Endocrine Abstracts

May 2022 Volume 81
ISSN 1479-6848 (online)

24th European Congress of Endocrinology 2022

21–24 May 2022, Milan, Italy

ECE 2022
24th European Congress of Endocrinology

published by
bioscientifica

Online version available at
www.endocrine-abstracts.org

Endocrine Abstracts

Volume 81
May 2022

24th European Congress of Endocrinology 2022

European Society of Endocrinology

21–24 May 2022, Milan, Italy

The European Society of Endocrinology would like to thank its ECE 2022 sponsors and supporters:

Silver Sponsors
Abiogen Pharma
HRA Pharma Rare Diseases
Recordati Rare Diseases
Takeda

Bronze Sponsors
ACE Pharmaceuticals
Alexion
Diurnal
Ipsen
Kyowa Kirin
Novo Nordisk
Pfizer
Rare Bone Consortium
Uni-Pharma

Supporters
Ascendis Pharma
Concept Life Sciences
Consilient Health
Crinetics Pharmaceuticals
Neurocrine Biosciences
Rhythm Pharmaceuticals
Soleno Therapeutics

European Society for Endocrinology
Starling House
1600 Bristol
Parkway North
Bristol BS34 8YU, UK

Tel: +44 (0)1454 642247
Fax: +44 (0)1454 642222
E-mail: info@euro-endo.org
Web site: http://www.ese-hormones.org

Conference Secretariat
Bioscientifica Ltd
Starling House
1600 Bristol
Parkway North
Bristol BS34 8YU, UK

Tel: +44 (0)1454 642240
Fax: +44 (0)1454 642222
E-mail: ece2022@endocrinology.org
Website: https://www.ese-hormones.org/ece-2022

CONTENTS

24th European Congress of Endocrinology 2022

PRIZE LECTURES

PLENARY LECTURES

SYMPOSIA

JOINT SESSIONS

EYES SYMPOSIUM

ECAS SYMPOSIUM

NEW SCIENTIFIC APPROACHES

DEBATE SESSIONS

MEET THE EXPERT BASIC SCIENTIST SESSIONS

MEET THE EXPERT SESSIONS

ORAL COMMUNICATIONS

RAPID COMMUNICATIONS

POSTER PRESENTATIONS

EPOSTER PRESENTATIONS

AUTHOR INDEX

Prize Lectures

European Journal of Endocrinology Award Lecture

AP1

The regulation of human brown adipose tissue

Roland Stimson
University of Edinburgh, Edinburgh, United Kingdom

The obesity epidemic has underlined the need for new treatments to aid weight loss and prevent the associated cardiometabolic sequelae of obesity. The relatively recent discovery of brown adipose tissue (BAT) in adult humans has revived interest in activating this tissue to increase energy expenditure as a novel treatment for these conditions. BAT is a thermogenic organ that generates heat to maintain body temperature in a cold environment. While BAT mass and activity are reduced in obesity, BAT is a plastic organ and activity can be increased in response to certain stimuli such as repeated cold exposure. In addition, the presence of BAT in obese subjects is associated with improved metabolic health and reduced incidence of cardiovascular disease. Therefore, it is important to determine how to safely increase BAT mass and thermogenesis to determine its therapeutic potential. However, our understanding of the pathways regulating human BAT remains limited, in part due to its location and the difficulty in quantifying activity in vivo. To improve our understanding of human brown adipose tissue function, we have performed a series of physiological studies in healthy volunteers using techniques such as PET imaging, microdialysis and thermal imaging. We have determined key differences in the regulation of brown adipose tissue function between species, such as identifying how glucocorticoids regulate brown adipose tissue activation in humans. We have also determined how brown adipose tissue utilises energy substrates to fuel thermogenesis. Most recently, we have undertaken hypothesis-free transcriptomics in human brown adipocytes to identify novel pathways regulating BAT function and have demonstrated their relevance in vivo. Understanding the pathways regulating cold-induced thermogenesis in humans may ultimately lead to novel therapies to enhance energy expenditure and improve metabolic function.

DOI: 10.1530/endoabs.81.AP1

The Geoffrey Harris Award Lecture

AP2

Abstract unavailable

DOI: 10.1530/endoabs.81.AP2

The Transatlantic Alliance Award Lecture

AP3

Growth Hormone: An Adult Endocrine Misnomer

Vera Chesnokova, Svetlana Zonis & Shlomo Melmed
Pituitary Center, Department of Medicine, Cedars-Sinai Medical Center, Los Angeles, California, United States

Growth hormone (GH) secreted by the anterior pituitary gland regulates skeletal growth, metabolism and body composition. Although several of these actions are mediated by production of hepatic and local tissue IGF1, GH also acts independent of IGF1. GH is mainly produced from the pituitary as a systemic endocrine hormone, yet is also expressed in local tissues acting in an autocrine/paracrine/intracrine manner. Locally produced non-pituitary GH (npGH) signals the GHR to induce epithelial cell proliferation by suppressing p53, thereby enabling epithelial cell proliferation. Although endocrine GH levels drop markedly with aging, npGH increases with aging, blocking repair of age-associated DNA damage. Consistent with these findings, npGH is a component of the senescence-associated secretory phenotype thereby enabling a pro-proliferative epithelial milieu. As p53 is increased in vivo by blocking GHR signalling these mechanisms may explain the known cancer- protective effects of GH deficiency and GHR signaling disruption, as well as contributing to age-associated pathologies. Thus, GH is a powerful inducer of skeletal growth during childhood,and maintains body composition in the adult, after maturation and with aging, GHR actions are transformed to accumulate DNA damage. Unraveling these mechanisms supports a hypothesis whereby adverse aging-related processes are in fact accelerated by GHR signalling. This notion supports the protective function of low circulating GH during aging, and also would call for vigilance against inappropriate adult GH abuse .This premise also supports the potential for trials designed to block GH action to enable extended healthspan. These insights point to pituitary and non-pituitary adult GH as a regulator of DNA damage contributing to the cellular micro-environment in addition to functioning as a promoter of skeletal growth.

DOI: 10.1530/endoabs.81.AP3

Clinical Endocrinology Trust Award Lecture

AP4

Setting the scene for (rare) endocrine diseases in Europe

Alberto M Pereira
Amsterdam UMC, Amsterdam, Netherlands

My research focuses on the long-term consequences of pituitary diseases, and on the effects of stress hormones on the central nervous system (CNS) in specific. This has elucidated long-term effects of hormone excess on the CNS, as well as on other organs that affect stress-resilience, and consequently, general well-being and quality of life. This profoundly affects our understanding of the biological effects of stress hormone excess on the CNS, and on the care for patients with specific rare endocrine conditions. Endocrine tumours are characterized by low incidence, genetic predisposition (either isolated or as manifestation of a hereditary tumour syndrome), abnormal hormone secretion and expression of hormone receptors, specific genetic patterns, and generally slow growth. The special biology provides unique opportunities for systems biology and for development of targeted therapies. The complexity precludes that the diagnosis and treatment modalities fit in standard concepts of care, and the low prevalence implicates that screening and clinical decision making is very important. The installation of the European Reference Networks formed the foundation to improve quality and safety and access to highly specialized health care across Europe for patients affected by rare, or low prevalence and complex conditions. The European Reference Network on Rare Endocrine Conditions (Endo-ERN) covers specific expertise from birth to senescence and provides equal responsibilities for patient representatives and health care providers. The scope and mission of Endo-ERN is complex but ultimately will thrive toward reducing health care inequalities across Europe.

DOI: 10.1530/endoabs.81.AP4

Jens Sandahl Christiansen Awards

JSC1

Abstract unavailable

DOI: 10.1530/endoabs.81.JSC1

JSC2

Abstract unavailable

DOI: 10.1530/endoabs.81.JSC2

European Hormone Medal Award Lecture

AP5.1

Great impact in low quantities - thyroid hormones, trace elements and endocrine disruptors

Josef Köhrle
Institut für Experimentelle Endokrinologie, Charité Universitätsmedizin Berlin, Berlin, Germany

Thyroid hormones (TH) regulate (brain) development, growth, body temperature, most pathways involved in energy and structural metabolism as well as anabolic and catabolic reactions. Inadequate availability of essential trace elements (iodine, selenium, iron, zinc) limits TH biosynthesis, metabolism and action. Endocrine-disrupting chemicals (EDC), i.e., exogenous chemicals or their mixtures, can interfere with any aspect of TH synthesis, distribution, transport, metabolism, and action via (non-)canonical T3 receptor mediated signalling. Only a limited number of EDC exert their adverse effects by directly interfering with follicular TH production. Majority of EDC effects occurs by disruption of protein-protected TH distribution via bloodstream, specific TH transport across cellular membranes and/or intracellular (in-)activation and/or TH metabolism. This pre-receptor control of local T3 availability to intracellular T3 receptors, which act as ligand-modulated transcription factors for gene expression, represents the main operation field for EDC in the TH system (THS). Only few EDC modulate functions of T3 receptors, which contrasts adverse EDC actions on the sex steroid dependent reproductive processes, most of which are known to be associated with direct disruption of sex steroid receptor functions. Thus, individual blood TH concentrations only provide limited information about adverse action and consequences for EDC exposed individuals, e.g., mother-child pairs. TH, trace elements and EDC exert their direct and permissive effects in very low, locally regulated, physiological concentrations frequently not reflected at the systemic level as impressively illustrated during TH-regulated amphibian metamorphosis, embryonal development of fish or mammalian species, including humans. Considering that anthropogenic mass recently exceeded our blue planet's biomass, we must minimize exposure to EDC, contained in and released from anthropogenic products, as EDC interfere already at very low concentrations with the THS. Concomitantly, the THS needs to be fortified and protected by globally adequate supply with those essential trace elements (I, Se, Fe) required for its proper function.

DOI: 10.1530/endoabs.81.AP5.1

AP5.2

Diabetic kidney disease: after years of darkness came light – finally new options for treatment!

Peter Rossing[1,2]
[1]Steno Diabetes Center Copenhagen, Gentofte, Denmark; [2]Department of Clinical Medicine, University of Copenhagen, Copenhagen, Denmark

Unfortunately diabetes is a growing problem with now more than 537 million people worldwide having diabetes according to International Diabetes Federation. Excess morbidity and mortality in diabetes is related to the development of diabetic kidney disease seen in 30-40%, which not only causes end stage kidney disease, but also increases risk for cardiovascular events and mortality, which is the leading cause of death. Treatment of diabetic kidney disease has been control of glucose, lipids, and blood pressure including blockade of the renin angiotensin system, but the residual risk on optimal treatment was large. Multiple interventions have been tested and failed in this condition, but in the past few years, we have suddenly been able to find new treatment options. First cardiovascular outcome trials in diabetes found the SGLT2 inhibitors reduced progression of kidney disease or heart failure, and GLP1 receptor agonists reduced cardiovascular events and maybe also improved kidney parameters. Then an endothelin receptor antagonist demonstrated reduced progression of kidney disease, and most recently the nonsteroidal mineralocorticoid receptor antagonist finerenone demonstrated reduction in progression of kidney and cardiovascular disease. Now we suddenly have the opportunity to improve on the most deadly complications to diabetes with several interventions, and as they work on different disease pathways (hemodynamic, metabolic, inflammatory) data suggest they can be combined with extra benefit for the person with diabetes. Now implementation is key, and quality monitoring systems should be in place to ensure this.

DOI: 10.1530/endoabs.81.AP5.2

Plenary Lectures

Genotype-phenotype analyses permit prediction of cure from Primary Aldosteronism
PL1

Abstract unavailable
DOI: 10.1530/endoabs.81.PL1

Cellular and molecular mechanisms regulating muscle regeneration in aging
PL2

Abstract unavailable
DOI: 10.1530/endoabs.81.PL2

Resilience Endocrinology
PL3

Abstract unavailable
DOI: 10.1530/endoabs.81.PL3

Fatty bone stem cells
PL4

Fatty bone stem cells
Clifford Rosen
Center for Clinical and Translational Research, Maine Medical Center Research Institute, Scarborough, United States

Bone marrow adipose tissue represents a unique depot surrounded by hematopoietic elements and trabecular bone. It expands during aging, and is dynamic in response to hormonal, nutritional and mechanical stimuli. The skeletal response to the increase in marrow adipocyte number and/or size is a relevant consideration, particularly since bone marrow adipose tissue is enhanced in states with low bone mass or rapid bone loss. Excess or deficient nutrient intake are powerful inducers of bone marrow adiposity in both humans and mice. We previously showed that 30% calorie restriction in mice stimulated bone marrow adiposity and drove bone loss. This led us to determine if fasting in humans also caused bone loss and expansion of marrow adipocytes. Volunteers were fasted for 10 days or given a high calorie diet for 10 days; bone marrow aspirates and skeletal quantitation was determined by uCT and MRI. Fasting induced a 10% increase in marrow fat, which was rapidly reversed by a 2 week return to a normal diet. In pathway analysis from marrow adipocytes using RNAseq, recruitment of progenitors (adipogenesis) was the major network activated, followed by the complement pathway. qRT-PCR demonstrated that adipsin, complement factor D (CFD), was one of the most up-regulated genes in the marrow adipocytes. In vitro analysis of adipocytes from the marrow of 30% CR mice revealed increased CFU-F and alkaline phosphatase staining, and enhanced adipogenic markers with increased oil-red O staining but suppressed genes associated with impaired in vitro osteogenesis. CFD mRNA was markedly increased similar to the human data. Addition of adipsin suppressed bone marrow stromal cell osteogenesis, and reduced gene expression for col1a1, osteocalcin and other bone markers. Taken together, nutrient intake regulates bone marrow adiposity and influences skeletal remodeling. We are now studying if intermittent fasting, which now is an extremely popular weight loss program, can cause bone loss and increased marrow adiposity.
DOI: 10.1530/endoabs.81.PL4

Old dogmas and new players in puberty and reproduction
PL5

Old dogmas and new players in puberty and reproduction
Manuel Tena-Sempere
Instituto Maimónides de Investigación Biomédica de Cordoba (IMIBIC); Department of Cell Biology, Physiology and Immunology, University of Cordoba, Cordoba, Spain; Hospital Universitario Reina Sofia, Spain; CIBER Fisiopatología de la Obesidad y Nutrición, Instituto de Salud Carlos III, Cordoba, Spain; Institute of Biomedicine, University of Turku, Turku, Finland

Reproduction, as essential function for the perpetuation of species, is controlled by precise maturational programs and sophisticated regulatory circuits, which have been the subject of active research. Seminal findings in the last decades of the 20th century set basic dogmas in reproductive endocrinology, including the identification of gonadotropin-releasing hormone (GnRH), as the master hypothalamic signal controlling reproduction, and the initial characterization of complex networks of central transmitters and peripheral hormones, from glutamate and GABA to nitric oxide and leptin, as key modulators of puberty and fertility. In fact, by the turn of the Millennium, there was the perception that the fundamentals of the neuroendocrine systems governing the reproductive axis had been already exposed, thus leaving little room for major conceptual developments in this apparently exhausted field of contemporary Endocrinology. Reality, however, turned out to be much more exiting, so that in the last twenty years, we have witnessed groundbreaking findings in this area, epitomized by the discovery of the reproductive roles of kisspeptins. These have not only revolutionized our understanding of the mechanisms controlling puberty and reproduction, but have also boosted kind of a New-Age in reproductive research, where basic, translational and clinical studies have surfaced novel players, neuroendocrine circuits and molecular regulatory mechanisms responsible for the precise control of the reproductive axis along the lifespan. Some examples of these recent developments will be summarized in this lecture, which aims also to identify new avenues for further progress of this fertile area of modern Endocrinology.
DOI: 10.1530/endoabs.81.PL5

Thyroid Hormone Resistance, Diagnosis and Treatment
PL6

Thyroid hormone resistance, diagnosis and treatment
Carla Moran
Department of Endocrinology, UPMC Beacon Hospital, Dublin, Ireland

Resistance to Thyroid hormone (RTH) encompasses various disorders of Thyroid Hormone (TH) Action, including defective signalling through TH Receptors (RTH alpha, RTH Beta), abnormal TH metabolism (Selenoprotein deficiency) and altered cellular entry of TH (MCT8 defects). In this talk, I will focus on RTH alpha and beta. RTH beta is usually associated with mutations in the *THRB* gene and is often readily identified, due to the associated typical biochemical pattern of raised TH levels and non-suppressed TSH. Resistance to the action of TH occurs in tissues expressing the beta form of the TH receptor (hypothalamus, pituitary, liver), but TR alpha expressing tissues are exposed to elevated TH levels. Patients with Resistance to Thyroid Hormone alpha (RTH alpha; due to mutations in the *THRA* gene) are highly challenging to identify because many patients only have mildly abnormal (or even normal) thyroid hormone levels. Resistance to the action of TH occurs in tissues expressing the alpha form of the TH receptor (bone, skeletal muscle, brain and heart). The clinical features/phenotype of both RTHalpha and RTHbeta are highly variable; from mild developmental delay to severe learning impairment and disability in RTHalpha, and asymptomatic states to significant tissue specific thyrotoxicosis in RTHbeta. Treatment for RTHbeta is not always required, but beta-blockade and tri-iodothyroacetic acid (TRIAC) can be considered. Many patients with RTHalpha respond to thyroxine therapy, but optimal dosing schedules and treatment targets are not known.
DOI: 10.1530/endoabs.81.PL6

Endocrine-disrupting chemicals: scientific, economic, regulatory, and policy implications

PL7

Endocrine-disrupting chemicals: scientific, economic, regulatory, and policy implications

Leonardo Trasande[1,2,3]

[1]NYU School of Medicine, New York, United States; [2]NYU Wagner School of Public Service, New York, United States; [3]NYU School of Global Public Health, New York, United States

Endocrine disrupting chemical (EDC) exposure contributes to disease and dysfunction, with annual costs >2% GDP in the US and >1% in Europe. Differences in policy explain differences in disease burden and cost. In Europe, general principles for EDCs call for minimization of human exposure, identification as substances of very high concern, and ban on use in pesticides. In the US, screening and testing programs are focused on estrogenic EDCs exclusively, and regulation is strictly risk-based. Since our reports describing 15 probable exposure-outcome associations due to EDCs, there has been a deepened understanding of their effects on human health. We have reviewed subsequent additions to the literature and identified new exposure-outcome associations with substantial human evidence. Although systematic evaluation is needed of their probability and strength, the growing evidence supports urgent action to reduce exposure. We suggest: expanded and comprehensive testing to conclusively identify EDCs, and a shift from a flawed, risk-based paradigm to one that proactively excludes chemicals with some evidence of hazardous properties. An international initiative on EDCs supported by the UN could address the weaknesses related to hazard identification and provide much-needed guidance for policies globally.

DOI: 10.1530/endoabs.81.PL7

Symposia

Endocrine malignancies - update on rare tumours

S1.1

Abstract unavailable
DOI: 10.1530/endoabs.81.S1.1

S1.2

Abstract unavailable
DOI: 10.1530/endoabs.81.S1.2

S1.3

Abstract unavailable
DOI: 10.1530/endoabs.81.S1.3

Genetic and epigenetic basis of PCOS heritability

S2.1

Prenatal androgen exposure causes transgenerational epigenetic transmission of PCOS

Elisabet Stener-Victorin
Department of Physiology and Pharmacology, Karolinska Institutet, Stockholm, Sweden

In a register-based and case-control studies it has been shown that daughters of women with or without PCOS have a five-fold increased risk of being diagnosed with the syndrom. Moreover, sons born to a mother with PCOS have two to three-fold increased risk of being obese. But how PCOS is inherited is unclear as PCOS loci identified by genome-wide association studies account for only 10% of the heritability. It has been suggested that epigenetic and developmental programming contributes to the inheritance of PCOS. In support for this, PCOS-like traits induced by androgen exposure during pregnancy in mice can be passed on from mothers (F_0) to daughters (F_1), granddaughters (F_2), and even great-granddaughters (F_3), and transcriptional and mitochondrial perturbations of oocytes accompany the transmission. Several of the oocyte gene signatures are detectable also in serum from daughters of women with PCOS and in adipose tissue of unrelated women with PCOS, indicating communication between germ cells, serum and somatic tissues/cells. Also, male offspring F_1 to F_3 of obese and androgen-exposed mothers develop aberrant reproductive and metabolic traits in adulthood. Small-noncoding (snc)RNA sequencing carried by the sperm contribute to a transgenerational epigenetic inheritance of phenotypic traits. As in females, several of sperm signatures are detectable in whole blood from sons of women with PCOS supporting the translational relevance of the mouse findings.

DOI: 10.1530/endoabs.81.S2.1

S2.2

Abstract unavailable
DOI: 10.1530/endoabs.81.S2.2

S2.3

Abstract unavailable
DOI: 10.1530/endoabs.81.S2.3

Nutritional and Metabolics aspects of the Thyroid

S3.1

Abstract unavailable
DOI: 10.1530/endoabs.81.S3.1

S3.2

Abstract unavailable
DOI: 10.1530/endoabs.81.S3.2

S3.3

Abstract unavailable
DOI: 10.1530/endoabs.81.S3.3

Parathyroid disorders clinical update (PARAT group)

S4.1

Management of primary hyperparathyroidism (PHPT)

Neil Gittoes
Department of Endocrinology, University Hospitals Birmingham NHS Foundation Trust, Birmingham, United Kingdom

The European PARAT group have recently explored a number of practical management issues in parathyroid diseases. Herein, we present expert opinion on areas of controversy in the diagnosis and management of primary hyperparathyroidism (PHPT). Although PHPT is common, its differential diagnosis from familial hypocalciuric hypercalcaemia (FHH) poses practical problems. Proposed approaches to addressing this will be discussed. The definition and clinical course of normocalcemic PHPT remains controversial and there is particular emphasis

on excluding causes of secondary hyperparathyroidism that can cause elevated PTH with normal blood calcium levels. An algorithm is presented to explore the approach to diagnosing normocalcaemic PHPT. Recurrent PHPT is rare but requires clear definition and approaches to reassessment and redo surgery should be performed at centres with great expertise in repeat surgery. Per- and post-operative management of patients with PHPT differs from centre to centre. We propose a structured approach to patient preparation for parathyroidectomy and review causes and management of post-operative hypocalcaemia. Longer term follow up and assessment of PHPT patients is also discussed. The recommendations on clinical management presented herein serve as background for further educational material aimed at a broad clinical audience and were developed with the focus on endocrinologists in training.

DOI: 10.1530/endoabs.81.S4.1

S4.2

Abstract unavailable

DOI: 10.1530/endoabs.81.S4.2

S4.3

Abstract unavailable

DOI: 10.1530/endoabs.81.S4.3

Organ crosstalk in metaflammation

S5.1

Beta cells and inflammation in diabetes

Thomas Mandrup-Poulsen
Department of Biomedical Sciences, University of Copenhagen, Copenhagen, Denmark

Innate immunity contributes to inducing functional inhibition and apoptosis of pancreatic beta-cells in the pathogenesis of both Type 1 diabetes (T1D) and Type 2 diabetes (T2D). The past four decades has provided overwhelming circumstantial evidence from in vitro studies and animal models that innate immune cells and cytokines are key effectors in beta-cell killing. Pro-inflammatory cytokines activate signaling pathways that reprogram the beta-cell transcriptome and proteome, adversely affecting most functions of the cell and triggering death by the intrinsic (mitochondrial) death pathway. On the other hand, these signaling pathways also elicit numerous adaptive and protective responses that may guide development of preventive therapies. Researchers increasingly agree that environmental stressors that enhance insulin biosynthetic demand may lead to increased proinsulin misfolding, misprocessing and posttranslational modifications, triggering inflammation and neoepitope formation and presentation in the beta-cell. This novel concept attracts focus to beta-cell stress as an initiating event in the development of both T1D and T2D. There is clinical proof-of-concept that blocking the action of the pro-inflammatory cytokines interleukin-1 (IL-1) or tumor necrosis factor (TNF) improves glycaemia and beta-cell function in T2D and T1D, respectively, and meta-analyses on >2000 T2D patients substantiates the efficacy of IL-1 blockade. Yet, anti-cytokine biologics have not yet been adopted in clinical practice. This lecture will review key basic and clinical findings supporting the importance of inflammatory beta-cell damage in the pathogenesis of T1D and T2D, and will highlight central barriers that prevent clinical translation.

DOI: 10.1530/endoabs.81.S5.1

S5.2

Abstract unavailable

DOI: 10.1530/endoabs.81.S5.2

S5.3

Abstract unavailable

DOI: 10.1530/endoabs.81.S5.3

Recent Advances in our understanding of pituitary disorders

S6.1

Abstract unavailable

DOI: 10.1530/endoabs.81.S6.1

S6.2

Abstract unavailable

DOI: 10.1530/endoabs.81.S6.2

S6.3

Abstract unavailable

DOI: 10.1530/endoabs.81.S6.3

Are adrenal steroids the guilty?

S7.1

Abstract unavailable

DOI: 10.1530/endoabs.81.S7.1

S7.2

Cardiometabolic outcomes and mortality in patients with autonomous cortisol secretion

Henrik Olsen[1,2]
[1]Department of Medicine, Ängeholm Hospital, Ängelholm, Sweden; [2]Department of Clinical Scien ces, Lund University, Lund, Sweden

Mild autonomous cortisol secretion (MACS) has been associated with cardiometabolic risk factors and cardiovascular disease in the 2000s and with increased mortality in the 2010s. Since the range of cortisol after dexamethasone suppression ($cortisol_{DST}$) in MACS is wide, the associated risk may vary. To adequately decide treatment, the risk associated to the different levels of $cortisol_{DST}$ must be known. This year the ENSAT group published a study on cardiometabolic complications in MACS. Patients with $cortisol_{DST}$ 138 nmol/l or more had an increased adjusted prevalence ratio of hypertension 1.15 and more often had treatment with three or more antihypertensives. The adjusted prevalence ratios of dyslipidaemia and diabetes were similar, but insulin treatment was more common. Patients with $cortisol_{DST}$ 50 to 137 nmol/l had no increase in the prevalence of hypertension, diabetes, and dyslipidaemia. Last year our group published a study on 1048 patients with a median follow-up of 6.4 years. Patients with $cortisol_{DST}$ 83 to 137 nmol/l had a hazard ratio of 2.30 for mortality and patients with $cortisol_{DST}$ 138 nmol/l or more 3.04. Patients with $cortisol_{DST}$ 50 to 82 nmol/l had no significant increase in mortality. The increase in mortality was found to be linear up to $cortisol_{DST}$ levels of 200 nmol/l. The cardiovascular event rate was increased in patients with $cortisol_{DST}$ 138 nmol/l or more but unchanged at $cortisol_{DST}$ levels 50 to 137 nmol/l. The risk ratios for mortality seem larger than the relative prevalence of cardiometabolic complications. Therefore, improved medical treatment may not normalise the mortality risk in MACS. We suggest treatment of cardiovascular risk factors and incorporation of our results into the decision of which patients to recommend for adrenalectomy.

DOI: 10.1530/endoabs.81.S7.2

S7.3

Abstract unavailable

DOI: 10.1530/endoabs.81.S7.3

Trace elements in endocrinology: too low or too high

S8.1

Abstract unavailable

DOI: 10.1530/endoabs.81.S8.1

S8.2

Abstract unavailable

DOI: 10.1530/endoabs.81.S8.2

S8.3

Iron and the thyroid

Michael Zimmermann
ETH Zurich, Switzerland

Despite significant progress, deficiencies of iron and iodine remain major public health problems affecting >30% of the global population. These deficiencies often coexist in populations. Iron deficiency has adverse effects on thyroid metabolism. Iron deficiency impairs thyroid hormone synthesis by reducing activity of heme-dependent thyroid peroxidase. Iron-deficiency anemia blunts, and iron supplementation improves the efficacy of iodine supplementation. Studies have demonstrated that a high prevalence of iron deficiency among children in areas of endemic goiter may reduce the effectiveness of iodized salt programs. These findings argue strongly for improving iron status in areas of overlapping deficiency, not only to combat anemia but also to increase the efficacy of iodine prophylaxis. Poor maternal iron status predicts both higher TSH and lower TT4 concentrations during pregnancy in an area of borderline iodine deficiency.

DOI: 10.1530/endoabs.81.S8.3

Genetics of adrenal endocrine tumors

S9.1

Genetic bases of pheochromocytoma and paraganglioma

Mercedes Robledo
Hereditary Endocrine Cancer Group, Spanish National Cancer Research Centre (CNIO), Madrid, Spain; [2]Rare Diseases Networking Biomedical Research Centre (CIBERER), Madrid, Spain

Pheochromocytoma and paraganglioma (PPGL) are rare tumours, whose genetic profile has gained complexity over the last two decades. The list of genes involved in the development of this disease has been steadily growing, and there are currently more than 20 driver genes capable of explaining either the hereditary or sporadic nature of the disease. Although genetic diagnosis is achieved in about 75-80% of cases, the genetic aetiology remains to be explained not only in patients with apparently sporadic PPGL, but also in patients with a family history or with multiple tumours, and who therefore meet the criteria to be considered as candidates for carrying mutations in as yet undiscovered genes. Taken together, the mutations in the known PPGL genes deregulate three distinct signalling pathways, which may be the starting point for personalised treatment of these patients. One of the most relevant features of PPGLs is that they show homogeneous genomic profiles according to the specific gene that is mutated in each case. This homegeneity is what is making it possible to identify new characteristics of PPGLs, including differential aspects of the tumour microenvironment, again dependent on the genetics of the tumour.

DOI: 10.1530/endoabs.81.S9.1

S9.2

Abstract unavailable

DOI: 10.1530/endoabs.81.S9.2

S9.3

Abstract unavailable

DOI: 10.1530/endoabs.81.S9.3

Transition from childhood to adulthood

S10.1

Abstract unavailable

DOI: 10.1530/endoabs.81.S10.1

S10.2

Abstract unavailable

DOI: 10.1530/endoabs.81.S10.2

S10.3

Abstract unavailable

DOI: 10.1530/endoabs.81.S10.3

Thyroid and Brain

S11.1

Abstract unavailable

DOI: 10.1530/endoabs.81.S11.1

S11.2

Abstract unavailable

DOI: 10.1530/endoabs.81.S11.2

S11.3

Abstract unavailable

DOI: 10.1530/endoabs.81.S11.3

Are all sugars the same with regard to the development of obesity, insulin resistance and NAFLD?

S12.1

Abstract unavailable

DOI: 10.1530/endoabs.81.S12.1

S12.2

Fructose but not glucose drives DNL

Philipp A Gerber
Department of Endocrinology, Diabetology and Clinical Nutrition, University Hospital Zurich and University of Zurich, Switzerland

Observational studies conducted during the past two decades provide evidence of an association of dietary fructose consumption with obesity and metabolic diseases as non-alcoholic fatty liver disease or insulin resistance / type 2 diabetes mellitus. However, these associations are challenged by the fact that it is difficult to adjust the results of such studies for excessive caloric intake, which often co-exists with high fructose intake, e.g., by consumption of sugar-sweetened beverages. Thus, there is a clear need for direct interventional studies exploring a possible causal role of fructose in the development of metabolic diseases, as compared to other sugars. To this aim, different controlled trials were conducted by our group as well as other investigators to assess this question. Such studies expose their participants to various amounts of different sugars for several weeks to months, and investigate different outcomes related to metabolic diseases as those outlined above. With these trials, it was possible to gain direct insights into the mechanisms by which different sugars may negatively influence metabolic health. In particular, latest research provides evidence of very distinct effects of fructose consumption on hepatic metabolism, in particular regarding a "metabolic switch" in hepatic tissue towards de novo lipogenesis. Furthermore, and in addition to the effects of fructose, the co-ingestion of fructose and glucose (which is very common due to their co-existence in the sucrose molecule) may have similar or even more deleterious effects than consumption of fructose alone. Thus, these results emphasize the importance of an overall reduction of added sugars in our diet, as suggested by the WHO and other organizations.

DOI: 10.1530/endoabs.81.S12.2

S12.3

Abstract unavailable

DOI: 10.1530/endoabs.81.S12.3

Hormones and emotions

S13.1

Abstract unavailable

DOI: 10.1530/endoabs.81.S13.1

S13.2

Abstract unavailable
DOI: 10.1530/endoabs.81.S13.2

S13.3

Abstract unavailable
DOI: 10.1530/endoabs.81.S13.3

Molecular aspects of clinical management in liver/ pancreatic cancer

S14.1

Abstract unavailable
DOI: 10.1530/endoabs.81.S14.1

S14.2

Abstract unavailable
DOI: 10.1530/endoabs.81.S14.2

S14.3

Abstract unavailable
DOI: 10.1530/endoabs.81.S14.3

Key targets of EDC action in humans

S15.1

Abstract unavailable
DOI: 10.1530/endoabs.81.S15.1

S15.2

Abstract unavailable
DOI: 10.1530/endoabs.81.S15.2

S15.3

Abstract unavailable
DOI: 10.1530/endoabs.81.S15.3

Tools for fracture risk assessment, and how to use them

S16.1

Abstract unavailable
DOI: 10.1530/endoabs.81.S16.1

S16.2

Bone microstructure - What techniques are there, what do they tell us

Carmelo Messina[1,2]
[1]University of Milan, Milan, Italy; [2]IRCCS Istituto Ortopedico Galeazzi, Milan, Italy

Areal BMD from Dual energy X-Ray absorptiometry (DXA) accounts for approximately two-thirds of bone strength and is used as a surrogate for bone strength in clinical practice to predict fracture risk. Nevertheless, a more in-depth assessment of bone quality requires second level imaging techniques to assess bone quality parameters. Bone quality is a key parameter in determining bone strength. During time, several non-invasive high-resolution imaging techniques have been developed to visualise bone structure. As bony trabeculae measure 50–200 μm in thickness, the spatial resolution of imaging techniques applied to the the non-invasive evaluation of bone microstructure must be higher than 200 μm to spatially solve the single trabeculae. High-resolution peripheral quantitative computed tomography (HR-pQCT) is a low-dose technique that enable to image bone microarchitecture in vivo at peripheral skeletal sites, such as distal forearm and tibia. Differences and reference data exist for HR-pQCT by age and sex, race/ethnic origin and body composition. We will review the role of HR-pQCT in fractured patients, to highlight those parameters of bone microarchitecture and bone strength useful as predictors of incident fractures, as well as in subject with prevalent fractures. The role of HR-pQCT in monitoring response of anti-osteoporotic therapy will be addressed, as well as its role in patients with secondary osteoporosis and metabolic bone disorders. Finally, novel application of Hr-pQCT will be briefly reviewed. The presentation will then deal with the evaluation and quantification of bone structure and microstructure with current available MRI techniques, also comparing the MRI performance with DXA and CT measurements. Limitation of each technique will be reviewed, as well as their current applicability in clinical practice.

DOI: 10.1530/endoabs.81.S16.2

S16.3

Artificial intelligence in osteoporosis management

Hans Peter Dimai
Department of Internal Medicine, Division of Endocrinology & Diabetology, Medical University of Graz, Graz, Austria

Background
Osteoporosis is a systemic skeletal disease characterized by low bone mass, microarchitectural deterioration of bone tissue, and the consequence of an increased fracture risk. The term "artificial intelligence (AI)" denotes a field in computer science which enables computers to simulate different aspects of human intelligence, such as natural language understanding, pattern recognition or data driven learning. Machine Learning is a subset of AI, and within this field, Convolutional Neural Networks (CNN) play a key role particularly in relation to medical imaging.
Methods
Various AI applications as currently available for the management of osteoporosis are presented, including their strengths and pitfalls.
Results
One of the mainstays of AI supported applications in osteoporosis is imaging based detection of fractures. Almost any medical imaging technique including – but not limited to - plain radiography, computed tomography (CT) and MRT, is represented in an increasing number of studies. There is evidence that AI based technical support can improve fracture detection rate. Furthermore, AI supported algorithms are used not only to assess quantitative aspects of the bone, such as bone mineral density (BMD) at the lumbar spine, the hip and the total body, but also to assess qualitative properties, such as microarchitecture and even fracture load. However, it is of note that many of the clinical studies involving AI in the field of osteoporosis are short of scientific diligence. For example, algorithms behind specific diagnostic approaches are not always published in detail. Also, the logic behind a chosen approach is not always comprehensible. In general, there is a clear lack in standardized procedures.
Conclusion
There are aspects in support of integrating AI based tools into osteoporosis management workflows in daily clinical practice. However, there is also a clear need for high quality clinical research in this field. In this regard, implementation of, e.g., internationally consented quality standards could help to improve the relevance of study outcomes and also their credibility.

DOI: 10.1530/endoabs.81.S16.3

Infections and endocrinology

S17.1

Sepsis as a pan-endocrine illness

Weronika Wasyluk[1,2]
[1]Department of Internal Medicine in Nursing, Faculty of Health Sciences, Medical University of Lublin, Lublin, Poland; [2]Doctoral School, Medical University of Lublin, Lublin, Poland

Sepsis is defined as "life-threatening organ dysfunction caused by a dysregulated host response to infection". This response is expressed, inter alia, in the endocrine system and affects almost all endocrine axes. Endocrine dysfunction, in turn, may contribute to other aspects of dysregulated host response to infection, such as metabolism. Endocrine disorders in the course of sepsis are particularly noticeable in the area of the hypothalamic-pituitary-target tissue axis. Disorders of the hypothalamic-pituitary-adrenal axis manifest mainly by hypercortisolemia in the acute phase. In the hypothalamic-pituitary-thyroid axis the most typical manifestation is a triiodothyronine concentration decrease and reverse triiodothyronine concentration increase. In terms of the somatrotropic axis, a change in the secretion pattern of growth hormone and peripheral resistance to this hormone is characteristic. Hypothalamic-pituitary-gonadal axis disorders are expressed by the stress-induced amenorrhea in women and the reduction in testosterone level in men. Other changes include insulin resistance and catecholamine and β-adrenergic stimulation disorders. It is also worth bearing in mind that a patient's endocrine profile is not the same for the entire duration of the disease, but changes over time, which is noticeable especially between the acute and the chronic phase. It is suggested that some of these changes are adaptive, but there is no doubt that all of them may have an impact on the patient's clinical condition. Since the endocrine system is responsible for the homeostasis of the system, disturbances in its scope contribute to the dysregulation of other functions of the body, including metabolism, which, according to some authors, is one of the main pillars of the pathophysiology of sepsis. As stated by Singer et al., a more sophisticated understanding of the sequence, dynamics and interaction between the occurring metabolic, hormonal and immunological changes would provide a logical basis for patient-tailored therapeutic interventions, therefore this issue undoubtedly requires further researches.

DOI: 10.1530/endoabs.81.S17.1

S17.2

Abstract unavailable

DOI: 10.1530/endoabs.81.S17.2

S17.3

Endocrine and metabolic aspects of COVID-19

Michal Kršek
Department of Internal Medicine 3, 1st Faculty of Medicine, Charles University, General University Hospital, Prague, Czech Republic

Coronavirus disease 19 (COVID-19) started to quickly spread worldwide in the end of 2019 and was declared by the WHO a pandemic on March 11, 2020. Prevailing signs and symptoms of COVID-19 comprise many organ systems and are very complex and variable and also even unpredictable and lead to tremendous increase in morbidity and mortality. Recently, there has been increasing evidence that COVID-19 affects in a complex way also the endocrine system. Renin-angiotensin-aldosterone system (RAAS) plays a crucial role in SARS-CoV-2 infection and pathogenesis. Angiotensin-converting enzyme 2 (ACE2) protein is crucial for the entry of the virus into the cells. However, it seems that overexpression of ACE2, which takes place also during the use of ACEs inhibitors, is not connected with higher susceptibility to SARS-CoV-2 infection. It is of note that the balance between ACE1 and ACE2 actions is disturbed during COVID-19 which favours proinflammatory pathways leading to tissue damage with that of lung tissue being critical for the course and prognosis of COVID-19. Thyroid gland disorders are frequently reported in relationship with COVID-19. During the severe course of COVID-19, the changes compatible with non-thyroidal illness syndrome are common. This, however, is a consequence of severe/critical illness rather than direct causal effect of COVID-19. Amongst thyroid disorders reported and studied in connection with either COVID-19 or vaccination, we can find autoimmune thyroid (AITD) disease manifestation and subacute thyroiditis. Several cases of adrenal insufficiency have been reported during or following COVID-19. These cases, however, are very likely a consequence of COVID-19 comorbidities such as antiphospholipide syndrome. It is necessary to point out that normal function of hypothalamic-pituitary adrenal axis is necessary for the survival of patients mainly with severe course of the disease and proper replacement regimens in patients with adrenal insufficiency have to be introduced. Other conditions also possibly related to COVID-19 will be mentioned, mainly diabetes and obesity.

DOI: 10.1530/endoabs.81.S17.3

Unmet needs in aggressive endocrine cancers

S18.1

Choosing the best treatment sequence for gepnet tumours

Eva Tiensuu Janson
Department of Medical Sciences, Uppsala University, Uppsala, Sweden

Background
Gastroenteropancreatic neuroendocrine tumors (GEP-NETs) are grouped according to the origin of the primary tumor and their proliferation index (Ki-67). The WHO classification divide GEP-NETs into G1 (Ki-67 $<3\%$), G2 (Ki-67 ≥ 3-20%) and G3 (Ki-67 $>20\%$). Both parameters are accounted for when treatment strategies are planned. Furthermore, the presence of hormone related symptoms warrant consideration.
Aim
To describe the treatment landscape for metastasized GEP-NETs.
Results/discussion
Surgery should always be discussed and performed if R0 is considered possible. Most GEP-NETs express somatostatin receptors (SSRs) and treatment with somatostatin analogs is the primary choice in metastatic low proliferating GEP-NETs, originating both in the small intestine and pancreas, and to reduce symptoms of carcinoid syndrome or in the rare event of a glucagonoma or VIPoma. SSR expression is also a prerequisite for peptide receptor radionuclide therapy (PRRT) which is usually recommended as second or third line treatment in both G1 and G2 tumors and for a selected population of GEP-NET G3. For patients with pancreatic tumors with Ki-67 $>10\%$, chemotherapy or the mTOR inhibitor everolimus may be used as first line treatment. Everolimus may also be

an option in progressing small intestinal NETs with a higher proliferation rate. Sunitinib is an alternative in progressing PanNETs. To reduce tumor burden in the liver, radiofrequency ablation or liver embolization may be used. In rare cases, liver transplantation may also be discussed, but a thorough preoperative work-up has to be performed before such an intervention is initiated. For those patients that does not respond to the traditional therapies, treatment in clinical studies can be an option.

Conclusion

The therapeutic landscape for metastasized GEP-NETs include several treatment options. However, the sequencing of therapy is still debated and choices should be made in order to preserve QoL and minimize the risk for severe side effects.

DOI: 10.1530/endoabs.81.S18.1

S18.2

Abstract unavailable

DOI: 10.1530/endoabs.81.S18.2

S18.3

Abstract unavailable

DOI: 10.1530/endoabs.81.S18.3

Systemic cues mediating neuroendocrine regulation of food intake and metabolism

S19.1

Abstract unavailable

DOI: 10.1530/endoabs.81.S19.1

S19.2

The aperitif: The neurobiology of appetite and hunger

Suzanne Dickson
Department of Physiology/Endocrine, Institute of Neuroscience and Physiology, The Sahlgrenska Academy at the University of Gothenburg, Sweden

Environmental cues recalling palatable foods motivate eating beyond metabolic need, yet the timing of this response and whether it can develop towards a less palatable but readily available food remain elusive. Increasing evidence indicates that external stimuli in the olfactory modality communicate with the major hub in the feeding neurocircuitry, namely the hypothalamic arcuate nucleus (Arc), but the neural substrates involved have been only partially uncovered. By means of a home-cage hidden palatable food paradigm, aiming to mimic ubiquitous exposure to olfactory food cues in Western societies, we investigated whether the latter could drive the overeating of plain chow in non-food-deprived male rats and explored the neural mechanisms involved, including the possible engagement of the orexigenic ghrelin system. The olfactory detection of a familiar, palatable food impacted upon meal patterns, by increasing meal frequency, to cause the persistent overconsumption of chow. In line with the orexigenic response observed, sensing the palatable food in the environment stimulated food-seeking and risk-taking behavior, which are intrinsic components of food acquisition, and caused active ghrelin release. Our results suggest that olfactory food cues recruited intermingled populations of cells embedded within the feeding circuitry within the Arc, including, notably, those containing the ghrelin receptor. These data demonstrate the leverage of ubiquitous food cues, not only for palatable food searching, but also to powerfully drive food consumption in ways that resonate with heightened hunger, for which the orexigenic ghrelin system is implicated.

DOI: 10.1530/endoabs.81.S19.2

S19.3

Central impact of growth hormone GH-axis negative feedback and metabolic function

José Donato Júnior
Department of Physiology and Biophysics, Institute of Biomedical Sciences, University of São Paulo, São Paulo, Brazil

Growth hormone (GH) responsive cells are extensively distributed in the brain, including in neurons of the arcuate nucleus (ARH) and ventromedial nucleus (VMH) of the hypothalamus, areas that control food intake, energy expenditure and blood glucose levels. However, the functional role of central GH signaling for energy and glucose homeostasis has not been unveiled yet. We generated mice lacking GH receptor (GHR) in multiple neuronal populations to investigate whether central GHR signaling modulates energy and glucose homeostasis during normal conditions or during situations of metabolic stress. GHR ablation in AgRP neurons did not affect the body weight, food intake, energy expenditure, glucose tolerance and leptin sensitivity, compared to control animals. However, fasting induced a lower c-Fos expression, a marker of neuronal activation, in the ARH of AgRP GHR KO, suggesting that AgRP neurons are unable to appropriately sense food deprivation without GH signaling. Remarkably, GHR ablation in AgRP cells mitigated highly characteristic hypothalamic and neuroendocrine adaptations induced by weight loss. Thus, while control mice adapted to a 60% food deprivation by progressively saving energy, AgRP GHR KO mice exhibited a higher T4 and testosterone concentrations as well as an increased energy expenditure and UCP-1 mRNA expression in the brown adipose tissue, compared to control animals. These effects led to a higher rate of weight loss, which was predominantly due to fat. In contrast, GHR ablation in steroidogenic factor-1 (SF1) cells, which include VMH neurons, did not affect the responses to food restriction in comparison with control group. However, a blunted counter-regulatory response to hypoglycemia was observed in SF1 GHR KO mice, indicating that GH signaling in VMH neurons helps the organism to recover from hypoglycemia. These findings indicate a previously unidentified function of GH to induce appropriate metabolic responses that ensure survival via its action on specific neuronal populations.

DOI: 10.1530/endoabs.81.S19.3

Osteoporosis treatment

S20.1

Abstract unavailable

DOI: 10.1530/endoabs.81.S20.1

S20.2

Abstract unavailable

DOI: 10.1530/endoabs.81.S20.2

S20.3

Abstract unavailable

DOI: 10.1530/endoabs.81.S20.3

Autoimmune polyendocrine syndromes

S21.1

Autoimmunity in families with Addison's disease

Marta Fichna
Poznan University of Medical Sciences, Poland

Since individuals with autoimmune Addison's disease (AD) present considerable co-occurrence of other autoimmune conditions, clustering of autoimmunity was also predicted among their relatives. We aimed to evaluate the burden of autoimmunity in families of patients with AD by means of a survey, serum autoantibody testing and correlating these data with the established genetic risk factors (*PTPN22* rs2476601, *CTLA4* rs231775, and *BACH2* rs3757247). 74.1% patients reported relative(s) with autoimmunity, and, inversely, 11.9% surveyed relatives, especially first-degree female family members, declared an autoimmune disease, most frequently Hashimoto's thyroiditis, followed by Graves' disease, vitiligo, and type 1 diabetes. Psoriasis, rheumatoid arthritis, pernicious anaemia, multiple sclerosis, and premature menopause were also quite common, while AD, alopecia, and celiac disease – less frequent. Significant correlation was noticed between the number of autoimmune conditions in AD proband and the number of affected relatives ($P=0.031$). Endocrine gland-specific serum autoantibodies were detectable in 39.8% first-degree relatives of patients with AD, including asymptomatic subjects. Antibodies to 21-hydroxylase were found in 6.2% relatives, thyroid peroxidase in 28.3%, thyroglobulin in 19.5%, glutamic acid decarboxylase in 8.0%, zinc transporter-8 in 7.1%, and islet antigen-2 in 2.6%. Autoantibodies were significantly more frequent in families of male patients ($P=0.008$; OR 3.31; 95% CI 1.334-8.234) and patients with polyglandular autoimmunity ($P=0.009$; OR 3.545; 95%CI 1.313-9.573). Autoimmunity-related genetic polymorphisms occurred more frequently among Addison's families vs controls (all $P<0.05$), and *PTPN22* rs2476601 was associated with all autoantibody prevalence, except for IA-2. In conclusion, there is convincing evidence of increased susceptibility for autoimmune endocrine conditions, especially thyroid disease, in the relatives of patients with AD, predominantly in females. Relatives of the male AD patients and of those with polyendocrine autoimmune AD are at particular risk and should undergo periodic screening for autoimmune endocrine disorders.

DOI: 10.1530/endoabs.81.S21.1

S21.2

Abstract unavailable

DOI: 10.1530/endoabs.81.S21.2

S21.3

Autoimmune regulator mutations and autoimmunity

Bergithe Oftedal
Department of Clinical Science, University of Bergen, Norway

The autoimmune regulator (AIRE) gene is crucial for establishing central immunological tolerance and preventing autoimmunity. Mutations in AIRE cause a rare autosomal-recessive disease, autoimmune polyendocrine syndrome type 1 (APS-1). The clinical picture is highly variable, however, most patients present severe chronic mucocutaneous candidiasis and organ-specific autoimmunity from early childhood and have high levels of autoantibodies against interferon alpha and omega. Recently, it has become evident that AIRE variants also associate with more common organ-specific autoimmune diseases such as autoimmune adrenal insufficiency, gastritis, and type 1 diabetes. We have identified multiple patients with heterozygous variants in AIRE and investigated their dominant negative effect on AIRE's gene regulation. We find that dominant negative AIRE variants cluster within the PHD1 and PHD2 domains and have a varying effect on AIRE's transcriptional activity. As a group, these patients have fewer and milder manifestations masquerading as "common" organ-specific autoimmunity where enteropathy was the most frequent manifestation. Interestingly, a few of these patients have autoantibodies against interferon omega. By scrutiny of our national registry, we identified two female and two male APS-1 patients from three different families with late-onset APS-1 sharing a homozygous or compound heterozygous splice mutation in AIRE's exon 7. In addition to the late onset, they also presented with a milder phenotype compared to classical APS-1. Both normal AIRE mRNA splicing and an altered splicing pattern including skipping of exon 7 were found in the patients and in the corresponding mouse model, indicating leaky rather than abolished mRNA splicing. Further, a moderately inhibited. Aire-regulated transcriptome was found in the mouse thymus. Our results underline the dose-effect of AIRE. Taken together, our results highlight the importance of functional validation of AIRE variants and suggest a dose-dependent function of AIRE.

DOI: 10.1530/endoabs.81.S21.3

Male infertility

S22.1

Abstract unavailable

DOI: 10.1530/endoabs.81.S22.1

S22.2

Abstract unavailable

DOI: 10.1530/endoabs.81.S22.2

S22.3

Abstract unavailable

DOI: 10.1530/endoabs.81.S22.3

Thyroid autoimmunity

S23.1

Abstract unavailable

DOI: 10.1530/endoabs.81.S23.1

S23.2

Thyroid autoimmunity, subfertility and assisted reproduction

Kris G Poppe[1,2]
[1]CHU St-Pierre, Brussels, Belgium; [2]ULB-Erasme, Brussels, Belgium

Severe thyroid dysfunction may lead to menstrual disorders and subfertility via direct and indirect interactions with the hypothalamo–pituitary–ovarian axis and the reproductive organs. However, the exact prevalence of subfertility in women with thyroid disorders remains unknown. Fertility problems may persist after restoring normal thyroid function, and then surgery and/or an assisted reproductive technology (ART) may be necessary to obtain a pregnancy. The initial step in an ART treatment is the ovarian stimulation, putting strain on the thyroid gland, potentially leading to (permanent) hypothyroidism in women with thyroid autoimmunity (TAI) or when already treated with thyroid hormones (LT4). Moreover, women with ovarian and unexplained causes of subfertility have a higher prevalence of TAI. In women with TSH levels >4.0 mIU/l, fertilisation rates, embryo quality and live birth rates may be impaired and improved with LT4 therapy. The increased use of intracytoplasmic sperm injection (ICSI) as a type of ART on pregnancy outcomes in women with TAI deserves more attention as therapeutic tool. In euthyroid women with TAI, LT4 should not be given systematically, but on a case-by-case basis if serum TSH is >2.5 mIU/l. Women already treated with LT4, should target a serum TSH level <2.5 mIU/l before ART. For all of the above reasons, women of subfertile couples should be screened systematically for the presence of thyroid disorders, and especially serum TSH and TPOAb. In this symposium, we will present the current state of art, discuss the gaps in the knowledge, and finally, make proposals for future investigations.

DOI: 10.1530/endoabs.81.S23.2

S23.3

Abstract unavailable

DOI: 10.1530/endoabs.81.S23.3

Diabetes remission: From dream to clinical goal

S24.1

Type 1 diabetes remission: who, how and when

Paolo Pozzilli[1,2]
[1]Unit of Endocrinology and Diabetes, Campus Bio-Medico University of Rome, Italy; [2]Centre of Immunobiology, St Bartholomew's and the London School of Medicine, Queen Mary, University of London, United Kingdom

Type 1 diabetes (T1D) is a chronic disease of childhood that also presents in adults, resulting from the destruction of insulin-producing β-cells by auto-reactive T cells that have escaped central and peripheral immune tolerance. It is now well established that T1D is characterised by a wide heterogeneity especially in terms of age at onset, representing a major barrier for both pathogenesis and translational efforts aimed to develop novel therapeutics approach. This concept represents a key factor in defining who should be treated with an intervention capable of inducing disease remission. The insulin secretory capacity assessed by the residual β-cell function (measurement of C-peptide) at the time of diagnosis and during the first few year after T1D diagnosis is a crucial factor to define when and how to intervene with the aim of modifying the natural history of the disease on the short and long term. We have to remember that in the vast majority of T1D patients at diagnosis a significant mass of functional islets has been destroyed by the autoimmune attack, thus lacking the chance to be either preserved or rescued by a therapeutic approach able to reverse the course of disease onset. However, some T1D patients show a substantial residual β-cell function at diagnosis and also in the first year after disease manifestation, thus representing an interesting population to target for an intervention able to protect endogenous insulin secretion. Furthermore, some patients may be overweight and become insulin resistant, thus implying that also this pathophysiological condition should be tackled. Patients with T1D and substantial residual β-cell function with or without signs of insulin resistance identify a specific endotypes of T1D. These novel concepts pave the way for new and diverse therapeutic options which can be applied to well characterised patients accordingly.

DOI: 10.1530/endoabs.81.S24.1

S24.2

Abstract unavailable

DOI: 10.1530/endoabs.81.S24.2

S24.3

Abstract unavailable

DOI: 10.1530/endoabs.81.S24.3

Joint Sessions

Safety of growth hormone treatment in survivors of cancer and intra-cranial tumours – A Growth Hormone Research Society Consensus statement

JS1.1

Abstract unavailable

DOI: 10.1530/endoabs.81.JS1.1

JS1.2

Abstract unavailable

DOI: 10.1530/endoabs.81.JS1.2

JS1.3

Abstract unavailable

DOI: 10.1530/endoabs.81.JS1.3

JS1.4

Abstract unavailable

DOI: 10.1530/endoabs.81.JS1.4

ESE-EndoERN Joint Session: Retrospect and prospect

JS2.1

Abstract unavailable

DOI: 10.1530/endoabs.81.JS2.1

JS2.2

Abstract unavailable

DOI: 10.1530/endoabs.81.JS2.2

JS2.3

Abstract unavailable

DOI: 10.1530/endoabs.81.JS2.3

JS2.4

Abstract unavailable

DOI: 10.1530/endoabs.81.JS2.4

ESE-SBEM, FASEN and SMNE Joint Session: New horizons in rare diseases

JS3.1

Is familial hypercholesterolemia an underdiagnosed and undertreated disease?

Juan Patricio Nogueira
Centro de Investigación en Endocrinología, Nutrición y Metabolismo (CIENM), Facultad de Ciencias de la Salud, Universidad Nacional de Formosa, Argentina

Familial Hypercholesterolemia (FH) is a monogenic disease, associated with variants in the LDLR, APOB, and PCSK9 genes. The initial diagnosis is based on clinical criteria like the DLCN criteria. A score $>$ 8 points qualifies the patient as "definite" for the diagnosis of FH. It is characterized by lifelong elevations in plasma low-density lipoprotein cholesterol (LDL-C) levels and premature coronary heart disease (CHD). FH is an underdiagnosed and undertreated genetic disorder, which affects 1 in 200 to 250 people worldwide of all races and ethnicities. The general lack of awareness about FH among the public and the medical community has resulted in only 10% of the FH population being diagnosed and adequately treated. It is recommended that children, adults, and families should be screened for FH if an individual or family member has FH, an adult plasma cholesterol level $\geq$8 mmol/l ($\geq$310 mg/dl) or in a child $\geq$6 mmol/l ($\geq$230 mg/dl), premature CHD, tendon xanthomas, or sudden premature cardiac death. In FH, low-density lipoprotein cholesterol goals are $<$3.5 mmol/l ($<$135 mg/dl) for children, $<$2.5 mmol/l ($<$100 mg/dl) for adults, and $<$1.8 mmol/l ($<$70 mg/dl) for adults with known CHD or diabetes. In addition to lifestyle and dietary advice, priority treatments are (i) in children, statins, ezetimibe, and bile acid-binding resins, and (ii) in adults, maximal potent statin dose, ezetimibe, bile acid-binding resins, and monoclonal antibodies directed against PCSK9. Lipoprotein apheresis can be offered in homozygotes and in heterozygotes with CHD refractory to treatment. FH is usually diagnosed late. Guidelines-recommended LDL cholesterol concentrations are rarely achieved with single-agent therapy. Cardiovascular risk factors and the presence of CHD were lower among non-index cases, who were diagnosed earlier. Earlier detection and an increase in the use of combination therapies are required to reduce the global burden of FH.

DOI: 10.1530/endoabs.81.JS3.1

JS3.2

Abstract unavailable

DOI: 10.1530/endoabs.81.JS3.2

JS3.3

Abstract unavailable
DOI: 10.1530/endoabs.81.JS3.3

JS4.2

Abstract unavailable
DOI: 10.1530/endoabs.81.JS4.2

ESE-EASO & ESPE Joint Session: Challenges in obesity care from childhood to adulthood

JS4.1

Abstract unavailable
DOI: 10.1530/endoabs.81.JS4.1

JS4.3

Abstract unavailable
DOI: 10.1530/endoabs.81.JS4.3

EYES Symposium

How artificial intelligence could change our vision on assisted reproduction. Is it time to change the view?

EYES1.1

Abstract unavailable

DOI: 10.1530/endoabs.81.EYES1.1

EYES1.2

Abstract unavailable

DOI: 10.1530/endoabs.81.EYES1.2

EYES1.3

The challenges in male infertility research. Which are the future topics of research?

Lærke Priskorn[1,2]

[1]Department of Growth and Reproduction, Copenhagen University Hospital – Rigshospitalet, Copenhagen, Denmark; [2]International Center for Research Training in Endocrine Disruption of Male Reproduction and Child Health (EDMaRC), Copenhagen University Hospital – Rigshospitalet, Copenhagen, Denmark

Infertility affects 15%–25% of couples, and male reproductive issues related primarily to semen quality play a role in many cases. Furthermore, impaired semen quality has been linked to adverse long-term health outcomes. A key pillar in the evaluation of men from infertile couples is the traditional semen analysis, which by and large has remained unchanged for decades, including assessment of semen volume, sperm concentration, motility and morphology. Though, the process of fertilization (*in vivo*) is much more complex that what is covered with these parameters. At present, most treatment options bypass natural reproduction barriers by enhancing ovulation and/or increasing the chance of oocyte/sperm interaction, whereas only few treatments target the underlying cause of infertility. The causes of male infertility are multifactorial involving both genetic factors and exposures in fetal life and adulthood. However, the interplay between and relative contributions of health behavior, psychosocial, environmental, genetic, endocrine, metabolic, immunologic, and epigenetic factors as well as pathogenic processes at different stages of life are still poorly understood. Despite the availability of increasingly advanced diagnostic and therapeutic techniques, approximately 30% of infertile couples do not obtain a live birth after fertility treatment. Reaching beyond the traditional semen analysis and implementing artificial intelligence methods is essential to further improve our ability to **a)** study risk factors for male (and female) infertility, **b)** identify new biomarkers to diagnose subfertility and predict fecundity and response to treatment, and **c)** identify subgroups of infertility patients at risk of long-term health impairment. With the establishment of the ReproUnion Biobank and Infertility Cohort (RUBIC), including 5000 well-characterized infertile Danish and Swedish couples, we hope to create a framework for this approach in a multidisciplinary research environment. An unresolved issue is, however, how to apply the artificial intelligence methods and develop the new interdisciplinary collaborations needed.

DOI: 10.1530/endoabs.81.EYES1.3

ECAS Symposium

Europe needs more endocrinology

ECAS1.1

Abstract unavailable

DOI: 10.1530/endoabs.81.ECAS1.1

ECAS1.2

Abstract unavailable

DOI: 10.1530/endoabs.81.ECAS1.2

ECAS1.3

Abstract unavailable

DOI: 10.1530/endoabs.81.ECAS1.3

ECAS1.4

Laboratory chaos diverted – the case of the in vitro diagnostics regulation

Michael Vogeser
Institute of Laboratory Medicine, University Hospital, LMU Munich, Germany

In vitro diagnostics (IVD) in the European Union is facing a fundamental change with the introduction of a new regulation, the so-called In Vitro Diagnostics Regulation (IVDR). Originally, the IVDR was scheduled to enter into force in May 2022, however, in January 2022, the EU legislator made a differentiated partial postponement of the application of important parts of the IVDR. The major innovation and achievement of the IVDR is that most commercially manufactured IVD products must now be certified by independent (albeit commercial) notified bodies - replacing the system of self-certification by manufacturers. Notified bodies are under surveillance by member states. Because key regulatory processes have not been implemented in time, the entry into force of the IVDR for commercial IVDs has been delayed to 2025 to 2027, depending on the risk class. For the IVD industry, the product certification process requires significant additional resources for compliance. This may result in niche products being phased out of the market by some manufacturers. In addition to commercial products, some elements of the IVDR are also mandatory for in-house manufactured products, particularly Annex I (general safety and performance requirements), starting as early as May 2022, particularly for calibration and control materials and reagents manufactured in-house. The definition of in-house products in Article 2 (IVDR) does not include measurement methods, and the term LDT (laboratory developed test) is not used by the IVDR. Compliance with this regulation is not assessed at EU level, but is the responsibility of the Member States.

DOI: 10.1530/endoabs.81.ECAS1.4

ECAS1.5

Abstract unavailable

DOI: 10.1530/endoabs.81.ECAS1.5

ECAS1.6

Fighting endocrine disruption - Are we getting somewhere?

Barbara Demeneix
Unité PhyMA, Department 'Adaptation du Vivant', Muséum national d'Histoire naturelle, Centre National de la Recherche Scientifique, Sorbonne University, 7 rue Cuvier, 75005, Paris, France

The Daily Tolerable Intake (DTI) was reduced by BPA (bisphenol A) 100,000 fold. This is an unprecedented action to protect consumers and the environment from the most commonly used plasticizer. However, one problem identified was the fact that regrettable substitutes, such as BPS and BPF, were not included in the recommendation. There will be a fight to ensure that this passes into the European legislation. In the meantime, BP-B (,4'-(1-methylpropylidene) bisphenol (a substitute for BPA) and a sunscreen agent 4-MBC were proposed to be endocrine disruptors. Resorcinol was identified as a Substance of Very High Concern (SVHC). This was primarily due to its effects on the thyroid and other endocrine systems. GenX produced by Chemours lost their suit. Chemours had taken the EU Chemicals Agency (ECHA) to court over the inclusion of GenX chemicals in the SVHC list under REACH – the main EU law used to stop chemical pollution. Already, a multitude of other PFAS, per (and poly) fluoroalkyl substances are classed as SVHCs, mainly due to their mobility and persistence. Next, the question of mixtures. As we showed in our paper 'From Cohorts to Molecules' (https://www.science.org/-doi/epdf/10.1126/science.abe8244) the thyroid gland was among those endocrine systems affected. We showed the mixture of 8 chemicals affected language delay in children at 30 months and at 7 years of age. Given that in the US current figures for autism spectrum disorder have reached 1 in 44 children and the thyroid axis is needed for brain development the two could be linked.

DOI: 10.1530/endoabs.81.ECAS1.6

ECAS1.7

Hormones and public awareness – the need for better estimates of hormonal exposure

Bruno Lapauw
Ghent University Hospital, Ghent, Belgium

Hormones are key regulators of numerous physiological processes. While most hormones are produced in select organs, their effects are felt throughout the body. Hormonal exposure is not only mediated by hormone production, but also by circulating binding proteins, and by local metabolism. Although we still heavily rely on total serum levels for the diagnosis of endocrine disorders and abnormalities, it is increasingly clear that total serum hormone levels do not always accurately reflect true exposure. Patients with binding protein defects presenting with low total hormone levels - but no profound clinical features - are a key example of this. Free serum hormone levels, the minor fractions of circulating non-protein bound (steroid) hormones, are recognized as superior markers of hormonal exposure and are increasingly used in the clinic. For example, using free testosterone is now recommended in the diagnosis of male hypogonadism and female hyperandrogenism. However, free serum hormone levels are mostly estimated using calculators, as access to direct measurements is limited because it is technically demanding and laborious. Also, alternative measurements in different matrices such as saliva and hair are being explored. Advantages of these measurements include more accurate reflections of hormonal exposure, over longer periods of time, minimizing patient discomfort, and the ability to collect samples ambulatory. Despite recent advances, further insight is necessary for a broader adaption of these new markers. In the BEED-ED project, we want to improve the clinical applicability of free steroid hormone concentrations in patients with specific conditions. As the number of available tests increases, so too does the need to educate both healthcare providers and patients. Increasing public awareness about the importance, implication and interpretation of these new measures of hormonal exposure is key to advancing both the immediate care for patients and the utility of these novel estimates of hormonal exposure.

DOI: 10.1530/endoabs.81.ECAS1.7

New Scientific Approaches

Human gonadal development at single-cell resolution
NSA1

Abstract unavailable

DOI: 10.1530/endoabs.81.NSA1

Scaling down the study of pituitary tumours for better understanding their behaviour and intra-tumoral heterogeneity
NSA2

Scaling down the study of pituitary tumours for better understanding their behaviour and intra-tumoral heterogeneity

Philippe Bertolino
Inserm U1052, CNRS UMR5286, University Claude Bernard Lyon 1, Cancer Research Center of Lyon, Lyon, France

Gonadotroph tumours (GoTs) are frequent intracranial neoplasms that represent 30% of all pituitary tumours (PiTs). While GoTs are responsible of an important morbidity, their tumorigenesis is not yet understood, and their treatment is limited to surgical resection and radiotherapy. The absence of identified driver-genes combined with their heterogeneity and silent behaviour (i.e. lack of hormone hypersecretion) limit the development of medical treatment. The current lack of relevant preclinical animal-models and patient-derived cell-lines has further slowed the study of the biological and molecular mechanism underlying gonadotroph tumorigenesis. Here we questioned whether we could scale down the culture and the functional analysis of tumour-cells derived from resected gonadotroph tumour to improve our knowledge of GoTs behaviour and intra-tumoral heterogeneity. We developed a series of approaches combining custom-made agarose-based micro-culture inserts and computerized-analyses of 3D-images to: i) characterize GoT intra-tumoral heterogeneity and ii) screen molecules to develop new therapeutics. The feasibility of these approaches was first addressed through the analysis of pituispheres obtained from rodent-pituitary cell-lines. Subsequently pituispheres obtained from GoT-patients were analyzed. Parameters such a size and percentage of tumor cells (CHGA+) vs non tumor-cells (i.e. Microenvironment, TME) and response to candidate therapeutic molecule were addresses in a 3D semi-high throughput manner (30-50 spheroids acquired through confocal scanning). Magnetic sort based on surface expressing-markers was also performed on surgically-resected gonadotroph tumours to compare the growing capabilities of different tumour-cell-populations isolated from single patients. In conclusion, we have built and validated custom-made micro-culture inserts for growing, imaging and analyzing pituitary rodent cell-lines and patient-derived cells. This work confirms that scaling down the analysis of patient-derived pituispheres could overcome the lack of patient-derived cell lines and could serve the screening of novel therapeutics for personalized medicine.

DOI: 10.1530/endoabs.81.NSA2

How liquid biopsies can change clinical practice in oncology
NSA3

Abstract unavailable

DOI: 10.1530/endoabs.81.NSA3

Debate Sessions

PRRT or targeted molecular therapies as preferred line of treatment

D1.1

For: PRRT or targeted molecular therapies as preferred line of treatment

Wouter W de Herder
Internal Medicine - Endocrinology, Erasmus Medical Center, Rotterdam, Netherlands

Purpose
Bronchopulmonary (BP) and gastroenteropancreatic (GEP) neuroendocrine neoplasms (NEN) are slow-growing tumors, which frequently express somatostatin receptors on their cell membranes. These receptors are targets for therapy with ^{177}Lutetium-labeled somatostatin analogues.
Experimental Design
Patients receive four treatments of ^{177}Lu-DOTATATE at a dose of 7.4 GBq every 8 weeks
Results
An objective response rate of 39% was found for all BP & GEP NEN. Stable disease was reached in 43% of patients. Progression-free survival (PFS) and overall survival (OS) for all NET patients were 29 months (95% confidence interval (CI), 26–33) and 63 months (95% CI, 55–72). Long-term toxicity included acute leukemia (0.7%) and myelodysplastic syndrome (1.5%). No therapy-related long-term renal or hepatic failure occurred. The NETTER-1 study was the first randomized phase III study of ^{177}Lu-DOTATATE and evaluated patients with midgut NENs who had progressed on standard doses of octreotide LAR. Patients were randomized to receive ^{177}Lu-DOTATATE in combination with standard-dose octreotide or high-dose octreotide (60 mg/4 weeks) alone. Median OS was 48 months (95% CI, 37-55) in the ^{177}Lu-DOTATATE group and 36 months (95% CI, 26-52) in the control group.
Conclusions
PRRT with ^{177}Lu-DOTATATE is a favorable therapeutic option in patients with metastatic bronchial and gastroenteropancreatic NETs that express somatostatin receptors. PRRT with ^{177}Lu-DOTATATE is safe with few side-effects and shows good response rates.
Speaker fees Ipsen, AAA-Novartis; research support AAA-Novartis.

DOI: 10.1530/endoabs.81.D1.1

D1.2

Abstract unavailable

DOI: 10.1530/endoabs.81.D1.2

Pituitary adenoma or pituitary tumor?

D2.1

Abstract unavailable

DOI: 10.1530/endoabs.81.D2.1

D2.2

Abstract unavailable

DOI: 10.1530/endoabs.81.D2.2

Adjuvant Radioactive Iodine Therapy for low to intermediate risk differentiated thyroid cancer patients

D3.1

Abstract unavailable

DOI: 10.1530/endoabs.81.D3.1

D3.2

For: Adjuvant radioactive iodine therapy for low to intermediate risk differentiated thyroid cancer patients

Juan Carlos Galofré
Department of Endocrinology and Nutrition, Clínica Universidad de Navarra, Pamplona, Spain

Current indications for adjuvant Radioactive Iodine (RAI) in low- and intermediate-risk differentiated thyroid cancer (DTC) are controversial. At the same time, there is universal consensus for personalized DTC management according to individual patient needs, as there does not appear to be a ''right'' way to treat patients with DTC. According to the *Martinique Principles* [1], adjuvant RAI treatment has many goals, including: initial staging of the disease, facilitate follow-up, improve disease-specific survival, decrease recurrence, improve progression-free survival and, in some cases, curative intent. The same principles state that the key elements in adjuvant treatment decision-making are post-op risk assessment, impact on outcomes of interest, side effect profile, patient values and preferences, improved initial staging, and facilitate sensitive follow-up. In addition, other factors must be consider such as the availability and quality of pre- and post-op ultrasound, the quality of RAI imaging, thyroglobulin assay accuracy, the access to an experienced thyroid surgeon, the presence of anti-thyroglobulin antibodies and preferences of local disease management multi-disciplinary team. All these factors (or a combination of them) could tip the balance for or against adjuvant RAI administration in DTC. There are fresh retrospective data showing that a decrease in the administration of adjuvant RAI in low- to intermediate-risk DTC individuals generates a substantial number of patients stranded in a misleading status labeled as "gray zone"[2]. These patients are those appropriately identified as *indeterminate* or *biochemical incomplete* response to treatment when ablative RAI is administered. A large number of patients in a broad "gray zone" could likely complicate their follow-up, with more diagnostic tests that will lead to increasing costs and raise the anxiety level of both patient and attending physician. A very recent European Thyroid Association Consensus Statement[3], recommends adjuvant RAI in intermediate-risk DTC patients who meet any of the following frequent conditions: advanced age (>45), aggressive histology, increase volume of nodal disease, extranodal extension, multiple lymph node or lymph node outside the central neck. In this conundrum we should bear in mind that changes that downgrade the intensity in the treatment of oncologic patients are normally based on the results emerging from large tertiary academic hospitals (those which are most often published). However, these results may not accurately reflect real-life outcomes. In other words, broad recommendations are not always applicable to individual cases. Finally, any proposal for change in the practice of medicine must be considered in light of both its ethical aspects and the precautionary principle, the latter emphasizes caution, pausing and review before embracing innovations that may in time prove disastrous.
References
1. Tuttle RM, et al. *Thyroid*. 2019; **29**: 461-470.
2. Grani G, et al. *J Clin Endocrinol Metab*. 2021; **106**: e1717-e1727.
3. Pacini F, et al. *Eur Thyroid J* .2022; **11**: e210046.

DOI: 10.1530/endoabs.81.D3.2

Meet The Expert Basic Scientist Sessions

Extracellular vesicles as theranostic tools in metabolic and cardiovascular diseases

MTEBS1

Extracellular vesicles in cardiometabolic disorders: from waste product to reliable disease biomarkers

Maria Felice Brizzi
Department of Medical Sciences, University of Torino, Torino, Italy

Circulating extracellular vesicles (EVs) are nano-sized bilayer membrane particles mainly released by platelets, inflammatory, endothelial cells and cancer cells, which play a pivotal role in inter-cellular communication. EV cargo, which consists of RNAs, proteins, DNA, and lipids, reflects the cell of origin and its activation state and the microenvironment; for this reason, it can be used as source of potential biomarkers in several conditions related to tumour development/progression, inflammation, atherosclerosis, thrombosis, and endothelial dysfunction. Therefore, cardiometabolic diseases can advantage of EVs for diagnostic/prognostic (theranostic) purposes. Recent advances in -omics technologies combined with artificial intelligence approaches allow high-throughput analysis, with the possibility to generate a biomolecular signature featuring a specific pathophysiological condition. An increase of specific EV sub-populations may even anticipate the rise of conventional biomarkers which usually require cell death or tissue necrosis (i.e., the rise of hs-troponin after cardiomyocyte death in cardiac ischemic disease). A change in EV secretome is expected in suffering, but still alive cells, thus providing great advantage for early diagnosis. Data on the impact of EV for diagnostic and therapeutic purposes in cardiometabolic settings will be discussed.

DOI: 10.1530/endoabs.81.MTEBS1

How to assess hazard of EDC mixtures?

MTEBS2

Abstract unavailable

DOI: 10.1530/endoabs.81.MTEBS2

The role of macrophages in the endocrine system

MTEBS3

Purinergic targeting of macrophages in obesity and diabetes

György Haskó
Department of Anesthesiology, Columbia University, New York City, New York, United States

The purinergic signaling complex comprising extracellular nucleotides and nucleosides, and their receptors, the P2 and P1 purinergic receptors, respectively, as well as catabolic enzymes and nucleoside transporters is a major regulatory system in the body. Macrophages are cells of the innate immune system that play myriad roles in the body. Macrophages are subject to regulation by the purinergic signaling complex. Macrophages are known to reside in endocrine glands and a body of evidence now suggests that these cells interact closely with endocrine cells and play important roles in both physiological and pathophysiological states. In the realm of inflammatory and auto-immune diseases, endocrine organs are known to be a frequent target, possibly due to the expression of a high density of major histocomptability complex (MHC)-II molecules on resident macrophages. This implicates a key role of macrophages in the pathogenesis of auto-immune endocrine diseases and making them attractive targets for pharmacotherapy. Here I summarize the diverse roles played by the purinergic signaling complex in regulating macrophages in the endocrine system and identify potential targets for pharmacotherapy in endocrine diseases.

DOI: 10.1530/endoabs.81.MTEBS3

Meet The Expert Sessions

Personalized therapy in acromegaly
MTE1

Personalized therapy in acromegaly
Maria Chiara Zatelli
Section of Endocrinology and Internal Medicine, Department of Medical Sciences, University of Ferrara, Ferrara, Italy

Personalized medicine aims at providing indications concerning the management of each patient according to her/his specific needs and disease characteristics. Acromegaly, although a rare disease, has a profound impact on patients' quality and expectancy of life, due to increased morbidity and mortality as compared to the general population in correlation mainly due to cardiovascular disease and cancer. Several clinical variables have been investigated as predictors of response to treatment (either surgical or medical) and as prognostic factors. Tumor diameter, invasiveness, genetic predisposition are recognized as the main predictors for surgical success. Adenoma granulation at electron microscopy, somatostatin receptor status, T2-intensity at MRI, age, and AIP mutation status have been indicated as predictive of response to treatment with somatostatin receptor ligands (SRLs). If resistance to SRL is foreseen, treatment with the growth hormone receptor antagonist pegvisomant or second-generation SRL pasireotide can be proposed, with the possibility of a combination therapy. In addition to tumor characteristics, a very important issue is represented by assessment of symptoms and of quality of life (QoL). Several quaestionnaires have been developed to specifically evaluate QoL in patients with acromegaly. The patient-assessed acromegaly symptom questionnaire consists of 5 acromegaly-related symptoms (soft-tissue swelling, arthralgia, headache, excessive perspiration, and fatigue) has not yet been clinically validated. The acromegaly quality of life questionnaire is used to assess the disease-specific physical and psychologic aspects. The acromegaly treatment satisfaction questionnaire is clinically validated to assess patient satisfaction with monthly injectable SRLs. Therefore, several items are available to clinicians to aid the best therapeutic managements of acromegaly and its complications on the basis of patient charcteristics, but also (and mainly) on the basis of patiet's choice and specific health issues.

DOI: 10.1530/endoabs.81.MTE1

Ultrasound-based approach in the management of thyroid nodules/ Does AI improve the accuracy of the current risk stratification systems
MTE2

Abstract unavailable

DOI: 10.1530/endoabs.81.MTE2

24h steroid measurements as new tools for the diagnosis of adrenal disease
MTE3

Abstract unavailable

DOI: 10.1530/endoabs.81.MTE3

MicroRNA in Bone OR MicroRNA in bone diagnostics and treatment looking into the future
MTE4

MicroRNA in bone diagnostics and treatment looking into the future
Matthias Hackl
TAmiRNA GmbH, Vienna, Austria

MicroRNAs (miRNAs) are non-coding RNAs that control the expression of 70% of the protein-coding genes. Since their discovery in the late 1990s, the function of miRNAs in the context of biological pathways that are essential to bone homeostasis has been investigated. This has expanded our understanding of the mechanisms underlying bone health and disease and led to the identification of novel drug and biomarker candidates. From a diagnostic viewpoint the seminal finding that miRNAs can be actively or passively released from cells into biofluids such as serum or urine ("circulating miRNAs"), motivated researchers to investigate circulating miRNAs in several pathologic conditions, including bone diseases. Thus, several exploratory studies in cohorts representing various types of bone diseases have been performed. In this meet-the-expert session, the important molecular basics of intracellular miRNA function and extracellular release will be discussed, including recommendations for best (pre-)analytical practices and documentation standards for circulating miRNA research. In the second part evidence from pre-clinical and clinical studies that have investigated the utility of microRNAs as biomarkers and drug targets in musculoskeletal disorders will be presented, with a specific focus on type-2 diabetic osteopathy.

DOI: 10.1530/endoabs.81.MTE4

Artificial pancreas to treat type 1 diabetes
MTE5

Abstract unavailable

DOI: 10.1530/endoabs.81.MTE5

State of the art of clinical studies in the OMICS age
MTE6

Abstract unavailable

DOI: 10.1530/endoabs.81.MTE6

What an endocrinologist should know about in vitro fertilization treatment and egg storage
MTE7

What an endocrinologist should know about in vitro fertilization treatment and egg storage
Sophie Catteau-Jonard
CHU Lille, University of Lille, INSERM U 7211, Lille, France

Achieving pregnancy through in vitro fertilization requires a minimum number of oocytes recovered during egg retrieval. These oocytes come from ovarian hyperstimulation that allows the entire oocyte cohort to mature. In physiology in a natural cycle, a dozen follicles are recruited at the beginning of the menstrual cycle under the action of the elevation of the FSH (the « FSH window »). Then, follicles secrete estradiol through aromatase under the action of FSH. By negative feedback, FSH levels decrease (the FSH window closes) and only the follicle most independent of FSH will continue to grow until ovulation: the dominant follicle. The other follicles of the cohort attenuate allowing mono-ovulation. On the contrary, it is very important in the process of in vitro fertilization to have a multifollicular development, in order to increase the chances of pregnancy. Indeed, there are still many stages before pregnancy: puncture and selection of oocytes, obtaining fertilization and then a quality embryo to be transferred. The goal of the treatment is therefore to continue the administration of FSH to avoid the closing of the window and thus allow the maturation of all the follicles of the cohort. The other very important aspect of stimulation treatment during IVF is to control the exact time of ovulation. GnRH agonists or antagonists are used but the use of simple progestins is also possible! Finally, the triggering of ovulation is achieved through the administration of either hCG (with an LH like action) or a GnRH agonist in cycles slowed down by GnRH antagonists. Completely artificial cycles are also possible to transfer devitrified embryos.

DOI: 10.1530/endoabs.81.MTE7

Management of panNENs in MEN1 and vHL

MTE8

Management of pancreatic neuroendocrine tumors in Multiple Endocrine Neoplasia Type 1 and the von Hippel Lindau syndrome

Gerlof Valk
Department of Endocrine Oncology, University Medical Center Utrecht, Utrecht, Netherlands

Multiple Endocrine Neoplasia Type 1 (MEN1) and the von Hippel Lindau syndrome (VHL) are hereditary disease with an autosomal dominant inheritance. Among a wide variety of manifestations, both syndromes predispose patients to pancreatic neuro-endocrine neoplasms (PanNENs). Screening for presymptomatic diagnosis of PanNENs enables timely intervention with the intention to prevent metastasized disease and premature death. MEN1 and VHL lead to different manifestations and there are also distinct differences in occurrence and clinical course of PanNEN. Therefore the management of PanNEN occurring in both syndromes is different with consequences for the required multidisciplinary team. For both tumor syndromes screening for PanNEN should be based on clinical orientation, including general planning of screening and surveillance, utility of biochemical biomarkers, the optimal choice for imaging modality, and risk stratification for individual patients. Recent research gives more insight into the main aspects of MEN1 and VHL-related pancreatic manifestations and their clinical management. For care tailored to the needs of the individual patient and improving outcomes on an individual basis, studies are now needed to define predictors of tumor behavior and effects of more individualized interventions. Patients with MEN1 and VHL are therefore preferably treated in centers with specific expertise and dedication to collaborative research.

DOI: 10.1530/endoabs.81.MTE8

Changing spectrum of hypophysitis

MTE9

Abstract unavailable

DOI: 10.1530/endoabs.81.MTE9

How do we have to treat patients with CAH to avoid complications for under-and over-treatment?

MTE10

How do we have to treat patients with CAH to avoid complications for under- and over-treatment?

Richard J Auchus
University of Michigan, Ann Arbor, MI, United States

The management of adults with congenital adrenal hyperplasia due to classic 21-hydroxylase deficiency (21OHD) is a challenging balance of hormone replacement, disease control, and avoidance of adverse effects. The approach should emphasize the clinical evaluation and patient goals, and laboratory tests are used secondarily as ancillary data. Upon transition from pediatric to adult care, the concerns shift from growth and pubertal development to fertility, neoplasia formation, and long-term complications. Each visit requires a thorough physical exam to assess for cushingoid features such as skin thinning, bruising, muscle weakness, fat redistribution, and purple striae – much of this exam can be done via telemedicine. The most useful biomarkers to aid in glucocorticoid titration are androstenedione, the androstenedione/testosterone ratio in men, and follicular-phase progesterone in women attempting pregnancy. The major androgens in most 21OHD patients are the 11-oxygenated androgens, and these steroids appear to be useful analytes of disease control as well. Hydrocortisone remains the most effective glucocorticoid for cortisol replacement therapy. More potent synthetic glucocorticoids have narrower therapeutic indices and greater the risk of adverse effects than hydrocortisone. Attention to mineralocorticoid replacement is also important, and under-replacement is a common cause of chronic fatigue. Standing blood pressure, serum potassium, and plasma renin are used to titrate the fludrocortisone acetate dose in that order. Conceptually, the endocrinologist should distinguish doses used to replace the cortisol deficiency (first priority) and then additional doses to achieve adequate disease control. New treatments are under study to improve disease control while avoiding excessive glucocorticoid exposure.

DOI: 10.1530/endoabs.81.MTE10

Endocrine treatment in transgenders - when, who and how?

MTE11

Endocrine treatment in transgenders - when, who and how?

Matthias Auer
Medizinische Klinik and Poliklinik IV, Klinikum der Universität München, LMU München, Munich, Germany

Treatment of transgender patients has gained increasing importance in outpatient endocrinological care due to a steadily rising influx of patients in recent years. Many gaps in knowledge regarding hormonal therapy have been filled in recent years thanks to a growing body of literature based on larger cohort studies. Nowadays therapy can be regarded as safe and effective. While puberty arrest and peripubertal hormone treatment in transgender youth has gained growing acceptance in recent years, some questions still remain unsolved but will hopefully be answered in years to come, following the steadily growing knowledge and experience in this area. This talk summarizes the current knowledge on risks and benefits of endocrine treatment in transgender individuals and should open discussion based on patient cases on questions such as optimal treatment monitoring, the use of progestins/progesterone, fertility preservation, relevant comorbidities and ideal hormone treatment across the lifespan.

DOI: 10.1530/endoabs.81.MTE11

Diagnostic approach and clinical management of hypophosphatemia: Is it really an endocrine disorder?

MTE12

Diagnostic approach and clinical management of hypophosphatemia: Is it really an endocrine disorder?

Sabrina Corbetta
Endocrinology and Diabetology Service, Department of Biomedical, Surgical and Dentistry, University of Milan, IRCCS Istituto Ortopedico Galeazzi, Milan, Italy

Phosphorus is involved in energy storage, metabolism, nucleic acids, cell membrane function, cell signaling; it is a fundamental constituent of skeleton and teeth. Pi homeostasis is regulated mainly by three hormones, namely parathyroid hormone (PTH), vitamin D and Fibroblast Growth Factor 23 (FGF23). Additionally, sex hormones are known to decrease circulating Pi levels, by reducing renal tubular reabsorption through direct and indirect effects on renal phosphate channels and likely stimulating FGF23 release. Though some patients may complain of muscle weakness, mild hypophosphatemia (HP) is usually asymptomatic, and, consequently, often overlooked, so that its prevalence in the general population is not known. Indeed, HP is not a rare feature in patients with osteoporosis. On the other hand, severe and chronic HP causes muscle weakness, bone pain and deformity, fragility fractures (osteomalacia), rhabdomyolysis, impaired mental status, heart failure. Several mechanisms can be involved, and reduced Pi intestinal absorption, internal redistribution or urinary loss must be differentiated. Once urinary loss has been established, differential diagnosis includes FGF23-dependent conditions [renal transplantation, tumor induced osteomalacia (TIO), hereditary hypophosphatemic rickets] and FGF23-independent ones (primary and secondary hyperparathyroidism, renal tubular defects, diuretics, glucocorticoid therapy, hereditary hypophosphatemic rickets with hypercalciuria). Diagnostic workup is complex and often unrewarding, and the cause of chronic HP can remain unexplained in a number of patients. Finally, in patients affected with osteoporosis, HP may occur as an adverse effect of the anti-osteoporotic drugs (bisphosphonates, denosumab, teriparatide), though most studies show that HP is rare and generally self-limiting in this context. Indeed, a subset of osteoporotic patients developing chronic HP on anti-osteoporotic treatment can be observed in clinical practice, but frequency and implications of this condition are not known. Lastly, it should be considered that recently a specific anti-FGF23 treatment is available implying the need to correctly diagnose FGF23-related HP.

DOI: 10.1530/endoabs.81.MTE12

Oral Communications

Diabetes, Obesity, Metabolism and Nutrition 1

OC1.1

Clinical characteristics and outcomes in hospitalized COVID-19 patients with and without diabetes at Vilnius University Hospital Santaros Klinikos (VUHSK)

Zydrune Visockiene[1,2], Valentinas Jakubkevicius[1,2], Modesta Alekniene[1,2], Laura Šiauliene[1,2], Gerda Mekionyte[1] & Joana Scerbinkinaite[1,2]
[1]Vilnius University Faculty of Medicine, Clinic of Internal Diseases, Family Medicine and Oncology, Vilnius, Lithuania; [2]Vilnius University Hospital Santaros Klinikos, Center of Endocrinology, Vilnius, Lithuania

Background
Studies suggest that diabetes mellitus (DM) is associated with greater risk of developing severe forms of COVID-19 and mortality.
Aims
To compare clinical characteristics and outcomes in hospitalized COVID-19 patients with and without DM.
Methods
A single-center, retrospective, observational study included adult patients with laboratory-confirmed COVID-19 treated at VUHSK between 2020-01-01 and 2021-03-31. Patients were allocated to DM and non-DM grousp. The demographic, laboratory and outcomes data were compared. Disease severity was described as requirement of either high flow oxygen, intubation or inotropic support.
Results
A total of 2559 patients (median age 60 years, 1424 (55.6%) men) were included. Compared with the non-DM group ($n=2058$, 80.4%), patients with DM ($n=501$, 19.6%) were older, had more co-morbidities: hypertension, coronary artery disease, heart failure, dyslipidaemia, obesity, chronic kidney disease ($P<0.05$). Serum glucose, CRP, procalcitonin, D-dimer, creatinine and lactate were significantly higher ($P<0.05$), eGFR and LYM count - significantly lower ($P<0.05$) in the DM group compared to non-DM. Patients with DM were more likely to develop acute respiratory failure (31.3 vs 20.9%; OR 1.728, 95% CI 1.391-2.146), sepsis or septic shock (9.2 vs 6.3%, OR 1.512, CI 1.063-2.149) acute kidney failure (18.4 vs 11.6%, OR 1.712, CI 1.316-2.228), to require high flow oxygen or non-invasive ventilation (16.4 vs 9.3%, $P=0.000$), intubation (12.2 vs 8.1%, $P=0.004$), inotropic support (4.6 vs 2.5%, $P=0.014$), stayed longer at the hospital (median 11 vs 13 days, $P=0.000$), had higher prevalence of severe disease (23.0 vs 14.7%, OR 1.732, CI 1.361-2.205) and mortality rate compared to non-DM patients (19.6 vs 12.7%, OR 1.674, CI 1.296-2.163). After matching for age and gender, DM remained significant risk factor for developing respiratory failure (OR 1.533, CI 1.157-2.031) and severe disease (OR 1.569, CI 1.142-2.154), but not death (19.4 vs 15.4%, OR 1.322, CI 0.952-1.837; $P=0.095$).
Conclusions
Diabetes was prevalent in one fifth of patients hospitalized with COVID-19. It was associated with longer hospitalization, greater risk of severe COVID-19 disease and death. Further investigation of the relationship between COVID-19 severity and diabetes is warranted.

Keywords: coronavirus disease 2019 (COVID-19); diabetes; mortality; outcome.
DOI: 10.1530/endoabs.81.OC1.1

OC1.2

Glucose control and mortality in critically Ill patients, based on real world evidence

George Dafoulas[1], Ilias Kalamaras[2], Konstantinos Votis[2] & Alexandra Bargiota[1]
[1]Faculty of Medicine, University of Thessaly, Department of Endocrinology and Metabolic Diseases, Larisa, Greece; [2]Centre for Research and Technology Hellas, Informatics and Telematics Institute, Thermi Thessaloniki, Greece

Objective
Published results of reduced morbidity and mortality with tight Glycemic Control of critical patients could not be reproduced in large prospective trials. Glycemic goals according to current respective guidelines include a target blood glucose range 140-180 mg/dl, while lower blood glucose targets may be appropriate for some patients. This study aims to provide real world evidence to this field.
Methods
We performed a retrospective study using the Medical Information Mart for Intensive Care Units (ICU) IV open access, anonymized database (MIMIC-IV) based on 15619 ICU admissions between 2008 and 2019 at Beth Israel Deaconess Medical Center, USA. Logistic regression was performed, using age, sex, SOFA, OASIS and proportion of time in glucose bands per ICU stay as predictors, and death in ICU as the target. Glucose bands and time proportions were defined as in Finney et al.[1] (hypoglycemic: blood glucose level <80 mg/dl, stringent: 80-110 mg/dl, normal: 111-144 mg/dl, intermediate: 145-180 mg/dl, liberal: 181-200 mg/dl, hyperglycemic: ≥ 201 mg/dl), where proportions were time-weighted to cope with variable measurement frequency. The study protocol was approved by the respective Institutional Review Boards.
Results

Table 1 Relationship between ICU mortality and proportion of time spent in each glucose band, controlling for age (<0.001)., gender, SOFA score (<0.001). and OASIS score (<0.001). Odds Ratios correspond to 1 unit increase

ICU type	Model	ICU mortality (OR)	CI (95%)	*P*-value
Cardio ($n=7758$)	hypoglycemic	**4.583**	(1.12, 18.69)	**0.034**
	stringent	**0.111**	(0.06, 0.19)	**<0.001**
	normal	**0.096**	(0.06, 0.16)	**<0.001**
	intermediate	**5.050**	(2.69, 9.48)	**<0.001**
	liberal	**254.094**	(73.46, 878.95)	**<0.001**
	hyperglycemic	**28.657**	(17.18, 47.8)	**<0.001**
Medical ($n=3463$)	hypoglycemic	2.431	(0.95, 6.19)	0.063
	stringent	**0.508**	(0.34, 0.75)	**<0.001**
	normal	0.937	(0.62, 1.41)	0.753
	intermediate	**1.707**	(1.01, 2.9)	**0.048**
	liberal	2.596	(0.92, 7.31)	0.071
	hyperglycemic	1.230	(0.82, 1.83)	0.311
Surgical ($n=4398$)	hypoglycemic	**5.366**	(1.85, 15.54)	**0.002**
	stringent	**0.364**	(0.24, 0.56)	**<0.001**
	normal	**0.578**	(0.39, 0.87)	**0.008**
	intermediate	**2.558**	(1.59, 4.12)	**<0.001**
	liberal	**4.276**	(1.57, 11.62)	**0.004**
	hyperglycemic	**2.318**	(1.36, 3.96)	**0.002**

Conclusion
Overall, increased time in the hypoglycemic, intermediate, liberal and hyperglycemic bands is related to increased ICU mortality, while increased time in the stringent and normal bands is related to decreased mortality. However, in medical ICUs, these results are not statistically significant with the available data, e.g. the OR for the "normal" band being around 1.

References
1. Finney, S.J., T.W., 2003. Jama, 290(15), pp.2041-2047.

DOI: 10.1530/endoabs.81.OC1.2

OC1.3

Canakinumabin patients with COVID-19 and type 2 diabetes (CanCovDia) – a multicentric, randomised, double-blind, placebo-controlled phase 3 trial

Matthias Hepprich[1], Jonathan Mudry[1], Claudia Gregoriano[2], Francois R Jornayvaz[3], Sebastian Carballo[4], Anne Wojtusciszyn[5], Pierre-Alexandre Bart[6], Jean-Daniel Chiche[7], Stefan Fischli[8], Thomas Baumgartner[9], Claudia Cavelti-Weder[9], Felix Beuschlein[9], Dominque L Braun[10], Huldrych F Günthard[10], Emily West[10], Anna Conen[2], Egon Isenring[2], Gabriela Bucklar[1], Yoann Aubry[1], Ludovic Dey[1], Beat Müller[2], Philipp Schütz[2], Marco Cattaneo[11], Patrick Hunziker[12] & Marc Y Donath[1]
[1]University Hospital Basel, Division of Endocrinology, Diabetes and Metabolism, Switzerland; [2]Kantonsspital Aarau, Medical University Department of Medicine, Aarau, Switzerland; [3]Geneva University Hospital, Division of Endocrinology, Diabetes, Nutrition and Therapeutic Patient Education, Genève, Switzerland; [4]Geneva University Hospital, Division of General Internal Medicine, Department of Medicine, Genève, Switzerland; [5]Centre Hospitalier Universitaire Vaudois, Service d'Endocrinologie Diabète et Métabolisme, Lausanne, Switzerland; [6]Centre Hospitalier Universitaire Vaudois, Service of Internal Medicine, Lausanne, Switzerland; [7]Department of Intensive Care Medicine, Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland; [8]Luzerner Kantonsspital,

Department of Endocrinology, Luzern, Switzerland; [9]Klinik für Endokrinologie, Diabetologie und Klinische Ernährung, Universitätsspital Zürich, Zürich, Switzerland; [10]University Hospital Zurich, Division of Infectious Diseases and Hospital Epidemiology, Zürich, Switzerland; [11]University of Basel, Department of Clinical Research, Basel, Switzerland; [12]University Hospital Basel, University of Basel, Intensive Care Unit, Basel, Switzerland

Background
Patients with type 2 diabetes and overweight have a chronic activation of the innate immune system possibly explaining the increased risk of a hyperinflammatory response and severe COVID-19. We aimed to test whether blockade of interleukin-1β(IL-1β) using canakinumab improves clinical outcome.
Methods
CanCovDia was a multicenter, randomised, double-blind, placebo-controlled trial to assess the efficacy of canakinumab plus standard-of-care compared with placebo plus standard-of-care in patients with type 2 diabetes and a BMI $>$ 25 kg/m^2 hospitalised with SARS-CoV2 infection. Patients were randomly assigned 1:1 to a single dose of canakinumab (body weight-adapted dose of 450-750 mg) or placebo intravenously. Canakinumab and placebo were compared on the basis of an unmatched win-ratio approach consisting of length of survival, ventilation, ICU stay and hospitalization. This study is registered with ClinicalTrials.gov, NCT04510493.
Findings
Between October 23, 2020, and May 12, 2021, 116 patients were randomly assigned with 58 in each group. The win-ratio analysis between canakinumab vs placebo was 1·08 (95% CI 0·69-1·69; $P=0·72$). After four weeks, in the canakinumab group 4 people died (7·0%), 12 were hospitalized for more than 3 weeks (23·5%), and 11 were on ICU (20·0%), vs 7 (12·3%), 16 (28·3%) and 11 patients (21·6%) respectively. Median ventilation time at 29 days was 10 days [IQR 6.0, 16.5] in the canakinumab group and 16 days [IQR 14.0, 23.0] in the placebo group. Glycated haemoglobin A1c (HbA1c) in the canakinumab group after four weeks was 7·40 [6·65, 8·30] vs 7·50 in the placebo group ([6·68, 8·33] $P=0·955$) despite a lower number of antidiabetics administered in patients treated with canakinumab vs placebo (OR 0·47 [95% CI 0·23-0·95] $P=0·03$). Median ratio to baseline of endogenous Insulin (pmol/l) at four weeks was 0.94 [0.59, 1.66] in the canakinumab group vs placebo 0.64 [0.29, 1.44] (OR 2.21 [1.09, 4.48] ($P=0.029$). Serious adverse events were reported in 13 (11·4%) patients in each group treated with canakinumab and placebo, respectively.
Interpretation
In patients with type 2 diabetes who were hospitalised with COVID-19, treatment with canakinumab in addition to standard-of-care did not result in a significant improvement of the primary composite outcome despite a numerical benefit in survival, ICU and ventilation time. Patients treated with canakinumab required significant less antidiabetic drugs to achieve similar glycaemic control, possibly due to increased insulin production.

DOI: 10.1530/endoabs.81.OC1.3

OC1.4

β-Caryophyllene, a dietary CB2 receptor selective cannabinoid mitigates myocardial fibrosis in a mice model of diabetic cardiomyopathy

Hebaallah Mamdouh Hashiesh[1], Azimullah Sheikh[1], MF Nagoor Meeran[1], Ahmed Al Kaabi[1], Bassem Sadek[1], Ernest Adeghate[2] & Shreesh Kumar Ojha[1]
[1]UAE University, Pharmacology and Therapeutics, Al Ain, United Arab Emirates; [2]UAE University, Anatomy, Al Ain, United Arab Emirates

β-Caryophyllene, a dietary CB2 receptor selective cannabinoid mitigates myocardial fibrosis in a mice model of diabetic cardiomyopathy
Background and aim
Diabetic cardiomyopathy (DCM), a cardiac complication in diabetes is characterized by abnormal cardiac function accompanied with myocardial fibrosis. In recent years, the cannabinoid type 2 receptors (CB2) emerged as a crucial therapeutic target for diabetes and its complications. The downregulation of CB2 receptors has been documented in various cardiovascular diseases and diabetes, that supports the concepts that activation of CB2 receptors may protect against diabetic cardiomyopathy. The present study was designed to investigate the effect of a selective CB2 receptor agonist β-Caryophyllene (BCP), a dietary natural cannabinoid compound and chemically a bicyclic sesquiterpene on myocardial fibrosis in DCM mice.
Methods
Experimental DCM was developed in Male C57/B6 mice by feeding a high-fat diet for 4 weeks followed by a low dose of streptozotocin (100 mg/kg) injection. Both DCM and control mice were then treated with or without BCP (50 mg/kg, orally) for 12 weeks by continuous feeding of a high fat or normal diet. At the end of this period, hemodynamic parameters (systolic blood pressure, diastolic blood pressure, mean arterial pressure, heart rate), and heart weight/body weight were evaluated, fasting blood glucose, oral glucose tolerance test, insulin level, lipid parameters (triglyceride, total cholesterol, low-density lipoprotein, very-low-density lipoprotein, high-density lipoprotein), and lactate dehydrogenase in serum were detected. Hematoxylin-eosin and picrosirius red were employed to determine heart morphological changes and cardiac fibrosis, respectively. Immunohistochemistry of collagen I and III and western blotting were taken to determine the expression levels of cardiac-fibrosis markers (TGF-β, SMAD, α-SMA).
Results
DCM mice exhibited hyperglycemia, insulin resistance, hyperlipidemia, hemodynamic abnormalities, significantly increased serum lactate dehydrogenase along with increased myocardial fibrosis, and hypertrophy. Oral administration of BCP significantly decreased the levels of blood glucose, serum lipids, while increased serum insulin level with improving the insulin resistance. Additionally, the myocardial enzyme (lactate dehydrogenase) was significantly decreased. Furthermore, BCP significantly improved hemodynamic changes and attenuated the abnormal morphologic change in DCM hearts. Moreover, BCP treatment decreased the expression of TGF-β, SMAD, α-SMA and reduced collagen deposition in the heart of DCM mice. Most importantly, pre-administration of the CB2 receptor antagonist AM630, abrogated the protective effects of BCP in DCM mice.
Conclusion
These results suggest that activation of CB2 receptors by BCP alleviated diabetic cardiomyopathy by attenuating hyperglycemia/hyperlipidemia-induced cardiac fibrosis and remodeling via TGF-β/SMAD signaling pathway.

DOI: 10.1530/endoabs.81.OC1.4

OC1.5

Associations between alcohol consumption and body fat distribution in type 1 diabetes

Erika B. Parente[1,2,3], Ina Lampenius[1,2,3], Valma Harjutsalo[1,2,3], Maija Feodoroff[1,2,3], Carol Forsblom[1,2,3] & Per-Henrik Groop[1,2,3,4]
[1]Folkhälsan Research Center, Helsinki, Finland; [2]Department of Nephrology, University of Helsinki and Helsinki University Hospital, Helsinki, Finland; [3]Research Program for Clinical and Molecular Metabolism, Faculty of Medicine, University of Helsinki, Helsinki, Finland; [4]Department of Diabetes, Central Clinical School, Monash University, Melbourne, Australia

Background
Increased alcohol intake is associated with several health disorders. However, its impact on body composition is still controversial and data regarding this subject in people with type 1 diabetes (T1D) are limited. We have shown that central obesity is associated with diabetes complications in T1D, and now, we investigated whether the alcohol consumption is associated with body fat distribution in adults with T1D from the Finnish Diabetic Nephropathy (FinnDiane) Study cohort.
Methods
We included 548 individuals that had their body composition assessed by dual-energy-X-Ray absorptiometry and had answered the questionnaires regarding alcohol consumption during the FinnDiane visits. The amount of alcohol was converted into standard doses (1 dose = 12 g of pure alcohol). Then, participants were divided into groups based on their alcohol consumption (dose/week) and the risk of health problems: abstainers, low risk (0.1-6.9 doses for women, 0.1-13.9 for men), moderate risk (7-15.9 for women, 14-23.9 for men) and high risk ($\geq$16 for women, $\geq$24 for men). Percentages of body fat refers to total body weight. Central obesity was defined as having $\geq$0.7% of visceral fat for women and $\geq$1.1% for men, while general obesity was $\geq$40.4% of total body fat for women and $\geq$31.8% for men. Logistic regression models adjusted for confounders were used to study the associations between alcohol consumption, central and general obesity. Similar analysis was done using the groups of alcohol, considering abstainers as the reference group.
Results
From 548 individuals, 30% had general obesity and 47% central obesity. Median age was 42 (IQR 34-53) years, duration of diabetes was 25.4 (19.6-37.5) years and 40% were men. The high risk group had the highest visceral fat percentage [2.19 (0.93-2.48), $P=0.002$] and the lowest arms and legs fat percentage [12.2 (10.1-15.1), $P=0.04$]. Total body fat percentage did not differ between groups. Each dose increase of alcohol consumption increased the odds of central obesity [OR 1.03, $P=0.03$]. The high risk group was associated with increased odds of central obesity [OR 6.8, $P=0.004$] and general obesity [OR 5.1, $P=0.008$]. Low and moderate risk groups were not.

Conclusion
In adults with type 1 diabetes, each dose increase of alcohol consumption increases the odds of central obesity by 3%. A high risk consumption of alcohol is associated with both central and general obesity. Our results motivate further longitudinal studies to explore the relationship between alcohol consumption and body fat distribution, as well as its impact on diabetes complications.

DOI: 10.1530/endoabs.81.OC1.5

Adrenal and Cardiovascular Endocrinology 1

OC2.1

DLK1 expressing cells mark a population of progenitor cells in the adrenal cortex and contribute to the zonation of the adrenal gland

Katia Mariniello, Leonardo Guasti & Emanuel Rognoni
William Harvey Research Institute, Queen Mary University, Centre for Endocrinology, London, United Kingdom

The adrenal cortex is a dynamic organ that undergoes self-renewal. In the mouse it is divided into two concentric layers, the outer zona glomerulosa (ZG) and the inner zona fasciculata (ZF), that secrete aldosterone and corticosterone, respectively. Capsular and subcapsular stem/progenitor cells differentiate and migrate in a centripetal fashion to repopulate the gland until they reach the juxtamedullary region where they undergo senescence and apoptosis. Cell fate mapping studies have shown that the maintenance of the cortex relies on a pool of two interconnected cell populations, subcapsular undifferentiated cells secreting the morphogen Sonic Hedgehog (Shh) and capsular Gli1$^+$ cells, which can transduce the Shh signal. Our lab has shown that Delta like non-canonical Notch ligand 1 (Dlk1) is expressed in partially undifferentiated cells of the subcapsular region in rat and human adrenals, whilst it is mostly expressed in capsular cells in mice. Our recent lineage tracing analyses used a tamoxifen inducible Dlk1^{CreERT2} mouse model carrying the R26tdTom reporter. Injection of pregnant dames at embryonic day (e) 12.5 and analysis of tdTomato expression at postnatal day (p) 10 and p38 showed that 35% (p10) and 24% (p38) of Steroidogenic Factor 1(Sf1)+ cortical cells were tdTomato+. On the other hand, postnatal tamoxifen injections showed tdTomato+/Sf1+ cells only in 1-2% in cortical cells. This data indicates that capsular Dlk1 marks a population of adrenocortical progenitor cells, that are mostly active during embryonic development and near-dormant postnatally. However, postnatal Dlk1+ cells could be reactivated and contribute to the regeneration of the ZF after dexamethasone-induced atrophy. Mice were administered tamoxifen followed by 7 days of dexamethasone which resulted in ZF atrophy. Two weeks after removal of dexamethasone, regrowth of the ZF occurred and tdTomato+ cells were visible in the cortex suggesting that near-dormant capsular Dlk1+ cells are re-activated during ZF regeneration to become steroidogenic cells. Taken together, our results provide evidence for a role of DLK1+ cells as contributors to the development and zonation of the adrenal cortex.

DOI: 10.1530/endoabs.81.OC2.1

OC2.2

Loss of SUMO-specific protease 2 leads to adrenal insufficiency limited to glucocorticoids

Damien Dufour[1], Typhanie Dumontet[2], Isabelle Sahut-Barnola[1], Meline Onzon[1], Eric Pussard[3], James Wilmouth Jr[1], Julie Olabe[1], Adrien Levasseur[1], Guillaume Bossis[4], Edward Yeh[5], Pierre Val[1], Antoine Martinez[1] & Lefrançois-Martinez Anne-Marie[1]
[1]CRBC (Centre de Recherche Bio Clinique), GReD, Clermont-Ferrand, France; [2]Rogel Cancer Center, Ann Arbor, United States; [3]Bicetre Hospital, Le Kremlin-Bicêtre, France; [4]Institute of Molecular Genetics of Montpellier, Montpellier, France; [5]University of Missouri, Columbia, United States

The adrenal gland produces corticosteroids essential for hydromineral and metabolic homeostasis. It is organised, in mice, in two concentric layers. The zona glomerulosa (zG) and fasciculate (zF), renewed from progenitors located in the capsular periphery. Centripetal renewal and maintenance of cortical zonation are dependant of a balance between WNT/β-catenin and ACTH/PKA signalling pathways. They provide recruitment and consecutive differentiation of progenitors into zG and zF. SUMOylation is a reversible post-translational modification mandatory for embryonic development. It consists of the serial reactions of activation, conjugation and ligation that will enables SUMOylation of a specific target protein. The presence of deSUMOylases mainly represented by SENPs makes SUMOylation particularly dynamic. In the adrenal cortex, it follows a centripetal decreasing gradient whose function is unknown. Moreover, chronic and acute PKA signalling stimulation leads to a decrease in SUMOyaltion in the adrenal cortex. In order to study the impact of hyperSUMOylation in the adrenal differentiation, we have chosen to delete the deSUMOylase SENP2 since it is positively regulated by ACTH/PKA signalling. Hence, we developed a model of *Senp2* deficiency targeting specifically the adrenal cortex thanks to cre/loxP technology. *Senp2* loss induces, as soon as 4 weeks of age, a glucocorticoids deficiency caused by zF hypoplasia without any defect in zG physiology. Even though, mice manage to normalise glucocorticoid levels throughout time, they still fail to respond properly to ACTH stimulation. We demonstrate, by biochemical and genetic experiments, that this lack of response was neither due to signalling upstream of PKA nor downstream, pointing toward a direct change in intrinsic PKA catalytic activity. The hypoplasia is associated with a stimulation of apoptosis at the zG/zF boundary. We show that this apoptosis was linked to a lack of PKA dependant phosphorylation of DRP1, whose phosphorylation state can induce either apoptosis or steroidogenesis. Finally, β-catenin, which is supposed to be limited to zG cell membrane, is found in the zF nuclei in *Senp2* mutant adrenals. Moreover, this is associated with an increase in SUMOylation of β-catenin and mild activation of the WNT signalling pathway. In conclusion, we show that HyperSUMOylation affects zF homeostatic renewal by altering the balance between ACTH/PKA and WNT/β-catenin signalling pathways and by stimulating early apoptosis of the zF cells. SUMOylation is a central mechanism of adaptive cellular responses to stress. Our results suggest that it is a fundamental pathway in the processes of functional maintenance of the adrenal cortex.

DOI: 10.1530/endoabs.81.OC2.2

OC2.3

Loss of lysine demethylase KDM1A in GIP-dependent bilateral macronodular adrenal hyperplasia with Cushing's syndrome

Fanny Chasseloup[1], Isabelle Bourdeau[2], Antoine Tabarin[3], Daniela Regazzo[4], Charles Dumontet[5], Nataly Ladurelle[1], Lucie Tosca[6], Larbi Amazit[1,7], Alexis Proust[8], Raphael Scharfmann[9], Frederic Fiore[10], Stylianos Tsagarakis[11], Dimitra Vassiliadi[11], Dominique Maiter[12], Jacques Young[1,13], Anne-Lise Lecoq[1,13], Vianney Deméocq[1], Sylvie Salenave[1,13], Hervé Lefebvre[14], Lucie Cloix[15], Philippe Emy[15], Rachel Desailloud[16], Delphine Vezzosi[17], Carla Scaroni[4], Mattia Barbot[18], Wouter de Herder[19], Francois Pattou[20], Martine Tetreault[21], Gilles Corbeil[2], Margot Dupeux[22], Benoit Lambert[23], Gerard Tachdjian[6], Anne Guiochon-Mantel[1,8], Isabelle Beau[1], Philippe Chanson[1,13], Say Viengchareun[1], André Lacroix[2], Jérôme Bouligand[1,8] & Peter Kamenicky[1,13]
[1]Université Paris-Saclay, Inserm, Physiologie et Physiopathologie Endocriniennes, Le Kremlin-Bicêtre, France; [2]Division of Endocrinology, Department of Medicine and Research Center, Centre Hospitalier de l'Université de Montréal (CHUM), Canada; [3]Department of Endocrinology, Diabetes and Nutrition, Hôpital Haut Lévêque, CHU and University of Bordeaux, France; [4]Endocrinology Unit, Department of Medicine, DIMED, Hospital-University of Padova, Italy; [5]Inserm UMR 1052 / CNRS 5286 / Université Claude Bernard Lyon I, Centre de Recherche de Cancérologie de Lyon, France; [6]Université Paris-Saclay, Assistance Publique-Hôpitaux de Paris, Hôpital Antoine Béclère, Service d'Histologie, Embryologie et Cytogénétique, France; [7]UMS 44 IBVB, Le Kremlin Bicêtre, France; [8]Assistance Publique-Hôpitaux de Paris, Hôpital Bicêtre, Service de Génétique Moléculaire et d'Hormonologie, France; [9]U1016 INSERM-Institut Cochin, France; [10]US12 Ciphe, Parc Scientifique et Technologique de Luminy; [11]Department of Endocrinology, Diabetes and Metabolism, Evangelismos Hospital; [12]Department of Endocrinology and Nutrition, Université Catholique de Louvain, Cliniques Universitaires Saint-Luc, France; [13]Assistance Publique-Hôpitaux de Paris, Hôpital Bicêtre, Service d'Endocrinologie et des Maladies de la Reproduction, France; [14]Normandie University, UNIROUEN, Inserm, DC2N, the Rouen University Hospital, Department of Endocrinology, Diabetes and Metabolic Diseases, Clinical Investigation Centre, CIC1404, Tumor BioBank-Centre for Biological Resources, France; [15]CHR Orleans, Service d'Endocrinologie, Diabète et Nutrition, France; [16]Department of Endocrinology, Diabetes and Nutrition, and PériTox, UMR-I 01 INERIS, University Picardie Jules Verne (UPJV), France; [17]Service d'Endocrinologie, Hôpital Larrey, France; [18]Endocrinology Unit, Department of Medicine, DIMED & Department of Neuroscience, Hospital-University of Padova, Italy; [19]Department of Internal Medicine, Section of Endocrinology, Erasmus MC, Netherlands; [20]Univ Lille, CHU Lille, Inserm U1190, Institut Pasteur Lille, Chirurgie Générale et Endocrinienne, France; [21]Department of Neuroscience, Faculté de Médecine, Université de Montréal, Centre de Recherche du Centre Hospitalier de l'Universiteé de Montreéal (CHUM), Canada; [22]Assistance Publique-Hôpitaux de Paris, Hôpital Bicêtre, Service d'Anatomie et

Cytologie Pathologiques, France; [23]Assistance Publique-Hôpitaux de Paris, Hôpital Bicêtre, Service de Chirurgie Digestive et Endocrinienne, France

Context
Primary bilateral macronodular adrenal hyperplasia (PBMAH) with glucose-dependent insulinotropic polypeptide (GIP)-dependent Cushing's syndrome is caused by ectopic expression of GIP receptor in the adrenal tissue. The bilateral nature of this adrenal disease suggests germline genetic predisposition. We aimed to identify the molecular driver event responsible for ectopic GIP receptor expression in PBMAH.
Methods
We conducted an international, multicenter, retrospective, cohort study to collect blood and adrenal samples from patients who had undergone unilateral or bilateral adrenalectomy for familial or sporadic GIP-dependent PBMAH with Cushing's syndrome. We performed sequencing and copy-number analyses of blood and adrenal DNA. Adrenal samples from patients with PBMAH and Cushing's syndrome without food-dependent cortisol production were used as controls. RNA-sequencing on adrenal samples was performed to study gene expression in GIP-dependent Cushing's syndrome and in control samples. Functional *in vitro* studies were performed to study the impact of the genetic event identified in human adrenocortical H295R cells.
Results
17 patients with familial or sporadic GIP-dependent PBMAH with Cushing's syndrome were studied. We identified germline heterozygous pathogenic or likely pathogenic variants in the lysine demethylase 1A (*KDM1A*, or *LSD1*) gene in all 17 patients. We further identified a recurrent deletion of the short arm of chromosome 1 harboring the *KDM1A* locus in the adrenal lesions of affected patients. None of the 25 patients in the control group had *KDM1A* germline or somatic alterations. Concomitant genetic inactivation of both *KDM1A* alleles resulted in loss of *KDM1A* expression in the adrenal lesions. Transcriptome analysis of adrenals from affected patients revealed the global effect of KDM1A loss in adrenal tissue on gene transcription and identified differentially regulated genes, including those encoding for GIP receptor and some other G protein-coupled receptors involved in adrenal tumorigenesis and regulation of steroidogenesis. *In vitro* pharmacologic inhibition, silencing and knock-out by CRISPR-Cas9 genome editing of *KDM1A* led to an increase in GIP receptor transcripts and protein in H295R cells.
Discussion
We found that familial and sporadic GIP-dependent PBMAH is a genetic disease caused in 100% of cases studied by germline inactivating pathogenic variants of the *KDM1A* gene with a loss of heterozygosity of the second *KDM1A* locus in the adrenal lesions. This stepwise inactivation of KDM1A is suggestive of a tumor suppressor gene model of tumorigenesis. Uncovering of a common genetic mechanism of GIP-dependent PBMAH will enable genetic testing and counselling of affected patients and earlier detection of the disease in their relatives.

DOI: 10.1530/endoabs.81.OC2.3

OC2.4

Autonomous cortisol secretion in adrenal incidentalomas and risk of fragility fractures: a large cross-sectional study

Guido Zavatta[1], Valentina Vicennati[1], Paola Altieri[1], Giacomo Colombin[1], Kimberly Coscia[1], Flaminia Fanelli[2], Matteo Malagrinò1[2], Matteo Magagnoli[2], Lorenzo Tucci[1], Uberto Pagotto[1] & Guido Di Dalmazi[1]
[1]Division of Endocrinology and Diabetes Prevention and Care, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Department of Medical and Surgical Sciences (DIMEC), Alma Mater Studiorum University of Bologna, Bologna, Italy.; [2]Division of Endocrinology and Diabetes Prevention and Care, IRCCS C.R.B.a. Azienda Ospedaliero-Universitaria di Bologna, Department of Medical and Surgical Sciences (DIMEC), Alma Mater Studiorum University of Bologna, Bologna, Italy

Context
Autonomous cortisol secretion (ACS) has been associated with a higher prevalence of osteoporosis and fragility fractures in several studies. However, the data rely on heterogeneous studies and criteria for osteoporosis screening in this population are still debated.
Objective
To assess the prevalence of fragility fractures and contributing factors in a large cohort of patients with adrenal incidentalomas.
Methods
We reviewed medical records of 1023 patients with adrenal incidentalomas from 1990 to 2019. Of these, 756 patients were selected after exclusion of confounders such as concomitant diseases or treatments, or missing data. Clinically-obtained electronic radiological images closest to the date of clinical evaluation, such as lateral views of spine X-rays or CT thoraco-abdominal scans, were reviewed by two experts blinded to clinical data to screen for asymptomatic morphometric vertebral fractures. Clinical fragility fractures were also recorded. 491 patients had non-secreting (NS) adrenal incidentalomas, 240 had ACS and 25 Cushing Syndrome (CS). Diagnosis of NS and ACS was based on cortisol after 1-mg dexamethasone suppression test (1 mgDST) (<50 and >50 nmol/l, respectively). Biochemical parameters of bone metabolism and hormonal data were recorded.
Results
ACS were older than NS patients (65.5 vs 60.5 years, $P<0.001$). Prevalence of fragility fractures was different ($P=0.021$) between groups, respectively 18.9% (NS), 27.1% (ACS) and 32% (CS), with significant difference between NS and ACS ($P=0.012$). When analyzed separately by sex and menopausal status, this difference remained significant in post-menopausal women ($P=0.003$), with a prevalence of 16.7% (NS), 28.2% (ACS) and 50% (CS). By contrast, prevalence of fractures was similar in males, even when analysis was adjusted for low testosterone levels (<3 ng/ml). Women with ACS aged ≥ 65 years reported a 40% prevalence of fragility fractures, as compared with 23.6% in NS ($P=0.016$). In younger women and in males with cut-off age set at 65 years, prevalence of fractures was similar between groups. Following logistic regression analysis including biochemistries and clinical data of the overall population, fragility fractures were predicted independently by age (OR = 1.04, $P<0.001$) and post-1 mgDST cortisol (OR = 2.07, $P=0.001$). After sex and menopausal status sub-analysis, an independent contributory effect from age (OR = 1.07, $P<0.001$) and 1 mgDST (OR = 4.49, $P=0.001$) remained significant only in post-menopausal women.
Conclusions
Post-menopausal women aged 65 or older with adrenal incidentalomas and ACS showed higher risk of fragility fractures than NS, with ACS likely playing an independent major pathogenetic role.

DOI: 10.1530/endoabs.81.OC2.4

OC2.5

Elevated serum free cortisol is a strong predictor of mortality in hospitalized patients with Covid-19 irrespective of dexamethasone treatment

Karina Rozenfeld[1], Elena Izkhakov[2,3], Miguel Moshiashvili[2], Howard Oster[1], Karen Tordjman[2,3], Gabi Shefer[2] & Yona Greenman[2,3]
[1]Tel Aviv-Sourasky Medical Center, Internal Medicine Department A, Tel Aviv, Israel; [2]Tel Aviv-Sourasky Medical Center, Institute of Endocrinology and Metabolism, Tel Aviv, Israel; [3]Tel Aviv University, Sackler Faculty of Medicine, Medicine, Tel Aviv, Israel

Serum total cortisol has been linked to increased mortality in patients with Covid-19, but its reliability in critically ill patients is limited. We examined the association between serum free cortisol (SFC) levels and clinical outcomes in patients hospitalized with Covid-19 between 5/5/2020 and 1/3/2021 in our institution.
Methods
SFC was measured in blood samples collected at patient's admission, prior to any medical treatment. Patients' files were reviewed retrospectively.
Results
There were 241 patients (78% female), mean (SD) age 67.4 (18.5), of whom 47.3% received dexamethasone treatment (DT). According to the NIH severity index, 46.9% had asymptomatic or mild disease, 17.4% moderate, and 35.7% had severe or critical disease. The in-hospital mortality, 30-day mortality and the need for assisted ventilation were 8.7%, 14.9% and 18.3% respectively. SFC levels were higher in patients who died in hospital [3.74 (2.8) vs 1.4 (0.85) µg/dl, $P<0.0001$), or within 30 days [3.01 (2.3) vs 1.32 (0.77) µg/dl, $P<0.0001$] or who required assisted ventilation [2.77 (2.4) vs 1.4 (0.8) µg/dl, $P<0.0001$]. SFC levels were significantly higher in patients with diabetes, hypertension, cardiovascular disease and chronic renal failure. There was a positive correlation between SFC and IL-6, CRP, ferritin, LDH, D-dimers, neutrophil/lymphocyte ratio (NLR) and a negative correlation with GFR and oxygen saturation at admission ($P<0.0001$ for all pair comparisons). The area under the ROC curve (AUC) to discriminate 30-day mortality was significantly higher for SFC (0.837) compared with IL-6 (0.733, $P=0.012$), CRP (0.634, $P<0.0001$), ferritin (0.618, $P<0.0001$), LDH (0.667, p-0.001) and NLR (0.759, $P=0.039$). The AUC to discriminate in-hospital mortality for SFC (0.837) was similar to IL-6 (0.811), LDH (0.790) and ferritin (0.716), but higher than CRP (0.665, $P=0.004$) and NLR (0.715, $P=0.008$). The SFC AUC for the need for assisted ventilation was 0.723, not significantly different from the other parameters. Among patients who received

DT, 71.1% had severe or critical disease, 17.5% had moderate and 11.4% had mild disease. SFC levels were higher [1.88 (1.5) μg/dl] in patients who received dexamethasone compared with those that did not [1.36 (1) μg/dl, $P<0.0001$]. Within treated patients, SFC levels were higher in those who died in hospital (3.58 (2.8) vs 1.56 (0.9) μg/dl, $P< 0.0001$] or within 30 days [3.1(2.6) vs 1.56 (0.9) μg/dl, $P<0.0001$], compared with those that survived.
Conclusions
SFC levels strongly predict in hospital and 30-day mortality as well as the need for ventilation support in hospitalized patients with Covid-19, irrespective of DT.
DOI: 10.1530/endoabs.81.OC2.5

OC2.6

Activity of abiraterone acetate in the management of cushing syndrome associated to advanced adrenocortical carcinoma: results of the ABACUS trial

Soraya Puglisi[1], Deborah Cosentini[2], Salvatore Grisanti[2], Vittoria Basile[1], Marta Laganà[2], VittorioDomenico Ferarri[2], Andrea Abate[3], Anna Calabrese[1], Elisa Rossini[3], Paola Perotti[1], Laura Saba[1], Anna Pia[1], Sandra Sigala[3], Alfredo Berruti[2] & Massimo Terzolo[1]
[1]Internal Medicine, Department of Clinical and Biological Sciences, San Luigi Hospital, University of Turin, Orbassano, Italy; [2]Medical Oncology, Department of Medical and Surgical Specialties, Radiological Sciences, and Public Health, Spedali Civili Hospital, University of Brescia, Brescia, Italy; [3]Section of Pharmacology, Department of Molecular and Translational Medicine, University of Brescia, Brescia, Italy

Background
More than 50% of adrenocortical carcinomas (ACC) in adults are associated with cortisol excess that makes tumor management challenging and has a negative impact on patient outcome. Abiraterone acetate (AA) is an irreversible inhibitor of the 17α-hydroxylase/C17, 20-lyase (CYP17 enzyme) that is used in patients with prostate cancer, in whom it leads to suppression of cortisol and androgens. The aim of this study was to assess the activity of AA to control cortisol excess in patients with advanced ACC and overt Cushing syndrome.
Methods
We designed the phase II trial ABACUS (NCT 03145285) whose primary endpoint was normalization of 24-h urinary free cortisol (UFC) excretion within 1 month from treatment start. Inclusion criteria were histologically proven ACC, locally advanced or metastatic disease, and Cushing syndrome confirmed by two 24-h UFC >1.5 times the upper normal limit with suppressed ACTH. No concomitant treatment with mitotane or chemotherapy was allowed for the first 4 weeks of the study. AA was given orally at the daily dose of 1000 mg. Data are expressed as median and interquartile range.
Results
From 2017 to 2019, we included 17 patients with ACC (2 stage III, 15 stage IV), 13 women (76%), aged 51 years (18-76), of whom 8 have been heavily pretreated and 9 were treatment naïve. In 8 patients, multiple steroid secretion was found. Patients were treated with AA for 17 days (7-163). Median 24-h UFC was 368 μg/24 h (121-7422) at baseline and 94 μg/24 h (20-1793) at end of treatment ($P=0.01$). Normalization of 24-h UFC was attained in 8 patients (53%) and a > 50% decrement in 11 patients (73%). The median time to effect was 21 days and median 24-h UFC reduction 81.8% (-97.7 - +25.9). Androgen and precursor steroids were also significantly reduced by AA treatment. Cushing Syndrome Score and blood pressure significantly decreased during treatment. In 2 patients, treatment was discontinued for toxicity. Seven patients died of ACC progression during follow-up with an overall survival of 5.4 months (0.5-39.3).
Conclusions
AA was able to control rapidly cortisol excess in most patients with a good safety profile. The results of this proof-of-concept study show that AA looks promising and may be viewed as an additional weapon to manage Cushing syndrome in patients with ACC. These findings pose the basis for power calculation and implementation of a prospective long-term study to establish AA efficacy in patients with a steroid-secreting ACC.
DOI: 10.1530/endoabs.81.OC2.6

Thyroid 1

OC3.1

Real world prospective application of ATA guidelines in over 500 aspirated thyroid nodules: Is it time for changing the size cut-offs for FNA?

Stamatina Ioakim[1], George Zavros[2], Michalis Picolos[3], Akheel Syed[4,5] & Angelos Kyriacou[2,4,6]
[1]Medical School, University of Milan, Milan, Italy; [2]CEDM, Centre of Endocrinology, Diabetes & Metabolism, Limassol, Cyprus; [3]Alithias Endocrinology Centre, Nicosia, Cyprus; [4]Department of Diabetes, Endocrinology & Obesity Medicine, Salford Royal NHS Foundation & University Teaching Trust, Salford, United Kingdom; [5]Division of Diabetes, Endocrinology & Gastroenterology, Faculty of Biology, Medicine and Health, The University of Manchester, Manchester, United Kingdom; [6]Medical School, European University of Cyprus, Nicosia, Cyprus

Introduction
The 2015 American Thyroid Association (ATA) guidelines on the management of thyroid nodules and cancer recommend specific size cut-offs for fine needle aspiration (FNA) cytology. We assessed the correlation between sonographic and cytological stratification as per the guidelines, with emphasis on the size cut-offs.
Methods
In a 'real world' prospective study, we sonographically stratified 562 thyroid nodules prior to performing ultrasound-guided FNA as cysts (1.4%), very low (3.9%), low (54.8%), intermediate (19.9%), or high (19.9%) risk. Their Bethesda cytological classification was B1, B2, B3, B4, B5 and B6 in 3.6%, 77.9%, 3.9%, 5%, 2.8% and 6.8% of nodules, respectively. Strong sonographic-cytological correlation was observed ($P<0.0001$); for example, B2 (benign) cytology was reported in 100% of very low, 91.2% of low, 81.3% of intermediate and 32% of high risk nodules. Excluding B1 (non-diagnostic) results and nodules without size data, the diagnostic performance of ATA-proposed cut-offs for FNA based on sonographic appearance was compared to higher cut-offs. Increasing the size-threshold for sonographically low and intermediate risk thyroid nodules would spare FNAs at the expense of missing a small proportion of B3–B6 cytological nodules and differentiated thyroid carcinomas (DTCs). The size cut-offs are compared against the cytological result of B2 ('negative outcome') or B3–B6 ('positive outcome'). †Relative to number of available histopathology results. PPV, positive predictive value. NPV, negative predictive value.
Discussion
By increasing the size cut-off for low-risk nodules, the NPV value retains its excellent performance, whereas PPV remains unaffected with poor performance. By using a higher cut-off in intermediate-risk nodules, NPV and PPV performance remain unchanged. In high-risk nodules, both NPV and PPV perform poorly regardless of the size cut-off. The 20 mm and 40 mm cut-offs may have greater clinical significance in case of carcinoma, as they correspond to higher tumour grades (≥T2 and ≥T3), altering the clinical management.
Conclusion
Our results suggest that increasing the ATA size cut-off from 15 mm to 20 mm in sonographically low-risk nodules is clinically safe whilst reducing FNAs.
DOI: 10.1530/endoabs.81.OC3.1

		Cut-off	Sensitivity	Specificity	PPV	NPV	Spared FNAs	Missed B3–B6 cytology	Missed DTCs†
Sonographic classification as per ATA guidelines	Low-risk ($n=301$)	15 mm	87.5%	15.9%	8.3%	93.6%			
		20 mm	58.3%	42%	8%	92.1%	80 (26.6%)	7	0/4
		40 mm	4.2%	93.9%	5.6%	91.9%	236 (78.4%)	20	1/15
	Intermediate-risk ($n=102$)	10 mm	75%	18.9%	11%	85%			
		20 mm	8.3%	88.9%	9.1%	87.9%	71 (69.6%)	8	1/7
	High-risk ($n=103$)	10 mm	58.2%	30.6%	60.9%	28.2%			
		20 mm	13.4%	88.9%	69.2%	35.6%	51 (49.5%)	30	17/29

OC3.2

Cabozantinib versus placebo in patients with radioiodine-refractory differentiated thyroid cancer (DTC) who have progressed after prior VEGFR-Targeted yherapy: updated results from the phase 3 COSMIC-311 trial and prespecified subgroup analyses based on prior therapy

Cosimo Durante[1], Marcia Brose[2,3], Bruce Robinson[4], Steven I Sherman[5], Barbara Jarzab[6], Chia-Chi Lin[7], Fernanda Vaisman[8], Ana O Hoff[9], Erika Hitre[10], Daniel W Bowles[11], Suvajit Sen[12], Purvi Patel[12], Bhumsuk Keam[13] & Jaume Capdevila[14]

[1]Sapienza University of Rome, Department of Translational and Precision Medicine, Roma, Italy; [2]University of Pennsylvania, Abramson Cancer Center, Philadelphia, United States; [3]Thomas Jefferson University Medical School, Sidney Kimmel Cancer Center, Philadelphia, Pennsylvania, United States; [4]The University of Sydney, Sydney Medical School, Sydney, New South Wales, Australia; [5]The University of Texas MD Anderson Cancer Center, Department of Endocrine Neoplasia and Hormonal Disorders, Houston, United States; [6]M. Sklodowska-Curie National Research Institute of Oncology, Gliwie Branch, Poland; [7]National Taiwan University Hospital, Department of Oncology, Taiwan; [8]The National Cancer Institute, Rio de Janeiro, Mexico; [9]University of São Paulo, Department of Endocrinology, Instituto do Câncer do Estado de São Paulo, , Brazil; [10]National Institute of Oncology, Department of Medical Oncology and Clinical Pharmacology "B," , Budapest, Hungary; [11]University of Colorado Anschutz Medical Campus, Division of Medical Oncology, Department of Medicine, Aurora, United States; [12]Exelixis Inc, Alameda, California, United States; [13]Seoul National University Hospital , Seoul, Rep. of South Korea; [14]VHIO Vall d'Hebron Institut d'Oncologia, Barcelona, Spain

Background
At a preplanned interim analysis (median follow-up 6.2 months) of the double-blind, phase 3 COSMIC-311 trial (NCT03690388), cabozantinib significantly improved progression-free survival (PFS) vs placebo (HR 0.22, 96% CI 0.13-0.36; $P<0.0001$) in 187 patients with previously treated radioiodine-refractory DTC (Brose, Lancet Oncol; 2021). Patients must have received lenvatinib or sorafenib and progressed during or after 1-2 prior VEGFR inhibitors. We present the final analysis with an extended datacut of all randomized patients (ITT population) and for prespecified subgroups who received prior lenvatinib, sorafenib, or both.
Methods
Patients were randomized 2:1 to cabozantinib (60 mg QD) or placebo. Placebo patients could cross over to open-label cabozantinib upon disease progression per blinded independent radiology committee (BIRC). PFS (ITT) and objective response rate (ORR, first 100 randomized patients) per RECIST v1.1 by BIRC were the primary endpoints.
Results
At final analysis 258 patients (170 cabozantinib, 88 placebo) were randomized at data cut (8 Feb 2021); 96 had received prior sorafenib/no lenvatinib, 102 prior lenvatinib/no sorafenib, and 60 prior sorafenib and lenvatinib. Median follow-up was 10.1 months. Forty patients crossed over to receive cabozantinib. Median PFS was 11 months for cabozantinib vs 1.9 months for placebo in the ITT population (HR = 0.22, 95% CI 0.15-0.31; $P<0.0001$). For subgroups, median PFS was 16.6 vs 3.2 months for prior sorafenib/no lenvatinib (HR = 0.13, 95% CI 0.06-0.26); 5.8 vs 1.9 months for prior lenvatinib/no sorafenib (HR = 0.28, 95% CI 0.17-0.48), and 7.6 vs 1.9 months for prior sorafenib and lenvatinib (HR = 0.27, 95% CI 0.13-0.54). In the ITT population, ORR was 11% for cabozantinib vs 0% for placebo & overall survival HR = 0.76 (95% CI 0.45-1.31). Grade 3/4 treatment emergent adverse events (TEAEs) were 62% in the cabozantinib arm vs 28% in placebo with no treatment-related grade 5 events; 67% vs 5% required dose reductions due to TEAEs; 8.8% vs 0% discontinued treatment due to TEAEs not causally related to disease.
Conclusion
In the final analysis of COSMIC-311 with longer follow-up, cabozantinib maintained its superior efficacy versus placebo. The PFS-HR was consistent with the interim analysis, in patients with previously treated radioiodine-refractory DTC irrespective of prior treatment, with no unexpected toxicities.

DOI: 10.1530/endoabs.81.OC3.2

OC3.3

Adata-driven approach reveals emerging risk factors for recurrent and persistent differentiated thyroid cancer

Michele Gentili, Giorgio Grani & Federico Siciliano
on behalf of Italian Thyroid Cancer Observatory, Italy

Background
The appropriate risk stratification of patients with differentiated thyroid cancer (DTC) is crucial because most cases have an indolent behavior and need a conservative approach. One of the most widely used tools is included in the American Thyroid Association (ATA) Guidelines, based on heterogeneous literature data derived by different populations, settings, and timeframes. Recent research focused on the inclusion of other features or questioned the clinical relevance of some of the included ones. In this prospective cohort study, we analyzed data of DTCs managed in 40 Italian clinical centers. The aims were to develop comprehensive, data-driven prediction models, able to capture all available features and to determine the weight of the potential predictors.
Methods
The Italian Thyroid Cancer Observatory (ITCO) web-based database (NCT04031339) now includes prospectively collected data of 10000 patients with histologically confirmed thyroid cancer. Each record contains information on patient demographics and biometrics, circumstances of the diagnosis, tumor pathology, treatments, and periodic follow-up examinations. We selected consecutive cases with DTC ($n=4773$) and at least early follow-up data. We built a decision tree, a relatively simple prediction model, to assign a risk index to each patient. The model allows to investigate the impact of different variables in the prediction of the risk level.Results. 2492 patients (52.2%) are classified as low, 1873 (39.2%) as intermediate, and 408 as high risk, according to the ATA risk estimation. Their response to treatment during their whole follow-up is excellent response in 2188 (45.8%), indeterminate in 1957 (41%), biochemical incomplete response in 250 (5.2%), and structural incomplete response in 378 (7.9%). The decision-tree model outperformed the ATA risk stratification system: the sensitivity of high-risk classification for structural disease increased from 37% to 49%, and the negative predictive value for low-risk patients also slightly increased by 3%), even without including information derived from radioiodine treatment (performed only in a subgroup of patients). The feature importance was estimated: several variables not included in the ATA system significantly impact the prediction of disease persistence/recurrence: age at diagnosis, gender, body-mass index, cytology, family history of thyroid cancer, surgical approach, pre-surgical cytology, and circumstances of the diagnosis.
Conclusions
The current risk stratification systems may be complemented by the inclusion of other demographic, clinical and anthropometric data, to improve the prediction of response to treatment. The use of a complete set of variables allows for a more precise clustering of patients, to predict their responses to treatment.

DOI: 10.1530/endoabs.81.OC3.3

OC3.4

Effect of age on efficacy and safety of cabozantinib vs placebo in patients with radioiodine refractory (RAI-R)-differentiated thyroid cancer (DTC) with progression after VEGFR-targeted therapy: subgroup analysis from Phase 3 COSMIC 311 study

Cosimo Durante[1], Bruce Robinson[2], Steven I Sherman[3], Jolanta Krajewska[4], Chia-Chi Lin[5], Fernanda Vaisman[6], Ana O Hoff[7], Erika Hitre[8], Daniel W Bowles[9], Jorge Hernando[10], Kamalika Banerjee[11], Roman M Levytskyy[11], Jennifer W Oliver[11], Bhumsuk Keam[12], Jaume Capdevila[10] & Marcia Brose[13,14]

[1]Sapienza University of Rome, Department of Translational and Precision Medicine, Roma, Italy; [2]University of Sydney School of Medicine, Sydney Medical School, Camperdown, Australia; [3]The University of Texas MD Anderson Cancer Center, Department of Endocrine Neoplasia and Hormonal Disorders, Houston, United States; [4]M. Sklodowska-Curie National Research Institute of Oncology , Gliwie Branch, Gliwice, Poland; [5]National Taiwan University Hospital, Department of Oncology, Taiwan; [6]National Institute of Cancer, Brazil; [7]Instituto do Câncer do Estado de São Paulo, Department of Endocrinology, Brazil; [8]National Institute of Oncology, Department of Medical Oncology and Clinical Pharmacology "B," , Budapest, Hungary; [9]University of Colorado Anschutz Medical Campus, Division of Medical Oncology, Department of Medicine, Aurora, United States; [10]VHIO Vall d'Hebron Institut d'Oncologia, Barcelona, Spain; [11]Exelixis Inc, Alameda, United States; [12]Seoul National University Hospital Medical Research and Innovation Center, Rep. of South Korea; [13]University of Pennsylvania, Abramson Cancer Center, Philadelphia, United States; [14]Thomas Jefferson University Medical School, Sidney Kimmel Cancer Center, Philadelphia, Pennsylvania, United States

Background
Increasing age is associated with poorer survival in DTC [Oyer SL, 2012]. In the phase 3 COSMIC-311 trial (NCT03690388), cabozantinib, an inhibitor of VEGFR2, MET, AXL and RET, significantly improved the progression-free survival (PFS) vs placebo in previously treated patients with RAI-R DTC (HR 0.22, 96% CI 0.13-0.36; $P<0.0001$; median follow-up 6.2 months). The impact of age on efficacy and safety was included in the prespecified subgroup analysis.

Methods
258 patients were randomized 2:1 to receive cabozantinib (60 mg QD) or placebo. Patients were stratified by prior lenvatinib treatment and age (younger subgroup: ≤65 y, older subgroup: >65 y). Patients with RAI-R DTC must have progressed on or after 1-2 prior VEGFR-targeted therapy. The primary endpoint of PFS and other outcomes in the extended follow-up data (8 Feb 2021) were analyzed by subgroups based on age.
Results
In the younger subgroup, 49% patients had papillary thyroid cancer (PTC) in the cabozantinib arm vs 66% in placebo, whereas 53% vs 36% had follicular thyroid cancer (FTC). In the older subgroup, 64% had PTC in the cabozantinib arm vs 57% in placebo, whereas 38% vs 43% had FTC. In the younger subgroup, 65% received prior sorafenib and 61% prior lenvatinib whereas in the older subgroup 55% received prior sorafenib and 65% prior lenvatinib. Median PFS for the cabozantinib arm was 11.1 months (95% CI 7.2-NE) with HR 0.19 (95% CI 0.12-0.32) for the younger subgroup and 11.1 months (95% CI 5.9-13.8) with HR 0.27 (95% CI 0.16-0.45) for the older subgroup. ORR with cabozantinib was 10% (95% CI 4.9%–18.9%) for the younger and 12% (95% CI 5.9%–20.8%) for the older subgroup vs 0% (95% CI 0.0-8.0) for both placebo subgroups. The discontinuation rate of cabozantinib due to AE related to study treatment was 6% both in the younger and the older subgroup and the percentage of patients with any dose reduction was 65% vs 69%. The safety profile in both age groups was similar and consistent with that of the overall population. No treatment-related grade 5 adverse events were observed.
Conclusion
This subgroup analysis demonstrates that clinical benefit with cabozantinib is maintained irrespective of age in previously treated RAIR DTC patients.
Keywords
Cabozantinib; COSMIC-311; DTC; VEGFR; age; differentiated thyroid
DOI: 10.1530/endoabs.81.OC3.4

OC3.5

Functional analysis of exosomal miRNAs secreted by thyroid cancer cells

Antonella Verrienti[1], Valentina Maggisano[2], Fancesca Capriglione[2], Marialuisa Sponziello[1], Valeria Pecce[1], Cosimo Durante[1], Marilena Celano[2], Stefania Bulotta[2] & Diego Russo[2]
[1]Sapienza University of Rome, Translational and Precision Medicine, Rome, Italy; [2]Università Magna Graecia di Catanzaro, Health Sciences, Italy

Background
MiRNAs transported by exosomes play a role in various processes of tumorigenesis and tumor progression. They can function as oncogenes able to structurally and biologically change the tumor microenvironment (TME) therefore playing a crucial role in cell-to-cell communication during tumor development and allowing cancer cells to become invasive and disseminate from the primary site to distant locations.We aimed to identify the exosome miRNAs that may be involved in thyroid cancer development and progression and to investigate their functional effects.
Methods
We searched for the presence of specific miRNA profiles in exosomes secreted by a non-tumorigenic thyroid cell line (Nthy-ori-3-1) and two papillary thyroid cancer cell lines (TPC1 and K1) and compared them with intracellular miRNA profile of each cell line. Exosomes isolated from the cells' conditioned medium were characterized by dynamic light scattering and the expression of exosome-specific markers. We evaluated the expression of 46 miRNAs by Real-Time PCR using custom TaqMan Array cards on RNA from exosomes of each cell line. Mienturnet web tool was used for the microRNA-target enrichment and network-based analysis.
Results
Exosomes secreted by thyroid cancer cell lines were enriched in five miRNAs (miR21-5p, miR221-3p, miR22-3p, miR31-5p, and miR-let7i-3p) compared to normal cell lines, with higher levels observed in more aggressive K1 compared to less aggressive TPC1 cell lines. The levels of exosome miRNAs reflected those of intracellular miRNAs. The microRNA-target enrichment analysis revealed that VEGFA−VEGFR2 Signaling Pathway, ATM-dependent DNA damage response, EGF/EGFR Signaling Pathway, and PI3K−AKT−mTOR signaling pathway may be the most affected cellular processes. Finally, Network-based analysis found seven genes (ICAM1, FOXO3, SELE, ETS1, RECK, PTEN and TIMP3) which are targets of at least three identified miRNAs. Notably, ICAM1, target of 4 out 5 identified exosome miRNAs, is known to be the most important adhesion molecule involved in the extravasation of leukocytes into the surrounding tissue.
Conclusion
We identified five exosomal miRNAs that may be involved in thyroid cancer development and progression by playing paracrine effects on the tumor microenvironment. The findings of "in silico" analysis suggest a potential role even in angiogenesis, promotion and immune-surveillance impairment. Further studies will be performed to define the effects of these exosomal miRNAs.
DOI: 10.1530/endoabs.81.OC3.5

OC3.6

RET Fusion Genes in Thyroid Carcinomas

Barbora Pekova[1], Vlasta Sykorova[1], Karolina Mastnikova[1], Eliska Vaclavikova[1], Jitka Moravcova[1], Petr Vlcek[2], Petr Lastuvka[2], Rami Katra[2], Petr Bavor[2], Daniela Kodetova[2], Martin Chovanec[3], Jana Drozenova[3], Jaromir Astl[4], Petr Hrabal[4], Josef Vcelak[1] & Bela Bendlova[1]
[1]Institute of Endocrinology, Department of Molecular Endocrinology, Prague 1, Czech Republic; [2]Motol University Hospital, Prague, Czech Republic; [3]University Hospital Kralovske Vinohrady, Prague, Czech Republic; [4]Military University Hospital, Prague,

Objective
RET fusion genes are known driver mutation in thyroid cancer and have been described mainly in pediatric thyroid carcinomas, in which they represent the most common genetic alteration. In large cohorts of adult patients, *RET* fusions have not yet been well characterized. The aims of this study were to identify *RET* fusion-positive thyroid tumors in a cohort of different types of thyroid carcinomas and to correlate them with clinical and histopathological features and to determine the prognostic significance of *RET* fusion genes based on long-term follow-up of patients with thyroid cancer harboring this mutation.
Methods
The cohort consisted of 1067 different thyroid cancer samples (fresh frozen tissues). Based on the detected mutation, samples were triaged. Samples positive for the *BRAF*, *HRAS*, *KRAS*, *NRAS*, *RET* or *NTRK* fusion gene mutation were excluded from the further *RET* fusion gene analyses. Samples were analyzed using Real-Time PCR (LC480, Roche) or using the FusionPlex Comprehensive Thyroid and Lung panel (ArcherDx) by next generation sequencing on MiSeq sequencer (Illumina).
Results
RET fusion genes were detected in 103/914 (11.3%) papillary thyroid carcinomas, from which 32/118 (27.1%) were from pediatric patients (7-20 years old) and 71/796 (8.9%) were from adult patients. A total of 17 types of *RET* fusions were found, including the following partner genes: *CCDC6*, *NCOA4*, *PRKAR1A*, *SQSTM1*, *IKBKG*, *RASAL2*, *TPR*, *ACBD5*, *RUFY2*, *BBIP1*, *AFAP1L2*, *AKAP13*, *TRIM27*, *SPECC1L*, *FBXO41*, *GOLGA5*, *SSBP2*. The *RET* fusion-positive carcinomas were associated with follicular growth pattern, multifocality, extrathyroidal invasion, lymph node and distant metastases. Lymph node metastases were found in almost all (93.8%) pediatric cases. On the other hand, most patients responded well to radioiodine treatment.
Conclusion
In summary, RET fusion gene were found only in papillary thyroid carcinomas. The frequency was approximately three times higher in pediatric patients than in adult patients. *RET* fusion-positive carcinomas correlated with aggressive tumor behavior. In conclusion, the genetic molecular testing of *RET* fusions is important not only for patient's diagnosis and prognosis, but also for possible targeted therapy.
Supported by the Ministry of Health of the Czech Republic DRO (Institute of Endocrinology – EU, 00023761) and AZV NU21-01-00448 grant.
DOI: 10.1530/endoabs.81.OC3.6

Pituitary and Neuroendocrinology 1

OC4.1

Significant weight loss resulted in reduced levothyroxine requirements during a tesomet trial of hypopituitary patients with acquired hypothalamic obesity

Marianne Klose[1], Kim Huynh[1], Jacob Tfelt[2], Kim Krogsgaard[3], Jørgen Drejer[3], Sarah Byberg[4], Sten Madsbad[5], Faidon Magkos[6], Abdellatif Aharaz[7], Berit Edsberg[3], Arne Astrup[8] & Ulla Feldt-Rasmussen[1]
[1]Copenhagen University Hospital, Rigshospitalet, Dept of Endocrinology and Metabolism, Copenhagen, Denmark; [2]Copenhagen University Hospital, Rigshospitalet, Dept of Cardiology, Copenhagen, Denmark; [3]Saniona A/S, Glostrup, Denmark; [4]Copenhagen University Hospital, Department of

Biomedical Sciences, Copenhagen, Denmark; [5]Copenhagen University Hospital, Hvidovre, Dept of Endocrinology and Metabolism, Copenhagen, Denmark; [6]Copenhagen University , Department of Nutrition, Exercise and Sports (NEXS), Frederiksberg, Denmark; [7]Slagelse Hospital, Dept of Endocrinology and Metabolism, Slagelse, Denmark; [8]Novo Nordisk Foundation, Hellerup, Denmark

Objective
Hypothalamic obesity results in severe weight-gain and increased risk of cardiovascular and metabolic mortality. We aimed to assess the safety and efficacy of Tesomet (tesofensine plus metoprolol), and ongoing requirements in pituitary hormone replacement adjustments in adults with acquired hypothalamic obesity, a rare disease with no approved therapy
Research design, patients and methods
Twenty-one adults with hypothalamic obesity (16 females, 5 males, mean(SD) age 46(14.6) years; 90% with a BMI "≥" 30 kg/m^2) were randomized to Tesomet (0.5 mg tesofensine/50 mg metoprolol)($n=14$) or placebo ($n=8$) during a 24-week double-blind treatment period. Seventeen subjects (11 Tesomet; 6 placebo) continued in 24-week open-label extension, all treated with Tesomet. Primary endpoint was safety; secondary endpoints included body weight and waist circumference. Almost half had a craniopharyngioma, 86% had undergone pituitary/hypothalamic surgery, 52% irradiation. All received one or more anterior pituitary hormone replacements. Trial NCT03845075.
Results
Most common adverse events were sleep disorders, dizziness, dry mouth, and headache; mostly of mild to moderate severity. No clinically meaningful changes in heart rate or blood pressure were observed. On completion of the double-blind period, mean change in body weight from baseline was -7.84 kg for the Tesomet group vs -0.34 kg for placebo ($P=0.03$), and at the end of the open-label extension period it was -6.34 kg for the Tesomet-Tesomet group and -6.03 kg for the placebo-Tesomet group. Mean change in waist circumference from baseline was -7.1 cm for the Tesomet group vs -1.2 cm for the placebo group at the end of the double-blind period, and -5.7 cm for the Tesomet-Tesomet group and -3.0 cm for the placebo-Tesomet group at the end of the open-label extension period. Most subjects (65%) had Levothyroxine reduced; adjustments in pituitary replacement and diabetic medications were otherwise few and did not differ significantly from baseline. Mean (SD) change in levothyroxine daily dose from baseline was -6.6% (6.1) and -6.4% (9.1) in Tesomet and placebo, respectively. In both groups, change in Levothyroxine correlated with weight-loss at time of adjustment (r2 = 0.37, $P=0.006$). This tendency was maintained during the extension period and implementing the reduction of levothyroxine in the management stabilised thyroid function.
Conclusion
Tesomet was generally well tolerated after 48 weeks of treatment, did not affect heart rate or blood pressure, and resulted in significant reductions in body weight in this cohort of hypopituitary patients with hypothalamic obesity. Weight-loss necessitated reductions in levothyroxine dose in most subjects to maintain stable thyroid function.

DOI: 10.1530/endoabs.81.OC4.1

OC4.2

Measurements of growth hormone in neonatal screening cards as a non-invasive and feasible tool: reference values in healthy term newborns

Federico Giacchetti[1], Matteo Vidali[2], Andrea Sangiorgio[3], Giulia Rodari[4], Chiara Vantaggiato[5], Adriana Di Modugno[5], Daniela Morniroli[4], Lorenzo Colombo[6], Eriselda Profka[1], Alberta Dall'Antonia[7], Fabio Mosca[4,6], Ferruccio Ceriotti[5], Maura Arosio[1,4], Maria Lorella Gianni'[2,4] & Claudia Giavoli[1,4]
[1]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Endocrinology Unit, Milan, Italy; [2]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy; [3]University of Milan, International Medical School, Milan, Italy; [4]University of Milan, Department of Clinical Sciences and Community Health, Milan, Italy; [5]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Clinical Laboratory, Milan, Italy; [6]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, NICU, Milan, Italy; [7]University of Milan, Milan, Italy

Background
Severe congenital growth hormone deficiency (cGHD) is a rare but potentially life-threatening condition. Even though random growth hormone (GH) can confirm cGHD during the first week of life, the diagnosis remains extremely challenging in the absence of reliable reference values in healthy neonates and thus of a best diagnostic cut-off.
Aims
First, to provide solid reference values for GH concentrations in term newborns, by means of a non-invasive procedure (GH from screening cards), using a current ultrasensitive GH assay. Secondly, to investigate eventual maternal and neonatal predictors of GH concentrations.
Methods
Using Immulite 2000 assay, GH was measured simultaneously from 200 dried blood spots (DBS) and serum samples of controls, thus validating this method for DBS. With the same assay, GH concentrations were measured in 444 filter papers of term newborns after 48 hours of life. Maternal and neonatal anamnestic data were collected from clinical records.
Results
In our cohort (444 neonates, 212 males and 232 females), the auxological parameters were spread according with the reference neonatal anthropometric charts of Italian population (median length -0.05 SDS, median head circumference -0.07 SDS, median weight -0.12 SDS). Median GH value was 16.9 μg/l (IQR 11.2 - 23.1 μg/l), with no significant gender difference. We defined a lower limit of 6.5 μg/l as 5° centile through Harrell-Davis' method with a confidence interval at 90% between 5.9 and 7 μg/l by bootstrap BCA method. Considering our lower limit of GH < 6.5 μg/l, at logistic regression analysis, jaundice presented the greater association with GH concentrations ($P<0.001$). Indeed, neonates with jaundice had 5-fold increased risk of presenting a GH < 6.5 μg/l. No other significant correlation was found between GH and maternal or neonatal characteristics. Yet, the association between neonatal hypoglycaemia and lower GH concentrations was suggestive, though not significant ($P=0.077$).
Conclusions
We defined the lower limit of reference values for GH in term healthy new-borns independently from sex, gestational age and auxological parameters using for the first time a widely available assay. The relationship found between symptoms/-signs suggestive for cGHD and lower GH concentrations, even in healthy subjects, confirmed the crucial role of clinical presentation in the diagnosis of cGHD. Providing solid reference values in term newborns, we put the basis for further studies aiming at defining a reliable diagnostic cut-off of cGHD.

DOI: 10.1530/endoabs.81.OC4.2

OC4.3

Long-term efficacy and safety data for oral octreotide capsules in acromegaly: mpowered trial open-label extension phase

Maria Fleseriu[1], Mark E Molitch[2], Alexander Dreval[3], Yulia G Pokramovich[4], Irina Bondar[5], Yury E Poteshkin[6], Djuro P Macut[7], Barbara Obermayer-Pietsch[8], Yossi Gilgun-Sherki[9], Asi Haviv[9], Nienke Biermasz[10], Shlomo Melmed[11] & Christian J Strasburger[12]
[1]Oregon Health & Science University, Pituitary Center, Portland, United States; [2]Northwestern University Feinberg School of Medicine, Endocrinology, Metabolism & Molecular Medicine, Boston, United States; [3]M.F. Vladimirsky Moscow Regional Research Clinical Institute, Department of Clinical Endocrinology of Postgraduate Education Faculty, Moscow, Russian Federation; [4]M.F. Vladimirsky Moscow Regional Research & Clinical Institute; [5]Novosibirsk State Medical University, Department of Endocrinology, Novosibirsk, Russian Federation; [6]Pirogov Russian National Research Medical University, Department of Endocrinology, Moscow, Russian Federation; [7]University of Belgrade, Department of Endocrine Tumors and Hereditary Cancer Syndromes, Belgrade, Serbia; [8]Medical University Graz, Division of Endocrinology and Diabetology, Graz, Austria; [9]Amryt Pharmaceuticals DAC, Dublin, Ireland; [10]Leiden University Medical Center (LUMC), Leiden, Netherlands; [11]Cedars-Sinai Medical Center, Los Angeles, United States; [12]Charite-Universitätsmedizin, Campus Mitte, Department of Endocrinology and Metabolism, Berlin, Germany

Background
Oral octreotide capsules (OOC) are a treatment option for patients with acromegaly in the United States. The MPOWERED trial (NCT02685709) showed that OOC were noninferior to injectable somatostatin receptor ligands (iSRLs; octreotide or lanreotide) in maintenance of biochemical control in patients previously responding to both treatments, as well as demonstrated improvements in patient-reported outcomes among patients receiving OOC.
Objective
Report long-term safety and efficacy outcomes with OOC from the open-label extension (OLE) of MPOWERED.
Methods
Patients were eligible for and could voluntarily enroll into the OLE if they had completed the 15-month core treatment phase of MPOWERED (6-month Run-in phase plus 9-month randomized controlled treatment [RCT] phase or, for OOC nonresponders during/at end of Run-in at participating sites, combination substudy evaluating OOC in combination with cabergoline) and were adequately biochemically controlled per investigator assessment. Maintenance of response

(definition: IGF-I $<1.3\times$ULN; single timepoint) was assessed in each year of the OLE in patients responding at the start of that year. Additional analyses were performed on patients switching to OOC in the OLE from iSRLs in the core study.
Results
Sixty patients elected to enroll in the OLE (35 who received OOC and 19 who received iSRLs in the RCT phase, 6 from the combination sub-study). Median and maximal OOC exposure durations in the OLE were 2.2 and 3.5 years, respectively. A total of 94%, 90%, and 93% of patients receiving OOC monotherapy maintained biochemical response at the end of years 1, 2, and 3 of the OLE, respectively (using last observation carried forward imputation). Of patients switching from iSRLs to OOC during the OLE, 79% reported very good (47%) or excellent (32%) symptom control at the end of the OLE, compared with 47% (42% very good, 5% excellent) at the end of the RCT phase while receiving iSRLs. Patients switching from iSRLs also experienced significant improvements in the treatment convenience and treatment satisfaction domains (both $P<0.05$) of the Acromegaly Treatment Satisfaction Questionnaire. Median OOC compliance rate during the OLE was 99%. OOC safety during the OLE was consistent with that observed during the core study, with no new safety signals observed with long-term exposure.
Conclusions
The OLE of MPOWERED demonstrated a high percentage ($\geq$90%) of patients maintaining biochemical response while receiving OOC monotherapy with a favorable long-term safety profile of OOC. Those who switched from iSRLs to OOC demonstrated improvements in symptom control, treatment convenience, and treatment satisfaction.

DOI: 10.1530/endoabs.81.OC4.3

OC4.4

Recurrence in acromegaly: a two tertiary centers experience

Elisa Sala[1], Arianna Cremaschi[1,2], Giulia Carosi[1,3], Nazarena Betella[4], Giulia Del Sindaco[1,2], Alessandra Mangone[1,2], Roberta Mungari[1], Angela Pagnano[1,2], Rita Indirli[1,2], Emanuele Ferrante[1], Gherardo Mazziotti[4,5], Marco Locatelli[6,7], Davide Milani[8], Andrea Gerardo Lania[4,5], Maura Arosio[1,2] & Giovanna Mantovani[1,2]
[1]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Endocrinology Unit, Milan,; [2]Department of Clinical Sciences and Community Health University of Milan, Milan,; [3]Department of Experimental Medicine, Sapienza University of Rome, Rome,; [4]Endocrinology, Diabetology and Medical Andrology Unit, Humanitas Clinical and Research Hospital, Rozzano, Italy; [5]Department of Biomedical Sciences, Humanitas University,, Rozzano, Italy; [6]Neurosurgery Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy; [7]Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy; [8]Neurosurgery Unit, Humanitas Clinical and Research Hospital, Rozzano, Italy

The aim of this study was to evaluate in a long follow-up time patients with acromegaly successfully treated by transphenoidal surgery (TNS) in order to establish the recurrence rate and the need of subsequent follow up.
Methods
We retrospectively analyzed data of 283 acromegalic patients (168 females, mean age: 44.2 $\pm$12.9 years) who underwent TNS for a GH secreting pituitary adenoma between 1980 and 2020, on regular follow-up at two Pituitary Units in the city of Milan (Fondazione IRCCS Ospedale Maggiore Policlinico and IC Humanitas). Diagnosis of acromegaly was defined by the presence of clinical signs and symptoms, an elevated serum IGF-1 level, age and sex matched, and lack of GH suppression based on appropriated criteria for the assay used at the time of diagnosis (GH <2 µg/l using a RIA, 1 µg/l with a modern IRMA or <0.4 µg/l with chemiluminescent assays, CLIA). For recurrence the same biochemical parameters were used.
Results
All patients had preoperative confirmation of acromegaly (mean IGF1: $+13.7\pm9.2$ SDS, mean GH nadir: 15.9 ± 26 µg/l). MRI confirmed the presence of a pituitary adenoma in all patients (192 macro) and all patients underwent TNS. At the first follow-up after surgery (mean distance: 3.63 ± 5 months) we defined as not cured 143 patients (50%), as cured 132 (47%) and as "partially cured", i.e. with normalization of only one parameter between GH suppression and IGF-1 levels, 8 patients (3%). Considering the group of cured patients, at the last follow-up (mean: 109 months after surgery) 5/132 (3.7%) patients needed medical therapy for recurrence. In particular, only 1 patient (0.7%) after 15 months form surgery showed a biochemical status of active acromegaly (IGF1 $+5.61$ SDS, and GH nadir 1.27 µg/l assessed with CLIA). Four additional patients (3%), after a mean follow-up of 81 months, started therapy for an isolated increase in IGF1 levels (mean IGF1SDS $+3.65$). In the "partially cured" group, 2/8 (25%) patients showed after 12 and 37 months from surgery a biochemical status of active acromegaly (IGF1 SDS $+2.75$ and $+3.62$; GH nadir 0.6 and 0.5 µg/l respectively assessed with CLIA).
Conclusions
Recurrence of acromegaly occurred in less than 1% of patients successfully treated with surgery. More frequently (25%), recurrence occurred in patients with incomplete normalization of either IGF1 or GH after surgery. Our data suggest that most acromegalic patients with complete remission after surgery may be considered as definitely cured, while those in partial remission need a strict endocrinological follow-up.

DOI: 10.1530/endoabs.81.OC4.4

OC4.5

Real-world injection experience and use of independent injection among patients using lanreotide autogel/depot (LAN) prefilled syringe or octreotide long-acting release (OCT) to treat acromegaly or neuroendocrine tumors (NETs): international PRESTO 2 survey

Susan Webb[1,2], Dermot O'Toole[3], Pamela Kunz[4], Aude Houchard[5], Sandra Boiziau[5], Antonio Ribeiro-Oliveira[6] & Ally Prebtani[7]
[1]Centro de Investigación Biomédica en Red de Enfermedades Raras (CIBERER, Unidad 747), ISCIII, Endocrinology Department, Spain; [2]Universitat Autònoma de Barcelona (UAB), Research Center for Pituitary Diseases, Hospital Sant Pau, IIB-Sant Pau, and Dept Medicine, Spain; [3]St. Vincent's University Hospital, Neuro Endocrine Tumours-ENETS Centre of Excellence, Dublin, Ireland; [4]Yale School of Medicine, Medicine (Oncology), New Haven, CT, United States; [5]Ipsen, Boulogne Billancourt, France; [6]Ipsen, Boston, MA, United States; [7]McMaster University, Faculty of Health Sciences, Ontario, Canada

Introduction
Long-acting (LA) somatostatin analog (SSA) therapy is a common first-line medical treatment for acromegaly and NETs. There are limited real-world data on patients' injection experience with the latest LA SSA devices/formulations.
Aims
To compare the injection experience of patients with acromegaly or NETs who were receiving treatment with LAN prefilled syringe vs OCT syringe.
Methods
A 2021 e-survey of adults with acromegaly or NETs from Canada, USA, UK and Ireland who had received $\geq$3 months' treatment with LAN or OCT (planned sample size, 304 [min 76/cohort]; 50:50 ratio [+/- 10%]). The primary endpoint was the proportion of patients with pain at injection site lasting >2 days after last injection. Secondary endpoints included interference with daily life due to injection-site pain and occurrence of technical injection problems. Benefits of independent injection (by self or partner) were assessed among patients receiving LAN, excluding patients in the USA, where LAN independent injection is not in the approved labelling.
Results
There were 304 respondents (acromegaly, $n=85$; NETs, $n=219$; LAN, $n=168$; OCT, $n=136$; 69.2% female; mean age 59.6 years). Fewer patients had injection-site pain lasting >2 days after last dose with LAN (6.0%) vs OCT (22.8%); the odds of pain lasting >2 days were significantly lower for LAN vs OCT, adjusted for disease group and occurrence of injection-site reaction (OR 0.13 [95% CI 0.06–0.30]; $P<0.0001$). Secondary endpoints are summarized in the table. In the LAN group (excluding USA), 40.7% ($n=11$) of patients with acromegaly and 38.7% ($n=29$) with NETs received their last treatment via independent injection and indicated they chose this for flexibility (80.0%), time saved (70.0%) and it was easy to do (60.0%).
Conclusions

Endpoint	LAN	OCT
Interference with daily life due to injection-site pain, %[a]	$n=78$	$n=80$
Not at all	59.0	40.0
A little bit	37.2	52.5
Quite a bit	3.8	7.5
Very much	0	0
Frequency of technical problems with injection, %[b]	$n=155$	$n=126$
Never	76.8	42.9
Rarely	17.4	39.7
About half the time	1.9	11.1
Most of the time	1.3	5.6
Don't know/remember	2.6	0.8

[a]Patients with pain at last injection [b]Patients with >6 months' experience with current SSA

In this e-survey, LAN was associated with advantages relative to OCT beyond improvements in the occurrence of technical problems, especially regarding duration of pain at injection site and its interference with daily life. A substantial proportion of LAN patients had received independent injection, demonstrating the value of this treatment option.

DOI: 10.1530/endoabs.81.OC4.5

OC4.6

ACROBAT advance: once daily, oral paltusotine treatment maintained long-term igf-1 at levels previously achieved with injectable long-acting somatostatin receptor ligands (LA-SRLs)

Mônica R Gadelha[1], Harpal Randeva[2], Murray B Gordon[3], Emese Mezosi[4], Mirjana Doknic[5], Miklós Tóth[6], Cesar L Boguszewski[7], Melissa Nichols[8], Theresa Jochelson[8], Scott Henley[8], Meenal Patel[8], Debbie Koh Mendez[8], Christine Ferrara-Cook[8], Alan Krasner[8], Alessandra Casagrande[8] & R Scott Struthers[8]

[1]Neuroendocrinology Research Center/Endocrinology Division–Medical School and Hospital Universitario Clementino Fraga Filho–Universidade Federal do Rio de Janeiro, Brazil; [2]University Hospitals Coventry and Warwickshire NHS Trust, United Kingdom; [3]Allegheny Neuroendocrinology Center, Allegheny General Hospital, United States; [4]University of Pécs Medical School, 1st Department of Internal Medicine, Hungary; [5]Clinical Centre Serbia, Clinic for Endocrinology, Diabetes and Metabolic Diseases, Serbia; [6]Semmelweis University, Department of Internal Medicine and Oncology, Hungary; [7]SEMPR, Endocrine Division, Department of Internal Medicine, Federal University of Parana, Brazil; [8]Crinetics Pharmaceuticals, United States

Paltusotine is a once-daily, oral, nonpeptide somatostatin receptor type 2 (SST2) specific agonist, in development for the treatment of acromegaly and neuroendocrine tumors. We report interim results from ACROBAT Advance (NCT04261712), an ongoing, multicenter, open-label, long-term extension study of paltusotine in subjects with acromegaly who previously completed either Phase 2 study ACROBAT Edge (NCT03789656) or Evolve (NCT03792555). ACROBAT Edge enrolled 47 subjects with elevated ($n=35$) or normal ($n=12$) IGF-1 taking LA-SRLs either as mono- or combination therapy at baseline. ACROBAT Evolve enrolled 13 subjects with a normal IGF-1 using octreotide LAR or lanreotide depot monotherapy. Both ACROBAT Edge and Evolve involved up to 13-weeks of paltusotine treatment followed by a 1-month drug washout period. In ACROBAT Advance, paltusotine was re-initiated at a dose of 10 mg/day with titration up to 40 mg/day based on IGF-1 and tolerability. For subjects not achieving a normal IGF-1 with 40 mg/day of paltusotine monotherapy, adjunctive treatment was allowed. Of 49 eligible subjects, 41 (84%) [median age 52 (IQR 46-62) years, 56.1% female] were enrolled at the time of the interim analysis, 23 had reached 51 weeks of treatment, and 4 had discontinued from the study. Paltusotine dose was titrated to 40 mg/day in most subjects (73%) by week 51. The frequency of adjunctive cabergoline use during the trial was the same as that prior to the trial (24%). Median IGF-1 was maintained for up to 51 weeks at levels achieved with previous parenteral LA-SRL therapy (Table 1). The most common treatment-emergent adverse events were headache [12 (29.3%)], arthralgia [9 (22%)], and fatigue [6 (14.6%)]. Most adverse events were transient and of mild-to-moderate intensity. There were 3 non-treatment-related SAEs in 2 subjects. There were 4 discontinuations (1 for headache and 3 for study drug unrelated reasons). Median HbA1c levels remained stable [baseline 6.0% (5.7-6.2), 5.9% (5.7-6.1) at week 23, and 5.8% (5.6-6.4) at week 51]. Oral once-daily paltusotine treatment was well tolerated and resulted in maintenance of IGF-1 at levels comparable to prior LA-SRL therapy for up to 51 weeks. This was seen in all subsets of acromegaly patients representing a variety of previous treatment regimens and a range of baseline disease control.

	Previous LA-SRL therapy*	ACROBAT Advance Week 31*	ACROBAT Advance Week 51*
ACROBAT Edge subjects	1.31×ULN (1.02,1.48) ($n=30$)	1.30×ULN (0.91,1.54) ($n=21$)	1.15×ULN (1.01,1.49) ($n=17$)
ACROBAT Evolve subjects	0.83×ULN (0.64,0.94) ($n=11$)	0.84 (0.75,0.96) ($n=10$)	0.89 (0.83,1.06) ($n=6$)

*Median IGF-1×Upper Limit Normal (IQR)

DOI: 10.1530/endoabs.81.OC4.6

Diabetes, Obesity, Metabolism and Nutrition 2

OC5.1

Pdgfrα-driven Alms1 deletion in mice recapitulates the obesity and insulin resistance of Alms1 global knockout

Eleanor McKay, Ineke Luijten, Dominique McCormick, Adrian Thomson, Gillian Gray & Robert Semple

University of Edinburgh, Centre for Cardiovascular Science, Edinburgh, United Kingdom

Background

Alström Syndrome (AS) is a rare autosomal recessive disease featuring highly accelerated insulin resistance, fatty liver, diabetes and heart failure among other syndromic features. Heart failure leads to significant early mortality, but is complex and likely multifactorial, with developmental defects, accelerated atherosclerosis, and fibrosis all implicated. These cardiometabolic complications occur in the face of only moderate obesity in many patients. AS is caused by biallelic loss-of-function mutations in the *ALMS1* gene, encoding a large centrosomal protein. The precise derangement of centrosomal and/or primary ciliary function caused by loss of ALMS1 is unknown. There is currently no specific treatment for AS. Further research is needed to address this unmet clinical need. Several global knockout (KO) mouse models have been described to recapitulate key metabolic components of AS, but none have characterised cardiac function in-vivo, and tissue-specific KO approaches have not yet been used to tease out contributions of different cell types to pathology.

Hypothesis

The metabolic profile of AS closely resembles that of lipodystrophy. We thus hypothesised that loss of Alms1 function in mesenchymal stem cell populations, such as adipose precursor cells, would recapitulate the metabolic derangement in AS. We secondarily hypothesised that this would mitigate some but not all cardiac complications.

Methods

A novel global KO mouse was generated by crossing the EUCOMM Tm1c Alms1 line with the global CAG-Cre driver. A Pdgfrα-Cre driver was used to abrogate Alms1 function only in mesenchymal progenitor cells and their descendants including preadipocytes and adipocytes. We undertook metabolic phenotyping and echocardiography of global and Pdgfrα+ Alms1-KO mouse models in both sexes on a 45% high-fat diet.

Results

Consistent with previous models and the human disease, global Alms1 KO mice were hyperphagic, obese, insulin resistant, and had severe hepatosteatosis. We show novel evidence of restrictive cardiomyopathy in 23-week-old female global KO mice, manifesting as increased left-atrial area and decreased intraventricular relaxation time. This was not seen in male global KO mice. Initial assessment did not reveal cardiac apical fibrosis on histological examination. KO of Alms1 only in MSCs and their descendants recapitulated key metabolic phenotypes of global KO animals including obesity and insulin resistance. Interestingly hyperphagia was also seen despite lack of neuronal Alms1 KO.

Conclusions

1. Female-specific restrictive cardiomyopathy is seen in mice deficient in Alms1.
2. MSC-derived lineages are critical in driving the severe metabolic syndrome in AS.
3. Hyperphagia in AS does not depend on neuronal Alms1 deficiency.

DOI: 10.1530/endoabs.81.OC5.1

OC5.2

Once-weekly semaglutide delays a late phase gastric emptying of solid meal measured by repeated scintigraphic imaging in obese women with PCOS

Mojca Jensterle[1], Simona Ferjan[1], Luka Lezaic[2], Aljaz Socan[2], Katja Zaletel[2] & Andrej Janez[1]

[1]University Medical Centre Ljubljana, Department of Endocrinology, Diabetes and Metabolic Diseases, Ljubljana, Slovenia; [2]University Medical Centre Ljubljana, Department of Nuclear Medicine, Ljubljana, Slovenia

Background

GLP-1 agonism have the potential to affect gastric emptying (GE), yet the reports for subcutaneous semaglutide, currently the most effective GLP-1 RA approved for weight management, remain inconclusive. It has been demonstrated that semaglutide either had no effect on GE or it delayed GE only within the first hour,

without late phase retention. Notably, those conclusions were made by an indirect method of estimation of GE through ingestion, absorption and determination of plasma level of paracetamol. Furthermore, in previous studies GE has been evaluated as a part of the composite outcome. The indirect method with paracetamol was shown to be appropriate for evaluation of kinetics of liquid meals, whereas it might lead to inaccurate estimation of late phase GE. Scintigraphic evaluation is considered as a reference method for the purpose.
Aim
This is the first study that evaluates the effect of once weekly subcutaneous semaglutide on late phase GE of a solid meal by scintigraphy as a primary outcome in obese women with PCOS without other comorbidities.
Materials and Methods
A single-blind, placebo-controlled trial was conducted in 20 women with PCOS and obesity, without diabetes and other comorbidities, randomized to once weekly subcutaneous semaglutide 1 .0 mg (S) or placebo (P) for 8 weeks. Gastric emptying was assessed by scintigraphy after ingestion of 99mTC colloid in pancake labelled with radiopharmaceutical that maintained a stable binding within gastric environment by scintigraphy using sequential static imaging and dynamic acquisition. Estimation of GE was obtained by repeated imaging of remaining 99mTC activity (RA) at fixed time intervals over 4 hours and the half time (T1/2) of gastric emptying had been calculated. Additionally, we evaluated anthropometric, metabolic, hormonal and appetite parameters.
Results
At 30 min after ingestion significant difference in RA was observed between semaglutide group and placebo (92.5% in S vs 89% in P ($P=0,05$)) and persisted throughout the observation period up to 4 hour (37% in S vs 0% in P ($P=0,002$)). T1/2 was significantly longer in S as compared to P (171 min vs 118 min, respectively ($P<0.001$)). In addition, semaglutide led to significant decrease in weight, waist and neck circumference, HbA1c and androgen levels. Subjective ratings of appetite suppression correlated with T1/2.
Conclusion
Semaglutide 1.0 mg resulted in a significant late-phase retention of solid meal measured by repeated scintigraphic imaging. This effect correlated with appetite suppression and likely contributed to weight loss.

DOI: 10.1530/endoabs.81.OC5.2

OC5.3

Weight loss attempts and weight perception in women with polycystic ovary syndrome (PCOS) - a 15-year follow-up in a population-based cohort study

Emilia Pesonen[1,2], Meri-Maija Ollila[1], Laure Morin-Papunen[1], Juha S Tapanainen[1,3], Timo Jämsä[4], Raija Korpelainen[2,5,6], Maisa Niemelä[4], Marjukka Nurkkala[2,5,6] & Terhi T Piltonen[1]
[1]University of Oulu and Oulu University Hospital, Department of Obstetrics and Gynaecology, PEDEGO Research Unit, Medical Research Center, Oulu, Finland; [2]Oulu Deaconess Institute Foundation sr., Department of Sports and Exercise Medicine, Oulu, Finland; [3]University of Helsinki, Department of Obstetrics and Gynaecology, Helsinki, Finland; [4]University of Oulu and Oulu University Hospital, Research Unit of Medical Imaging, Physics and Technology, Medical Research Center , Oulu, Finland; [5]University of Oulu and Oulu University Hospital, The Center for Life Course Health Research (CLCHR), Faculty of Medicine; [6]University of Oulu and Oulu University Hospital, Medical Research Center

Background
Women with polycystic ovary syndrome (PCOS) experience increased weight gain during life, thus weight management and preventing weight gain should be the first line treatment. Weight loss is usually self-initiated because practical support for weight management is often limited or even lacking. Perception of overweight is considered an important prerequisite for weight loss attempts, although there is no prior research regarding women with PCOS. The main aim of the study was to investigate whether women with PCOS are more likely to have multiple weight loss attempts compared to non-PCOS controls regardless of weight. In addition, we evaluated women's weight perception in relation to weight loss attempts.
Methods
The study is part of Northern Finland Birth Cohort 1966 including women with PCOS ($n=280$) and non-PCOS controls ($n=1573$) examined at ages 31 and 46 years. Multiple weight loss attempts, weight perception, body mass index (BMI), and psychological distress were analyzed along with sociodemographic factors at both time points. Binary logistic regression analysis was performed, and the results were reported as odds ratios (ORs) with 95% confidence intervals. A *P*-value <0.05 was considered statistically significant.
Results
Women with PCOS had higher prevalence of multiple weight loss attempts by age 31 and 46 years compared to controls ($P<0.001$). Despite this, women with PCOS had significantly higher BMI at both time points ($P<0.001$). PCOS was independently associated with multiple weight loss attempts at age 46 when adjusted for psychological distress and BMI (OR 1.44 [95% CI, 1.01–2.05]) or perception of overweight (OR 1.45 [95% CI, 1.03–2.03]). Perception of overweight was the most significant factor contributing to multiple weight loss attempts at both time points. Perception of overweight was more prevalent in PCOS compared to controls, and interestingly, perception of overweight was more common even among normal weight women with PCOS at age 31 ($P=0.004$) and age 46 ($P<0.001$) years. Indeed, PCOS was independently associated with perception of overweight at age 31 when adjusted for BMI and leisure-time physical activity (OR 1.69 [95% CI, 1.01–2.85]), and at age 46 when adjusted for BMI and psychological distress (OR 2.65 [95% CI, 1.37–5.13]).
Conclusions
Women with PCOS are more likely to experience multiple weight loss attempts as well as perception of overweight independent of BMI until late fertile age compared to non-PCOS controls. In clinical practice, adequate support and resources should be offered to reduce inefficient weight loss attempts and stress.

DOI: 10.1530/endoabs.81.OC5.3

OC5.4

Body composition during childhood, adolescence and adulthood influences the odds of developing polycystic ovary syndrome: a mendelian randomisation study with a systematic review and meta-analysis

Laurence J Dobbie[1,2], Sizheng Steven Zhao[3], Bradley Pittam[4], Uazman Alam[1,2], Thomas M Barber[5] & Daniel J Cuthbertson[1,2]
[1]University Hospital Aintree, Liverpool University Hospitals NHS Foundation Trust, Liverpool, United Kingdom; [2]Department of Cardiovascular and Metabolic Medicine, Institute of Life Course and Medical Sciences, University of Liverpool, Liverpool, United Kingdom; [3]Centre for Epidemiology Versus Arthritis, Division of Musculoskeletal and Dermatological Sciences, School of Biological Sciences, Faculty of Biology Medicine and Health, University of Manchester, Manchester, United Kingdom; [4]Manchester University Hospital NHS Foundation Trust, Manchester, United Kingdom; [5]Warwick Medical School, University of Warwick, Coventry, United Kingdom

Background
Observational and genetic Mendelian randomisation (MR) data has demonstrated the association of adulthood overweight/obesity with development of polycystic ovary syndrome (PCOS). However, the contribution of early life (i.e. childhood/adolescence) body composition on incident PCOS is unclear. This study determines the influence of body composition on the likelihood of developing PCOS.
Methods
We conducted a 2-sample Mendelian randomisation study to determine the impact of body composition and metabolic parameters (fasting serum insulin or sex-hormone binding globulin) on the odds of PCOS. PCOS genome-wide association study meta-analysis data (from 10,074 people with PCOS, 103,164 controls) was interrogated using the inverse-variance weighted method. Furthermore, we conducted a systematic review (71 studies) and meta-analysis (63 studies) of the role of overweight, obesity and central obesity (defined via waist circumference / waist-hip ratio) on odds of PCOS in adults and adolescents.
Results
From Mendelian randomisation, significant associations were shown between body composition and odds of PCOS. For every standard deviation increase in BMI (a BMI increase of 4.8 kg/m^2), odds of PCOS increased significantly (OR: 2.76, 2.27 - 3.35). Similar associations were demonstrated between body fat percentage (OR: 3.05 per 8.5%, 2.24 - 4.15), whole-body fat mass (OR: 2.53 per 9.6 kg, 2.04 - 3.14), fasting insulin (OR: 6.98 per 0.79 pmol/l, 2.02 - 24.13) and sex-hormone binding globulin (OR: 0.74 per 28 nmol/l, 0.64 - 0.87). Genetically determined childhood body size increased odds of PCOS after adjusting for adult body size (OR: 2.56, 1.57 - 4.20). *From meta-analysis*, women with overweight (OR 3.80, 2.87- 5.03)), obesity (OR 4.99, 3.74 – 6.67) and central obesity (OR 2.93, 2.08 – 4.12) had increased odds of PCOS. For adolescents with overweight and/or obesity the PCOS odds were greater than for adults (adult vs adolescent: overweight: OR 3.57 and 5.32; Obese: OR 4.66 and 7.86).
Conclusions
Using two complementary epidemiological techniques we demonstrate a clear relationship between markers of body composition, indicative of excess body fat accumulation, and odds of developing PCOS, especially in childhood and adolescence. MR reports that genetically determined childhood body composition increases PCOS likelihood independent of adult body composition. From meta-analysis, women with overweight, obesity and central obesity had increased odds of PCOS, with odds even higher in adolescents with overweight and obesity.

Overall, this study has implications for the prevention and treatment of obesity and the importance of effective weight maintenance from early years and beyond.

DOI: 10.1530/endoabs.81.OC5.4

OC5.5

The glucocorticoid transporter ATP-binding cassette subfamily C member 1 (ABCC1) influences adiposity, glucose homeostasis and insulin sensitivity in male mice

Elisa Villalobos[1], Allende Miguelez-Crespo[1], Ruth A Morgan[1], Ruth Andrew[1], Mark Nixon[1] & Brian R Walker[1,2]
[1]The Queen's Medical Research Institute - University of Edinburgh, British Heart Foundation Centre for Cardiovascular Science, Edinburgh, United Kingdom; [2]Translational and Clinical Research Institute - Newcastle University , Newcastle upon Tyne, United Kingdom

Background
Glucocorticoids (GCs) modulate glucose homeostasis by acting on metabolic tissues including liver, adipose and skeletal muscle. GC access to corticosteroid receptors in these tissues is regulated e.g. by pre-receptor metabolism. We recently identified a role for ABCC1, a transmembrane 'drug-resistance' transporter, as a GC exporter which limits intracellular GC concentrations and action in adipose tissue. Here, we tested the hypothesis that ABCC1, which is also highly expressed in skeletal muscle, influences glucose metabolism and insulin sensitivity, through regulation of tissue GC action.
Methods
Male global *Abcc1* knockout (*Abcc1*$^{-/-}$) and wild-type (WT) littermate mice were fed chow diet or high-fat diet (HFD - 58% fat and sucrose) for 9 weeks, starting at 8-12 weeks of age ($n=10$-13 each group). Glucose and insulin tolerance tests were performed (week 7-8), all procedures were done with ethical approval. Plasma and tissue GC concentrations were measured by Liquid Chromatography Tandem Mass Spectrometry, and tissue GC-responsive genes and metabolic markers (mRNA and protein) by RT-qPCR and Western blot.
Results
Our findings show that on chow diet, *Abcc1*$^{-/-}$ mice have similar body weight, despite reduced fat mass (subcutaneous, gonadal and brown adipose tissue), normal glucose tolerance in the presence of reduced fasting insulin levels, and increased levels of corticosterone in plasma, subcutaneous adipose tissue (sWAT) and gastrocnemius muscle compared to WT mice, By contrast, on HFD, *Abcc1*$^{-/-}$ mice had similar body weight gain and fat mass to WT mice, but impaired glucose and insulin tolerance and fasting hyperinsulinemia, without measurable alterations in plasma or tissue GC levels. Interestingly, on HFD, WT mice protein levels of ABCC1 were upregulated in sWAT but not in skeletal muscle. Further, we investigated a number of genes and pathways that might be affected by the changes in insulin e.g GSK-3β We identified upregulation on the levels of pGSK-3β in skeletal muscle, but not in adipose tissue from *Abcc1*$^{-/-}$ mice on chow diet. By contrast, on HFD, the levels of pGSK-3β were upregulated in skeletal muscle from WT mice but not in *Abcc1*$^{-/-}$. These changes were absent in adipose tissue.
Conclusions
Abcc1 influences adiposity, insulin sensitivity and glucose homeostasis differently according to diet and obesity, and by mechanisms which are likely to be only in part GC-dependent. Further dissection of the substrates for ABCC1 which mediate these effects may reveal new avenues for therapy in metabolic disease.

DOI: 10.1530/endoabs.81.OC5.5

OC5.6

Fetal sex predicts perinatal outcomes in women with gestational diabetes

Catarina Cidade-Rodrigues[1], Catarina Chaves[1], Anabela Melo[2], Odete Figueiredo[2], Ana Morgado[2], M Céu Almeida[3], Mariana Martinho[1], Margarida Almeida[1] & Filipe M Cunha[1]
[1]Centro Hospitalar do Tamega e Sousa, Endocrinology, Portugal; [2]Centro Hospitalar do Tamega e Sousa, Gynaecology and Obstetrics, Portugal; [3]Maternidade Bissaya Barreto, Centro Hospitalar e Universitário de Coimbra, Obstetrics, Portugal

Introduction
Gestational diabetes (GD) is a known risk factor for delivery, fetal and perinatal complications. Fetal male sex is known to be associated with worse perinatal outcomes, such as macrosomia, neonatal hypoglycemia, low Apgar scores, birth defects and mortality. However, studies evaluating the impact of fetal sex on perinatal outcomes in women with GD are scarce.
Objectives
We aimed to study whether male newborn sex is associated with neonatal outcomes, in women with GD.
Methods and Methods
Retrospective study based on the national register of GD. Included women with live-born singleton pregnancies followed between 2012 and 2017. Excluded women without data on variables of interest. Primary endpoint: Neonatal hypoglycaemia, neonatal macrosomia, respiratory distress syndrome (RDS) and neonatal intensive care unit admission (NICUA). BMI as pregestational weight divided by squared height. Female and male newborns were compared. Multivariate logistic regression models were built and included variables with different distribution between groups and with known association with the endpoint under analysis.
Results and Conclusions
We studied a total of 10768 newborns in mothers with GD, 5635 (52.3%) male, 438 (4.1%) had neonatal hypoglycaemia, 406 (3.8%) were macrosomic, 671 (6.2%) had RDS, and 671 (6.2%) had a NICUA. Male sex newborns were heavier, more frequently small and large for gestational age. No differences were observed on maternal age, BMI, HbA1c, anti-hyperglycaemic treatment, pregnancy complications or gestational age at delivery. In the multivariate regression analysis, male sex was independently associated with neonatal hypoglycaemia [OR 1.27 (IC 95%:1.04-1.55), $P=0.02$], neonatal macrosomia [1.98 (1.58-2.48), $P<0.001$], NICUA [1.27 (1.06-1.55), $P=0.01$] and RDS [1.33 (1.03-1.71), $P=0.03$]. Male newborns from mothers with GD have a 27% higher risk of neonatal hypoglycaemia, almost 2-fold higher risk of macrosomia, 33% higher risk of RDS and 27% higher risk of NICUA.

DOI: 10.1530/endoabs.81.OC5.6

Endocrine-Related Cancer

OC6.1

Recurrent disease in patients with sporadic pheochromocytoma and paraganglioma

Minghao Li[1], Tamara Prodanov[2], Leah Meuter[2], Michiel Kerstens[3], Nicole Bechmann[1,4], Aleksander Prejbisz[5], Martin Fassnacht[6], Henri Timmers[7], Felix Beuschlein[8,9], Stephanie Fliedner[10], Mercedes Robledo[11], Jacques Lenders[1,7], Karel Pacak[2], Graeme Eisenhofer[1,4] & Christina Pamporaki[1]
[1]University Hospital Carl Gustav Carus at the TU Dresden, Department of Medicine III, Dresden, Germany; [2]National Institutes of Health, Section on Medical Neuroendocrinology, Eunice Kennedy Shriver National Institute of Child Health and Human Development, Bethesda, United States; [3]University of Groningen, University Medical Center Groningen, Department of Endocrinology, Groningen, Netherlands; [4]University Hospital Carl Gustav Carus at the TU Dresden, Institute of Clinical Chemistry and Laboratory Medicine, Dresden, Germany; [5]Institute of Cardiology, Warsaw, Department of Hypertension, Warsaw, Poland; [6]University Hospital of Würzburg, 6Department of Internal Medicine, Würzburg, Germany; [7]Radboud University Hospital, Nijmegen, Department of Internal Medicine, Nijmegen, Netherlands; [8]University Hospital of Munich, Department of Internal Medicine, Munich, Germany; [9]University Hospital, Zurich, Department of Endocrinology, Diabetology, and Clinical Nutrition, Switzerland; [10]University Medical Center Schleswig-Holstein, Luebeck, Department of Medicine, Luebeck, Germany; [11]Human Cancer Genetics Programme, Spanish National Cancer Research Centre, Hereditary Endocrine Cancer Group, Spain

Background
It is well established that life-long follow-up is required for patients with hereditary pheochromocytomas and paragangliomas (PPGLs), due to the potential of developing recurrent disease. However, whether follow-up of patients with sporadic PPGLs is necessary, remains unclear.
Aims
To examine the prevalence and predictors of recurrent disease in patients with sporadic PPGLs.Materials and method: This multicenter study included retrospective clinical data of 528 patients with PPGLs. Recurrent disease was defined as presence of new tumor and/or locoregional recurrence and/or metastases one year after initial tumor diagnosis. Patients with sporadic PPGLs were defined as

those without germline mutations in known genes associated with hypoxia (cluster 1) or kinase (cluster 2) signaling pathways.
Results
Fifty-three percent of the patients had sporadic PPGLs and presented with a recurrence rate of 17.3%, which mainly reflected metastatic disease (10%). This was significantly lower than those with cluster 1 (54.3%), but similar to those with cluster 2 mutations (14.1%). Among patients with sporadic PPGLs and recurrent disease, 70.7% developed recurrence within 10 years from initial tumor diagnosis. Multivariable Cox regression analysis showed that larger (>4.5 cm) size (HR 1.8, 95% CI 1.13-3.0, $P=0.015$) and extra-adrenal location (HR 2.4, 95% CI 1.4-4.11, $P=0.001$) of the primary tumor, were independent predictors of recurrence in patients with sporadic PPGLs. Indeed, patients with small (≤4.5 cm) sporadic pheochromocytomas presented with the lowest (7.8%) rate of recurrent disease ($P<0.001$).
Conclusion
Among patients with sporadic PPGLs, prevalence of recurrence was mainly due to metastases and high enough to mandate long-term follow-up. Importantly, our findings indicate that size and tumor location are important to consider for further stratification and management of patients with sporadic PPGLs.

DOI: 10.1530/endoabs.81.OC6.1

OC6.2

Translational evidence for splicing factor RBM22 as a novel prognostic biomarker and therapeutic target in prostate cancer

Prudencio Sáez-Martínez[1,2,3,4], Juan M Jiménez-Vacas[1,2,3,4], Antonio J Montero-Hidalgo[1,2,3,4], Ana D Rosa-Herencia[1,2,3,4], Vicente Herrero-Aguayo[1,2,3,4], Antonio J León-González[1,2,3,4], Rafael Sánchez-Sánchez[1,3,5], Teresa González-Serrano[1,3,5], Enrique Gómez-Gómez[1,3,6], Manuel D Gahete[1,2,3,4] & Raúl M Luque[1,2,3,4]
[1]Maimonides Institute of Biomedical Research of Cordoba (IMIBIC); [2]Department of Cell Biology, Physiology and Immunology, University of Cordoba, 14004 Cordoba, Spain; [3]Reina Sofia University Hospital (HURS), 14004 Cordoba, Spain; [4]CIBER Physiopathology of Obesity and Nutrition (CIBERobn), 14004 Cordoba, Spain; [5]Anatomical Pathology Service, HURS/IMIBIC, 14004 Cordoba, Spain.; [6]Urology Service, HURS/IMIBIC, 14004 Cordoba, Spain

Prostate cancer (PCa) is one the leading causes of cancer-related deaths among men in developed countries. Therefore, identification of novel molecular and therapeutic approaches to tackle this pathology are urgently needed. In this scenario, our group has recently reported that elements of the cellular machinery controlling alternative splicing processes might be used as potential novel therapeutic tools against PCa and castration-resistant PCa (CRPC). In this context, RBM22 has been identified as a key spliceosome component, playing a crucial role for normal development; however, the potential dysregulation and functional role of RBM22 in cancer still remain unknown. Here, we identify for the first time a profound downregulation of RBM22 (at mRNA/protein-levels) in two well-characterized cohorts of PCa patients, compared to non-tumor control samples. Notably, RBM22 levels were inversely associated to key clinical aggressiveness features in PCa (i.e. extraprostatic extension and perineural invasion). These results were confirmed in two additional, independent *in silico* human cohorts. Overexpression of RBM22 in PCa cells decreased aggressiveness parameters *in vitro* (e.g. proliferation, migration, tumorsphere- and colony-formation, etc.), and drastically decreased tumor development and progression *in vivo* (using a preclinical mouse model), which would underlie a relevant direct association of lower RBM22 levels with enhanced tumor progression. These results were corroborated using the TRAMP mouse model, wherein gradual reduction of RBM22 from prostatic intraepithelial neoplasia to moderately differentiated PCa and to poorly differentiated PCa was observed. These actions are likely mediated through the modulation of key signaling pathways (i.e. cycle-apoptosis, PI3K pathways, etc.) and critical molecular regulators (i.e. MYC, MCYN and E2F), and may also involve the alteration of alternative splicing events of key genes involved in these pathways. Therefore, our study demonstrates for the first time that RBM22 plays a critical functional role in the pathophysiology of PCa and suggests that targeting negative regulators of RBM22 could represent a novel therapeutic strategy to tackle this devastating pathology.
Fundings
MINECO (PID2019-105564RB-I00/FPU16-06190/FPU17-00263/FPU18-02485), Junta de Andalucía (BIO-0139/PI-0152-2019) and CIBERobn.

DOI: 10.1530/endoabs.81.OC6.2

OC6.3

Systematic detection of mosaicism by using digital NGS in a cohort of 119 unresolved MEN1 cases reveals 3 new MEN1 mosaicisms

Arnaud Lagarde[1], Grégory Mougel[1], Lucie Coppin[2], Magalie Haissaguerre[3], Lauriane Le Collen[4], Marc Klein[5], Marie-Françoise Odou[6], Antoine Tabarin[3], Hedia Brixi[7], Brigitte Delemer[4], Anne Barlier[1] & Pauline Romanet[1]
[1]Aix Marseille Univ, APHM, INSERM, MMG, Laboratory of Molecular Biology Hospital La Conception, Marseille, France; [2]Univ. Lille, CNRS, Inserm, CHU Lille, UMR9020-U1277 - CANTHER - Cancer - Heterogeneity Plasticity and Resistance to Therapies, F-59000, Lille, France; [3]Service d'Endocrinologie, Centre Hospitalier Universitaire, Hôpital du Haut Levêque, Pessac, France; [4]Endocrinology, Diabetology and Nutrition Unit, University Hospital of Reims, Reims, France; [5]Service endocrinologie, CHU de Nancy, hôpital de Brabois, Vandoeuvre-lès-Nancy, France; [6]CHU Lille, Service de Biochimie et Biologie moléculaire « Hormonologie, Métabolisme-Nutrition, Oncologie », Lille, France; [7]Department of Gastroenterology and Digestive Oncology, Reims University Hospital, Reims, France

Context
Mosaicism is a feature of several inherited tumor syndromes but is rarely systematically looked for in routine. MEN1 is an autosomal dominant hereditary syndrome characterized by several endocrine tumors affecting parathyroids, pancreas, and anterior pituitary most of the time, due to inactivating mutations in the *MEN1* gene. Few cases of mosaicism in Multiple Endocrine Neoplasia type 1 (MEN1) have been described. *MEN1* mosaicism is probably under-diagnosed because it is not routinely investigated. At present, Next generation sequencing (NGS) offers new possibilities to detect mosaicism. The challenge is to distinguish true mosaicism from sequencing artifacts. We reported the first study systematically looking for *MEN1* mosaicism in MEN1 suspected patient but without MENI pathogenic variants (PV) at heterozygote state.
Methods
For that, we set up in routine a digital targeted NGS including unique molecular identifiers (UMIs). UMIs are tools for improving molecular detection of rare events in somatic DNA. We established the analytic performance of such method. Next *MEN1* mosaicism was then looked for in a cohort of unresolved MEN1 cases addressed in the molecular biology laboratory between 2017 and 2019.
Results
For *MEN1*, sensitivity was 100% for detecting the variants up to an allelic frequency (AF) of 1%. By using UMIs, false positives were reduced by 98.4% for *MEN1*. Among a cohort of 119 patients harboring from 2 to 5 MEN1 lesions, we identified 3 patients with *MEN1* mosaic PVs. The allelic frequencies ranged from 2.3 to 9.5%. The detection rate of MEN1 mosaicism in patients bearing at least 3 MEN1 lesions was 17% (3/18). No cases are detected in patients with 2 lesions.
Conclusion
we reported here 3 new cases with *MEN1* mosaicism. This study deciphered the performances of UMI in *MEN1* mosaic diagnosis in routine and underlined that the frequency of mosaicism is probably underestimated in MEN1 suspected patients.

DOI: 10.1530/endoabs.81.OC6.3

OC6.4

Clinical correlates of a large Israeli cohort of Cys 618 Arg RET mutation

Rachel Chava Rosenblum[1], Dania Hirsch[2], Simona Glasberg[3], Carlos Benbassat[4], Uri Yoel[5], Avraham Ishay[6], Sagit Zolotov Lamprecht[7], Gideon Bachar[8], Ehud Banne[9] & Orit Twito[9]
[1]Wolfson Medical Center, Endocrinology Unit, Holon, Israel; [2]Beilinson Hospital Rabin Medical Center, Petah Tikva, Israel; [3]Hadassah Ein Kerem, Jerusalem, Israel; [4]Shamir Medical Center (Assaf Harofeh), Be'er Ya'akov, Israel; [5]Soroka Medical Center, Be'er Sheva, Israel; [6]HaEmek Hospital, Afula, Israel; [7]Rambam Health Care Campus, Haifa, Israel; [8]Beilinson Medical Center, Petah Tikva, Israel; [9]Wolfson Medical Center, Holon, Israel

Introduction
A syndrome of MEN2A and Hirschsprung's disease described in Israeli Jews of Moroccan descent is caused by Cys 618 Arg mutation, one of the less common causes of MEN2A. We aimed to define the clinical characteristics of a large cohort with this mutation from a multi-center Israeli registry.

Methods
The Israeli MTC registry including 8 centers was searched retrospectively for results of RET mutational analysis. Patients with a Cys 618 Arg mutation belonging to a single large extended family were included in the study, as were their first-degree family members with MTC without available genetic test results. Clinical, laboratory and pathological data, as well as long-term surveillance data were retrieved.
Results
Of the 274 patients in the Israeli registry, 53 (19.3%) had documented RET mutations, and 29/53 (54.7%) had the Cys 618 Arg mutation. Through development of a family tree spanning five generations, a familial connection was determined for 28/29 patients, descendants of one large family of Moroccan Jewish descent. Another 4 patients from the MTC registry without available genetic test results belonged to this extended family. Clinical and pathological data pertaining to these 32 patients was analyzed. Nineteen patients (59%) were female; mean age at surgery was 26.6 $\pm$12.8 years. Tumor size was 10.8 $\pm$9.3 mm. Extrathyroidal extension was described in 4/19 (21.0%); vascular invasion in 5/18 (27.8%); multifocality in 17/21 (81.0%) and bilateral lesions in 17/22 (77.3%). Ki67 was mentioned for only one patient and was 3%. Lymph nodes were removed in 8 patients, and metastases found in 3. Extranodal extension was found in 1 case. Three patients had distant metastases at diagnosis. Of 22 patients with one-year follow-up, 11 were cured, 10 had persistent disease and 1 suffered disease-related mortality. Of those with persistent disease, 6 were biochemical, 2 structural and 2 unknown. Surveillance duration was 9.3 $\pm$12.9 years. Recurrence occurred in 4/19 patients (21.2%), 3 with distant metastases. Seven patients had additional therapy: 4 surgery, 2 radiotherapy and 1 tyrosine kinase inhibitors. One more patient died during follow-up; whether his death was disease-related is unclear. Comorbidities included pheochromocytoma in 2 patients, Hirschsprung disease in 2 and primary hyperparathyroidism in 1 patient.
Conclusion
The prevalent RET mutation in Israel is Cys 618 Arg, and almost all cases are linked to one large family of Moroccan Jewish descent. Genotype-phenotype correlation are similar to that described previously with cases of pheochomocytoma and hyperparathyroidism, rendering screening for these conditions essential.

DOI: 10.1530/endoabs.81.OC6.4

OC6.5

Antagonist of growth hormone-releasing hormone (GHRH) potentiates the antitumor effect of chemotherapy in human malignant pleural mesothelioma

Iacopo Gesmundo[1], Nicoletta Vitale[2], Giulia Orlando[3], Alessia Bertoldo[1], Mauro Papotti[3], Silvia Deaglio[2,4], Ezio Ghigo[1], Andrew V Schally[5,6] & Riccarda Granata[1]
[1], Division of Endocrinology, Diabetology and Metabolism, Department of Medical Sciences, University of Turin, Italy, Turin, Italy; [2], Laboratory of Cancer Immunogenetics, Department of Medical Sciences, University of Turin, Italy, Turin, Italy; [3], Pathology Unit, Department of Oncology, "Città della Salute e della Scienza di Torino" University Hospital, University of Turin, 10126 Turin, Italy, Turin, Italy; [4], Immunogenetics and Transplant Biology Service, Città della Salute e della Scienza University Hospital, Turin, Italy, Turin, Italy; [5]Endocrine, Polypeptide, and Cancer Institute, Veterans Affairs Medical Center, Miami, FL, USA, Florida, Miami, United States; [6], Department of Pathology and Department of Medicine, Divisions of Hematology, Oncology and Endocrinology, University of Miami Miller School of Medicine, Miami, FL, USA , Florida, Miami, United States

Human malignant pleural mesothelioma (MPM) is a rare but aggressive neoplasm, arising from pleural mesothelial cells, generally due exposure to asbestos. Of note, different growth factors and their receptors are involved in the pathogenesis of MPM and resistance to therapy. Chemotherapy with cisplatin (cis) and antifolates, like pemetrexed (PEM), is the first-line treatment for inoperable MPM. Growth hormone-releasing hormone (GHRH), besides stimulating GH secretion in the anterior pituitary, exerts many peripheral functions, such as stimulation of cell proliferation and survival. GHRH and GHRH receptors (GHRH-Rs) are expressed in different cancer cell types, where they modulate their proliferative effects. Conversely, GHRH-R antagonists were found to inhibit the proliferation of different cancer cells *in vitro* and *in vivo*. Moreover, we recently demonstrated the antitumor activity of GHRH antagonists MIA-602 and MIA-690, in both *in vitro* and *in in vivo* models of MPM. However, the antitumor functions of GHRH-antagonists in combination with cis and PEM (cis/PEM) remain to be elucidated. Thus, in the present study, we assessed the antitumor effects of MIA-690 in combination with cis/PEM *in vitro*, in human biphasic MPM cell line MSTO-211H, and *in vivo*, in mice bearing MPM xenografts. *In vitro*, MIA-690 showed synergistic inhibitory activity with cis/PEM, by reducing cell survival and proliferation at 48 h in MSTO-211H and increasing the chemotherapy-induced apoptosis. *In vivo*, subcutaneous administration of MIA-690, at the dose of 5 µg/d for 4 weeks, potentiated the antitumor activity of cis/PEM by strongly inhibiting the growth of MPM xenografts, as demonstrated by the reduction of tumor volume and weight and inhibition of survival/proliferative markers, as revealed by immunohistochemistry analysis. MIA-690 also influenced the expression levels of cell cycle regulators (cyclinB1, D1 and D2), cell migration effectors (MMP-2 and MMP-9) and epithelial-mesenchymal transition markers (E-cadherin, N-cadherin, and vimentin), compared with cis/PEM treatment alone. Moreover, mice treated with both MIA-690 and cis/PEM showed increased expression of apoptotic molecules, along with a reduction of tumor insulin-like growth factor-I (IGF-I) and vascular endothelial growth factor (VEGF) in tumor xenografts. Collectively, these results further confirm the antitumor role of GHRH antagonists in MPM and suggest the potential therapeutic efficacy of these molecules in combination with chemotherapy, by potentially reducing anticancer drug doses and associated side effects.

DOI: 10.1530/endoabs.81.OC6.5

OC6.6

SF3B1 inhibition disrupts malignancy and prolongs survival in glioblastoma patients through BCL2L1-splicing and mTOR/ß-catenin pathways imbalances

Miguel E G-Garcia[1,2,3], Antonio C Fuentes-Fayos[1,2,3], Jesus Perez Gomez[1,2,3], Juan M Jiménez-Vacas[1,2,3], Cristobal Blanco-Acevedo[1,4], Rafael Sánchez-Sánchez[1,2,5], Juan Solivera[1,4], Joshua Breunig[6], Manuel D Gahete[1,2,3], Justo P Castaño[1,2,3] & Raul M Luque[1,2,3]
[1]Maimonides Biomedical Research Institute of Cordoba (IMIBIC), Department of Cell Biology, Physiology and Immunology, University of Cordoba (UCO), CÓRDOBA, Spain; [2]Reina Sofia University Hospital (HURS), Cordoba, CÓRDOBA, Spain; [3]CIBER Physiopathology of Obesity and Nutrition (CIBERobn), Spain; [4]Reina Sofia University Hospital (HURS), Cordoba, Department of Neurosurgery, Spain; [5]Reina Sofia University Hospital (HURS), Cordoba, Pathology Service, CÓRDOBA, Spain; [6]Board of Governors Regenerative Medicine Institute, Cedars-Sinai Medical Center, Department of Biomedical Sciences, United States

Glioblastoma (GBM; grade IV astrocytoma) is one of the most devastating endocrine-related cancer worldwide based on its locally aggressive behavior and because it cannot be cured by current therapies. Therefore, the identification of novel diagnostic and prognostic biomarkers, and especially efficient therapeutic targets is urgently needed. In this sense, defects in alternative splicing process are associated with poor survival and high aggressiveness in cancer, including GBM. Specifically, splicing factor SF3B1 (splicing-factor-3B-subunit-1), an essential and druggable component of spliceosome (machinery responsible for splicing process), has been identified as a key dysregulated factor in some endocrine-related cancer (e.g. prolactinomas and breast cancer); however, the oncogenic implication of SF3B1, its somatic mutations, and expression profile or its association with molecular features and clinical parameters have not been characterized in GBM, nor its putative therapeutic potential. Therefore, different human cohorts and dataset from different glioma mouse models were analyzed to determine the mutation frequency as well as the gene and protein expression levels between tumor and control samples of SF3B1. SF3B1 expression was also explored at the single cell level across all cell subpopulation and transcriptomic programs. The association of *SF3B1* expression with relevant clinical data in different human cohorts was also analyzed. Moreover, different functional (proliferation/migration/tumorspheres-formation/ VEGF-secretion/apoptosis) and molecular/mechanistic (gene expression/signaling-pathways) assays were performed in different glioblastomas cell models (human primary-cultures and cell-lines) in response to SF3B1 blockade (using pladienolide B treatment). Additionally, tumor onset, formation and progression were monitored in response to SF3B1 blockade in a preclininal mouse model. Our data provide novel evidence demonstrating that SF3B1 is low-frequency mutated in human gliomas (1%) but widely overexpressed in glioblastoma compared with control samples from the different human cohorts and mouse models included in the present study, wherein SF3B1 levels are associated with key molecular and clinical features (e.g., overall survival, poor prognosis and/or drug-resistance). Remarkably, in vitro and in vivo blockade of SF3B1 activity with pladienolide B drastically altered multiple glioblastoma pathophysiological processes (i.e., reduction in proliferation, migration, tumorspheres-formation, VEGF-secretion, tumor initiation and increase in apoptosis) likely by suppressing AKT/mTOR/ß-catenin pathways, causing an imbalance of *BCL2L1* splicing. Together, we highlight

SF3B1 as a potential diagnostic and prognostic biomarker and an efficient pharmacological target in glioblastoma, offering a clinically relevant opportunity worth to be explored in humans.
Fundings: MINECO (PID2019-105564RB-I00), Junta de Andalucía (P20_00442, BIO-0139) and CIBERobn.
DOI: 10.1530/endoabs.81.OC6.6

Pituitary and Neuroendocrinology 2

OC7.1

Splicing factor 3 subunit B1 (SF3B1) inhibition in PRL-secreting PitNETs and cross-talk with dopamine receptor type 2 (DRD2)

Genesio Di Muro[1,2], Federica Mangili[2], Anna Maria Barbieri[2], Emanuela Esposito[2], Donatella Treppiedi[2], Federico Arlati[2], Rosa Catalano[2], Giusy Marra[2], Emma Nozza[2], Maura Arosio[2,3], Giovanna Mantovani[2,3] & Erika Peverelli[2]
[1]University Sapienza of Rome, PhD Program in Endocrinological Sciences, Italy; [2]University of Milan, Department of Clinical Sciences and Community Health, Italy; [3]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Endocrinology Unit, Italy

Somatic mutations in splicing factor 3 subunit B1 (SF3B1) were found in about 20% of PRL-secreting PitNETs. SF3B1 is involved in pre-mRNA splicing and required for assembly of the U2 complex, which is critical for branch site recognition and the early stages of spliceosome assembly. Patients with mutant prolactinomas showed higher PRL levels and shorter progression-free survival compared to wild-type patients. Aims of the present study were: 1) to characterize the genetic profile of a cohort of 14 patients with PRL-secreting PitNETs, searching for somatic mutations in SF3B1 hotspot region; 2) to test the effects of SF3B1 inhibitor pladienolide-B on tumoral lactotroph cells; 3) to investigate dopamine receptor type 2 (DRD2) agonist effects in tumoral lactotroph cells silenced for SF3B1. We found no SF3B1 mutated patients in our cohort. In rat PRL-secreting pituitary tumoral cells MMQ, pladienolide-B was effective in reducing cell proliferation (-40 $\pm$ 10% at 20 nM, $P<0.001$ vs basal), viability (-42 $\pm$ 7% at 10 nM, $P<0.05$ vs basal) and in promoting apoptosis (6-fold increase at 50 nM, $P<0.05$ vs basal). In primary cultured cells from one PRL-secreting PitNET, bearing wild-type SF3B1, pladienolide-B reduced cell proliferation and cyclin D3 expression and increased cell apoptosis. SF3B1 silencing in MMQ cells induced a reduction of DRD2 expression (-51 $\pm$ 13.2%, $P<0.001$ vs control cells). Moreover, in MMQ cells lacking SF3B1, cabergoline completely lost its ability to reduce cell proliferation (-22 $\pm$ 4.8%, $P<0.001$ vs basal), AKT phosphorylation (-31 $\pm$ 24,6%, $P<0.01$ vs basal), cyclin D3 expression (-23 $\pm$ 7,6%, $P<0.05$ vs basal) and to increase p27 (+20 $\pm$ 8,6%, $P<0.05$ vs basal). Interestingly, cabergoline treatment reduced SF3B1 protein expression levels in MMQ cells (-60 $\pm$ 40%, $P<0.05$ vs control cells) and in primary cultured cells from 2 PRL-secreting PitNETs (-43 $\pm$ 6,4%, $P<0.01$). In conclusion, our data demonstrated that SF3B1 inhibitor pladienolide-B exerts antitumoral actions in PRL-secreting PitNET cells bearing wild-type SF3B1. In MMQ cells, SF3B1 silencing reduced DRD2 expression and signaling, and cabergoline negatively regulated SF3B1 expression.

DOI: 10.1530/endoabs.81.OC7.1

OC7.2

Kisspeptin administration has therapeutic potential for men with low sexual desire by increasing penile tumescence and sexual brain processing

Edouard Mills[1], Natalie Ertl[2], Matt B Wall[2], Layla Thurston[1], Lisa Yang[1], Sofiya Suladze[1], Tia Hunjan[1], Maria Phylactou[1], Bijal Patel[1], Beatrice Muzi[1], Dena Ettehad[1], Jonathan Howard[2], Eugenii A Rabiner[2], Paul Bech[1], Ali Abbara[1], David Goldmeier[3], Alexander Comninos[1] & Waljit Dhillo[1]
[1]Imperial College London, Hammersmith Campus, Section of Endocrinology and Investigative Medicine, London, United Kingdom; [2]Invicro London, London, United Kingdom; [3]Imperial College Healthcare NHS Trust, Sexual Function Clinic, London, United Kingdom

Background
Hypoactive Sexual Desire Disorder (HSDD) is associated with dysfunctional brain activation in regions governing sexual responses, resulting in a deficiency/absence of sexual desire with marked distress. It affects up to 8% of men with detrimental effects on quality of life, interpersonal relationships and fertility, but so far has no licensed treatment options. The reproductive neuropeptide kisspeptin offers a putative therapeutic target owing to its emerging role in modulating reproductive behaviour in animal models and healthy men. However, there are no studies examining its effects in HSDD. To address this, we performed the first clinical study of kisspeptin in men with HSDD.
Methods
We examined the effects of kisspeptin administration (vs placebo) on brain activity during short and long erotic video tasks using functional MRI in 32 men with HSDD (mean $\pm$SEM age 37.9 $\pm$1.5 y, BMI 24.9 $\pm$1.0 kg/m^2). To provide functional and behavioural relevance for the associated fMRI brain responses during the long erotic video, simultaneous penile tumescence and subjective level of arousal were recorded. Participants also completed psychometric and behavioural questionnaires. Standard analysis methods were used for fMRI data from the short videos task, and the long videos task used regressors derived from the subjective arousal and penile tumescence data. The statistical threshold used for both was $Z=2.3$, $P<0.05$ (cluster-corrected).
Results
In response to visual erotic stimuli, kisspeptin administration significantly increased penile tumescence during the long video task compared to placebo, with kisspeptin increasing penile tumescence by 56% ($P=0.002$). Moreover, kisspeptin increased participant-reported happiness about sex ($P=0.02$). During both video tasks, kisspeptin significantly modulated brain activity, compared to placebo, in key structures of the sexual-processing network. In response to short erotic videos, kisspeptin enhanced left middle frontal gyrus and left anterior cingulate activity, and decreased activity in bilateral parahippocampus (all $p<0.05$). During the long video task, kisspeptin enhanced right fusiform gyrus and bilateral visual cortex activity, and decreased left frontal pole, right posterior cingulate and bilateral precuneus activity (all <0.05). Additionally, we observed positive correlations between kisspeptin's effects on aforementioned brain activity and psychometric parameters of sexual desire and arousal (all $P<0.01$).
Conclusion
Collectively, we demonstrate for the first time that kisspeptin administration in men with HSDD increases penile tumescence and psychometric measures of sexual desire and arousal by modulating sexual brain processing. Taken together, our data suggest that kisspeptin-based therapeutics may offer a novel, effective and much-needed clinical strategy for men with HSDD.

DOI: 10.1530/endoabs.OC7.2

OC7.3

Clinical practice outcomes from 107 patients with Cushing's syndrome treated with osilodrostat in France

Alexandre Dormoy[1], Magalie Haissaguerre[2], Dephine Drui[3], Lea Demarquet[4], Christine Do Cao[5], Laurence Guignat[1], C Vaillant[6], Anne-Cecile Papegaey[1], Yves Raznik[7], Maelle Le Bras[8], S Salenave[1], Isabelle Raingeard[9], I Tauveron[10], Marie Christine Vantyghem[11], M Francois[12], B Delemer[13], Florina Luca[14], Anne Mayer[15], Jean-Michel Petit[16], Eric Baudin[17], Philippe Chanson[1], Frederic Castinetti[18], Gerald Raverot[19], Olivier Chabre[20], Antoine Tabarin[21] & Jacques Young[1]
[1]Université Paris-Saclay – Assistance Publique-Hôpitaux de Paris, Endocrinology, Paris, France; [2]Centre Hospitalier Universitaire Bordeaux, Bordeaux, France, Endocrinology, France; [3]Centre Hospitalier Universitaire Nantes, Nantes, France, Endocrinology, France; [4]Centre Hospitalier Régional Universitaire Nancy, Nancy, Endocrinology, France; [5]Centre Hospitalier Régional Universitaire Lille, Endocrinology, France; [6]Le Centre Hospitalier du Mans, Endocrinology, France; [7]Centre Hospitalier Universitaire Caen, Endocrinology, France; [8]Centre Hospitalier Universitaire Nantes, Endocrinology, France; [9]Centre Hospitalier Universitaire Montpellier, Endocrinology, France; [10]Hospital Center Universitaire, Clermont-Ferrand, France; [11]Centre Hospitalier Régional Universitaire Lille, Endocrinology, Lille, France; [12]Centre Hospitalier Universitaire Reims, Endocrinology, France; [13]Centre Hospitalier Universitaire Reims, Reims,

France; [14]Centre Hospitalier Régional Universitaire Strasbourg, Endocrinology, France; [15]Centre Hospitalier de Chambéry - Hôpital Savoie, Endocrinology, France; [16]Centre Hospitalier Universitaire Dijon, Endocrinology, France; [17]Institut Gustave Roussy, Endocrinology, France; [18]Centre Hospitalier Universitaire Marseille, Endocrinology, France; [19]Centre Hospitalier Universitaire Lyon, Endocrinology, France; [20]CHU Grenoble, Endocrinology, France; [21]Centre Hospitalier Universitaire Bordeaux, Endocrinology, France

Background
Osilodrostat is a potent oral inhibitor of the adrenal enzymes aldosterone synthase and 11b-hydroxylase and decreases glucocorticoid and mineralocorticoid production and secretion. Phase 2 and 3 studies from the osilodrostat clinical trial programme have demonstrated the drug's efficacy and safety in patients with Cushing's disease. Osilodrostat received European Marketing Authorization (MA) for the treatment of Cushing's syndrome (CS) in adults.
Objective
Evaluate the use of osilodrostat for the treatment of CS in clinical practice in France (Autorisation Temporaire d'Utilisation [ATU], post-ATU, post-MA; authorization IDRCB2021A0140140).
Methods
This multicentre analysis included patients with CS who were treated with osilodrostat between 2019 and 2021. Causes of CS, therapeutic approaches, dosages, and efficacy and safety of osilodrostat were analysed in patients where data was available.
Results
Patients ($n=107$) with CS aged 11–85 years were analysed; 68 patients were female and 39 were male. At diagnosis, urinary free cortisol (UFC; median ± standard deviation (SD) [range; n]) was 135 µg/24 h ±1703 (10–27188; $n=79$). Causes of CS in these patients include ACTH-dependent (Cushing's disease [$n=57$]; ectopic [$n=28$]; uncertain [$n=5$]) and ACTH-independent (adrenocortical carcinoma [$n=9$]; macronodular adrenocortical hyperplasia [$n=5$]; adrenocortical adenoma [$n=2$]). UFC levels (median ± SD [range; n]) at the time of initiating osilodrostat therapy were 135 µg/24 h ±1703 (5–10000; $n=78$). Regarding therapeutic approaches (n/N, %), 17/87 patients (20%) received osilodrostat as first-line therapy, whereas 36 patients (41%) received it as second-line therapy. Methods of osilodrostat administration included: titration (59/95, 62%), block and replace (9/84, 11%) and titration followed by block and replace (33/85, 39%). The initial osilodrostat dose (median ± SD [range; n]) was 4.0 mg/day ±8.7 (1–60; $n=96$), whereas the maximum dose was 12.0 mg/day ±18 (1–80; $n=103$). UFC normalization with osilodrostat was achieved in 64/78 patients (82%). Improvements of clinical signs and symptoms were reported in 67/89 patients (75%), and improvement of comorbidities with osilodrostat was reported in 39/62 patients (63%). In terms of safety in patients treated with osilodrostat, adrenal insufficiency was reported in 30/91 patients (33%) and hyperandrogenism was reported in 6/54 patients (11%).
Conclusion
These findings from clinical practice confirm the efficacy of osilodrostat in patients with various aetiologies of CS, in agreement with the European MA. The main side effect observed was adrenal insufficiency, which was expected and related to the mechanism of action of osilodrostat. Use of the block and replace approach may prevent the development of adrenal insufficiency.

DOI: 10.1530/endoabs.OC7.3

OC7.4

HPLC-MSMS steroidogenic profiles in ACTH-dependent Cushing Syndrome patients treated by osilodrostat or metyrapone suggest differences in the spectrum of steroidogenic enzyme inhibition between the two CYP11B1 inhibitors in clinical care

Bonnet Fideline[1,2,3], Jonathan Poirier[4], Anna Vaczlavik[2,3,4], Christelle Laguillier-Morizot[1,2,5], Benoît Blanchet[6], Laurence Guignat[4], Laura Bessiene[4], Léopoldine Bricaire[4], Lionel Groussin[2,3,4], Guillaume Assié[2,3,4], Jean Guibourdenche[1,2,5] & Jerome Bertherat[2,3,4]
[1]Hôpital Cochin-APHP, UF d'Hormonologie, Paris, France; [2]Université de Paris, Paris, France; [3]INSERM, U1016, Paris, France; [4]Hôpital Cochin-APHP, Endocrinologie, Paris, France; [5]INSERM, Physiopathologie et Pharmacotoxicologie Placentaire Humaine : Microbiote Pré & Post Natal, Paris, France; [6]Hôpital Cochin-APHP, Biologie du Médicament et Toxicologie, Paris, France

Introduction
Osilodrostat is a new 11 ß-hydroxylase inhibitor with a mode of action analogue to metyrapone. It has become increasingly used in recent years for treatment of Cushing's Syndrome (CS). However, few in vivo studies are currently available to accurately compare both drugs characteristics. The objective of our study was to compare steroidogenic profiles in patients treated by either Osilodrostat or Metyrapone for ACTH-dependent CS.
Methods
Patients followed in Cochin hospital Endocrinology department between March 2019 and December 2021 for an ACTH-dependent CS, controlled by either Osilodrostat or Metyrapone were included. A serum profile of 5 steroids (cortisol, 11-deoxycortisol, 17-hydroxyprogesterone, androstenedione and testosterone) was determined in high performance liquid chromatography-tandem mass spectrometry (HPLC-MS/MS).
Results
Twenty-five patients treated by Osilodrostat and 14 patients treated by Metyrapone were thus included. Cortisol level was lower in Osilodrostat group (175 [22-421] nmol/l) in comparison to Metyrapone group (307 [68-547] nmol/), $P=0.025$; hypocortisolism (basal 8:00 AM cortisol < 100 nmol/l) being found in 48% of patients treated by Osilodrostat and 7% of patients treated by Metyrapone. 11-deoxycortisol level was higher in patients treated by Metyrapone (80.9 [2.2-688.4] nmol/l) than in patients treated by Osilodrostat (10.3 [0.5-71.9] nmol/l), $P=0.0009$. Similarly, androstenedione level was higher in Metyrapone group (14.9 [2.5-54.3] nmol/l) than in Osilodrostat group (4.0 [0.3-13.3] nmol/l), $P=0.0005$. Testosterone level in women patients was also higher in Metyrapone group (3.3 [0.93-4.82] nmol/l) than in Osilodrostat group (1.31[0.13-5.09] nmol/l), $P=0.0146$. Steroidogenic enzymes activity was evaluated by upstream/downstream steroids ratio, a higher ratio thus reflecting an accumulation of the enzyme substrate, i.e a lower enzymatic activity. CYP11B1 activity, evaluated by 11-deoxycortisol/cortisol ratio, was not different between Metyrapone group (22.4 [0.7-410]) and Osilodrostat group (7.53 [1.0-47.3]), $P=0.1254$. CYP21A2 activity, assessed by 17OHprogesterone/11-deoxycortisol ratio, was significantly decreased in Osilodrostat group (18.6 [4.89-101.9]) in comparison to Metyrapone group (3.1[1.3-31.8]), $P<0.0001$, as well as CYP17A1 activity, evaluated by 17OHprogesterone/androstenedione ratio: 56.9 [17.7-136.5] in Osilodrostat group in comparison to 18.3 [5.8-46.8] in Metyrapone group, $P<0.0001$.
Conclusion
In patients with ACTH-dependent CS, the use of CYP11B1 inhibitors in standard routine care suggest that Osilodrostat has a less specific effect on the inhibition of steroidogenic enzymes than Metyrapone. This might explain a smaller increase in 11-deoxycortisol and in androgens levels in patients treated by Osilodrostat and should be taken in consideration for patients management.

DOI: 10.1530/endoabs.OC7.4

OC7.5

Epigenomic and somatic mutation profile of pituitary adenomas (PAs)/ pituitary neuroendocrine tumors (PitNETs)

Federica Guaraldi[1], Luca Morandi[2], Matteo Zoli[1,2], Alberto Righi[3], Stefania Evangelisti[2], Caterina Tonon[2], Diego Mazzatenta[1,2] & Sofia Asioli[2]
[1]IRCCS Istituto delle Scienze Neurologiche di Bologna, Pituitary Unit, Bologna, Italy; [2]Alma Mater Studiorum - Bologna University, Department of Biomedical and Neuromotor Sciences (DIBINEM), Bologna, Italy; [3]Rizzoli Orthopedic Institute, Anatomopathology and Histopathology Service, Bologna, Italy

Background
Pituitary adenomas (PAs)/Pituitary Neuroendocrine Tumors (PitNETs) are a complex and heterogeneous group of lesions. Genetic and epigenetic studies have been performed to identify predictors of treatment outcome.
Study aim
To profile clinically non-aggressive (NA) and aggressive (A) PAs/PitNETs, and carcinomas for somatic mutations and epigenetic alterations of genes involved in cell proliferation/differentiation, miRNA/lncRNA-post-transcriptional regulators, and therapy targets.
Patients and Methods
64 NA and 41 A PAs/PitNETs (40 males; 21 ACTH-, 50 FSH-/lH-, 16 GH-, 3 GH/PRL-, 12 PRL-secreting; 1 null cell; 2 plurihormonal PIT-1+) and 6 carcinomas (3 males; 3 ACTH-, 2 PRL- and 1 FSH/lH-secreting) treated by endoscopic surgery from 2003 to 2017, with ≥1-year follow-up were included. Clinico-radiological and histological data were collected. Somatic mutations of 17, and DNA methylation of 22 genes were assessed in fresh frozen and/or formalin-fixed paraffin-embedded tumor tissue (20% VAF and 100x coverage in both strands). Ten normal pituitaries were used as control.

Results
6/64 (9.4%) NA and 9/41 (22%) A PAs/PitNETs and 1/6 (16.6%) carcinoma showed ≥1 mutation ($P=0.0024$), involving *TP53* ($n=3$; 2.7%), *NOTCH1* ($n=4$; 3.6%), *AIP* ($n=6$; 5.4%), *USP8* ($n=3$; 2.7%) or *PIK3CA* ($n=3$; 2.7%). Carcinomas presented the highest methylation levels of *PARP15*, *LINC00599*, *MIR193a*, *MIR137HG* and *ZAP70* followed by A and NA PAs/PitNETs ($P<0.05$). *LRRTM1*, *NTM*, *CDH1* were hypermethylated in carcinomas only. *GNAS*, *PDCD1* and *AIP* methylation was higher in NA than A PAs/PitNETs and carcinomas ($P<0.05$). Hypermethylation could silence genes and reduce the expression of PARP15, LINC00599 and miR-193a, thus inducing cancer cells growth and proliferation by modulating p53 expression and related apoptotic pathways in aggressive tumors. *PDCD1* methylation could predict the response to anti-PD1 and PDL-1 inhibitors, as well as the escape of tumor cells from immunological control. Methylation levels of *MAGEA family, UXT* and *FLNA* gens, interacting with the androgen receptor (AR) and p53, differed between males and females in PAs/PitNETs and carcinomas, supporting the role of AR expression and the synergy of epigenetics and somatic gene mutations in pituitary tumorigenesis.
Conclusions
Different profiles of somatic gene mutations and methylation were identified in NA and A PAs/PitNETs, and carcinomas. Altered methylation appears an early event that could contribute to tumor aggressiveness, response to treatment and progression to carcinoma directly, or indirectly by inducing gene mutation. Involvement of X-linked genes could underly gender variability in tumor behavior. These data reinforce the importance of combining molecular analysis with clinico-radiological and pathological data in attempting to predict tumor behavior.

DOI: 10.1530/endoabs.OC7.5

OC7.6

A tumor-borne Angpt2/Tie2 autostimulatory loop controls tumorigenesis

Natalia Pellegata[1], Ninelia Minaskan[1], Sebastian Gulde[1], Hermine Mohr[1], Julia Geppert[1], Maria Rohm[1], Giovanni Vitale[2], Germano Gaudenzi[2], Alessandra Dicitore[2], Schilling Franz[3], Mathias Schillmaier[3], Graeme Eisenhofer[4], Stephan Herzig[1], Federico Roncaroli[5] & Jürgen Honegger[6]
[1]Helmholtz Zentrum München, Institute for Diabetes and Cancer, Munich, Germany; [2]Istituto Auxologico Italiano IRCCS, Milan, Italy; [3]Technical University Munich, Munich, Germany; [4]Technical University Dresden, Dresden, Germany; [5]University of Manchester, Manchester, United Kingdom; [6]Eberhard Karls University Tübingen, Tübingen, Germany

Background
Invasive nonfunctioning (NF) pituitary neuroendocrine tumors (PitNETs) are non-resectable neoplasms associated to frequent relapse and significant comorbidities. As current treatments often fail against NF-PitNETs, identifying actionable therapeutic targets is essential. We focused on the angiopoietin-2 (Angpt2)/Tie2 axis, usually active in endothelial cells (ECs).
Methods
ANGPT2 plasma levels in NF-PitNET patients and healthy controls were measured by ELISA. qRT-PCR and immunohistochemistry assessed Angpt2 and Tie2 expression in rat and human NF-PitNETs. The role of endogenous Angpt2 in PitNET cells was investigated by gene knockdown (siRNA, shRNA) followed by proliferation/apoptosis assays. Xenografts of sh*Angpt2* PitNET cells in zebrafish embryos demonstrated that tumor cell-borne Angpt2 is pro-angiogenic. Proximity ligation assay (PLA) showed Angpt2/Tie2 interaction on primary NF-PitNET cells. Downstream targets activation upon Angpt2-mediated receptor stimulation was assessed by western blotting. Mouse xenografts of CRISPR/Cas9-generated Tie2-knockout PitNET cells proved the role of Tie-2 in pituitary tumorigenesis *in vivo*. Drugs inhibiting Angpt2/Tie2 signaling were tested against primary rat/human NF-PitNET cultures. Treatment of mouse xenografts of PitNET cells with an angiopoietin-neutralizing peptibody (AMG386), followed by MRI imaging, determined the effects of Angpt2/Tie2 inhibition on tumor growth *in vivo*. The efficacy of Angpt/Tie2 inhibition was also assessed in MENX rats, the only spontaneous and autochthonous NF-PitNET model. MENX rats were treated with AMG386 and longitudinally monitored using anatomical and functional (diffusion weighted) MRI.
Results
In NF-PitNET patients, circulating Angpt2 levels are elevated and correlate with tumor aggressiveness. PitNET cells express and secrete bioactive Angpt2, which stimulates tumor cell proliferation *in vitro*, and angiogenesis in zebrafish xenografts *in vivo*. Noteworthy, NF-PitNET cells possess a functional Tie2 receptor, which is activated by Angpt2 and stimulates downstream mitogenic signals. This establishes an autocrine/paracrine stimulatory loop in NF-PitNET cells, as so far only demonstrated in ECs. Tie2 knockout blunts PitNETs growth *in vivo*. Proof-of-principle pharmacological inhibition of Angpt2/Tie2 signaling antagonizes NF-PitNETs *ex vivo* (primary cultures of human/rat tumors) and *in vivo* (mouse xenografts, MENX rats).
Conclusion
The Angpt2/Tie2 axis emerges as exploitable therapeutic target in NF-PitNETs, hence addressing an unmet clinical need. The ability of tumor cells to coopt angiogenic signals classically viewed as EC-specific expands our view on microenvironmental cues essential for tumor progression. Tumor-targeted Angpt2/Tie2 inhibition is a novel concept in anti-cancer strategies applicable to tumors expressing Angpt2/Tie2.

DOI: 10.1530/endoabs.OC7.6

Calcium and Bone

OC8.1

Effectiveness of anti-resorptive drugs on risk of vertebral fractures in women receiving aromatase inhibitors: a prospective study in real-life clinical practice

Gherardo Mazziotti[1,2], Walter Vena[2], Stella Pigni[2], Flaminia Carrone[2], Rebecca Pedersini[3], Deborah Cosentini[3], Rosalba Torrisi[4], Maria Francesca Birtolo[2], Giulia Maida[2], Alfredo Berruti[3,5] & Andrea Lania[1,2]
[1]Humanitas University, Department of Biomedical Sciences, Pieve Emanuele (MI), Italy; [2]IRCCS Humanitas Research Hospital, Endocrinology, Diabetology and Andrology Unit, Rozzano (MI), Italy; [3]ASST Spedali Civili of Brescia, Medical Oncology, Brescia, Italy; [4]IRCCS Humanitas Research Hospital, Cancer Center, Rozzano (MI), Italy; [5]University of Brescia, Department of Medical and Surgical Specialties, Radiological Sciences and Public Health, Brescia, Italy

Bone loss is a frequent complication of aromatase inhibitors (AIs) therapy in women with breast cancer. Bone-active drugs are effective in protecting the skeleton from detrimental actions of AIs. However, bone mineral density (BMD) was the primary end-point in most of published studies, whereas data on fractures were scant and mainly limited to denosumab. In this prospective study, we investigated the effects of denosumab, oral bisphosphonates and intravenous zoledronate on risk of morphometric vertebral fractures (VFs; primary end-point) and BMD at lumbar spine, femoral neck and total hip (explorative end-point). To address these aims, 567 consecutive women (median age 62 years, range 28-83) were evaluated for BMD and morphometric VFs at baseline and after 18-24 months of follow-up. The inclusion criteria were: 1) hormone receptor-positive breast cancer with indication to AIs; 2) duration of AIs therapy at study entry ≤12 months. After enrolment, 268 women (47.3%) started denosumab 60 mg subcutaneously every 6 months, 59 (10.4%) oral bisphosphonates (BPs), 56 (9.9%) intravenous zoledronate 5 mg every 12 months, whereas 184 women (32.5%) were not treated with bone-active drugs because of patient preference, contraindications and/or clinical judgment. Vitamin D, with or without calcium, was given to all women during study period. Denosumab was given more frequently to women with pre-existing VFs ($P=0.019$) and/or lower BMD values ($P<0.01$ at all skeletal sites) as compared to women treated with oral BPs or zoledronate. During 18-24 months of follow-up, 54 women (9.5%) developed new morphometric VFs, with incidence being higher in untreated women vs those treated with any bone-active drug (17.4% vs 5.7%; $P<0.001$). Stratifying women for type of anti-osteoporotic medications, risk of VFs resulted to be significantly decreased by denosumab [odds ratio (OR) 0.22, 95% confidence interval (C.I.) 0.11-0.46; $P<0.001$) and zoledronate (OR 0.27, 95% C.I. 0.08-0.91; $P=0.035$) , but not by oral BPs (OR 0.64, 95% C.I. 0.27-1.54; $P=0.317$). All anti-osteoporotic medications induced significant increase in median BMD at any skeletal site, whereas BMD decreased significantly in women who were not treated with bone-active drugs. In conclusion, this prospective study, reflecting the real-life clinical practice, shows that in women exposed to AI therapy, denosumab and zoledronate are more effective than oral BPs in decreasing the risk of VFs during the first 24 months of treatment. Future prospective studies will clarify whether in the long-term also oral BPs

could reduce the risk of fractures in women exposed to estrogen-deprivation therapies.

DOI: 10.1530/endoabs.81.OC8.1

OC8.2

SGLT2 inhibitor treatment does not increase risk of osteoporotic fractures compared to GLP-1 receptor agonists: a Danish population-based cohort study

Zheer Kejlberg Al-Mashhadi[1,2], Rikke Viggers[3,4], Jakob Starup-Linde[1,2,5], Peter Vestergaard[3,4] & Søren Gregersen[1,2]

[1]Aarhus University Hospital, Steno Diabetes Center Aarhus, Aarhus, Denmark; [2]Aarhus University, Department of Clinical Medicine, Aarhus, Denmark; [3]Aalborg University Hospital, Steno Diabetes Center North Jutland, Department of Endocrinology, Aalborg, Denmark; [4]Aalborg University, Department of Clinical Medicine, Aalborg, Denmark; [5]Aarhus University Hospital, Department of Endocrinology and Internal Medicine, Aarhus, Denmark

Background

Type 2 diabetes mellitus (T2D) is associated with an increased risk of fractures. Research on the effects of sodium-glucose cotransporter 2 (SGLT-2) inhibitors is scarce and unsettled. We aimed to investigate the risk of major osteoporotic fractures (MOF) – i.e., hip, vertebral, humerus, and forearm fractures – with SGLT2 inhibitors compared to glucagon-like peptide 1 (GLP-1) receptor agonists when either is used in combination with metformin.

Methods

We conducted a population-based cohort study using discharge diagnosis codes from the Danish National Patient Registry and data on all redeemed drug prescriptions from the Danish National Prescription Registry. Subjects treated with metformin in combination with either SGLT2 inhibitors or GLP-1 receptor agonists between 2012 and 2018 were identified. Subjects were then propensity-score matched 1:1 based on age, sex, and index date. Survival curves were plotted using the Kaplan-Meier estimator. A Cox proportional hazards model was utilized to estimate crude and adjusted hazard rate ratios (HR) for MOF. Finally, Aalen's Additive Regression (AAR) model was used to examine a possible additive rather than multiplicative effect of SGLT2 inhibitors on fracture hazard while allowing time-varying covariate effects.

Results

We identified 27,543 individuals treated with either combination. After matching, 18,390 individuals were included in the main analysis (9,190 in each group). Median follow-up times were 355 [interquartile range (IQR) 126-780] and 372 [IQR 136-766] days in the SGLT2 inhibitor and GLP-1 receptor agonist group, respectively. The crude HR for MOPF was 0.77 [95% CI 0.56-1.04] with SGLT2 inhibitors compared to GLP-1 receptor agonists. The fully adjusted model yielded an unaltered HR of 0.77 [95% CI 0.56-1.05]. Results were similar across subgroup- and sensitivity analyses. Similarly, the multivariate AAR model yielded a non-significant difference between the two exposure groups.

Conclusion

These results suggest that SGLT2 inhibitors have no effect on fracture risk when compared to GLP-1 receptor agonists. This is in line with results from previous studies.

DOI: 10.1530/endoabs.81.OC8.2

OC8.3

Impact of preoperative zoledronic acid on hungry bone syndrome and bone health indices in patients with primary hyperparathyroidism after curative parathyroidectomy: a randomized controlled trial

Akanksha Gautam[1], Sanjay Bhadada[2], Anil Bhansali[2], Divya Dahiya[3], Arunanshu Behera[3], Uma Nahar Saikia[4], Ashwani Sood[5] & Tulika Singh[6]

[1]Post Graduate Institute of Medical Education & Research, Chandigarh, Endocrinology, Chandigarh, India; [2]Post Graduate Institute of Medical Education & Research, Chandigarh, Endocrinology , Chandigarh, India; [3]Post Graduate Institute of Medical Education & Research, Chandigarh, Surgery, Chandigarh, India; [4]Post Graduate Institute of Medical Education & Research, Chandigarh, Histopathology , Chandigarh, India; [5]Post Graduate Institute of Medical Education & Research, Chandigarh, Nuclear Medicine , Chandigarh, India; [6]Post Graduate Institute of Medical Education & Research, Chandigarh, Radiodiagnosis , Chandigarh, India

Background

In individuals with primary hyperparathyroidism (PHPT), the utility of preoperative bisphosphonate administration in prevention of post-curative-parathyroidectomy hungry bone syndrome (HBS) and effects on long-term bone accrual are uncertain.

Objectives

To estimate the effect of preoperative administration of single infusion of zoledronic acid (ZA) on occurrence of HBS and gain in bone mineral density (BMD) at one year in individuals with PHPT undergoing curative parathyroidectomy.

Methods

In this single-centre, randomized (1:1), single-blind, placebo-controlled study (CTRI/2019/10/021762), a total of 48 adults (age $>$ 18 years) with PHPT (serum Calcium $\geq$ 11 mg/dl) were enrolled. Prior to parathyroidectomy ($\leq$ 2 weeks), participants received either a single intravenous infusion of 5 mg ZA ($n=24$) or placebo ($n=24$). Post-curative-parathyroidectomy, participants were monitored for occurrence of HBS until discharge. HBS was defined by the presence of hypocalcemia (Ca$<$ 8.5 mg/dl) and hypophosphatemia ($P<$ 2.7 mg/dl) with rise in alkaline phosphatase (ALP) ($>$5%) on any day after surgery. BMD (Hologic Discovery 4500) and trabecular bone score (TBS) were assessed at baseline and one year after surgery. In addition, bone turnover markers (CTX, P1NP) were assessed at baseline, first week, 3-, 9- and 12- months post-surgery. Occurrence of HBS was assessed using binary logistic regression model. Changes in BMD and BTM were assessed using linear mixed model for repeated measures.

Results

Forty five out of 48 participants had succesful curative parathyroidectomy. HBS occured in 6 (27.3%) individuals in ZA and 6 (26.1%) in placebo group [OR: 1.06 (0.28 - 3.98);$P=0.928$]. The odds for developing HBS were comparable after adjusting for baseline severity and serum 25(OH)D levels ($P=0.075$). Individuals in ZA group had a higher gain in BMD at lumbar spine (7.54%; 95% CI, 0.06 to 15.02; $P=0.048$), comparable gain at neck of femur (9.74%; 95% CI, - 5.005 to 24.49; $P=$ 0.190) and a fall in BMD at distal radius (3.29% ; 95% CI, -10.17 to 2.31; $P=0.008$). Rise in TBS was comparable between the two groups ($P=0.396$). The higher gain in BMD at lumbar spine was paralleled by a higher decline in CTX (27.8%; 95% CI, -48.44 to -7.12; $P=0.009$) in ZA group while ALP (10.9%; 95% CI, -23.39 to 1.44; $P=0.082$) and P1NP levels remained comparable (9.50%; 95% CI, -22.36 to 41.37; $P=0.360$).

Conclusion

In PHPT, preoperative administration of single infusion of ZA is associated with increased bone mineral accrual at lumbar spine without significant effect on occurrence of HBS.

DOI: 10.1530/endoabs.81.OC8.3

OC8.4

Is the "rebound phenomenon" following Denosumab discontinuation a risk factor for Zoledronic acid acute phase adverse reactions?

Marta Zampogna[1], Giorgia Grassi[1], Alberto Ghielmetti[1], Serena Palmieri[2], Maura Arosio[1] & Cristina Eller Vainicher[2]

[1]University of Milan, Department of Clinical Sciences and Community Health, Italy; [2]Fondazione IRCCS Cà Granda Ospedale Maggiore Policlinico, Unit of Endocrinology, Italy

Background

Zoledronic acid (ZOL) administration may cause acute phase adverse reactions (APR), which manifest with fever, malaise, bone and muscular pain, headache

and/or gastrointestinal disturbances. Previous data suggest that high N-terminal propeptide of type 1 collagen (P1NP) and low 25,OH-vitaminD (VitD) levels are associated with higher incidence of APR, while the previous use of bisphosphonates is a protective factor. Lately, ZOL has been frequently used to mitigate the "rebound phenomenon" following Denosumab (Dmab) discontinuation. The aim of our study is to evaluate whether the use of ZOL in patients discontinuing Dmab (postDmab) may be associated with an increase in incidence and severity of APR, as compared with patients without prior antiosteoporotic therapy (naïve) and the presence of possible factors associated with APR.

Methods

we retrospectively evaluated 112 patients (56 postDmab and 56 naïve) treated with ZOL 5 mg intravenously for osteoporosis in our center during the last 24 months. Bisphosphonates treatment preceding ZOL administration, including previous ZOL infusions, was considered an exclusion criterion. All patients were taking vitamin D and calcium. In all patients we evaluated femoral neck (FN) and lumbar spine (LS) bone mineral density (BMD), C-terminal telopeptide (CTX) and VitD levels.

Results

PostDmab patients were older (71.4±8.7 vs 65.1±11.4 years, $P=0.001$), had higher BMD (LS T-score -2.3±0.8 vs -3.1±1.2, $P=0.0001$, FN T-score -2.0±0.8 vs -2.4±0.8, $P=0.011$) and lower CTX levels (452±350 vs 630±307 pg/ml $P=0.008$) as compared to naïve patients, while the prevalence of fractures (56.3 vs 43.8% $P=0.333$; respectively postDmab and naïve) and the VitD levels (40.4±13.9 vs 42.8±23.1 ng/ml, $P=0.509$; respectively postDmab and naïve) were comparable in the two groups. No difference was found in the overall APR rate (65.3 vs 58%, $P=0.156$; respectively postDmab and naïve) or in the moderate-severe APR rate (34.7 vs 42%, $P=0.156$ respectively postDmab and naïve) between the two groups. The logistic regression analysis showed a significant association between CTX levels and the occurrence of moderate-severe APR, regardless of age, group (naïve or postDmab) and VitD levels (OR 1.002, 95% CI 1.000-1.003, $P=0.027$).

Conclusions

In our cohort of ZOL treated patients we found a higher incidence of APR than reported in literature without significant differences between postDmab and naïve patients. In our cohort of VitD sufficient patients, CTX seems to be the only factor significantly associated with an increased risk of moderate-severe APR post ZOL infusion.

DOI: 10.1530/endoabs.81.OC8.4

OC8.5

Key4OI: Development and implementation of a standard set of outcome measures for osteogenesis imperfecta

Anton Franken[1] & Dagmar Mekking[2]
[1]Isala Hospital Zwolle, Endocrinology, Netherlands; [2]Care4brittlebones, Netherlands

Key4OI : Development and implementation of a Standard set of Outcome measures for Osteogenesis Imperfecta. Osteogenesis Imperfecta (OI) is a genetic disorder also known as 'brittle bone disease'. The clinical manifestation of OI shows a wide variation. Therefore, care for patients with OI requires an interdisciplinary approach. The effectiveness of particular interventions and treatment protocols of interdisciplinary teams is not clear due to a non-standardized and wide variation of patient outcomes thus making the comparison of outcome measures available in the literature difficult. In 2018 the Key4OI project was started, an international interdisciplinary working group of 27 experts used a consensus-driven modified Delphi approach to develop a set of global outcome measures for patients with OI. More than 400 different outcome measures were identified in our literature search. After three Delphi rounds, 24 domains were selected. After the focus group sessions with members from OI community, the number of domains were reduced to 15. A consensus was reached on the measuring instruments to cover these domains for both children and adults. The entire approach was in line with the International Consortium for Health Outcomes Measurement ICHOM methodology. The Key4OI project resulted in a standard set of outcome measures focused on the needs and wishes of individuals with OI and their families. This outcome set will enable healthcare teams and systems to compare and to improve their care pathways and quality of care world. Implementation was started in 5 different countries (6 hospitals): China, Norway, USA, Canada and the Netherlands (Isala Zwolle and UMC Utrecht). Various other countries will start implementation in 2022. Anton Franken, D. Mekking on behalf of the international Key4OI expertgroup.

DOI: 10.1530/endoabs.81.OC8.5

OC8.6

Dose-range analysis of the effects of the long-acting parathyroid hormone analog AZP-3601 versus PTH(1-34) delivered by daily injection or continuous infusion on blood calcium levels and bone metabolism in thyroparathyroidectomized (TPTX) rats

Cagri Aksu[1,2], Michael D Culler[3] & Thomas Gardella[1,2]
[1]Massachusetts General Hospital, Boston, United States; [2]Harvard Medical School, Boston, United States; [3]Amolyt Pharma, Écully, France

AZP-3601, a long-acting PTH/PTHrP(1-36) analog, is a candidate new treatment option for hypoparathyroidism (HP). As compared to conventional PTH(1-34), AZP-3601 binds with higher affinity to the R0 conformation of the PTH-1 receptor, resulting in prolonged signaling and sustained elevations in blood calcium (Ca^{++}) in vivo, despite a very short circulating half-life. We assessed whether repeated injection of AZP-3601 into TPTX rats at doses aimed to normalize serum Ca^{++} levels would produce different effects on bone than PTH(1-34) administered either intermittently or continuously.

Methods

Male S-D rats at age 9 weeks and 2 weeks after TPTX surgery received either a daily sc injection of AZP-3601 at doses of 1.0, 2.0 or 4.0 nmol/kg, daily sc injection of PTH(1-34) at 50, 100 or 150 nmol/kg, or continuous infusion of PTH(1-34) via ALZET mini pump at 1.5, 2.0 or 3.0 nmol/kg/day ($n=8$/group) for 16 days. TPTX controls received vehicle injections or infusion. Tail vein blood Ca^{++} was analyzed on days 7 and 14 at 6 h post-injection. Rats were euthanized on day16 (24 h post injection) and blood and femurs collected for analysis.

Results

Each treatment modality resulted in dose-dependent increases in blood Ca^{++} levels. Optimal doses for raising blood Ca^{++} to normal range (1.2-1.4 mM vs 0.9-1.1 mM in TPTX-vehicle controls, $P<0.001$) on days 7 and 14 were identified as 1.0 nmol/kg for AZP-3601 daily injection, 50 nmol/kg for PTH(1-34) daily injection and 3.0 nmol/kg/day for PTH(1-34) continuous infusion. Effects on bone markers and uCT parameters at these optimal doses were as follows: Continuous infusion of PTH(1-34) significantly increased serum levels of the bone formation marker P1NP ($P=0.03$) and the bone resorption markers CTX1 ($P=0.02$) and TRAP-5b ($P=0.03$), and decreased distal femur trabecular (Tb) bone volume relative to tissue volume (BV/TV, $P=0.002$), as well as mid-femur cortical thickness (Ct.Th $P=0.01$). Daily injection of PTH(1-34) significantly increased serum P1NP ($P<0.001$) and TRAP-5b ($P=0.001$), and increased distal femur trabecular BV/TV ($P=0.01$) as well as mid-femur cortical thickness($P=0.02$). Daily injection of AZP-3601 caused no significant change in these bone turnover and structural parameters.

Conclusion

At doses that similarly normalized blood Ca^{++} levels in TPTX rats, continuous infusion of PTH(1-34) was bone-catabolic, daily injection of PTH(1-34) was bone-anabolic and daily injection of AZP-3601 was bone-neutral. The distinct mechanism used by AZP-3601 may lead to less impact on bone, as compared to either daily injection or sustained, continuous delivery of PTH(1-34), when used as chronic treatments for HP.

DOI: 10.1530/endoabs.81.OC8.6

Environmental Endocrinology

OC9.1

Higher free thyroxine associated with pfas exposure in first trimester. The odense child cohort

Richard Christian Jensen[1,2], Dorte Glintborg[1,3], Clara Amalie Gade Timmermann[2,4], Flemming Nielsen[2], Henriette Boye[5], Niels Bilenberg[3,5,6], Jeppe Buur Madsen[7], Philippe Grandjean[2,8], Tina Kold Jensen[2,5,9] & Marianne Andersen[1,3]

[1]Odense University Hospital, Department of Endocrinology, Odense, Denmark; [2]University of Southern Denmark, Department of Clinical Pharmacology, Pharmacy and Environmental Medicine, Odense, Denmark; [3]University of Southern Denmark, Department of Clinical Research, Odense, Denmark; [4]University of Southern Denmark, National Institute of Public Health, København K, Denmark; [5]Odense University Hospital, Odense Child Cohort, Hans Christian Andersen Children's Hospital, , Odense, Denmark; [6]Odense University Hospital, Department of Child and Adolescent Mental Health Odense, Odense, Denmark; [7]Vejle Hospital, Hospital Lillebælt, Department of Biochemistry and Immunology, Vejle, Denmark; [8]Harvard T.H. Chan School of Public Health, Department of Environmental Health, Boston, United States; [9]University of Southern Denmark, OPEN, Odense, Denmark

Background
Perfluoroalkyl substances (PFAS) are endocrine disrupting chemicals, with elimination half-lives ranging from four to eight years. Experimental studies found PFAS able to interfere with thyroid hormone-binding proteins. During the first 20 weeks of gestation (GW), the fetus is reliant on placental transfer of maternal thyroid hormones, mainly free thyroxine (FT4). However, previous studies investigating associations between exposure to PFAS and thyroid hormone status mainly focused on blood samples from late pregnancy or umbilical cord with mixed findings.
Objectives
To investigate associations between concentrations of PFAS and FT4 and thyroid-stimulating hormone (TSH) in early pregnancy.
Methods
In Odense Child Cohort (OCC), a single-center study, we measured maternal pregnancy serum concentrations of five PFAS: perfluorohexane sulfonic acid (PFHxS), perfluorooctane sulfonic acid (PFOS), perfluorooctanoic acid (PFOA), perfluorononanoic acid (PFNA), perfluorodecanoic acid (PFDA); and FT4 and TSH in 1,048 pregnant women at median gestational week 12 (25th, 75th percentile: 10, 15). Multivariate linear regression models were performed to estimate associations between concentrations of PFAS and FT4 and TSH.
Results
Included women had a mean age of 30.2 ($\pm$ 4.5 SD) years and median pre-pregnancy BMI of 23.5 (5th, 95th percentiles: 19.2, 32.5) kg/^{2}, and 58.7% were nulliparous. A doubling in PFOS, PFOA, and PFNA concentrations was associated with an increment in FT4 concentration by 1.85% (95% CI: 0.66%, 3.05%), 1.29% (95% CI: 0.21%, 2.39%), and 1.70% (95% CI: 0.48%, 2.94%), respectively, in adjusted analyses. A statistically significant dose-response relationship was observed across exposure quartiles for PFOS, PFOA, and PFNA in the association with FT4. No association was found between concentrations of PFAS and TSH in adjusted analyses.
Conclusion and persepectives
Exposure to PFOS, PFOA, and PFNA was associated with higher FT4 concentrations in women during early pregnancy. Our observed associations between exposure to PFAS and FT4 concentrations were small in magnitude, nonetheless, the effects may be greater in populations with higher concentrations of PFAS exposure. The clinical significance of these findings remains to be elucidated. At population level, the demonstrated potential disruption of maternal thyroid hormone status in response to PFAS exposure during early pregnancy may affect offspring neurodevelopment. Hence, the findings are of general public interest, which supports the necessity of a follow-up of offspring in the OCC to assess putative long-term implications on neurodevelopment.

DOI: 10.1530/endoabs.81.OC9.1

OC9.2

Effect of legacy and new generation PFAS on thyrocyte function

Luca De Toni[1], Andrea Di Nisio[1], Stefano Dall'Acqua[2], Stefania Sut[2], Maria Santa Rocca[3], Alberto Ferlin[1] & Carlo Foresta[1]

[1]University of Padova, Department of Medicine, Italy; [2]University of Padova, Department of Pharmacological Sciences, Italy; [3]Padova University Hospital, Italy

Perfluoroalkyl substances (PFASs) have been claimed as thyroid disrupting chemicals since the exposure to several PFASs was significantly associated with thyroid hormones derangements. Demographics such as sex, age, and disease status likely influence the associations between PFASs exposure and thyroid hormones since major hypothyroidism effects were observed among pregnant women and infants. This study aims to evaluate of the possible impact of legacy and new-generation PFAS exposure on the thyroid stimulating hormone (TSH) receptor (THSR)-mediated effects on available cell models of thyrocytes. Based on their surfactant properties, PFAS are supposed to interfere with the cell function through the alteration of the biophysical properties of plasma membrane. FRTL-5 normal rat thyroid follicular cell line was exposed to C6O4, perfluorooctanoic-acid (PFOA) or perfluoro-octan-sulphonate (PFOS) at a concentration ranging from 0 ng/ml (CTRL) to 100 ng/ml for 24 hours and the possible cell accumulation was evaluated by LC-MS/MS. The cell content of all tesetd PFAS was below the limit of detection and, accordingly, membrane fluidity evaluated by Merocyanin 540 (MC540) showed no obvious variation showed no variation compared to CTRL. The quantification of intracellular cAMP levels upon stimulation with 10 mIU/ml of TSH for 30 minutes showed a significant reduction, compared to CTRL sample, when cells were exposed for 24 hours exposure to PFAS. A dose-dependent effect detected for PFOA whilst, for C6O4 and PFOS, a sharp blunt of cAMP was observed at the lowest concentration tested. The possible interaction of TSHR with PFAS was evaluated by computational docking methods, addressing the possible binding of C6O4 or PFOA to TSHR extracellular domain. Molecular dynamics also showed that the receptor bound by C6O4 or PFOA displayed major conformational differences related to the unbound receptor. Specifically, the root-mean-square deviation (RMSF) profile of the atomic positions in LEU100-GLN170 range, the most involved in the binding to TSH, showed a modified flexibility than the unbound structure, particularly for PFOA. The cell iodide uptake upon 10 mIU/ml TSH stimulation was then evaluated with the Sandell-Kolthoff (SK) reaction. Stimulation with TSH was associated with a strong and significant increase of the intracellular iodide levels in CTRL conditions. Differently, the exposure to PFOA was associated with a significant reduction of iodide uptake at the highest concentration tested of 10 ng/ml, whilst C6O4 and PFOS were essentially unaffected. Further gene expression experiments are planned to clarify whether this effect is mediated by a down-regulation of downstream event related to TSHR-signaling.

DOI: 10.1530/endoabs.81.OC9.2

OC9.3

Transcriptional profiling of developing male rat perineum and phallus following exposure to the anti-androgenic fungicide triticonazole

Monica Kam Draskau[1], Camilla Lindgren Schwartz[1], Bertrand Evrard[2], Aurélie Lardenois[2], Andrew Pask[3], Frédéric Chalmel[2] & Terje Svingen[1]

[1]National Food Institute, Technical University of Denmark, Kgs Lyngby, Denmark; [2]Université de Rennes, Inserm, EHESP, Irset (Institut de recherche en santé, environnement et travail), Rennes, France; [3]School of BioSciences, University of Melbourne, Melbourne, Australia

Androgen signaling is essential for male reproductive development and masculinization during fetal life. Developmental exposure to endocrine disrupting chemicals, not least those that disrupt androgen action, can lead to reproductive disorders such as cryptorchidism, hypospadias, and poor fertility. In rodent toxicity studies, as well as human epidemiological studies, a general biomarker for compromised fetal androgen signaling is a shorter

anogenital distance (AGD) in male offspring. Some outstanding questions, however, is if AGD is strictly sensitive to anti-androgenic effects or if other signaling pathways are involved such as estrogen signaling. Similarly, penis development and hypospadias formation also involve additional signaling pathways, but which pathways that are vulnerable to developmental exposure to endocrine disruptors are not well characterized. Therefore, we need a better molecular understanding of how these tissues are regulated and vulnerable to chemical exposures. Triticonazole, an agricultural azole fungicide, inhibits androgen receptor activity in vitro and induces short AGD in male rat offspring following gestational exposure. Though triticonazole has anti-androgenic properties, we previously showed that intrauterine exposure does not affect the transcriptome of the fetal rat testes. We thus investigated the transcriptional effects in the androgen-sensitive fetal male rat perineum and phallus. Pregnant Sprague Dawley rats were exposed via oral gavage to triticonazole (450 mg/kg bw/day) or corn oil (control) from gestational day (GD) 7-21. Fetuses (n=11-12) were collected at GD17 or GD21 and perineum and phallus were isolated. Bulk RNA barcoding and sequencing (BRB-seq) was used to analyze the transcriptomes. The transcriptomes of the developing rat perineum and phallus changed significantly during late gestation, showing distinct regional differences between these adjacent tissues and revealing 2,703 differentially expressed genes (DEGs). The transcriptional changes induced by triticonazole exposure (190 DEGs) were different between perineum and phallus, but also between different stages of development. Interestingly, DEGs not only included several androgen receptor (AR) target genes, but also estrogen receptor (ER) target genes. Our results highlight the importance of considering chemical mode of action and spatiotemporal effects when using transcriptomics approaches in characterizing complex in vivo adverse outcomes in toxicity studies. These data furthermore constitute a rich resource for studying the spatiotemporal gene networks that are involved in the development of rat perineum and phallus and the regulatory networks that can be disrupted upon exposure to xenobiotics that prevent normal masculinization of the male fetus and lead to reproductive disorders.

DOI: 10.1530/endoabs.81.OC9.3

OC9.4

Morphostructural characterization of the testis in a large cohort of men living in highly polluted areas of Campania Region in south Italy: a focus on cadmium exposure

Francesco Garifalos[1], Cristina De Angelis[1], Aldo Di Nunzio[2], Davide Menafra[1], Michele Castoro[1], NUNZIA VERDE[1], Giacomo Galdiero[1], Mariangela Piscopo[1], Claudia Pivonello[1], Renata Simona Auriemma[1], Paolo Chiodini[3], Marco Trifuoggi[2], Annamaria Colao[1,4] & Rosario Pivonello[1,4]

[1]Università Federico II di Napoli, Dipartimento di Medicina Clinica e Chirurgia, Sezione di Endocrinologia, Unità di Andrologia e Medicina della Riproduzione e della Sessualità Maschile e Femminile (FERTISEX-CARES), Naples, Italy; [2]Università degli Studi di Napoli Federico II, Dipartimento di Scienze Chimiche, Naples, Italy; [3]University of Campania "Luigi Vanvitelli", Medical Statistics Unit, Naples, Italy; [4]Università Federico II di Napoli, Unesco Chair for Health Education and Sustainable Development, Naples, Italy

Campania Region has been facing waste management crisis since 1980, characterized by urban, toxic and industrial waste illegal disposal, burying and incineration. Cadmium (Cd) is consistently shown to affect male reproductive function by multiple mechanisms, mostly elucidated in experimental models. The aim of the current single-center, observational, cross-sectional cohort study was to evaluate the prevalence of testis morphostructural alterations in a large cohort of men living in 3 municipalities of Campania Region (Acerra, Afragola, Giugliano) belonging to the high-environmental impact area "Land of Fires", by addressing the potential association with seminal Cd (sCd) levels. Study cohort included 465 males (age range: 14-50 yrs mean: 29.5±7.23 yrs). Morphostructural testis characteristics were assessed by ultrasound and sCd determination was performed in 385 samples by inductively coupled plasma-mass spectrometry. Prevalences of testis morphostructural alterations, unilateral or bilateral, included varicocele (35.4%), hydrocele (34.8%), parenchymal structure inhomogeneity (19%), hypotrophy (14.6%), microlithiasis (2.5%), solid lesions >5 mm (0.2%). Participants with detectable sCd levels (n=128) displayed significantly reduced mean testicular volume (16.56 ± 4.68 vs 17.66 ± 4.34; P=0.0153) and higher prevalence of hypotrophy (21% vs 10%; P=0.0059) and varicocele I-V° grade (47.5% vs 29.5%; P=0.0008), but not clinically relevant varicocele III-V grade (18% vs 11%, P=0.09), together with a slightly higher parenchymal structure prevalence of inhomogeneity (25.8% vs 16.7%; P=0.059) compared to participants with undetectable sCd levels (n=257). Furthermore, a significant difference in mean testicular volume was detected when comparing participants with sCd levels above (n=49) and below median value (n=79) and undetectable sCd levels, respectively (14.88 ± 3.79 vs 17.22 ± 5.03 vs 17.66 ± 4.34; P< 0.001). sCd level was persistently correlated with mean testicular volume after correction for the presence of clinically relevant varicocele (r=-0.185; P=0.001). sCd levels was identified as the best predictor of mean testicular volume in linear regression analysis performed by setting sCd, smoking habit, age and BMI as independent variables. ROC curve analysis highlighted that a sCd level >0.76 µg/l correctly identified testicular hypotrophy with a 60% sensibility and 70% specificity. In conclusion, the current study demonstrated for the first time, in a large cohort of adult males living in high-environmental impact areas of Campania Region, an inverse relationship between sCd levels and mean testicular volume and prevalence of varicocele, independently from age, BMI and smoking habit, therefore further strengthening the concept of gonadal toxicity exerted by Cd, potentially explained by Cd-induced damage to testicular vascular endothelium.

DOI: 10.1530/endoabs.81.OC9.4

OC9.5

Decoding the role of environmental cadmium exposure in thyroid disorders

Aleksandra Buha[1], Dragana Javorac[1], Katarina Baralic[1], Stefan Mandic-Rajcevic[2], Djurdjica Maric[1], Evica Antonijevic-Miljakovic[1], Danijela Djukic-Cosis[1], Milos Zarkovic[3], Biljana Antonijevic[1] & Zorica Bulat[1]

[1]University of Belgrade - Faculty of Pharmacy, Department of Toxicology, Belgrade, Serbia; [2]Institute of Social Medicine and School of Public Health and Health Management, Belgrade, Serbia; [3]Department of Endocrinology, Diabetes and Metabolic Diseases, Belgrade, Serbia

As a ubiquitously present metal, cadmium (Cd) represents a matter of great concern, especially considering its potential thyroid disrupting capacity. The study evaluated the connection between this environmentally relevant metal exposure and thyroid hormone levels. The DecodExpo study enrolled 425 participants (207 males and 218 females) with various disorders (236 participants) and healthy controls (189 participants). Collected blood samples were digested, and Cd levels were determined by flame atomic absorption method (AAS GTA 120 graphite tube atomizer and FAAS, Agilent technologies, Santa Clara, CA, USA). In contrast, thyroid-stimulating hormone (TSH) and free thyroxine (FT4) were measured in serum. The dose-response relationship between Cd in thyroid hormone disturbances was elucidated using a novel Benchmark dose (BMD) approach previously proposed as applicable to human data by the EFSA guidance. The Benchmark response (BMR) was set at 10% in the modeling procedure, expressed as an additional risk in% - an absolute change in response frequency divided by the non-affected fraction in the control population. PROAST 70.1 software was used for the calculations. Out of 435 participants, 76 had various thyroid disorders, and nearest-neighbor matching was performed to select the closest eligible healthy control unit paired with each patient with a thyroid disorder. Blood Cd levels were then compared between the two newly established

groups: cases, and controls using the Man-Whitney-Wilcoxon test. The statistical analyses were performed using the R language and environment for statistical computing with additional packages. The BMD calculations revealed the following confidence interval for FT4 1.22-915 µg/l for men and 0.784-721 µg/l for women, while confidence intervals obtained for TSH were even wider. Although dose dependence was observed for Cd's relationship with investigated hormones, the intervals calculated were wide, suggesting a high level of uncertainty. When comparing Cd levels in two established groups, the medium measured Cd blood level was 2.185 µg/l in cases while measured levels were 1.794 µg/l in corresponding controls, with no statistical differences observed between the Cd levels in these two groups. However, lower confidence intervals of BMD calculated for FT4 and TSH in both sexes were lower than the medium blood Cd levels obtained for the entire study, i.e., 1.8 µg/l (0.03-5.80 µg/l), which could suggest an additional risk of thyroid hormone disturbances due to Cd environmental exposure. Even though inconclusive, the results of this study urge the need for further investigations to elucidate the role of environmental exposure to Cd in thyroid disorders.

DOI: 10.1530/endoabs.81.OC9.5

OC9.6

Iodine nutrition among adolescent Faroese comply with recommendations – are we home-safe?

Herborg Líggjasardóttir Johannesen[1], Stig Andersen[2], Kári Rubek Nielsen[3], Pál Weihe[4], Maria Skaalum Petersen[4] & Anna Sofía Veyhe[4]
[1]The National Hospital of the Faroe Islands, Department of Endocrinology and Medicine, Torshavn, Faroe Islands; [2]Aalborg University, Department of Clinical Medicine,, Aalborg, Denmark; [3]The National Hospital of the Faroe Islands, Department of Gasteroenterology and Medicine, Torshavn, Faroe Islands; [4]The Faroese Hospital System, Department of Occupational Medicine and Public Health, Torshavn, Faroe Islands

Introduction
Iodine nutrition is critical for human health. In recent years the main focus was on the developing brain during pregnancy. In addition, iodine nutrition is essential for growth and development during adolescence. Iodine nutrition was recently low within the recommended range among adult Faroese living on local, iodine-rich marine food items. Dietary habits among young generations are drifting away from local foods, and this raises a concern that led us to perform the first study of iodine nutrition among Faroese teenagers.
Method
We surveyed 14-year olds aiming for the number of participants recommended for a 90% precision of the estimated iodine nutrition level: Urin from one hundred twenty-nine girls ($n=65$) and boys ($n=64$) sampled in iodine-free containers. Iodine was measured using standard laboratory methods using the ceri/arsen method after alkaline ashing and creatinine. We calculated the iodine/creatinine ratio to adjust for dilution. A food frequency questionnaire recorded intake of iodine-rich foods.
Results
The median urinary iodine concentration was 166 µg/l, creatinine adjusted 124 µg/g. Iodine was in recommended range in 102 urine samples (79%), above the recommended range in 22 (17%), and in the range of insufficiency in 4%. No single sample suggested severe iodine deficiency. The urinary iodine concentration was markedly higher in those who reported higher "fish dinners per week" than those who reported limited or no fish intake.
Conclusion
Our nationwide study demonstrated Faroese teenagers to be iodine replete according to the WHO recommendations. However, the Faroese may have adapted to a high iodine intake from the formerly frequent intake of marine foods. Dietary habits change with new generations, and surveying iodine deficiency disorders is needed. In addition, the changing dietary habits emphasise the need for continuous monitoring of iodine nutrition.

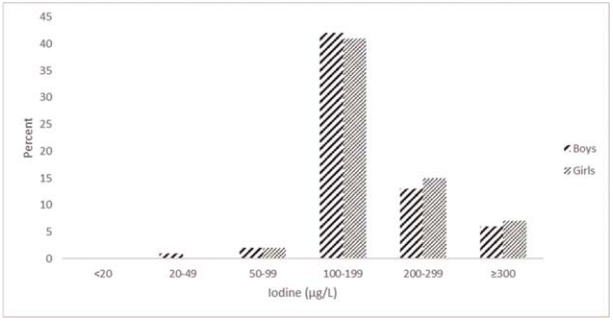


Figure 1 Proportions of urinary iodine concentrations among 14-year-old Faroese boys and girls, from a population-based sample of 129 participants divided into the following groups: moderate (20-49), mild deficiency (50-99), adequate (100-199), slightly increased (200-299) and excess (300+).

DOI: 10.1530/endoabs.81.OC9.6

Diabetes, Obesity, Metabolism and Nutrition 3

OC10.1

Single-cell molecular and functional mapping of POMC neurons in obesity: a multi-modal approach

Stéphane Léon[1], Vincent Simon[1], Thomas H Lee[1], Samantha Clark[1], Nathalie Dupuy[1], Yves Le Feuvre[1], Xavier Fioramonti[2], Daniela Cota[1] & Carmelo Quarta[1]
[1]University of Bordeaux, INSERM, Neurocentre Magendie, U1215, Bordeaux, France; [2]University of Bordeaux, INRAe, NutriNeuro, UMR 1286, Bordeaux, France

The brain plays a crucial role in maintaining the body's energy needs, a process involving the activity of a group of hypothalamic neurons that express the neuropeptidergic marker pro-opiomelanocortin (POMC). POMC neuronal dysfunction can cause obesity and its associated metabolic sequelae. However, this population of neurons is highly diverse at a molecular and functional level, and whether or not such heterogeneity is implicated in disease establishment or progression has yet to be elucidated. Here, using a lineage-tracing approach in combination with histological and electrophysiological tools, we have characterized POMC neuronal cells at a single-cell resolution in control of lean and diet-induced obese (DIO) mice. Thanks to this genetic strategy, we 'traced' with a reporter protein POMC neurons in adult mice, thus studying these neuronal cells independently from the expression of their main marker POMC. Different histological techniques, including immunohistochemistry, fluorescent in-situ hybridization, and RNAscope, have been used to cluster genetically 'traced' POMC neuronal cells based on their expression of the main marker POMC. These different approaches consistently allowed the identification of a previously uncharacterized sub-population that expresses negligible POMC mRNA and protein levels, which we named Ghost-POMC neurons. We also observed that Ghost-POMC neurons are insensitive to acute nutritional cues (fasting and refeeding) relative to 'classic' POMC positive neurons. Intriguingly, DIO mice presented an increased number of Ghost-POMC neurons relative to control animals. Furthermore, we developed an approach that combines whole-cell patch-clamp of traced POMC neurons with the subsequent molecular profiling of the patched cell by single-cell qPCR. Thanks to this approach, we observed that DIO leads to electrical alterations only in a fraction of POMC neurons expressing undetectable levels of POMC mRNA, which is reminiscent of the Ghost population previously identified by histological techniques. Thus, Ghost-POMC neurons might constitute a novel subpopulation of POMC neurons that undergo dysfunction in response to prolonged dietary cues, perhaps contributing to obesity establishment or progression.
Keywords: POMC neurons; heterogeneity; neuroanatomy; electrophysiology.
DOI: 10.1530/endoabs.81.OC10.1

OC10.2

Success in implementing changes in macronutrients intake in a high-protein and high-unsaturated fatty acids dietary intervention: 36-months results of the NutriAct randomized controlled multi-center trial

Laura Pletsch-Borba[1], Charlotte Wernicke[1], Nina Meyer[1], Thu Nguyen[1], Anne Pohrt[2], Christiana Gerbracht[3], Andreas Pfeiffer[1], Joachim Spranger[1] & Knut Mai[1]
[1]Charité Universitätsmedizin Berlin, Endocrinology and Metabolism, Berlin, Germany; [2]Charité Universitätsmedizin Berlin, Institute of Biometry and Clinical Epidemiology, Germany; [3]Human Study Center, German Institute of Human Nutrition Potsdam-Rehbrücke, Germany

Background & Aims
NutriAct is a 36-month randomized controlled multi-center trial aiming to analyze the effects of a dietary pattern focusing on a high-protein and high-unsaturated fatty acids (UFA) intake on healthy aging. We aimed to explore changes in intake of macronutrients and determine factors associated with a successful modulation of dietary pattern after 36 months in elderly community dwelling participants.
Methods
502 participants were randomized into a usual care control group including dietary recommendations of the German Nutrition Society or an intervention group, which used supplementation of rapeseed oil and specifically designed foods as well as repetitive advices to implement a food pattern based on high intake of predominantly plant proteins and UFA. Food intake was repeatedly assessed by 3-day food records at months 0, 3, 6, 12, 24 and 36 months. Linear regression models were carried out to investigate differences in changes in macronutrients intake between the intervention arms and determinants of modulation of dietary pattern during the intervention in 36 months.
Results
148 intervention and 164 control participants (median age 66 y, 36% males) with available food records at baseline and at month 36 and were included. The intervention resulted in higher intake of protein, mono- and polyunsaturated fatty acids (MUFA and PUFA) and fiber, and lower carbohydrate and saturated fat consumption (all $P < 0.05$). While individuals who were already at baseline closer to the NutriAct pattern also achieved a diet closer to the proposed pattern at month 36, the strongest relative changes of dietary behavior were seen in those with dietary patterns further away from the proposed pattern at baseline. Sex, age, baseline BMI, education, comorbidities, smoking, cognitive status and shared household were not associated to a higher implementation of the proposed diet.
Conclusions
A successfully modification of dietary pattern was achieved by the intervention within 36 months. Baseline dietary habits were substantial determinants predicting change in dietary pattern.

Table. Changes in macronutrients intake between baseline and month 36 between intervention and control groups

Macronutrient	Beta coefficient (95% CI)	*P*-value
Protein (%E)	2.35 (1.44, 3.25)	<0.01
Total fat (%E)	2.70 (1.00, 4.39)	<0.01
Carbohydrate (%E)	-4.83 (-6.60, -3.05)	<0.01
Sat. Fatty acids (%E)	-2.30 (-3.24, -1.32)	<0.01
PUFA (%E)	3.57 (2.70, 4.44)	<0.01
MUFA (%E)	0.82 (0.08, 1.60)	0.03
Fiber (%E)	3.64 (1.72, 5.56)	<0.01

DOI: 10.1530/endoabs.81.OC10.2

OC10.3

Glucose-dependent insulin secretion is regulated by mitochondrial-associated cannabinoid receptor type 1 (mtCB1)

Camille Allard[1], Philippe Zizzari[1], Samantha Clark[1], Nathalie Dupuy[1], Francisco-Javier Bermudez-Silva[2], Concepción Lillo Delgado[3], Luigi Bellocchio[4], Giovanni Marsicano[4], Carmelo Quarta[1] & Daniela Cota[1]
[1]University of Bordeaux, Neurocentre Magendie, INSERM U1215, Team Energy Balance and Obesity, Bordeaux, France; [2]Laboratorio de Investigación-Hormonas, Hospital Regional de Málaga – IBIMA, Malaga, Spain; [3]Instituto de Neurociencias de Castilla y León (INCyL), Universidad de Salamanca, Salamanca, Spain; [4]University of Bordeaux, Neurocentre Magendie, INSERM U1215, Team Endocannabinoids and Neuromodulation, Bordeaux, France

Type 2 diabetes is among the most prevalent chronic diseases worldwide. Further research is needed to identify new mechanisms that may help preserve the function of insulin-secreting pancreatic β-cells. The cannabinoid receptors type 1 (CB1) and their endogenous ligands, endocannabinoids, exert a key role in regulating of glucose homeostasis, β-cells function, and insulin secretion. Intriguingly, CB1 is not only located at the plasma membrane (pmCB1), but also at the mitochondrial membrane component (mtCB1), albeit the relative contribution of subcellular CB1 signaling on β-cell function and glucose control has yet to be determined. This study aimed to uncover the relative role(s) of pmCB1 and mtCB1 in β-cell physiopathology, with a particular focus on the differential impact on insulin secretion and mitochondrial function. For this purpose, we used an animal model expressing a mutant form of CB1 (named DN22-CB1) which lacks in vivo mitochondrial localization and functions but retains pmCB1-related signaling. DN22-CB1 mice present no difference in body weight and insulin sensitivity compared to control littermates, nor when fed chow or a hypercaloric high-fat diet (HFD). However, chow-fed DN22-CB1 mice are hyperglycemic after an overnight fast, and following a glucose load. Hyperglycemia in DN22-CB1 mice is then further worsened under HFD feeding. Regardless the diet, DN22-CB1 mice display reduced in vivo plasma insulin relative to controls. Glucose-stimulated insulin secretion (GSIS) data obtained ex-vivo from isolated islets of chow-fed DN22-CB1, full CB1-KO and control littermates suggest that pmCB1 and mtCB1 act as Ying-Yang partners to influence insulin secretion. Indeed, CB1KO islets display an increased GSIS, whereas GSIS and mitochondrial respiration is blunted in DN22-CB1 islets, with no significant changes in cytosolic calcium signaling. Our work pinpoints a novel molecular mechanism whereby subcellular CB1-dependent signaling orchestrate mitochondrial functions and glucose-dependent insulin secretion in β-cells to influence systemic glucose homeostasis. These findings might have implications for type 2 diabetes pharmacotherapy, thus resurrecting the interest in the use of CB1 receptor modulators in metabolic diseases.

DOI: 10.1530/endoabs.81.OC10.3

OC10.4

Variants in obesity-related genes in a population with early-onset obesity

Patrick Kleyn, Ilia Ichetovkin & Ida H Moeller
Rhythm Pharmaceuticals, Boston, United States

Introduction
Genetic testing can improve the diagnosis of rare genetic diseases of obesity and identify patients who may benefit from targeted therapeutic intervention. For example, patients with genetic defects in the melanocortin-4 (MC4R) pathway may present with severe early-onset obesity and hyperphagia. Historically, however, genetic testing in patients with obesity has been limited. The Uncovering Rare Obesity® diagnostic genetic testing program aims to enhance access to genetic testing for these patients. The frequency of rare genetic variants in this clinical patient population is currently unknown.
Methods
We sequenced 8599 individuals with severe, early-onset obesity as part of the US-based Uncovering Rare Obesity® program. Genes selected include those with well-established associations with obesity, as well as genes associated with the MC4R pathway. In this program, we sequenced 7811 individuals for 40 genes, and recently expanded the gene panel to include an additional 39 genes and the 16p11.2 chromosomal region; 788 individuals have been sequenced on the broader panel. Yield estimates were weighted by the number of individuals sequenced for each gene.
Results
Integrating across the two panels using weighted yield estimates, 54.6% of sequenced individuals had variants that may qualify them for commercial or investigational treatment with the MC4R agonist setmelanotide. An additional 9.9% of individuals had variants not eligible for setmelanotide treatment, but that may support a genetic diagnosis of obesity. Overall, 2.7% of individuals carried pathogenic or likely pathogenic variants that also met mode of inheritance criteria (2 or more alleles in autosomal recessive conditions and 1 or more alleles in autosomal dominant conditions).
Conclusions
In this selected cohort of individuals with severe, early-onset obesity, 64.5% carried potentially clinically relevant variants. As additional data become available about the investigational genes and obesity, and/or as new obesity-related genes are identified, these estimates may change. Genetic testing of patients with severe obesity, particularly those with a history of early-onset

obesity suggestive of a potential genetic origin, may therefore be an important component of understanding the etiology of these patients' phenotypes, and may potentially impact the course of care for these patients.

DOI: 10.1530/endoabs.81.OC10.4

OC10.5

Splicing dysregulation is associated with aggresive and metabolic-associated liver disease-derived hepatocellular carcinoma

Natalia Hermán Sánchez[1,2,3,4], Juan L López-Cánovas[1,2,3,4], Mercedes del Rio-Morenos[1,2,3,4], Víctor Amado[1,5,6], Manuel de la Mata[1,5,6], Manuel Rodríguez-Perálvarez[1,5,6], Raúl M Luque[1,2,3,4] & Manuel D Gahete[1,2,3,4]

[1]Maimónides Institute of Biomedical Research of Córdoba (IMIBIC), Córdoba, Spain; [2]University of Córdoba, Department of Cell Biology, Physiology and Immunology, Córdoba, Spain; [3]Reina Sofía University Hospital, Córdoba, Spain; [4]CIBER Pathophysiology of Obesity and Nutrition (CIBERobn), Córdoba, Spain; [5]Reina Sofía University Hospital, Department of Hepatology and Liver Transplantation, Córdoba, Spain; [6]CIBER Hepatic and Digestive Diseases (CIBERehd), Córdoba, Spain

Metabolic-associated fatty liver disease (MAFLD) is a growing cause of hepatocellular carcinoma (HCC), but the molecular mechanisms associated with the pathological progression from MAFLD to HCC are still to be fully elucidated. The genomic and transcriptomic profile of HCC samples have been widely described; however, the proteomic landscape of MAFLD-derived HCC samples is mostly unknown. Here, we sought to perform the first quantitative proteomic analysis of HCC samples from different aetiologies using a representative, well-characterized cohort of patients. To that end, cytosolic and nuclear proteome of liver tissues from HCC patients ($n=42$; HCC vs adjacent tissue) and healthy controls ($n=5$) were determined by SWATH-MS-based proteomics and the results were analyzed using different bioinformatics tools. Non-targeted proteomics revealed the dysregulation of the cytosolic ($n=507$ proteins) and nuclear ($n=925$ proteins) tumor proteomes. Enrichment analysis revealed altered cellular functions such as mRNA processing, including mRNA splicing. Indeed, the dysregulation of the splicing machinery was confirmed in two retrospective human cohorts [cohort 1: HCC vs adjacent ($n=93$); cohort 2: HCC vs adjacent ($n=58$), cirrhosis ($n=39$), and healthy livers ($n=5$)] and in different *in silico* HCC cohorts. Specifically, from the 94 splicing factors identified in the proteomic analysis, 31 were validated in the retrospective and *in silico* cohorts, and were associated with key clinical parameters of aggresiveness (tumoral diameter, survival). Interestingly, some of these splicing factors (ej. KHSRP) were associated to metabolic alterations such as diabetes. When comparing between aetologies, we identified cellular pathways (ej. "nucleotide excision repair", EIF4 and p70S6K signalling) speciffically dysregulated in MAFLD-derived HCC patients, and a battery of more than 20 splicing factors specifically dysregulated in this aetiology [e.g. SNRPD1 and LSM2, two critical components of the small nucleolar ribonucleoproteins (snRNPs) U1/U2/U4/U5 and U6]. Accordingly, culstering analysis defined a HCC subgroup with lower survival and higher recurrence that was associated to the dysregulation of the splicing machinery and included all patients with MAFLD-derived HCC. Finally, *in vitro* assays (proliferation, colonies/tumorspheres) were performed in liver cancer cell lines (HepG2, Hep3B, SNU-387) after silencing *SNRPD1* and *LSM2* with specific siRNAs. Remarkably, *in vitro* silencing of these splicing factors significantly reduced proliferation and dedifferentiation capacity in cancer cells. Our study demonstrates the usefullness of quantitative proteomics for the identification of tumoral subgroups in HCC and the potential of the splicing machinery as a tool for HCC management, specially in less described aetiologies, such as MAFLD.

Fundings: ISCIII (PI20/01301), JdA (PEMP-0036-2020, BIO-0139), FSEEN and CIBERobn.

DOI: 10.1530/endoabs.81.OC10.5

OC10.6

Opposite actions of LEAP-2 and ghrelin in energy homeostasis

Sabela Casado Masa[1,2,3], Tadeu De Oliveira Diz[1,3], Marta Varela Miguéns[1], Carlos Diéguez González[1,2,3] & Sulay Tovar Carro[1,2,3]

[1]Centro Singular de Investigación en Medicina Molecular y Enfermedades Crónicas (CIMUS)-Universidad de Santiago de Compostela, Fisiología, Santiago de Compostela, Spain; [2]Centro de Investigación Biomédica en Red de la Fisiopatología de la Obesidad y la Nutrición (CIBERobn), Spain; [3]Instituto de Investigación Sanitaria de Santiago de Compostela (IDIS), Santiago de Compostela, Spain

Liver-expressed antimicrobial peptide 2 (LEAP-2) has been recently characterized as an endogenous GHSR1a antagonist. LEAP-2 is produced mainly in the liver, and it was described that an acute ghrelin administration blocks food intake, GH release and normalize glucose levels during chronic caloric restriction. For this reason, it could be considered as a key endocrine factor in the regulation of systemic energy metabolism. Nevertheless, the exact mechanism of action is still unknown. Our aim was to investigate the central LEAP-2 effects in energy homeostasis in mice with standard diet and in a ghrelin resistance mice model induced by diet. We used male C57BL/6 mice fed standard or high fat diet (60% fat, 12 weeks). We performance an acute or chronic ICV administration of vehicle, ghrelin, LEAP-2 or ghrelin and LEAP-2. Food intake, body weight and circulating cholesterol and leptin plasma levels were measured. Human HEPG2 hepatocytes treated with oleic acid were used and they were co-treated with LEAP-2. Hepatic fat accumulation was analysed using oil red-O staining. Genes related to glucose and lipid metabolism were studied by qPCR. Statistical analysis conducted through t-student and ANOVA. The results obtained showed that LEAP-2 inhibits food intake, and body weight in all the mice models studied and in an acute and chronic treatment. Moreover, chronic treatment is able to decrease the orexigenic response of ghrelin when they are co-administered. Furthermore, LEAP-2 decreases leptin and cholesterol plasma levels, and decreases the liver lipid content. When we analysed human hepatocytes treated with LEAP-2, they exhibit a lower lipid accumulation with a reduction in the expression of genes of gluconeogenesis and *de novo* lipogenesis in standard conditions and under oleic acid effect. As a conclusion, chronic central administration of LEAP-2 in mice antagonizes the major effects of ghrelin in vivo and the co-administration with ghrelin attenuates the ghrelin orexigenic and obesogenic effects, in a diet independent manner. Moreover, it decreases fat accumulation directly in human hepatic cells. These novel results place LEAP-2 as a counter-regulatory hormone in the ghrelin system, and as a promising therapeutic target in the treatment of obesity, MAFLD and other metabolic diseases.

DOI: 10.1530/endoabs.81.OC10.6

Thyroid 2

OC11.1

Thr92Ala polymorphism of the type 2 deiodinase (DIO2) is associated with higher risk of iatrogenic thyrotoxicosis in thyroidectomized subjects treated with levothyroxine and liothyronine

Gisella Boselli[1,2], Gianluca Margiotta[1,2], Rossella Corleto[1,2], Maria Laura Monzani[1,2], Andrea Craparo[1,2], Michela Locaso[1,2], Samantha Sperduti[1,3], Manuela Simoni[1,2], Vincenzo Rochira[1,2], Daniele Santi[1,2] & Giulia Brigante[1,2]

[1]University of Modena and Reggio Emilia, Department of Biomedical, Metabolic and Neural Sciences, Modena, Italy; [2]Azienda Ospedaliero-Universitaria of Modena, Department of Medical Specialities, Unit of Endocrinology, Modena, Italy; [3]University of Modena e Reggio Emilia, Center for Genomic Research, Modena, Italy

Introduction

Hypothyroidism treatment is classically based on levothyroxine (LT4). However, 10% of hypothyroid patients treated with LT4 complain of hypothyroidism symptoms, despite normal thyroid stimulating hormone (TSH) serum levels. This "peripheral hypothyroidism" has been linked to decreased availability of free triiodothyronine (fT3), likely related to single nucleotide polymorphisms (SNP) in deiodinase genes (*DIO*), reducing enzymatic activity. Since *Thr92Ala-DIO2* was associated to altered responsiveness to LT4, combined levothyroxine/liothyronine (LT4/lT3) therapy was suggested to improve quality of life in hypothyroid patients encoding *Thr92Ala-DIO2*.

Aims

To evaluate the influence of *Thr92Ala-DIO2* variant on thyroid therapeutic compensation in thyroidectomized subjects treated with LT4 or LT4/lT3.

Methods

An interim analysis of a prospective, randomized, placebo-controlled, double-blinded clinical trial was performed. Totally thyroidectomized patients treated with LT4 and with TSH levels within reference range in the previous 3 months were enrolled. Subjects were randomized in two groups: personalized-combined-twice-daily therapy with LT4/lT3 at 13-20:1 ratio (study group) and LT4 + placebo (control group). Subjects were evaluated three times during the 6-month treatment. Iatrogenic thyrotoxicosis and hypothyroidism rates were assessed at each visit, measuring serum levels of TSH, fT4 and fT3. DNA was extracted from blood samples and the DIO2 genotype was analysed by Sanger's sequencing. The *Thr92Ala-DIO2* rate was calculated in both groups.

Results

A total of 139 patients (age 55.6±12.1 years, TSH 1.3±1.4 microIU/ml) were enrolled, 70 in the study (age 55.1±10.9 years) and 69

in the control group (age 56.0±13.4 years). *Thr92Ala-DIO2* frequency (11.4%) was similar to general population (12-36%). Drop-out rate did not differ between groups (11.4 vs 14.5%, respectively, $P=0.591$) and no difference was found in biochemical thyroid function examinations (considering also fT3/fT4 ratio) and LT4 pro-Kg dosage comparing study and control groups at baseline. Combined LT4/lT3 therapy resulted in more frequent iatrogenic thyrotoxicosis than LT4 monotherapy (9.8% vs 2.2%; $P<0.05$), with a significantly higher incidence in *Thr92Ala-DIO2* carriers. More frequent dose adjustments were required in the study group compared to controls (44.5% vs 22.5%; $P<0.001$) and, among cases, in those with *Thr92Ala-DIO2 compared to wild-type* (52.0% vs 37.6%; $P<0.05$).

Conclusion

Thr92Ala-DIO2 variant seems to have no influence on LT4 monotherapy effectiveness. In our interim analysis, carriers of *Thr92Ala-DIO2* are at higher risk of iatrogenic thyrotoxicosis when treated with LT4/lT3: this result surprisingly suggest an increased enzymatic activity in SNP carriers. Accordingly, the management of these patients is more challenging, requiring more frequent dose adjustments in the first six months of therapy.

DOI: 10.1530/endoabs.81.OC11.1

OC11.2

What you choose makes the difference: the first medical therapy for amiodarone-induced thyrotoxicosis has significant implications on cardiovascular events and hospitalizations

Daniele Cappellani[1], Giada Cosentino[1], Riccardo Morganti[2], Luca Manetti[1], Luigi Bartalena[3] & Fausto Bogazzi[1]

[1]University of Pisa, Department of Clinical and Experimental Medicine, Pisa, Italy; [2]University Hospital of Pisa, Unit of Statistics, Pisa, Italy; [3]University of Insubria, Department of Medicine and Surgery, Varese, Italy

Context

Amiodarone is a widely used anti-arrhythmic medication, however associated with a 15-20% rate of thyroid adverse effects. Amiodarone-induced thyrotoxicosis (AIT) is a complex disease due to diagnostic difficulties and therapeutic challenges. AIT patients often receive initial therapy for thyrotoxicosis before admission to a referral center. Whether the first-line medical therapy (i.e. therapies for thyrotoxicosis at first diagnosis of AIT) may affect the outcome of AIT patients is unknown.

Study design

Single-center historical-prospective cohort study of 313 AIT patients admitted to our university referral center for amiodarone-induced thyroid disorders.

Methods

Clinical and biochemical data at first diagnosis, at a referral center, and during the course of AIT were collected. The medical figures responsible for the first approach to the disease were recorded. Primary outcomes were cardiovascular (CV) events and hospitalizations. First-line therapies were appropriate when included glucocorticoids for type 2 AIT and methimazole for type 1 AIT at the approved dosage, either alone (optimal medical therapy, OMT) or in combination (right-dose combination therapy, RCT). Other therapies were considered not appropriate, including no therapy. Duration of exposure to thyrotoxicosis was the time from first diagnosis of AIT to its remission.

Results

34.5% patients received appropriate therapy (28.1% OMT and 6.4% RCT), whereas non-appropriate therapies accounted for 65.6% of cases: specifically most patients originally approached by general practitioners and cardiologists received no therapy at all (56.9% and 50% respectively), whereas inappropriate therapies for the AIT-type (i.e. glucocorticoids for type 1 AIT and methimazole for type 2 AIT) was the most common therapy for patients originally approached by endocrinologists outside the referral center. CV events, and hospitalizations were more frequent in patients who received non-appropriate therapies (33.2% vs 4.5%, and 24.9% vs 6.5%, respectively; $P<0.0001$ for both). Appropriate therapies reduced serum thyroid hormone concentrations ($P=0.018$) at variance with non-appropriate therapies. The duration of exposure to thyrotoxicosis was longer in patients receiving non appropriate therapies and was a risk factor for arrhythmias (HR 1.004, $P=0.0008$), MACEs (HR 1.004, $P=0.020$) and hospitalizations (HR 1.006, $P<.0001$).

Conclusions

The first medical therapy of AIT influences the exposure to thyrotoxicosis and the occurrence of cardiovascular events and hospitalizations.

DOI: 10.1530/endoabs.81.OC11.2

OC11.3

PD-1/PD-L1 inhibitors and immune-related thyroid toxicity according to pre-existing thyroid dysfunction and TPO antibody levels: a single centre experience

Giovanni Gruosso[1], Alice Anna Nervo[1], Sara Basile[1], Enrica Migliore[2], Valentina D'Angelo[1], Matteo Ferrari[1], Anna Roux[1], Alessandro Piovesan[1] & Emanuela Arvat[1]

[1]Azienda Ospedaliero-Universitaria Città della Salute e della Scienza di Torino, Oncological Endocrinology Unit, Torino, Italy; [2]Azienda Ospedaliero-Universitaria Città della Salute e della Scienza di Torino, Cancer Epidemiology Unit, Torino, Italy

Background

Immune checkpoint inhibitors (ICIs) have modified the outcome of several advanced malignancies. Thyroid dysfunctions (DYSTHYR) are the most common endocrine immune-related adverse events (IRAEs) during treatment with the programmed cell death protein-1 (PD-1) and its ligand (PD-L1) inhibitors. Data regarding predictive biomarkers enabling stratification of DYSTHYR risk are still limited.

Patients and methods

We retrospectively analyzed patients who started treatment with PD-1/PD-L1 inhibitors between 2017 and 2020 at Città della Salute e della Scienza Hospital (Department of Oncology). Both the onset of new DYSTHYR during ICI and the worsening of pre-existing DYSTHYR were recorded; patients with central hypothyroidism were excluded. In subjects without pre-existing hormonal thyroid alterations, it was evaluated the relationship between thyroid peroxidase antibody (Ab-TPO) level before the start of ICI and the onset of DYSTHYR during treatment. These patients were divided into two groups (MED-TPO+ and MED-TPO-) using the median Ab-TPO titer of the population as a cut-off value.

Results

In our cohort (median age 67 years, 70.7% males, 49.4% lung cancer, 95.4% anti PD-1 therapy), we observed a high frequency of DYSTHYR (80 out of 324 patients; 24.7%); thyrotoxicosis was detected in 7.7% of the population, while hypothyroidism occurred in 21% of subjects (after a median time of 1.8 and 3.7 months, respectively). Among cases with pre-existing thyroid hormonal alterations (14.5% of the sample), the worsening of DYSTHYR was found in 42.6% of cases after the start of ICI; the risk of DYSTHYR was significantly higher in comparison to patients without a thyroid disease history (OR 2.68 at univariate analysis, P 0.03). Baseline Ab-TPO levels were available for 97 patients (Ab-TPO median value 12 U/ml). Mean AbTPO level in the group with DYSTHYR during ICI (42.5 U/ml) was significantly higher than AbTPO titer in patients without DYSTHYR (16.1 U/ml, $P=0.0003$). DYSTHYR after the start of ICI occurred in 33.9% of MED-TPO+ patients vs 7.9% of MED-TPO- subjects ($P=0.003$); a significantly increased risk of developing DYSTHYR was observed in MED-TPO+ patients when compared to MED-TPO- cases (OR 5.98 at univariate analysis; $P=0.007$).

Conclusion

Our data confirm the high frequency of DYSTHYR (mostly hypothyroidism) during PD1/PD-L1 inhibitors. We observed a greater risk of DISTHYR during ICI in patients with pre-existing thyroid function alterations and in case of higher baseline Ab-TPO level. These results may help the oncologist to identify the patients who are most likely to require an endocrinologist consultation during ICIs.

DOI: 10.1530/endoabs.81.OC11.3

OC11.4

Association of thyroid function and TPO positivity with the risk of postpartum depression: a population-based cohort study and systematic review

Federica Sileo[1,2], Joris Osinga[3,4], Edward Visser[3,4], Arash Derakhshan[3,4], valeria citterio[1,2], Luca Persani[1,2] & Tim Korevaar[3,4]

[1]University of Milan, Milan, Italy, Department of Biotechnology and Experimental Medicine, Milan, Italy; [2]IRCCS Istituto Auxologico Italiano, Milan, Italy, Lab of Endocrine and Metabolic Research, Department of Endocrine and Metabolic Diseases, Milan, Italy; [3]Erasmus Medical Center, Postbus 2040, 3000 CA, Rotterdam, The Netherlands, Department of Internal Medicine, Rotterdam, Netherlands; [4]Erasmus Medical Center, Postbus 2040, 3000 CA, Rotterdam, The Netherlands, Academic Center for Thyroid Diseases, Rotterdam, Netherlands

Background

Postpartum depression (PPD) is a common mental health disorder with a major impact on maternal health and wellbeing and offspring development. Thyroperoxidase antibody (TPOAb) positivity is a major risk factor for

postpartum thyroiditis and via this link, it is hypothesized that TPOAb positivity is a risk factor for PPD. However, the results of currently available single center studies are heterogeneous and affected by major study limitations.
Objective
To examine the association of TPOAb and thyroid function with the risk of PPD.
Methods
In the Generation R Study, a population-based prospective birth cohort in Rotterdam, The Netherlands, we measured TSH, FT4 and TPOAb in blood samples collected between 8-18 weeks of pregnancy. Postpartum depressive symptoms were assessed with the Edinburgh Postpartum Depression Scale (EPDS) at 2 months postpartum and with the Brief Symptom Inventory (BSI) at 2, 6 and 36 months postpartum. In addition, we performed a systematic review of literature assessing the association of thyroid function and/or TPOAb positivity with risk of PPD.
Results
There was no association of TSH or FT4 levels with the risk of postpartum depression (log_TSH OR:0.79, 95%CI 0.56-1.13, $P=0.20$; fT4 OR:1.02, 95%CI 0.96-1.08, $P=0.57$). There was also no association of TPOAb positivity with PPD (OR:0.79, 95%CI 0.39-1.19, $P=0.39$). Additional analyses assessed an impaired thyroidal response to hCG stimulation and defined the combined effects of a high hCG with either a high TSH or low FT4 as an alternative marker of TPOAb positivity. We identified that an impaired thyroidal response to hCG stimulation was associated with a lower risk of PPD (P for interaction TSH $=0.04$ and FT4 $=0.06$). In our systematic review, ten out of 1219 identified articles were included: four studies showed an association of TPOAb positivity with PPD, two showed an association of thyroid function with PPD, the remaining studies showed no association of either thyroid function or autoimmunity with PPD.
Conclusions
Our original study is by far the largest study on this topic showing that neither TPOAb positivity nor TSH or FT4 were associated with PPD. Our systematic review revealed high heterogeneity and suboptimal methodological quality in the current literature, but overall does not support a link with PPD. Although TPOAb positive women should be monitored for postpartum thyroiditis, there does not seem to be an indication to screen for postpartum depression. Further research should focus on other factors potentially involved in the etiology of PPD.

DOI: 10.1530/endoabs.81.OC11.4

OC11.5

Positive correlation of thyroid nodule cytology with molecular profiling – analysis of over 4000 nodules from multicenter study and systematic literature review

Idit Tessler[1], Isaac Shochat[2], Oded Cohen[3], Richard J Payne[4] & Galit Avior[1]
[1]Sheba Medical Center, Department of Otolaryngology Head and Neck Surgery, Ramat Gan, Israel; [2]Hillel Yaffe Medical Center, Hadera, Israel; [3]Hebrew University, Jerusalem, Israel; [4]Sir Mortimer B. Davis-Jewish General Hospital, McGill University, Department of Otolaryngology Head and Neck Surgery, Montréal, QC, Canada

Objectives
Despite the increasing role of molecular profiling, the association between mutation expression and pre-operative cytology for thyroid nodules has not been established.
Methods
We collected data on patients who underwent molecular profiling of thyroid nodules in Bethesda categories III to VI from two tertiary academic hospitals and via systematic literature review. We tested the associations between Bethesda categories and molecular mutation stratified by risk levels, according to the 2015 ATA guidelines. When thyroidectomy was preformed, we also evaluated association with postoperative diagnosis and aggressivity of disease based on histopathological variants, nodal metastasis or extra-thyroidal extension.
Results
We analyzed data from 452 nodules in our institutional cohort and 3912 nodules from the systematic literature review. A significant positive correlation was found between Bethesda categories and mutations, demonstrated by an increase in the intermediate to high-risk mutation rate in the higher BSRTC categories (Rs $=$ 0.660, $P\leq$ 0.001). In the institutional cohort malignancy rate for BSRTC III and IV was 56.7% and 75.7%, respectively. The most common mutation was BRAFV600E, with 95.9% (93/97) of those patients in Bethesda category V or VI ($P<.001$). All had confirmed thyroid cancer on pathology, with aggressive tumor behavior in most (60%). Patients with low-risk mutation, as H, K or N RAS alterations showed an association with Bethesda categories III and IV ($P\leq.01$). In mutation-negative nodules of BSATC III to VI who underwent surgery, we found a lower incidence of aggressive thyroid cancer compared to those with an identified mutation (12.6% vs 44.3%, $P<.01$).
Conclusion
We found positive correlation between cytology results and molecular testing. These findings may provide clinicians with better interpretation for BSRTC results and may contribute to the identification of aggressive thyroid nodules associated with indeterminate Bethesda categories.

DOI: 10.1530/endoabs.81.OC11.5

OC11.6

A new grading system for medullary thyroid cancer

Alessandro Prete[1], Carla Gambale[1], Liborio Torregrossa[2], Valeria Bottici[1], Virginia Cappagli[1], Fulvio Basolo[2], Rossella Elisei[1] & Antonio Matrone[1]
[1]Unit of Endocrinology, Department of Clinical and Experimental Medicine, Pisa, Italy; [2]Unit of Pathology, Department of Surgical, Medical, Molecular Pathology and Critical Area, Pisa, Italy

Introduction
medullary thyroid carcinoma (MTC) is a neuroendocrine thyroidal cancer. World Health Organization recognizes a grading system for almost all neuroendocrine tumors; however, a shared grading system for MTC is still lacking. We performed a clinical and pathological review of 257 MTCs to evaluate which histologic features have an impact on the disease specific survival and to propose a new grading system.
Method
We retrospectively reviewed clinical data of 257 consecutive patients with sporadic MTC, surgically treated at the Endocrine Surgery Unit and followed at the Endocrine Unit of the University Hospital of Pisa, from 2000 to 2018. In this cohort, MTC histopathologic variants (classical, follicular, papillary, oncocytic, clear cell, small cell and spindle cell), desmoplastic reaction (fibrosis $\geq$ 10%), number of mitosis for 10 high-power field (x10HPF), Ki67 percentage and necrosis were evaluated.
Results
Patients were followed for a median time of 9.3 years. The MTC variants were distributed as follows: 164/257 (63.3%) classical variant, 50/257 (19.3%) spindle cell variant and 43/257 (17.4%) other variants with a frequency $<5\%$ each. Desmoplastic reaction was present in 159/257 (61.9%). Number of mitosis and Ki-67 percentage higher than 2 were present in 57/257 (22.2%) and 97/257 (37.7%), respectively. Necrosis was present in 19/257 samples (7.4%). According to Kaplan-Meier analysis, MTC with desmoplastic reaction, mitosis number >2, Ki-67 $>2\%$ or necrosis had lower disease specific survival ($P<0.001$). After preliminary analysis, we proposed the following grading system composed by desmoplastic reaction and Ki-67 percentage: high grade (presence of desmoplastic reaction and Ki-67 $>2\%$) and low grade (all other combinations). At Kaplan-Meier analysis, high grade MTC had lower disease specific survival compared to low grade (74.7% vs 98.6%, $P<0.001$). Intriguingly, this grading system was able to predict DSM, both in intrathyroidal (stage I-II) ($P=0.034$) and extrathyroidal (stage III-IV) MTCs ($P<0.001$).
Conclusions
In our large MTC series, presence of desmoplastic reaction and necrosis, mitosis number $\times$10HPF >2, and Ki-67 $>2\%$ were negative prognostic factors for DSM. Grading system composed by Ki-67 $>2\%$ and desmoplastic reaction was able to identify the MTCs with the worst prognosis, both in lower (I-II) than in more advanced (III-IV) stages.

DOI: 10.1530/endoabs.81.OC11.6

Reproductive and Developmental Endocrinology

OC12.1

The European Registries for Rare Endocrine Conditions (EuRRECa): the use of a core registry for collecting common data elements and clinician and patient reported outcomes

Ana Luisa Priego Zurita[1], Salma Rashid Ali[2], Jillian Bryce[3], Martine Cools[4], Thomas Danne[5], Olaf M Dekkers[1], Olaf Hiort[6], Harshini Katugampola[7], Agnès Linglart[8], Irene Netchine[9], Anna Nordenström[10], Attila Patócs[11], Alberto M Pereira[1], Luca Persani[12,13], Nicole Reisch[14], Arelene Smyth[3], Zdenek Sumnik[15], Domenica Taruscio[16], Edward Visser[17], Natasha Appelman-Dijkstra[1] & Faisal Ahmed[1,2,3]
[1]Leiden University Medical Centre, Department of Medicine, Division of Endocrinology, Leiden, Netherlands; [2]University of Glasgow , Developmental Endocrinology Research Group, Royal Hospital For Children , Glasgow, United Kingdom; [3]University of Glasgow , Office for Rare Conditions, Glasgow, United Kingdom; [4]Ghent University, Department of Internal Medicine and Paediatrics, Department of Paediatric Endocrinology,

Ghent University Hospital, Ghent, Belgium; [5]Diabetes Center Auf Der Bult, Hannover, Germany; [6]University of Lübeck, Division of Paediatric Endocrinology and Diabetes, Department of Paediatrics and Adolescent Medicine, Lübeck, Germany; [7]University College London Great Ormond Street Institute Of Child Health, Genetics & Genomic Medicine Programme, London, United Kingdom; [8]AP-HP, Department of Pediatric Endocrinology and Diabetology for Children, Le Kremlin Bicetre, France; [9]Sorbonne Universite , INSERM, Centre De Recherche Sainte Antoine, APHP, Hopital des Enfants Armand Trousseau, Paris, France; [10]Karolinska University Hospital, S-17176 , Pediatric Endocrinology and Inborn Errors of Metabolism, Stockholm , Sweden; [11]Semmelweis University, Clinical Genetics And Endocrinology Laboratory, Department Of Laboratory Medicine, Budapest, Hungary; [12]Istituto Auxologico Italiano, Division of Endocrine and Metabolic Diseases, Milan, Italy; [13]University of Milan, Dept of Biotechnology and Experimental Medicine, Milan, Italy; [14]Klinikum der Universität München, Med. Klinik und Poliklinik IV, Munich, Germany; [15]Motol University Hospital, Department of Pediatrics, Prague, Czech Republic; [16]Istituto Superiore di Sanità, National Centre for Rare Diseases, Rome, Italy; [17]Erasmus Medical Centre, Department of Internal Medicine, Academic Centre for Thyroid Diseases, Rotterdam, Netherlands

Introduction
The European Registries for Rare Endocrine Conditions (EuRRECa) was created in collaboration with the European Reference Network on Rare Endocrine Conditions (Endo-ERN), the European Society for Paediatric Endocrinology and the European Society of Endocrinology to support the needs of the endocrine community.
Aim
To describe the patient population and data entered in the EuRRECa Core Registry between June 2019 and December 2021.
Methods
Core Registry clinical contributors are invited to register new and existing cases of endocrine conditions seen in their centres. Diseases are organized in eight main condition groups. A core data set and a condition-specific data set collect information regarding demographics and diagnosis. Generic Patient-Reported Outcome Measures (PROMs) are available for clinicians and patients to complete. Patients can access the platform, view their data and complete outcomes.
Results
Twenty centres from 12 countries have registered cases. To date, a total of 644 cases have been added to the registry, 238 (36%) in the sex development and maturation condition group, 160 (24%) in the pituitary group, 153 (23%) in the calcium and phosphate group, 51 (8%) in the adrenal group, 24 (4%) in the thyroid group, 23 (3%) in the genetic endocrine tumour syndrome group, 10 (1%) in the growth and obesity group and 5 (0.7%) in the disorders of glucose and insulin metabolism. Of 664 cases, 183 (28%) were within the age range 0-9 years, 140 (22%) within 10-17 years and 321 (51%) over 18 years. The median age was 19 (0, 88) with 341(52%) cases over the age of 18 yrs. Of 664 cases, 442 (67%) were under active follow-up. One-hundred and thirteen (17%) had expressed an interest in using the patient platform; 76 (67%) had been sent an invitation to join the platform and of these, 18 (24%) activated their account. Thirty-two EQ-5D outcomes have been completed, 28 (87%) in cases of mineral conditions and 2 (6%) in pituitary and. Of these, 26 (94%) have been completed by clinicians and 2 by patients.
Conclusion
The EuRRECa Core Registry has shown its ability to collect information on a very wide range of endocrine conditions in patients of all ages. The additional functionality for collecting patient reported and clinician reported outcomes has now been tested and can be used for studying long-term clinical outcomes for rare endocrine conditions.

DOI: 10.1530/endoabs.81.OC12.1

OC12.2

Genetic cause of POI are common, the case for next generation sequencing?

Elinor Vogt[1,2], Eirik Bratland[3], Eystein Sverre Husebye[4,5], Sigridur Bjornsdottir[6], Siren Berland[5] & Marianne Øksnes[4,5]
[1]University of Bergen, Medicine, Bergen, Norway; [2]Haukeland University Hospital / Health Bergen, Norway; [3]Haukeland University Hospital / Health Bergen, Genetics, Norway; [4]University of Bergen, Medicine, Bergen, Norway; [5]Haukeland University Hospital / Health Bergen, Medicine, Norway; [6]Nya Karolinska, Sweden

Context
Premature ovarian insufficiency (POI) affects approximately 1-3% of women. Clinical presentations are heterogeneous and the underlying etiologies remain unknown in the majority of cases.
Objective/aim
To characterize presentations of POI and to evaluate the distribution of underlying etiologies in women with newly diagnosed POI of unknown cause.
Design
Prospective study of 100 women with newly diagnosed POI. Autoimmunity was examined by radio immune assays of autoantibodies associated with POI, i.e. 21-hydroxylase (21 OH), cholesterol side-chain cleavage enzyme (SCC), 17α-hydroxylase (17 OH), and NALP5. Extensive chromosomal and genetic analyses were performed in all, including FMR-1 premutation sequencing and next generation sequencing (NGS) of 100 POI associated genes.
Results
Three percent had autoimmune POI based on the presence of 21OH and SCC autoantibodies. Copy number profiling or chromosome analysis revealed X-chromosome abnormalities in 5%, and a large deletion on chromosome 8 in one patient. FMR-1 premutations were identified in 3%. NGS analysis found genetic variants classified as likely causes of POI in approximately one third of cases. These included genes SOHLH2, STAG3 and EIF4ENIF1. Furthermore, several patients carried highly suspicious variants of unknown significance (VUS) in genes such as SOX8, BUB1B and C14ORF39. One patient with primary amenorrhea was homozygous for a rare missense variant in MCM8. A family history of POI was less common (10% vs 28% vs *P* 0.040) and fewer women reported previous pregnancies (38% vs 61%, *P* 0.041), in genetic compared to idiopathic POI. FSH levels were higher in genetic compared with idiopathic POI (53.4 (4.0-149.2] vs 37.3 [1.6-120] IU/l, *P* 0.043]. There were no significant differences between the groups in frequency of primary amenorrhea (15%), timing of menarche (13 [9-17] years) or age at secondary amenorrhea (33 [12-3] years). A larger proportion of women with African heritage carried a VUS (9/17).
Conclusion
In women with newly diagnosed POI, screening for chromosomal abnormalities and FMR mutations identified genetic etiology in 8%, whereas the extensive NGS panel revealed a possible underlying genetic etiology in more than one third, actualizing the discussion of which tests should be a part of diagnostic screening in clinical practice.

DOI: 10.1530/endoabs.81.OC12.2

OC12.3

Defective Notch1/Jag1 signaling impacts GnRH development and contributes to hypogonadotropic hypogonadism

Cotellessa Ludovica[1,2,3], Marelli Federica[2], Paolo Duminuco[1], Bartoloni Lucia[4], Adamo Michela[4], Nelly Pitteloud[4], Luca Persani[1,2], Marco Bonomi[1,2], Paolo Giacobini[3] & Vezzoli Valeria[1]
[1]Istituto Auxologico Italinao, Dept of Endocrine and Metabolic Diseases and Lab of Endocrine and Metabolic Research, IRCCS Istituto Auxologico Italiano, Cusano Milanino, Milan, Italy; [2]University of Milan, Dept of Medical Biotechnology and Translational Medicine, University of Milan, Milan Italy; [3], Univ. Lille, Inserm, CHU Lille, U1172 -LilNCog(JPARC) – Lille Neurosciences & Cognition, F-59000, Lille, France, Lille, France; [4]Lausanne University Hospital, Service of Endocrinology, Diabetology, and Metabolism, Lausanne University Hospital, Lausanne, Switzerland

The precise development of the Gonadotropin Releasing Hormone (GnRH) neurons is essential for the proper function of the hypothalamic-pituitary-gonadal axis, as GnRH is the master regulator of reproductive functions in vertebrates. Mutations in genes involved in the development of GnRH neurons are associated with Congenital Hypogonadotropic Hypogonadism (CHH), a heterogeneous genetic disorder characterized by hypogonadism, lack of puberty onset, and infertility, which is named Kallmann Syndrome (KS) when the disease associates with anosmia. In this study, we identified in two European cohorts of CHH/KS patients rare missense variants in the NOTCH1 ligand gene *JAG1*. It is already reported in the literature the key role of the Notch signaling in the development of the olfactory system in both mouse and drosophila; therefore, considering the intimate connection between the olfactory and GnRH systems we studied its possible role in the development of the GnRH system. We first performed multiplex fluorescent in situ hybridization combined with immunofluorescence to assess the expression pattern of *JAG1* and its receptors *NOTCH1*, *NOTCH2*, *NOTCH3* and *NOTCH4* in human fetal sections of the nasal compartment during the first trimester of gestation. We showed that those molecules were expressed along the GnRH migratory pathway as well as by GnRH neurons, suggesting a paracrine and/or autocrine mechanism. Taking advantage of the zebrafish model, we observed that *jag1a*, *jag1b*, *notch1a*, and *GnRH3* (homologous of the mammalian GnRH1) were expressed in the olfactory placodes of zebrafish embryos. Moreover, we report that pharmacological and genetic inhibition of *jag1b* altered the development of the GnRH3 neurons and the olfactory scaffold used for their migratory process. Functional *in vitro* validation of the *JAG1* variants identified in CHH patients revealed that some were retained into the cytoplasm and did not reach the cell membrane. We also showed that some variants

did not properly activate the Notch Responsive Element, suggesting that they are loss-of-function mutations. Combining morphological analysis *in vivo*, together with genetic manipulation in zebrafish and human genetic analysis, we provide compelling evidence that Notch1/Jag1 signaling plays a role in the development of GnRH neurons and propose that Notch1/Jag1 signaling insufficiency may contribute to the pathogenesis of CHH in humans.

Key words: CHH, KS, GnRH, Notch signaling, Reproduction

DOI: 10.1530/endoabs.81.OC12.3

OC12.4

Sex-chromosome dosage effects on circular RNA: A circular transcriptome-wide study of Turner and Klinefelter syndrome across different tissues

Emma Bruun Johannsen[1], Jesper Just[1], Mette Viuff[1], Jens Fedder[2], Anne Skakkebæk[1,3] & Claus H Gravholt[1,4]

[1]Aarhus University Hospital, Department of Molecular Medicine, Aarhus, Denmark; [2]Odense University Hospital, Odense, Denmark; [3]Aarhus University Hospital, Department of Clinical Genetics, Aarhus, Denmark; [4]Aarhus University Hospital, Department of Endocrinology, Aarhus, Denmark

Background

Turner syndrome (45,X; TS) and Klinefelter syndrome (47,XXY; KS) present with a range of clinical features due to copy number aberrations of the X chromosome. The underlying genetics of these syndromes have revealed karyotype-dependent transcription and methylation patterns, and implicated genes that escape X chromosome inactivation (XCI). Alterations in the expression pattern of non-coding RNAs has previously been reported in TS and KS, yet the landscape of circular RNAs (circRNAs) has never been investigated. These endogenous circularized RNAs have the potential to facilitate regulatory processes, thereby affecting transcription, translation and epigenetics, and may contribute to the TS and KS phenotype.

Methods

Primary samples of blood, muscle and adipose tissue were collected from individuals with TS ($n=33$) and KS ($n=22$) and from males ($n=16$) and females ($n=44$) of normal karyotype. The circRNAs were identified and quantified from RNAseq data from these samples, using a combination of three different circRNA identification pipelines (CIRI2, CIRCexplorer2 and circRNA_finder). CircRNA differential expression, interaction prediction and functional enrichment analysis was carried out to describe the nature of the circRNA profile in KS and TS.

Results

Differential expression was observed throughout the genome in all tested tissues. The host-genes of these circRNAs were associated with known phenotypic traits. Furthermore, several differentially expressed circRNAs had the potential to sponge certain miRNAs and these miRNAs were predicted to interact with genes that were differentially expressed between TS and females and KS and males. CircRNAs arising specifically from the PAR-genes, displayed a general pattern of opposing expression with up-regulation in TS and down-regulation in KS, which was similar to that of their respective host-genes. Furthermore, we observed that CircRNA-miRNA-mRNA networks may compensate for altered X-chromosome dosage of the PAR-genes.

Conclusion

The present study shows pervasive changes in the circRNA transcriptome throughout three different relevant tissues in Turner and Klinefelter syndrome. It extends our understanding of TS and KS genomics, being is not only limited to changes in the mRNA transcriptome and methylome. The conceptual picture of these syndromes is clearly much more complex than hitherto thought and future studies will need to include multiple tissues, more components of the endogenous ceRNA complex, as well as the epigenome. We propose that the phenotype of these syndromes shall be seen through a lens of a complicated multi-tissue framework with multiple genomic mechanisms causing, regulating and compensating the resultant output – the patient.

DOI: 10.1530/endoabs.81.OC12.4

OC12.5

Luteinizing hormone (LH)- and choriogonadotropin (hCG)-induced internalization of the receptor (LHCGR) is responsible for hormone-specific signaling

Elia Paradiso[1], Clara Lazzaretti[1], Sara D'Alessandro[1,2], Samantha Sperduti[1,3], Neena Roy[1], Elisa Mascolo[1], Lara Baschieri[1,2], Claudia Anzivino[1,3], Manuela Simoni[1,3,4] & Livio Casarini[1,3]

[1]University of Modena and Reggio Emilia, Unit of Endocrinology. Department of Biomedical, Metabolic and Neural Sciences, Modena, Italy; [2]University of Modena and Reggio Emilia, International PhD School in Clinical and Experimental Medicine (CEM), Modena, Italy; [3]University of Modena and Reggio Emilia, Center for Genomic Research, Modena, Italy; [4]Azienda Ospedaliero-Universitaria di Modena, Department of Medical Specialties, Modena, Italy

Introduction

Luteinizing hormone (LH) and human choriogonadotropin (hCG) regulate reproduction through binding the same receptor (LHCGR). They act via activation of G protein- and β-arrestin-dependent signals, resulting in ligand-specific pattern of signaling cascades and LHCGR internalization into endosomal vesicles. Previous studies differentiated the action of these two hormones in LH-related proliferative signals and hCG-related steroidogenic signals.Aim. We compared the role of LHCGR internalization in determining LH- and hCG-specific signals.

Methods

Ligand-specific patterns of LHCGR trafficking and signaling were evaluated in HEK293 cells overexpressing the receptor and specific bioluminescence resonance energy transfer (BRET) biosensors, with or without internalization blockade by Dynasore. LH- and hCG-induced LHCGR internalization and trafficking were evaluated over 30 min, determining the interaction between receptor and endosomal type-specific markers RAB-GTPases (Rab) 5, 7, and 11, as well as β-arrestin 2. Ligand-specific receptor coupling to Gs, Gi, and Gq protein, and related cAMP, extracellularly-regulated kinases 1 and 2 (ERK1/2), and intracellular Ca^{2+} increase were evaluated as well. Results were compared by Kruskal Wallis test and Dunn's post-test; $P<0.05$; $n=4$-8.

Results

The interaction between LHCGR and markers of internalization/localization into early endosome, i.e. β-arrestin 2 and Rab5, is markedly more induced upon cell treatment with hCG, with than LH ($P<0.05$; $n=4$). Conversely, LH induces preferential LHCGR-Rab11 interaction, indicating the routing of the receptor toward recycling in cell membrane ($P<0.05$; $n=4$), while no hormone-specific LHCGR-Rab7 interaction was found ($P\geq 0.05$; $n=4$). Interestingly, LHCGR trafficking is modulated by the blockade of internalization with Dynasore. Under this condition, hCG-induced LHCGR-β-arrestin 2/Rab5, as well as LH-induced LHCGR-Rab11 interactions were lost ($P\geq 0.05$; $n=4$), suggesting missing ligand-specific receptor trafficking. Moreover, Dynasore treatment increases LH-, but not hCG-induced LHCGR-Rab7 interaction, indicating ligand-specific routing toward the degradation pathway. Hormone-specific trafficking reflects the downstream signaling pattern. hCG has higher efficacy than LH in inducing Gs- and Gq coupling to LHCGR ($P<0.05$; $n=8$), reflecting more pronounced activation of cAMP and intracellular Ca^{2+} increase ($P<0.05$; $n=4$), as two molecules upregulating the synthesis of gonadal steroids. Cell treatment with Dynasore did neither change the hCG-related G protein coupling to LHCGR, nor cAMP production, while it decreased intracellular Ca^{2+} increase. Conversely, LH was more effective than hCG in inducing LHCGR coupling to Gi protein ($P<0.05$; $n=8$), preferentially activating proliferation-related ERK1/2 downstream signaling ($P<0.05$; $n=4$). However, LH-induced LHCGR-Gi coupling and ERK1/2 activation were inhibited by Dynasore ($P\geq 0.05$; $n=4$).

Conclusion

We conclude that LH-related proliferative and hCG-linked steroidogenic signals require hormone-specific trafficking of the receptor.

DOI: 10.1530/endoabs.81.OC12.5

OC12.6

Analysis of cardiovascular comorbidities and events in a cohort of transgender people during GAHT

Lorenzo Marinelli, Andrea Camandona, Chiara Michela Crespi, Domiziana Magistri, Ezio Ghigo & Giovanna Motta

Università Degli Studi Di Torino Dipartimento Scienze Mediche, Torino, Italy

Introduction

According to the DSM-5, gender dysphoria (GD) is defined as a distress that results from an incongruence between one's sex assigned at birth and one's gender identity. This condition may require gender-affirming hormone therapy (GAHT), in order to reduce distress. GAHT, however, is not free from side effects and it could increase the risk of onset of new pathological conditions.

Aim of the study

To evaluate cardiovascular comorbidities and events in a cohort of patients with GD taking GAHT.

Subjects and methods

We enrolled subjects with GD [assigned male at birth (AMAB) and assigned female at birth (AFAB)] who were regularly followed by the local gender team in Molinette Hospital, Turin (Italy), between February 2007 and July 2021. For each

patient, at each access anthropometric parameters, smoking habit and a cardiovascular assessment (arterial hypertension, diabetes, dyslipidaemia, ACS, stroke, DVT) were recorded. A baseline analysis of the whole cohort was carried out; subsequently an evaluation of cumulative incidence of comorbidities during GAHT was performed. Finally, mortality was assessed in terms of SMR (standardized mortality ratio - ratio between observed and expected death).
Results
We enrolled 613 patients, 380 transgender-AMAB with a median age of 33.9 years [22.04-45.85] and 233 transgender-AFAB, aged 27.4 years old [22.01-39.54], observed for a median follow-up time of 43.50 [17-72.25] and 41.50 [19-74] months, respectively. Only transgender-AMAB showed a significant weight gain (+2 Kg after 24 months). At baseline, 39% of transgender-AMAB and 39.1% of transgender-AFAB were active smokers; no significant difference during follow-up was recorded. During observation time, new cases of arterial hypertension ($n=12$), diabetes ($n=4$) and dyslipidaemia ($n=28$) were recorded in transgender-AMAB, while 12 new cases of arterial hypertension, 2 of diabetes and 21 of dyslipidaemia were reported in transgender-AFAB. Three cases of DVT were registered within transgender-AMAB. One case of ACS and one stroke were described in transgender-AFAB group. Finally, 4 deaths were recorded in the transgender-AMAB group (1.04%) and 1 in the transgender-AFAB group (0.42%). In both groups, SMR was higher than age-matched cisgender women [AMAB SMR: 1.32 (IC 95% 0.42-3.19); AFAB SMR: 1.26 (IC 95% 0.04-3.91)].
Conclusions
Although transgender-AFAB and AMAB enrolled were relatively young and not fully representative of the general transgender population, during GAHT an increase of main cardiovascular comorbidities was observed. Thus, our data highlight the need of a proper follow-up and medical monitoring to manage these new conditions and to prevent the onset of major cardiovascular events.

DOI: 10.1530/endoabs.81.OC12.6

Adrenal and Cardiovascular Endocrinology 2

OC13.1

Development of [18F]AldoView as the first highly selective aldosterone synthase PET tracer for imaging of patients with primary hyperaldosteronism

Kerstin Sander[1], Tom Kurzawinski[1,2], Thibault Gendron[3], Klaudia Cybulska[3], Fatih Sirindil[4], Junhua Zhou[4], Tammy Kalber[5], Mark Lythgoe[5], Morris Brown[4], Bryan Williams[6] & Erik Arstad[1]
[1]University College London, Centre for Radiopharmaceutical Chemistry, London, United Kingdom; [2]University College Hospital, Endocrine Surgery, London, United Kingdom; [3]University College London, Centre for Radiopharmaceutical Chemistry, United Kingdom; [4]Barts and The London School of Medicine and Dentistry, London, United Kingdom; [5]University College London, Centre for Advanced Biomedical Imaging, London, United Kingdom; [6]University College Hospital, Biomedical Research Centre, London, United Kingdom

Background
Inappropriately high aldosterone in patients with primary hyperaldosteronism (PHA) is due to increased aldosterone synthase (CYP11B2) activity. Selective in vivo imaging of overexpressed CYP11B2 in adrenals with positron emission tomography (PET) has not yet been achieved due to close homology of enzymes involved in aldosterone and cortisol (CYP11B1) synthesis.
Aim
Synthesize a fluorine-18 labelled highly selective CYP11B2 inhibitor, [^{18}F] AldoView, and assess its potential for the detection of aldosterone producing adenomas (APAs) and aldosterone producing cell clusters (APCCs) with PET in patients with PHA.
Methods
[^{18}F]AldoView was synthesised in high radiochemical yields using a proprietary radiochemistry platform.[1] Dynamic PET/CT imaging, biodistribution studies and metabolite analysis was performed in wild type female BALB/c mice. [18F] AldoView binding to CYP11B2 was characterised by quantitative phosphorimaging in tissue sections prepared from adrenalectomy specimens of patients with PHA, Cushing, phaeochromocytoma and incidentaloma. CYP11B2 specific immunohistochemistry (IHC) was performed in directly adjacent sections.
Results
In mice, [^{18}F]AldoView showed a favourable pharmacokinetic profile, including rapid distribution and clearance. In tissue sections, [^{18}F]AldoView binding was visually consistent with CYP11B2 IHC staining. Specific tracer binding to CYP11B2 positive areas ranged from 8.6 to 19.1 kBq/cm^2 and was evenly distributed across tissue identified as APA, in contrast to cortex, which had diffuse patterns with hot spots in keeping with APCCs. There was no evidence of elevated tracer uptake in CYP11B2 negative areas in patients with or without PHA (3.2±1.1 kBq/cm^2 and 2.6±1.8 kBq/cm^2, respectively).[2]
Conclusion
Our results strongly suggest that [^{18}F]AldoView can image CYP11B2 expression in human adrenals and could become first highly selective radioactive tracer to be used to stratify patients with PHA for adrenalectomy.
References
1. Gendron et al. *J Am Chem Soc* 2018, 140, 35, 11125–11132.
2. Sander et al. *J Med Chem* 2021, epub ahead of print: doi.org/10.1021/acs.jmedchem.1c00539.

DOI: 10.1530/endoabs.81.OC13.1

OC13.2

Early post-operative ACTH-stimulated aldosterone predicts long-term biochemical outcome in primary aldosteronism

Denise Bruedgam[1], Christian Adolf[1], Holger Schneider[1], Verena Wegmann[1], Paul Schwarzlmueller[1], Lisa Mueller[1], Finn Holler[1], Benjamin Lechner[1], Laura Handgriff[1], Roland Ladurner[2], Sinan Deniz[3], Tracy Ann Williams[1,4], Felix Beuschlein[1,5], Martin Reincke[1] & Daniel Heinrich[1]
[1]LMU Klinikum Innenstadt, Medizinische Klinik und Poliklinik IV, München, Germany; [2]LMU Klinikum Innenstadt, Klinik für Allgemein-, Viszeral- und Transplantationschirurgie, Campus Innenstadt, Klinikum der Universität München, München, Germany; [3]LMU Klinikum Innenstadt, Klinik und Poliklinik für Radiologie, München, Germany; [4]Division of Internal Medicine and Hypertension, Department of Medical Sciences, University of Turin, Turin, Italy; [5]University Hospital of Zürich, Klinik für Endokrinologie, Diabetologie und Klinische Ernährung, Zürich, Switzerland

Introduction
Primary aldosteronism (PA) is the most common surgically curable cause for endocrine hypertension. Patients with unilateral aldosterone-producing adenoma undergo adrenalectomy (ADX). Clinical and biochemical outcome is assessed 6-12 months after ADX according to PASO consensus. To reduce unnecessary follow-up visits and change in medication for diagnostic purposes for potentially cured patients after ADX, a prediction tool is needed. Previous research had shown greater ACTH-responsiveness in unilateral disease. Thus, we analyzed if early post-operative ACTH-stimulated aldosterone can predict PASO outcomes.
Methods
We prospectively included 100 patients of the German Conn's registry from 2015-2021, who underwent ADX and post-operative ACTH stimulation tests. 6-12 months after ADX we assessed blood pressure and biochemical remission according to PASO criteria. In addition, serum cortisol and plasma aldosterone concentrations (PAC) were measured before and 30 min after the application of 250 µg Synacthen® within the first week after ADX. We used ROC (receiver operating curve) analysis and paired baseline and stimulated PAC and serum cortisol to PASO outcomes.
Results
81% of the patients had complete, 13% partial and 6% absent biochemical remission at 6-12 months after ADX. Complete clinical remission was observed in 28%. There was a significant correlation between biochemical outcome and ACTH-stimulated PAC values ($P=0.01$, $r=0.53$). Using 58.5 pg/ml as a cut-off, post-operative stimulated PAC had high sensitivity (95%) and reasonable specificity (74%) for predicting partial or absent biochemical remission at 6-12 months after ADX. Additionally, stimulated PAC AUC (area under the curve) values (0.89; CI 0.82-0.96) were significantly higher ($P=0.03$) than baseline PAC AUC ($P=0.28$). In contrast, baseline and stimulated serum cortisol levels were less useful (baseline cortisol AUC 0.60; CI 0.45-0.74), stimulated cortisol AUC 0.67; CI 0.54-0.80, ($P=0.01$; $P=0.01$). Blood pressure outcome AUC for baseline and stimulated serum cortisol and PAC ranged from 0.56-0.66, indicating a low predictive value.
Conclusions
In our series, low post-operative ACTH-stimulated PAC was predictive of biochemical remission after ADX. As post-operative ACTH stimulation tests are used to detect adrenal insufficiency, concurrent stimulated PAC measurements should be included in routine care. If confirmed, this approach could reduce follow-up visits to assess biochemical outcome.

DOI: 10.1530/endoabs.81.OC13.2

OC13.3

11-oxygenated C19 steroids are the predominant androgens responsible for hyperandrogenemia in Cushing's disease

Hanna Nowotny[1], Frederick Vogel[1], Martin Bidlingmaier[1], Leah Braun[1], Martin Reincke[1], Lea Tschaidse[1], Matthias Auer[1], Christian Lottspeich[1],

James M Hawley[2], Jo Adaway[2], Brian Keevil[2], Katharina Schilbach[1] & Nicole Reisch[1]
[1]Klinikum der Universität München, Medizinische Klinik und Poliklinik IV, München, Germany; [2]Manchester University Foundation NHS Trust, Manchester Academic Health Sciences Centre, Department of Clinical Biochemistry, Manchester, United Kingdom

Background
Symptoms of hyperandrogenism are common in patients with Cushing's disease (CD), but they cannot be sufficiently explained by measured concentrations of circulating androgens. In this study we analyzed the contribution of 11-oxygenated (11o×C19) androgens to hyperandrogenemia in female patients with CD as well as the influence of treatment with steroidogenesis inhibitors osilodrostat and metyrapone on 11o×C19 and classic androgens.
Methods
In this single-center study, we assessed saliva day profiles of 23 females with treatment naïve CD, 26 female controls, 5 females with CD treated with metyrapone and 5 treated with osilodrostat for cortisol, cortisone, androstenedione (A4), 11-hydroxyandrostenedione (11OHA4), testosterone (T) and 11-ketotestosterone (11KT) by liquid chromatography tandem mass spectrometry as well as morning baseline levels of gonadotropins and estradiol, sex hormone-binding globulin, cortisol and dehydroepiandrosterone sulfate (DHEAS) in serum and adrenocorticotropic hormone in plasma.
Results
Treatment naïve females with CD showed significantly elevated areas under the curve (AUC) of 11OHA4 and 11KT throughout the day compared to controls (11OHA4 mean rank difference (mrd) 18.13, $P=0.0002$; 11KT mrd 17.42; $P=0.0005$) whereas A4, T and DHEAS were comparable to controls. Patients with more symptoms of hyperandrogenism displayed higher concentrations of 11o×C19 androgens and had significantly lower SHBG concentrations. Gonadotropin levels were normal in all patients with CD (LH 7.18 U/l (SD 14.28 U/l); FSH 7.68 U/l (SD 12.0 U/l)) and did not correlate with any other parameters. Treatment with osilodrostat and metyrapone efficaciously blocked 11oxC19 androgen synthesis. In metyrapone but not in osilodrostat treatment a trend towards increased concentrations of T and significantly increased A4-concentrations were observed (A4 mrd 23.07, $P=0.0119$).
Conclusion
Hyperandrogenemia in CD is predominantly caused by excess of 11o×C19 androgens. Due to lower compensatory increase of A4 and T, osilodrostat seems to be more suitable for treatment of females with CD and hyperandrogenism than metyrapone.

DOI: 10.1530/endoabs.81.OC13.3

OC13.4

Classic and 11-oxygenated androgens in serum and saliva across adulthood and the menstrual cycle – a mass spectrometry-based cross-sectional study

Punith Kempegowda[1,2], Lina Schiffer[1], Jo Adaway[3], Fozia Shaheen[1], Andreas Ebbehoj[4,5], Sumitabh Singh[4], Alessandro Prete[1,2], James M Hawley[1,3], Alice J Sitch[6], Brian Keevil[3], Irina Bancos[4], Angela Taylor[1] & Wiebke Arlt[1]
[1]University of Birmingham, Institute of Metabolism and Systems Research, United Kingdom; [2]Queen Elizabeth Hospital Birmingham, United Kingdom; [3]Wythenshawe Hospital, Department of Clinical Biochemistry, United Kingdom; [4]Mayo Clinic, Division of Endocrinology, Metabolism, Diabetes and Nutrition, Department of Internal Medicine, United States; [5]Aarhus University, Department of Clinical Medicine, , Aarhus, Denmark; [6]University of Birmingham, Institute of Applied Health Research, Birmingham, United Kingdom

Objective
Quantify classic and 11-oxygenated androgens in serum and saliva and determine variations across age, sex, body mass index (BMI), menstruation and hormonal contraception use.
Methods
Morning serum samples were collected from 292 healthy volunteers (125 men, 22-95 years; 167 women, 21-91 years). Morning saliva was collected from 83 healthy volunteers (51 women, 32 men). 25 individuals (12 women, 13 men) also collected a 7-timepoint diurnal saliva profile; the 12 women also collected morning saliva on seven consecutive days during both follicular and luteal phase. The following steroids were quantified by liquid chromatography-tandem mass spectrometry: classic androgens and their precursors (dehydroepiandrosterone sulfate [DHEAS], dehydroepiandrosterone [DHEA], androstenedione [A4], testosterone [T], dihydrotestosterone [DHT]), and 11-oxygenated androgens and their precursors (11-hydroxy androstenedione [11OHA4], 11-keto androstenedione [11KA4], 11-hydroxy testosterone [11OHT], 11-keto testosterone [11KT]). Data were pooled Descriptive statistics and non-parametric tools were used for each variable to obtain median, IQR and significance (p-values). Multiple linear regressions were performed to delineate the distinct effects of age and BMI in a sex-specific analysis
Results
Age: In serum, DHEAS, DHEA, and A4 decreased with age in both men and women, while 11OHA4, 11KA4, 11OHT, 11KT remained stable. Sex: Serum concentrations of DHEA, A4, and 11-oxygentated androgens were similar in men and women while, as expecteded, T and DHT were higher in men. 11OHA4 levels were the highest of all 11-oxygenated androgens and were higher than A4 and similar to DHEA levels. BMI: There were no associations of DHEAS, DHEA, A4, 11OHA4 and 11KA4 with BMI. After adjusting for age, 11KT positively correlated with BMI in men (change/kg/m^2 (95% CI)=3.05(0.08, 6.03), $P=0.044$), while the relationship between 11OHT and BMI was not significant. Menstruation status: Saliva classic and 11-oxygenated androgens showed a clear diurnal pattern in men and in the follicular phase in women, but in the luteal phase only 11-oxygenated androgens showed diurnal variation. Postmenopausal women had lower serum DHEAS, DHEA, A4, T, and 11KA4 ($P<0.001$) compared to premenopausal women. 11OHT and 11KT were increased in postmenopausal compared to premenopausal women ($P<0.001$ and $P=0.005$, respectively). Impact of contraception: Women on hormonal contraceptives had lower T and 11-KT concentrations in saliva, but not in serum.
Conclusion
While classic androgens decline with age and are subject to menstrual cycle-dependent variation, 11-oxygenated androgens form a stable pool during adulthood. While all other measured androgens decreased after menopause, 11OHT and 11KT increased, which may have clinical implications for diagnostic work-up of hormonal pathologies.

DOI: 10.1530/endoabs.81.OC13.4

OC13.5

Machine learning-based texture analysis in the characterization of cortisol secreting vs non secreting adrenocortical incidentalomas in CT scan

Roberta Maggio[1], Filippo Messina[2], Benedetta D'Arrigo[2], Giacomo Maccagno[2], Pina Lardo[3], Claudia Palmisano[2], Irene Biondo[3], Iolanda Matarazzo[2], Andrea Laghi[2], Giuseppe Pugliese[3] & Antonio Stigliano[4]
[1]Endocrinology - Sant'Andrea Hospital, Sapienza University of Rome; [2]Department of Surgical and Medical Sciences and Translational Medicine, Sant'Andrea Hospital, sapienza University of Rome; [3]Endocrinology, Department of Clinical and Molecular Medicine, Sapienza University of Rome; [4]Endocrinology - Sant'Andrea Hospital, Sapienza University of Rome , Clinical and Molecular Medicine , Rome, Italy

Adrenal nodular disease is a frequently increasing in the general population with an incidence that reaches almost 10% in the seventh decade of life. More and more evidences show these lesions discovered through diagnostic imaging (CT, MRI) performed for other medical problems (incidentalomas). New radioimaging techniques, exploiting the quantitative variables of imaging, permit to identify an hypothetical pathological tissue. We have applied this potential in a retrospective series of 72 patients of both sexes with single adrenal lesion >1 cm in dimension with adrenal incidentalomas followed at our center. Patients were studied following ESE/ENSAT current criteria practice guideline in order to exclude any hormonal hypersecretion considering in this study only not secreting and cortisol secreting adrenal masses by dexamethasone-suppression test (DST). Based on cortisol value they were divided in two groups: functioning (32) and non-functioning (40) adrenal incidentalomas with cortisol values >50 nmol/l and <50 nmol/l respectively. Machine learning concept, through different algorithms offers the possibility to study several biological processes obtaining quantitative information from imaging and correlating it with outcomes. Radiomics is an emerging technique that translates radiological images into quantitative data to yield biological information and permits an in depth radiological characterization, thus improving diagnosis, decision support, and follow up monitoring. It is a multistage process in which features based on shape, pixel densities, and texture are extracted from CT or MR images. Each incidentaloma was studied in the preliminary non-contrast phase with a specific software (Mazda), surrounding a region of interest within each lesion. 314 features were extrapolated. Mean and standard deviations of features were obtained and the difference in means between the two groups was statistically analyzed. ROC curves were used to identify an optimal cut off for each variable and a prediction model was constructed via multivariate logistic regression with backward and stepwise selection. A 11-variables prediction model was constructed and a ROC curve was used to

differentiate patients with high probability of functioning incidentalomas. Using a specific threshold value we obtained a sensitivity of 93.75% and a specificity of 100% in diagnosing functioning incidentaloma. Based on these results, CT texture analysis appears a promising tool in the diagnostic definition of adrenal incidentalomas.

DOI: 10.1530/endoabs.81.OC13.5

OC13.6

Machine Learning models for the accurate prediction of malignant pheochromocytomas and paragangliomas

Christina Pamporaki[1], Annika MA Berends[2], Angelos Filippatos[3], Tamara Prodanov[4], Leah Meuter[4], Aleksander Prejbisz[5], Felix Beuschlein[6], Martin Fassnacht[7], Henri Timmers[8], Svenja Noelting[6], Kaushik Ganesh Abhyankar[3], Georgiana Contsantinescu[1], Carola Kunath[1], Katharina Wang[6], Hanna Remde[7], Andrzej Januszewicz[5], Mercedes Robledo[9], Jacques Lenders[8], Michiel Kerstens[2], Karel Pacak[4] & Graeme Eisenhofer[1]

[1]University Hospital Carl Gustav Carus at TU Dresden, Dresden, Germany; [2]Medical Center Groningen, Groningen, Netherlands; [3]Dresden Center of Intelligent Materials, at the TU Dresden, Dresden, Germany; [4]National Institutes of Health, Washington DC, United States; [5]Institute of Cardiology, Warsaw, Poland; [6]University Hospital Zurich, Zurich, Switzerland; [7]University Hospital Würzburg, Würzburg, Germany; [8]Radboud University Hospital, Nijmegen, Netherlands; [9]Spanish National Cancer Research Center, Madrid, Spain

Introduction

Pheochromocytomas and paragangliomas (PPGLs) exhibit an up to 20% malignancy rate. Various clinical, genetic, and pathological features have been proposed as predictors of malignancy. However, until present there are no robust indices to reliably predict metastatic PPGLs.

Aim

The aim of the present study was to prospectively validate the value of methoxytyramine as risk marker of metastatic disease and establish a machine learning (ML) model, based on clinical and biochemical features, to reliably predict malignancy in patients with PPGLs.

Methods

This study included retrospective data of 493 patients for the generation and training of ML models. Data of 295 patients prospectively enrolled in the multicenter international PMT-Study were used for the validation of the predictive value of methoxytyramine and the external validation of the selected ML model. The predefined features for selection analysis were sex, age at initial diagnosis, locations and size of tumor(s), previous history of PPGL, presence of SDHB mutation, plasma normetanephrine, metanephrine and methoxytyramine.

Results

Receiver operating characteristic curves indicated that plasma methoxytyramine using an optimal cutoff of 33 pg/ml provided an accurate biomarker for detecting patients with metastatic PPGLs. After feature selection and the use of 4 different models, ensemble trees model, which comprised 9 features, had the greatest discriminatory ability with an AUC of 0.9938 (95% CI:0.9903-0.9951). The ensemble trees model was validated externally and ranked based on the balanced accuracy with an AUC of approximately 0.9261 (95% CI:0.9293-0.9381).

Conclusion

Our study confirms in a prospective series the value of methoxytyramine as a strong predictor of metastatic PPGLs. Importantly we demonstrate predictive ML models, as the first effective, non-invasive and highly accurate approach to predict malignant disease in patients with PPGLs, providing immediate guidance to clinicians for individualized patient management and follow-up strategies.

DOI: 10.1530/endoabs.81.OC13.6

Late Breaking

OC14.1

Expression of luteinizing hormone-chorionic gonadotrophin receptor in pheochromocytomas

Antoine-Guy Lopez[1,2], Celine Duparc[1], Sylvie Renouf[1], Elise Machevin[3], Vincent Le Guillou[4], Jean-Christophe Sabourin[5], Guillaume Defortescu[6], Alexandre Buffet[7,8], Anne-Paule Gimenez-Roqueplo[7,8], Christophe Dubessy[1], Estelle Louiset[1] & Lefebvre Hervé[1,2]

[1]Normandie University, UNIROUEN, INSERM U1239, NorDiC, Rouen, France; [2]Rouen University Hospital, Endocrinology, Diabetes and Metabolic Diseases, Rouen, France; [3]Evreux Hospital Centre, Gynaecology-Obstetrics, Evreux, France; [4]Rouen University Hospital, Thoracic and Cardiovascular Surgery, Rouen, France; [5]Rouen University Hospital, Pathology and INSERM 1245, Rouen, France; [6]Rouen University Hospital, Urology, Rouen, France; [7]Université de Paris, PARCC, INSERM, Paris, France; [8]Assistance Publique-Hôpitaux de Paris, Hôpital Européen Georges Pompidou, Service de Génétique, Paris, France

Pheochromocytomas and paragangliomas (PPGL) are catecholamine-producing neuroendocrine tumors that display the highest heritability rate among all human tumors. Genomic analyses revealed the existence of 2 main clusters of PPGL, i.e. cluster 1 containing SDHx- and VHL-mutated tumors which do not produce epinephrine, and cluster 2 including epinephrine-secreting PPGL related to RET, NF1, TMEM127 and MAX mutations. Early diagnosis and treatment of PPGL is crucial to prevent adrenergic crises, especially in pregnant patients with previously undiagnosed pheochromocytoma (PCC). In this context, PCC are associated with a high risk of maternal or fetal complications due to catecholamine excess triggered by tumor compression induced by fetus growth, or labor and delivery. However, it is known that surges in plasma catecholamines may also occur during early gestation suggesting that pregnancy may also activate the secretory activity of PPGL through the involvement of non-mechanical factors, such as gestational hormones. Herein, we report a case of silent PCC in a pregnant woman with the first symptoms of catecholamine excess appearing during the first trimester and a life-threatening adrenergic myocarditis occurring at 31 weeks of gestation. Genetic analysis revealed the presence of a heterozygous germline RET variant of uncertain significance. The fact that the first symptoms of catecholamine excess had occurred during the first trimester of pregnancy led us to conduct in vitro studies to investigate the effects of estradiol and hormone chorionic gonadotropin (hCG) on epinephrine secretion by cultured cells derived from the patient's tumor. Expression of LH/hCG receptor (LHCGR) was searched for in the tumor and an additional series of 12 PCC by RT-qPCR and immunohistochemistry. LHCGR expression was also analyzed in silico in the PPGL cohorts of the COMETE network and The Cancer Genome Atlas (TCGA) databases. hCG stimulated epinephrine secretion by primary cultured PCC cells. The tumor expressed the LHCG receptor, which was colocalized with catecholamine-producing enzymes. LHCGR expression was also detected in 5 out of a series of 12 PCCs. In silico studies revealed that PPGL display the highest expression levels of LHCGR mRNA among the 32 solid tumor types of TCGA cohort. Interestingly, expression of LHCGR was higher in cluster 2 than in cluster 1 PPGL. These data show that PCC can express functional LHCG receptor. Consequently, pregnancy may activate catecholamine production by previously silent PCC as early as the first trimester of gestation especially in women with gene mutations that predispose to cluster 2 epinephrine-secreting PCC.

DOI: 10.1530/endoabs.81.OC14.1

OC14.2

Peripheral facial paralysis as first manifestation of hypophysary glioma: a case report

Jéssica Maria Telles[1], Laura Vilas Boas[2], Thielsen Cardoso da Silva[2], Gabrielle Andrusko dos Santos[1], Matheus Kowal Rosales[1], Bruno Melquíades da Rocha[2] & Mirnaluci Paulino Ribeiro Gama[1]

[1]Hospital Universitário Evangélico Mackenzie, Brazil; [2]Evangelical Mackenzie Faculty of Parana, Brazil

Introduction

Low-grade pituitary gliomas are extremely rare neoplasms, originating from the pituicytes of the posterior pituitary or infundibulum. The incidence of these tumors increases with age and peaks in the seventh decade of life. Gliomas are primary brain tumors of the supporting glial cells of the central nervous system, which derive from neuroglial stem cells or progenitor cells. They are responsible for nearly 30% of all primary brain tumors and 80% of all malignant tumors, as well as the majority of deaths from primary brain tumors. The clinical manifestation is mainly through visual impairment, due to optic nerve compression, headache, and pituitary deficits.

Case report

A 16-year-old female patient presented with left peripheral facial paralysis, with no change in the imaging tests, with spontaneous improvement. Evolved with progressive headache, severe nasal congestion, bilateral visual acuity alteration, and right peripheral facial paralysis, associated with findings of a tumor in the sellar topography, dilatation of the supratentorial ventricular system, and diffuse meningeal impregnation, suggestive of the spread of the pathology. She underwent a ventriculoperitoneal shunt and subsequent transsphenoidal excision of the mass (4.9 × 2.6 × 2.5 cm) which was successfully performed. Anatomopathological analysis showed a round cell neoplasm with fibrillar background and low-grade hyalinized vessels, suggestive of glial neoplasm. In the early postoperative period, developed diabetes insipidus, treated with desmopressin acetate nasal spray 0.1 mg/ml twice a day, and

hypothalamic obesity. In the outpatient follow-up, a diagnosis of panhypopituitarism was made, consisting of hypogonadotropic hypogonadism, central adrenal insufficiency, and central hypothyroidism, and replacement of estradiol valerate 2 mg + levonorgestrel 0.25 mg, hydrocortisone 17.5 mg, and levothyroxine 123 mg/day was initiated. The patient remains under outpatient follow-up, in good general condition, asymptomatic, and with good control of complications.

Conclusion

Although pituitary tumors are the most commonly found intracranial neoplasms, the low-grade pituitary glioma presented by the patient is an extremely rare pathology. However, as it has the potential to manifest in several forms, which go far beyond those described in the literature, it should always be considered in the differential diagnosis of pituitary neoplasms, given its potential for complications and the need for early radical treatment aimed at healing the patient.

DOI: 10.1530/endoabs.81.OC14.2

OC14.3

Are the neutrophil-to-lymphocyte ratio and large unstained cells (LUCs) different in hospitalized patients COVID-19 PCR positive with and without diabetes mellitus?

Müge Keskin[1], Şefika Burçak Polat[2], Ihsan Ates[3], Seval Izdes[4], Hatice Rahmet Guner[5], Oya Topaloglu[2], Reyhan Ersoy[2] & Bekir Cakir[2]
[1]Ankara City Hospital, Endocrinology and Metabolism, Ankara, Turkey; [2]Ankara Yildirim Beyazit University, Faculty of Medicine, Endocrinology and Metabolism, Ankara, Turkey; [3]Ankara City Hospital, Internal Medicine, Ankara, Turkey; [4]Ankara Yildirim Beyazit University, Faculty of Medicine, Anesthesia and Reanimation, Ankara, Turkey; [5]Ankara Yildirim Beyazit University, Faculty of Medicine, Infection Diseases, Ankara, Turkey

Objectives

The novel coronavirus disease-2019 (COVID-19) is the fastest-spreading disease worldwide, with over 380 million cases and 5 million deaths. The presence of diabetes mellitus (DM) in patients with COVID-19 was associated with mortality, acute respiratory distress syndrome, disease progression. COVID-19 was progressed with some hematological disorders, especially lymphopenia. Studies implicated that neutrophil-to-lymphocyte ratio (NLR) level can be a reliable marker in showing the severity of COVID-19 disease. A routine hematology analyzer measures the percentage of large unstained cells (%LUCs), reflecting activated lymphocytes and peroxidase-negative cells. In previous studies, the%LUCs was found to be associated with disease progression in patients with HIV. This study aims to investigate whether the%LUCs and NLR parameters are associated with disease progression in diabetic patients with COVID-19.

Materials and Methods

The data of the patients hospitalized in the Infectious Diseases Service and Intensive Care Unit with a COVID-19 in Ankara City Hospital between 15.03.2020 and 15.07.2020 were collected in our retrospective study. This study included 656 patients with COVID-19, 131 with DM, and 525 with the DM-free control group. White blood cell (WBC) count, neutrophils, neutrophil percentage, lymphocytes, lymphocyte percentage, LUCs,%LUCs, NLR, platelets, hemoglobin which was taken within the first 24 hours after admission, and history of DM were noted from the records.

Results

The mean age was 61.29 ± 13.81 years in the diabetic patient group and 44.37 ± 17.14 years in the non-diabetic control group with COVID-19, which was significantly higher in the diabetic group ($P < 0.001$). NLR, WBC count, neutrophils, and neutrophil percentage were statistically significantly higher in patients with DM (respectively, $P < 0.001$, $P = 0.008$, $P = 0.008$, $P = 0.003$, and $P = 0.049$). There were no significant differences between the groups regarding lymphocyte, platelet, LUCs, and%LUCs values ($P > 0.05$).

Conclusion

There are studies in the literature that a decrease in%LUCs value and an increase in NLR are indicators of severe disease in COVID-19. Our study did not detect a difference in%LUCs value in diabetic patients, but our study is a preliminary study. Analysis of the data with clinics continues with more patients.

Keywords: COVID-19, Diabetes Mellitus, neutrophil-to-lymphocyte ratio, large unstained cells

DOI: 10.1530/endoabs.81.OC14.3

OC14.4

Discovery of microRNA biomarkers in circulation and bone tissue from a type-2 diabetes mellitus rat model under different anti-osteoporotic treatments

David Carro Vázquez[1], Lejla Emini[2], Martina Rauner[2], Christine Hofbauer[2], Johannes Grillari[3], Richard Eastell[4], Lorenz C Hofbauer[2] & Matthias Hackl[1]
[1]TAmiRNA GmbH, Wien, Austria; [2]Dresden University of Technology, Department of Medicine III and Center for Healthy Aging, Dresden, Germany; [3]Ludwig Boltzmann Institut, Department of Experimental and Clinical Traumatology, Wien, Austria; [4]The University of Sheffield, Academic Unit of Bone Metabolism, and Mellanby Centre for Bone Research, Sheffield, United Kingdom

Metabolic changes in Type-2 Diabetes-Mellitus (T2DM) make patients more prone to develop osteoporosis and delayed bone healing. We hypothesize that microRNAs could be involved in the underlying mechanism and used as biomarkers in this context. To test this hypothesis, we analyzed microRNAs in samples from Zucker Diabetic Fatty (ZDF) rats, a T2DM model with reduced bone healing and bone mass. 11-week-old male ZDF and wildtype rats with a femur subcritical defect were treated with placebo, anti-sclerostin, PTH and insulin treatments for 12 weeks. After the treatment, metabolic and bone phenotype parameters of all the rats were measured and serum and ulna samples were obtained ($n =$ 4-5 per group). RNA isolation and small RNA next generation sequencing (NGS) were performed using serum and ulna samples for untargeted genome-wide miRNA analysis. Significantly (adj. $P < 0.2$) regulated miRNAs identified by NGS were further analyzed with the online tool miRnet 2.0 for miRNA target network construction and with the FANTOM5 browser for cell-type enrichment analysis. Our results show that insulin induced a strong dysregulation of circulating miRNAs mainly involved in metabolism, and even rescued seven circulating miRNAs in the ZDF model (rno-miR-802-5p, rno-miR-122-3p, rno-miR-375-3p, rno-miR-27a-5p, rno-miR-31a-5p, rno-miR-192-5p, rno-miR-122-5p). Anti-sclerostin caused a less intense miRNA dysregulation in serum but affected miRNAs shown to be enriched in bone tissue, rescuing particularly one of those miRNAs (rno-miR-145-5p). PTH treatment did not produce any effect on circulating neither on bone miRNAs in the ZDF rats, most probably due to a blunting effect of diabetes over the PTH. Altogether, this study shows the enhancement effect on bone mass and bone regeneration potentially caused by dysregulation of bone miRNAs and of the rescue of circulating miRNAs in ZDF rats under the three analyzed treatments.

DOI: 10.1530/endoabs.81.OC14.4

OC14.5

The effect of multiple passes to the same thyroid nodule in the fine needle aspiration biopsy session on obtaining adequate and/or the AUS/FLUS cytological result

Fatma Dilek Dellal Kahramanca[1], Fatma Neslihan Cuhaci Seyrek[2], Afra Alkan[3], Oya Topaloglu[2], Reyhan Ersoy[2] & Bekir Cakir[2]
[1]Ankara City Hospital, Endocrinology and Metabolism, Ankara, Turkey; [2]Ankara Yildirim Beyazit University, Faculty of Medicine, Endocrinology and Metabolism, Ankara, Turkey; [3]Ankara Yildirim Beyazit University, Faculty of Medicine, Biostatistics, Ankara, Turkey

Aim

To determine whether multiple fine needle passes to the same thyroid nodule in the fine needle aspiration biopsy (FNA) session affect sufficient and/or atypia of undetermined significance/follicular lesion of undetermined significance (AUS/FLUS) cytological result.

Materials and Methods

Ultrasonography (US) and cyto-histopathology results of the nodules of patients who were diagnosed with thyroid nodules and underwent FNA between May-August 2021 were retrospectively analyzed. The nodules were divided into two groups according to the number of needle passes performed in the same FNA session as those with one pass (one-pass group) and those with two or three passes (multiple-passes group). The two groups were compared in terms of cytological adequacy and the rate of AUS/FLUS diagnosis as well as US features and TIRADS scores.

Results

A total of 1500 thyroid nodules of 708 patients (575 female and 133 male) were included in the study. The mean age of the patients was 51.57 ± 12.51 years. 1409 (93.9%) nodules were performed one pass, and 91 (6.1%) were performed two ($n = 85$) or three passes ($n = 6$). While the cystic/mixed nodule ratio and macrocalcification rate were higher in the multiple-passes group, the rates of coalescent nodules and presence of halo were higher in the one-pass group ($P = 0.001$, $P = 0.039$, $P = 0.006$, and $P = 0.040$, respectively). TIRADS 3 score was higher in multiple-passes group ($P = 0.001$). The adequacy and AUS/FLUS ratios were similar in the two groups.When nodules with macrocalcifications and cystic/mixed structures were evaluated as two separate subgroups, the adequacy and AUS/FLUS ratios were similar in one-pass and multiple-passes groups.

Conclusion

Two or three passes to thyroid nodules have similar cytological adequacy and AUS/FLUS ratios compared to one pass.Although more passes are performed in

Features	One-pass ($n=1409$)	Multiple-passes ($n=91$)	P
Cystic/mixed structure [n (%)]	87 (6.2)	14 (15.4)	**0.001**
Presence of macrocalcification [n (%)]	119 (8.4)	14 (15.4)	**0.039**
Presence of peripheral halo [n (%)]	250 (17.7)	8 (8.8)	**0.040**
Coalescence [n (%)]	149 (10.6)	1 (1.1)	**0.006**
TIRADS Category			**0.003**
3	73 (5.2)	12 (13.2)	**0.001**
4a	702 (49.8)	40 (44.0)	0.278
4b	579 (41.1)	32 (35.2)	0.265
4c	55 (3.9)	7 (7.7)	0.078
5	0 (0.0)	0 (0.0)	
Cytological sufficiency [n (%)]	1033 (73.3)	65 (71.4)	0.694
AUS/FLUS cytology [n (%)]	240 (17.0)	9 (9.9)	0.103

cystic/mixed and macrocalcified nodules estimating that the material would be insufficient with macroscopic on-site evaluation, needle insertion of two or three times does not contribute to the adequacy and also the AUS/FLUS ratio compared to one pass.

DOI: 10.1530/endoabs.81.OC14.5

OC14.6

Engaging the Endocannabinoid System in Neuroendocrine Neoplasms (NENs) potentiates treatment outcomes and null drug resistance

Shani Avniel- Polak[1], David Polak[2], Kira Oleinikov[1], David J Gross[1], Ori Wald[3], Uzi Izhar[3], Haggi Mazeh[4], Yotam Drier[5] & Simona Glasberg[1]
[1]Hadassah Medical Organization, Hebrew University of Jerusalem, Department of Endocrinology and Metabolism, Neuroendocrine Tumor Unit, ENETs Center of Excellence, Jerusalem, Israel; [2]Hadassah Medical Organization, Hebrew University of Jerusalem, Department of Periodontics, Dental Medicine Faculty, Jerusalem, Israel; [3]Hadassah Medical Organization, Hebrew University of Jerusalem, Department of Cardiothoracic Surgery, Jerusalem, Israel; [4]Hadassah Medical Organization, Hebrew University of Jerusalem, Department of Surgery, Mount Scopus, Jerusalem, Israel; [5]Hadassah Medical Organization, Hebrew University of Jerusalem, The Lautenberg Center for Immunology and Cancer Research, Faculty of Medicine, Jerusalem, Israel

Introduction
Patients with unresectable NENs are offered a variety of non-curable therapeutic options, which eventually fail due to drug resistance. Increasing evidence suggest an anticancer trait of cannabinoids, via cellular pathways including mTOR, known to be associated with drug resistance development. Still, limited data exist on the anti-cancer effects of cannabinoids in NENs.
Aims
To understand the possible anti-tumor role of the cannabinoids and the endocannabinoid system in NENs, and their ability to overcome resistance to everolimus.
Materials and methods
The endocannabinoid receptors expression on NENs cell lines of lung (NCI-H727) and pancreatic (BON1) origin and on human samples was examined using FACS/immunofluorescence staining and RNA-Seq. Cells were treated with multiple cannabinoids extracts with different chemical profile. Viability and apoptosis were examined using WST-1 and Annexin/PI. Endocannabinoid receptors blocking with specific antagonists examined cannabis extracts -induced toxicity. The effect of everolimus $\pm$ cannabis extracts/ endocannabinoid receptors antagonists on cell viability was examined.
Results
The endocannabinoid receptor CB1, but not CB2, is highly expressed in NEN cell lines and tumor samples. The expression of other endocannabinoid receptors (TRPV1, TRPV2, PPARα and PPARγ) is heterogeneous. 50 cannabis extracts were initially tested, identifying 6 cannabis extracts that significantly reduced cell viability by ~40% via CB1. Also, CB1 blocking vigorously decreased cells viability and increased apoptosis. Cells viability decreased by 15% with everolimus alone; this effect was enhanced when cannabis extracts and mainly when CB1 antagonists were added (by 33% and 59%, respectively). Even more, combining everolimus with endocannabinoid receptor blocking in a NEN mouse model showed synergistic effect with impressive decrease in tumor size.
Conclusions
Our preliminary results suggest that modulation of endocannabinoid system seems promising in NENs models, mostly via the endocannabinoid receptor CB1. Addition of cannabis extracts /CB1 antagonist to everolimus may have synergistic effects that might lead to a novel and efficient modality to treat NEN and diminishes the development of drug resistance.

DOI: 10.1530/endoabs.81.OC14.6

Young Investigator Awards

YI1

Excessive bilateral adrenal hyperplasia associated with aldosterone synthase (CYP11B2) deficiency

Aristidis Diamantopoulos[1], Panagiotis Mourelatos[1], Amalia Sertedaki[2], Efthimia Botoula[1], Dimitra Vassiliadi[1] & Stylianos Tsagarakis[1]
[1]"Evangelismos" General Hospital of Athens, Greece, Department of Endocrinology, Diabetes and Metabolism, National Expertise Center for Rare Endocrine Disorders and member of the Endo-ERN, Athens, Greece; [2]"Agia Sofia" Children's Hospital, Athens, Greece, First Department of Peadiatrics, Division of Endocrinology, Metabolism and Diabetes, Medical School, National and Kapodistrian University of Athens, Athens, Greece

Introduction
Congenital adrenal hyperplasia (CAH) encompasses a group of enzymatic defects in cortisol biosynthesis resulting in adrenal hyperplasia through chronic compensatory ACTH stimulation. Aldosterone synthase deficiency, however, is associated with normal cortisol secretion and there are no reports on whether it may be associated with adrenocortical hyperplasia.
Case Presentation
A 37-year-old, Greek female was referred for further investigation of excessive diffuse bilateral adrenal hyperplasia discovered during investigations for post-partum weight gain (25 kg), fatigue, hirsutism, easy bruising, and depression associated with borderline cortisol status abnormalities (cortisol post-1mg dexamethasone: 100 nmol/l, basal ACTH: 7.3 pg/ml and 24-h urinary free cortisol (UFC): 1.32$\times$ULN; androgens, as well as 17-hydroxyprogesterone, were normal). In infancy, the patient was erroneously diagnosed with CAH when she presented with failure to thrive, hyponatremia and hyperkalemia. She was treated with methylprednisolone and fludrocortisone until the age of 2, when she was re-evaluated with a Cosyntropin Stimulation Test (CST) with normal basal and stimulated cortisol levels (0'/30': 811/822 nmol/l). Aldosterone was 13 ng/dl with PRA$>$40 ng/ml/h and 11-Deoxycortisol 2,2 ng/ml. On repeated testing, aldosterone was 15,6 ng/dl, PRA: 2,2 ng/ml/h, 17OHPR: 0,2 ng/ml and the diagnosis of pseudo-hypoaldosteronism was made. Subsequently, the patient had normal growth and pubertal development; she had oligomenorrhea until pregnancy and subsequently normalization of menstrual cycles. The coding regions of *CYP11B2*, *CYP21A2* and *CYP11B1* genes underwent Sanger sequencing.
Results
On physical examination, she had no clinical stigmata of Cushing's Syndrome. Cortisol post-dexamethasone was borderline (63 nmol/l) without any other features of hypercortisolism (normal midnight serum cortisol and UFC). Basal aldosterone levels were 5/4.4 ng/dl with marginally elevated renin levels (56/40 mcU/ml). Given her PMH we performed a CST, in which she had a normal cortisol response, a borderline increase of 17-OH PRG (0'/30': 7/30.2 nmol/l) but a remarkable lack of aldosterone response (0'/60':6.3/6.9 ng/dl). We suspected *CYP11B2* gene deficiency, which was confirmed by genetic testing, that revealed compound heterozygosity for two pathogenic variants (p.T185I and p.E255X). No mutations were identified in *CYP21A2* and *CYP11B1* genes.
Conclusion
To our knowledge, this is the first report that associates diffuse bilateral adrenal hyperplasia with *CYP11B2* deficiency, a rare defect that is usually diagnosed during infancy and improves with age so that adults are asymptomatic. Our patient presented with impressively enlarged adrenals without discrete nodules and no other evident cause of adrenal hyperplasia.

DOI: 10.1530/endoabs.81.YI1

YI2

Single-nuclei transcriptome of adult human adrenal glands reveals novel insights into molecular mechanisms intrinsic to adrenocortical tumourigenesis and cortisol secretion

Barbara Altieri[1], Ali Kerim Secener[2,3], Somesh Sai[2,3], Cornelius Fischer[2,3], Silviu Sbiera[1], Panagiota Arampatzi[4], Sarah Vitcetz[3], Caroline Braeuning[2], Sascha Sauer[2,3], Martin Fassnacht[1] & Cristina Ronchi[1,5]
[1]Division of Endocrinology and Diabetes, Department of Internal Medicine I, Würzburg, Germany; [2]Max Delbrück Center for Molecular Medicine, Berlin, Germany; [3]Berlin Institute of Health, Berlin, Germany; [4]Core Unit SysMed, University of Würzburg, Würzburg, Germany; [5]Institute of Metabolism and System Research, University of Birmingham, Birmingham, United Kingdom

Background
Molecular mechanisms underlying the pathogenesis of adrenocortical adenomas (ACAs) and autonomous cortisol secretion remains frequently unexplained despite previous comprehensive genomics studies.
Aim
To gain novel insights into molecular pathogenesis of adrenocortical tumours by investigating transcriptome profiles of ACAs at single-nuclei resolution (snRNA-Seq), using adult human normal adrenal glands (NAGs) as reference.
Methods
We isolated single nuclei from 6 NAGs and 12 ACAs, including 7 cortisol-producing adenomas (CPAs) and 5 endocrine inactive adenomas (EIAs) with different genetic background. snRNA-Seq was performed using inDrop™ technology. Data analysis, integration and exploration was performed using Seurat R package. Pathway enrichment analysis was performed using pathfindR withKEGG pathways as reference. Transcriptome profile from ACA was integrated with NAG using anchor pairs between the two datasets. Identification of tumour- and mutation-specific cell subpopulations (i.e. clusters) was done by differential gene expression analysis.
Results
Within the NAGs, we identified different satellite clusters of immune, myeloid and vascular origin, in addition to main clusters representing the three adrenal cortex zones, medulla and capsule. We also identified two subpopulations potentially representing adrenocortical and adrenomedullary progenitor cells, located within and underneath the capsule. Comparative analysis of the transcriptional profiles of NAGs and ACAs revealed the presence of six ACA-specific clusters, namely four "tumour-specific" (TC1-4), "tumour microenvironment" (TME), and one cluster overexpressing genes of cholesterol pathway (Chol-upreg). Specifically, the TC1 was mostly found in 2 *CTNNB1*-mutated samples (one EIA and one CPA), where a significant overexpression of *AFF3*, *FTO* and *ISM1*, as well as genes of spliceosome (fold enrichment, FE = 7.6), ECM-receptor interaction (FE = 7.3) and Hippo signaling (FE = 2.8) pathways were observed. The TC2 cluster was more abundant in EIA and characterized by overexpression of genes like *MMP26*, *SP100* and *EIF4H*, as well as genes of NOD-like receptor (FE = 3.6) and IL-17 signaling pathway (FE = 3.5) associated with tumour promotion. The Chol_upreg cluster was largely represented in CPAs and characterized by a very high expression of genes associated to steroid biosynthesis (FE = 34.2) and cortisol synthesis and secretion (FE = 9.5), including *HMGCS1*, *SQLE* and *FDX1*. The remaining clusters (TME, TC3-4) were quite homogeneously distributed in all ACAs, independently from mutational status (2 *PRKACA*-, 1 *GNAS*-, 6 *CTNNB1*-, 3 no driver-mutation) and cortisol secretion.
Conclusion
Our human adult NAG single-cell atlas represents a unique source for investigations of adrenal diseases and allowed us to investigate the molecular heterogeneity of ACAs at single-cell level, showing the presence of specific cell populations associated with cortisol secretion and genetic background.

DOI: 10.1530/endoabs.81.YI2

YI3

Generalization of TSH and FT4 reference intervals in pregnancy: an individual participant data meta-analysis

Joris Osinga[1,2], Arash Derakhshan[1,2], Consortium on thyroid and pregnancy working group on reference intervals [3], Robin Peeters[1,2] & Tim Korevaar[1,2]
[1]Erasmus University Medical Center, Department of Internal Medicine, Rotterdam, Netherlands; [2]Erasmus University Medical Center, Academic Center for Thyroid Diseases, Rotterdam, Netherlands; [3]Multiple, Nepal

Objective
Defining thyroid function test abnormalities in pregnancy is complicated by changes in maternal physiology. Ideally, reference intervals (RIs) should be population-based and pregnancy-specific. Large methodological differences between published reports limit the adoption of such RIs into clinical practice.
Methods
The study was performed in the Consortium on Thyroid and Pregnancy. In line with current consensus and the 2017 American Thyroid Association guidelines, cohort-specific RIs based on the 2.5th and 97.5th percentiles were calculated after exclusion of participants with pre-pregnancy thyroid disease, thyroid medication use and TPOAb positivity. To evaluate current recommendations and methodological variations, RIs were also calculated using the above mentioned methods and eight different methodologies often encountered in literature; 1) using the 5th to 95th percentiles, 2) without excluding TPOAb positivity, and using additional exclusion criteria defined as 3) exclusion of TgAb-positivity 4) pre-pregnancy diabetes mellitus, 5) essential hypertension, 6) obesity 7) active smoking, or 8) any pregnancy complications.
Results
The final study population comprised of $n = 63{,}198$ participants from 22 cohorts. Between cohorts, the upper limit for TSH calculated according to the current consensus ranged from 2.24 to 6.02 mU/l in the first trimester, from 2.67 to 6.15 mU/l in the second trimester and from 3.03 to 6.13 mU/l in the third trimester. Not excluding TPOAb positive participants led to a rise of the upper limits of TSH in all cohorts, especially in the first (+17.4% average, range +1.6 to +30.3%) and second (+9.8% average, range +0.6 to +32.3%) trimester. The use of the 95th percentile led to considerable changes in upper limits, varying from -10.8% to -21.8% for TSH and -1.2% to -13.2% for FT4 across all trimesters. All other additional exclusion criteria led to less than 3.5% variability around the 97.5th percentile, without a trend towards increase or decrease.
Conclusion
The large variability in reference limits between cohorts stress the importance of hospital- and pregnancy specific RIs. Furthermore, our data emphasize the importance of excluding TPOAb-positive participants and the use of appropriate percentiles cut-offs. Additional exclusions frequently encountered in literature did not affect TSH or FT4 reference intervals during pregnancy, indicating that the majority of published studies can be implemented into clinical practice despite methodological differences and future studies can adapt simplified study setups to define valid RIs.

DOI: 10.1530/endoabs.81.YI3

YI4

The role of miR-335-5p in the differentiation of thyroid cancers with BRAF mutation

Valeria Pecce[1], Antonella Verrienti[1], Marialuisa Sponziello[1], Giorgio Grani[1], Simone Bini[1], Sebastiano Filetti[2] & Cosimo Durante[1]
[1]Sapienza University of Rome, Translational and Precision Medicine, Rome, Italy; [2]Sapienza University of Rome, Unitelma

The most frequent mutation in papillary thyroid carcinoma (PTC) is the p.V600E of the *BRAF* gene. This mutation leads to the aberrant activation of the RAS / BRAF / MEK / ERK pathway and consequently to the under-regulation of thyroid-specific genes, resulting in uncontrolled growth and de-differentiation of cancer cells. In this work, we analyzed the transcriptomics data produced by the TCGA project using a network approach. The analysis led to the identification of regulatory genes, called switch genes, involved in the network changes between mutated *BRAF* papillary carcinomas and normal thyroid tissues. In particular, we identified 227 switch genes. Within the network generated by these genes, 63 were found to be targets of the same microRNA, the mir-335-5p. The role of this microRNA was then investigated through an *in vitro* study. We selected two primary cell lines and four immortalized lines of thyroid cancer, all of them carrying the *BRAF* mutation, which showed lower levels of mir-335-5p expression compared with normal control cells. A synthetic microRNA was transfected in all six cell lines. After transfection, the analyses showed an increase in *TSHR*, *PAX8*, and *NIS* expression in the two primary cell lines and in three out of four immortalized lines. Furthermore, all the studied lines showed an increased iodine uptake following treatment with mir-335-5p. Moreover, we obtained organoids by growing the transfected lines in a semi-solid culture medium. We studied the morphology of the 3D structures generated before and after the transfection of miR-335-5p, the interaction among organoid cells and extracellular matrix components, and the protein levels of thyroid-specific genes through immunofluorescence. Our results led us to conclude that the restoration of the intracellular levels of mir-335-5p could have a role in promoting the re-differentiation of thyroid tumors with *BRAF* mutation.

DOI: 10.1530/endoabs.81.YI4

YI5

Pseudohypoparathyroidism: focus on neonatal features, preliminary data from a retrospective analysis of a large cohort of patients

Giulia Del Sindaco[1,2,3], Angela Pagnano[2,3], Jugurtha Berkenou[1], Anya Rothenbuhler[1,4], Maura Arosio[2,3], Agnès Linglart[1,4,5] & Giovanna Mantovani[2,3]
[1]AP-HP, Service d'endocrinologie et diabète de l'enfant, ERN BOND, ERN for rare endocrine disorders, Platforme d'expertise des maladies rares, Hôpital Bicêtre Paris Saclay, Le Kremlin-Bicêtre, France; [2]Department of Clinical Sciences and Community Health, University of Milan, Milan, Italy; [3]Endocrinology Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy; [4]AP-HP, Centre de Référence des maladies rares du métabolisme du Calcium et du Phosphate, filière OSCAR, Paris, France; [5]Université de Paris Saclay, INSERM, U1185, Le Kremlin-Bicêtre, France

Since the first description of pseudohypoparathyroidism (PHP) a remarkable clinical variability was observed. In 2016 a new classification of this group of diseases have been published by the European Network on PHP and related disorders, proposing "inactivating PTH/PTHrP signaling disorder" (iPPSD) as a new term that encompasses all the clinical entities. PHP and related disorders vary in clinical presentation and disease severity, and clinical features usually develop during mid and late childhood. There are only few reports in literature about neonatal PHP, describing hypocalcemic seizures in late neonatal period. To our knowledge no others neonatal complications are described as associated to iPPSD. The aim of this study is to analyse a large cohort of iPPSD patients and to investigate early history of the disease, with special focus on neonatal complications. We collected data from 136 patients diagnosed with iPPSDs and in regular follow-up at the Endocrinology Unit of Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico (Milan, Italy) and at the Pediatric Endocrinology Unit of Hôpital Bicêtre (Paris, France). We have retrospectively collected data about birth, and we have then investigated the rate of neonatal complications occurring within the first month of life. Then, we have subdivided neonatal complications in several categories (respiratory, cardiac, neurological, gastrointestinal, metabolic, multiple districts, others) and we have assessed the number of complications for each patient. We analysed data from 83 children and 53 adults with diagnosis of iPPSD (mean age 18 $\pm$ 11 years). In our cohort 55.9% of patients were diagnosed with iPPSD2 (PHP1A) and 17.6% with iPPSD3 (PHP1B), 11.8% of patients suffered from acrodysostosis type 1 or 2 and 2.2% had a mutation of *PTHR1* (iPPSD1). In 12.5% of cases we couldn't find any mutations (iPPSDx). At least one neonatal complication occurred in 36% of patients (49/136). iPPSD2 patients represent the majority of our cohort and 47% of them experienced neonatal complications, being the category the most affected ($P=0.001$). At univariate analysis neonatal complications in iPPSD patients correlate with the risk of developing neurocognitive impairment ($P=0.01$) and constipation ($P=0.04$) later in life. Moreover, 38.9% iPPSD2 patients who developed neonatal complications had $>$ 2 complications at birth. We could also identify recurrent complications among iPPSD2 patients: 8 of them (10.5%) developed neonatal hypoglicemia and 13 (18.4%) experienced transient respiratory distress. To now we can conclude that iPPSD and especially iPPSD2 newborns need special care at birth, for the risk of developing neonatal complications.

DOI: 10.1530/endoabs.81.YI5

YI6

Integrated genomics reveals the molecular classification of Primary Bilateral Macronodular Adrenal Hyperplasia (PBMAH), correlating with specific profiles of illegitimate receptors expression and identifies KDM1A as the genetic cause of food-dependent Cushing syndrome

Lucas Bouys[1], Florian Violon[1], Anna Vaczlavik[1], Giannone Gaetan[1], Anne Jouinot[1], Roberta Armignacco[1], Isadora Pontes Cavalcante[1], Annabel Berthon[1], Eric Letouzé[2], Patricia Vaduva[3], Maxime Barat[1], Bonnet Fideline[1], Karine Perlemoine[1], Christopher Ribes[1], Mathilde Sibony[1], Marie-Odile North[4], Stéphanie Espiard[5], Magalie Haissaguerre[6], Igor TAUVERON[7], Laurence Guignat[4], Lionel Groussin[1], Bertrand Dousset[1], Martin Reincke[8], Maria Candida Barisson Villares Fragoso[9], Constantine A Stratakis[10,11,12], Eric Pasmant[1], Rossella Libe[1], Guillaume Assié[1], Bruno Ragazzon[1] & Jerome Bertherat[1]
[1]Institut Cochin, Paris, France; [2]Paris Artificial Intelligence Research Institute, Paris, France; [3]CHU de Rennes, Rennes, France; [4]Hôpital Cochin, APHP, Paris, France; [5]CHRU de Lille, Lille, France; [6]CHU de Bordeaux, Bordeaux, France; [7]CHU de Clermont-Ferrand, Clermont-Ferrand, France; [8]Klinikum der Universität München, Munich, Germany; [9]University of Sao Paulo, Sao Paulo, Brazil; [10]National Institute of Health, Bethesda, United States; [11]Research Institute, ELPEN, Pikermi, Athens, Greece; [12]Human Genetics & Precision Medicine, IMBB-FORTH, Heraklion, Crete, Greece

Introduction
In Primary Bilateral Macronodular Adrenal Hyperplasia (PBMAH), cortisol secretion may be consecutive to physiological stimuli, through the illegitimate expression of G-protein coupled receptors (GPCR) in adrenocortical cells. The most characterized is the overexpression of GIP receptor (GIPR) leading to food-dependent Cushing syndrome (FDCS) but it has not been associated with the consecutive inactivation of ARMC5 responsible for 25% of PBMAH. This work aimed to investigate the molecular heterogeneity of PBMAH and its genetic causes.
Methods
A multi-omics analysis (transcriptome, methylome, miRNome, SNP array and exome sequencing) was performed on PBMAH tissues from 36 operated patients.
Results
The integrative analysis revealed three molecular groups with different clinical features: G1, 16 patients with PBMAH due to ARMC5 inactivating variants; G2, 6 patients with FDCS; and G3, 14 patients with a less severe phenotype. Exome sequencing identified germline truncating variants of KDM1A in 5 G2 patients, constantly associated with a somatic loss of the KDM1A wild-type allele on 1p, leading to a loss of KDM1A expression both at mRNA and protein levels ($P=1.2\times10\text{-}12$ and $P<0.01$, respectively). G2 tumors are characterized by a specific pathological aspect including a large proportion of eosinophilic cells compared to G1 and G3 ($P<0.001$). The transcriptome analysis allows to show specific expression profiles of GPCR: G1/ARMC5 tumors showed a relative overexpression of the vasopressin receptors AVPR1A and AVPR1B compared to the two other groups (fold-change [FC] $=7.39$, $P<0.001$ and 3.98, $P<0.001$, respectively) but a lower expression of AVPR2 (FC$=0.43$, $P=0.015$); G2/KDM1A tumors showed a dramatic overexpression of GIPR compared to the two other groups (FC$=105.02$, $P<0.001$) but also of the adrenergic receptors ADRA1D and ADRA2A (FC$=2.93$, $P=0.027$ and 9.99, $P<0.001$, respectively) and of the LH/hCG receptor (LHCGR) (FC$=12.20$, $P<0.001$); G3 tumors showed a slight overexpression of the adrenergic receptors ADRA1B (FC$=3.49$, $P=0.001$) and in few tumors ADRA1D, AVPR2 and LHCGR were highly expressed suggesting molecular heterogeneity in G3.
Conclusion
This study reveals three distinct molecular groups of PBMAH with specific expression profiles of GPCR and identifies KDM1A inactivation as the genetic cause of FDCS. Besides GIPR, KDM1A inactivation seems to drive the overexpression of the LH/hCG receptor, potentially responsible for Cushing syndrome associated with pregnancy and menopause. KDM1A tumors present specific pathologic aspects including a large proportion of eosinophilic cells. ARMC5 and KDM1A genetic screening can now be offered for all PBMAH cases, opening the way to earlier diagnosis and improved management.

DOI: 10.1530/endoabs.81.YI6

YI7

Radiotherapy for adults with pituitary adenoma or craniopharyngioma is associated with increased risk of second brain tumour : A multi-centre study of 3,613 patients with long-term imaging surveillance

Ross Hamblin[1,2,3], Ashley Vardon[1,2,3], Josephine Akpalu[1,2,3], Metaxia Tampourlou[1,2,3], Ioannis Spiliotis[4], Emilia Sbardella[4], Julie Lynch[5], Vani Shankaran[5], Akash Mavilakandy[6], Irene Gagliardi[7], Sara Meade[8], Claire Hobbs[9], Alison Cameron[10], Miles J Levy[6], John Ayuk[3], Ashley Grossman[4], Maria Rosaria Ambrosio[7], Maria Chiara Zatelli[7], Narendra Reddy[6], Karin Bradley[11], Robert Murray[5], Aparna Pal[4] & Niki Karavitaki[1,2,3]
[1]Institute of Metabolism and Systems Research, College of Medical and Dental Sciences, University of Birmingham, Birmingham, United Kingdom; [2]Centre for Endocrinology, Diabetes and Metabolism, Birmingham Health Partners, Birmingham, United Kingdom; [3]Department of Endocrinology, Queen Elizabeth Hospital, University Hospitals Birmingham NHS Foundation Trust, Birmingham, United Kingdom; [4]Oxford Centre for Diabetes, Endocrinology and Metabolism, Oxford University Hospitals NHS Foundation Trust, Oxford, United Kingdom; [5]Department of Diabetes and Endocrinology, Leeds Teaching Hospitals NHS Trust, St James's University Hospital, Leeds, United Kingdom; [6]Department of Diabetes and Endocrinology, University Hospitals of Leicester NHS Trust, Leicester Royal Infirmary, Leicester, United Kingdom; [7]Section of Endocrinology & Internal Medicine, Department of Medical Sciences, University of Ferrara, Ferrara, Italy, Italy; [8]Department of Oncology, Queen Elizabeth Hospital, University Hospitals Birmingham NHS Foundation Trust, Birmingham, United Kingdom; [9]Department of Clinical Oncology, Oxford University Hospitals NHS Trust, Oxford, United Kingdom; [10]Bristol Haematology and Oncology Centre, University Hospitals Bristol and Weston NHS Foundation Trust, Bristol, United Kingdom; [11]Department of Endocrinology, Bristol Royal Infirmary, University Hospitals Bristol and Weston NHS Foundation Trust, Bristol, United Kingdom

Background
The risk of a second brain tumour following radiotherapy for pituitary adenoma or craniopharyngioma in adults is currently unclear. Studies are methodologically limited by small patient sample size, few case events, selection biases or the use of inappropriate controls.
Objective
To ascertain whether radiotherapy delivered to adults with pituitary adenoma or craniopharyngioma is associated with an increased second brain tumour risk using appropriate methodology.
Design
Multicentre, retrospective cohort study involving six adult endocrine centres.
Methods
4,292 patients with pituitary adenoma or craniopharyngioma detected until 31st December 2013 were identified from departmental registries. Patients with one image, unknown radiotherapy exposure status, genetic predisposition, history of brain tumour prior to study entry, or aged <18 years at the time of radiotherapy, were excluded ($n=598$). Recipients of proton or stereotactic radiotherapy ($n=81$) were also excluded from statistical analyses, such that data were explored for 930 patients exposed to conventional, 3D-CRT or IMRT and 2,683 controls. Follow-up was defined by imaging dates from the time of radiotherapy until last imaging in the exposure group, and from the time of pituitary tumour detection until last imaging in the control group.
Results
Over 43,887 patient-years (12,674 radiotherapy, 31,213 controls), second brain tumours were reported in 58 patients (27 radiotherapy, 31 controls): 6 were malignant (4 radiotherapy, 2 controls, and 52 benign (23 radiotherapy, 29 controls). Older age at pituitary tumour diagnosis and radiotherapy exposure were associated with increased risk of second brain tumour (HR 1.036, 95%CI 1.018-1.055, $P<0.0001$ and HR 1.744, 95% CI 1.040-2.927, $P=0.035$, respectively), but tumour type and sex were not. After adjusting for age, radiotherapy exposure was associated with an increased risk of second brain tumour (HR 1.728, 95%CI 1.029-2.902, $P=0.031$). Cumulative probability of second brain tumour at 20 years was 4.2% and 2.1%, for the radiotherapy group and control group, respectively. Incidence rate ratio of irradiated versus controls was 2.15 (95%CI 1.27-3.60, $P=0.005$). Median latency after radiotherapy was 8.1 years (7.5-27.3) for malignant and 17.2 years (3.0-50.8) for benign tumours, respectively.
Conclusions
This is the first study assessing the risk of a second brain tumour in a cohort of non-selected irradiated adults and appropriate controls with confirmed long-term imaging surveillance. The risk of second brain tumour following radiotherapy (conventional, 3DCRT or IMRT) for pituitary tumours is increased, although less than previously reported. Our results inform clinical practice and provide data to be used when counselling patients on the risks of radiotherapy.

DOI: 10.1530/endoabs.81.YI7

YI8

AKR1D1 knockdown identifies 7α-hydroxy-3-oxo-4-cholestenoic acid (7-HOCA) as a driver of metabolic dysfunction and hepatocellular cancer risk in patients with non-alcoholic fatty liver disease (NAFLD)

Nikolaos Nikolaou[1,2], Anastasia Arvaniti[2,3], Fabio Sanna[2], Ragazzon da Conceição[2], Niall Dempster[2], Laura Gathercole[3] & Jeremy Tomlinson[2]
[1]University of Cambridge, Department of Pathology, Cambridge, United Kingdom; [2]University of Oxford, Oxford Centre for Diabetes, Endocrinology and Metabolism, Oxford, United Kingdom; [3]Oxford Brookes University, Department of Biological and Medical Sciences, Oxford, United Kingdom

Non-alcoholic fatty liver disease (NAFLD) is a spectrum of disease ranging from simple intrahepatic lipid accumulation to fibrosis, cirrhosis, and hepatocellular carcinoma (HCC). 5β-reductase (AKR1D1) is a liver enzyme that catalyses a fundamental step in bile acid (BA) synthesis. Both BAs and BA intermediates are established as potent regulators of metabolic and proliferative phenotype. We have hypothesised that AKR1D1 plays a crucial role in NAFLD and HCC. Human liver biopsies and serum samples were obtained from healthy subjects and patients with established NAFLD, cirrhosis and HCC. Alterations in BA synthesis and composition were determined by LC-MS. Genetic manipulation of AKR1D1 (siRNA/shRNA) was performed in human hepatoma HepG2 cells. Effects on BA synthesis, fatty acid metabolism, cell cycle, proliferation and DNA damage were determined by LC-MS, qPCR, western blotting, flow cytometry, RNA-sequencing, ILab biochemistry analyser, and single cell gel electrophoresis (comet assay). Total serum BA and BA intermediate levels were significantly elevated across NALFD disease severity, with a particular increase in the concentration of the AKR1D1 substrate 7α-hydroxy-3-oxo-4-cholestenoic acid (7-HOCA) [control: 182.1 ± 14.9 ($n=19$) vs HCC: 350.6 ± 37.4 nM ($n=20$), $P=1e\text{-}4$). In line with this, *AKR1D1* expression was significantly decreased in liver biopsies from patients with advancing steatosis, fibrosis, inflammation and HCC. In HepG2 cells, AKR1D1 knockdown decreased primary BA and increased 7-HOCA concentrations. RNA-sequencing analysis in AKR1D1-knockdown cells identified dysregulated pathways impacting lipid metabolism, cell cycle and proliferation, consistent with increased intracellular triglyceride accumulation and decreased fatty acid oxidation. In addition, AKR1D1 knockdown induced DNA damage, downstream resulting in cell cycle arrest at G1/S phase, impaired cell proliferation and enhanced apoptosis, suggesting a role for 7-HOCA in liver cell health. Confirming this, RNA-sequencing and subsequent pathway enrichment analysis in wild-type, 7-HOCA-treated HepG2 cells revealed a transcriptional profile similar to the one observed following AKR1D1 knockdown, with increased lipid and decreased proliferative gene expression, accompanied by enhanced DNA damage. Complementing these findings, pharmacological inhibition of AKR1D1 using three novel AKR1D1 inhibitors (identified through a high-throughput drug screen of $>$ 300,000 compounds) similarly impaired proliferative gene expression and cell proliferation. In conclusion, AKR1D1 expression is decreased in patients with NAFLD and HCC, and results in increased accumulation of its substrate, 7-HOCA, with downstream detrimental effects on hepatic triglyceride metabolism, fatty acid oxidation and cell proliferation. Taken together, these data demonstrate the crucial role of 7-HOCA in NAFLD/HCC progression and reveal the potential of AKR1D1 manipulation for hepatoprotective therapies.

DOI: 10.1530/endoabs.81.YI8

YI9

Acute kidney injury: a strong risk factor for hypoglycaemia in hospitalized patients with type 2 Diabetes

Ana Carreira[1], Pedro Castro[2], Filipe Mira[2], Miguel Melo[1], Isabel Paiva[1], Pedro Ribeiro[3] & Lèlita Santos[3]
[1]Centro Hospitalar e Universitário de Coimbra, Department of Endocrinology, Diabetes and Metabolism, Coimbra, Portugal; [2]Centro Hospitalar e Universitário de Coimbra, Department of Nephrology, Coimbra, Portugal; [3]Centro Hospitalar e Universitário de Coimbra, Department of Internal Medicine, Coimbra,Portugal

Introduction
Acute Kidney Injury (AKI) is highly prevalent during hospitalization of patients with type 2 diabetes (T2D), and has been associated with increased risk of hypoglycaemia in Intensive Care Units. However, this association in non-critically ill patients is less clear and evidence on the impact of AKI's severity and duration on hypoglycaemia is lacking.
Objectives
To assess the impact of AKI and its severity and duration on the risk of hypoglycaemia during hospitalization of non-critically ill patients with T2D.
Methods
Retrospective cohort study of patients with T2D, hospitalized in Internal Medicine wards, from 01/01/2018 to 31/12/2019. AKI was defined as an increase in serum creatinine by ≥ 0.3 mg/dl in 48 hours or ≥ 1.5 times baseline within 7 days, and hypoglycaemia as blood glucose concentration <70mg/dl. Glomerular filtration rate (GFR) was calculated by CKD-EPI equation and patients with chronic kidney disease (CKD) stage ≥ 4 were excluded. 239 hospitalizations with AKI were obtained (Group 1) and an equivalent number without AKI was randomly selected (Group 2). Binary logistic regression was used to control for confounding factors and ROC curve analysis to determine cut-off values for AKI's duration.
Results
478 cases were analysed, with mean HbA1C of 7.4 ± 1.6%, 36.0% previously treated with insulin. Patients with AKI were older (82.7 ± 7.9 vs 80.3 ± 10.1 years, $P=0.004$) and had lower basal GFR (59.0 ± 17.3 vs 70.7 ± 19.1, $P<0.001$). The prevalence of hypoglycaemia was higher in Group 1 (40.2% vs 15.9%, $P<0.001$) and the risk increase was sustained when adjusted for confounding factors (including previous insulin therapy and insulin therapy protocol during hospitalization), with a 4.5 times greater risk of hypoglycaemia in the presence of AKI (95%CI: 1.9-10.3). AKI's severity was associated with mortality but not with hypoglycaemia. In contrast, each day of AKI's duration was associated with an increase of 15% on the risk of hypoglycaemia and 16% on the risk of 30-day mortality, independently of its severity. A cut-off of 5.5 days of AKI was obtained for increased risk of hypoglycaemia and mortality. Globally, patients with hypoglycaemia had 4.4 times greater risk of death in 30 days (95%CI: 2.4-8.1).
Conclusion
AKI was an important risk factor for hypoglycaemia in non-critically ill hospitalized patients with T2D, and its prevalence was superior in elderly patients with CKD. The duration of AKI was the main factor increasing the risk of hypoglycaemia and mortality. These results highlight the need to define specific protocols to avoid hypoglycaemia and its burden in patients with AKI.

DOI: 10.1530/endoabs.81.YI9

YI10

The developing rat thyroid gland transcriptome is sexually dimorphic and exhibit dynamic changes from fetal life to prepuberty

Louise Ramhøj[1], Anna Rosenmai[1], Aurélie Lardenois[2], Bertrand Evrard[2], Marta Axelstad[1], Frédéric Chalmel[2] & Terje Svingen[1]
[1]Technical University of Denmark, National Food Institute, Kgs. Lyngby, Denmark; [2]Univ Rennes, INSERM, EHESP, Irset, Rennes, France

Lifelong thyroid health depends on establishment of thyroid gland structure and function during early life development. However, thyroid development can be disrupted and lead to early- or adult life thyroid disorders. Still, the molecular machinery underpinning thyroid gland development remains poorly understood, particularly after the onset of fetal thyroid function. Here we used bulk-RNA-barcoding and sequencing (BRB-seq) to map the thyroid gland transcriptome as it undergoes transcriptional reprogramming after the onset of fetal thyroid gland function. We found 1619 differentially expressed genes (DEGs) during rat thyroid gland development from gestation day 21 to postnatal days 3, 6, 16 and 22. The DEGs partitioned into 6 clusters that display distinct temporal transcriptional patterns. Highly expressed genes in fetuses and neonates were primarily related to cell division, development and morphogenesis. This immaturity of the thyroid gland, even after the onset of thyroid function, was verified histologically, as the fetal thyroids displayed a dense structure with very little follicular lumen. Later on in postnatal development, as thyroid hormone concentrations peak, thyroid gland structure was more mature with larger follicles. This was also reflected in the postnatal transcriptome where genes important for thyroid hormone synthesis, such as *Tpo, Slc5a5(NIS)* and *Nkx2-1*, were upregulated. In addition to the temporal DEGs, we identified 205 DEGs between males and females. Some of these DEGs were related to thyroid hormone synthesis, *Tg, Duox1* and *Duox2*, but the enriched terms also showed that developmental processes as well as the immune system and response to hormones was different between males and females. Thus, it is possible that these differences mediate a sex-specific susceptibility to external stressors such as environmental chemicals. Our results show that, even after the onset of thyroid function, the thyroid gland is still developing with a distinct and sexually dimorphic transcriptional landscape. Disruptions to this transcriptional reprogramming could alter development and thus susceptibility to thyroid disorders in adult life.

DOI: 10.1530/endoabs.81.YI10

YI11

Diagnosing pancreatic neuroendocrine tumors in patients with multiple endocrine neoplasia type 1 in daily practice

Carolina Pieterman[1], Dirk-Jan Van Beek[2], Frank J Wessels[3], Annenienke C van de Ven[4], Wouter W de Herder[5], Olaf M Dekkers[6], Wouter T Zandee[7], Madeline L Drent[8], Peter H Bisschop[9], Bas Havekes[10], Inne HM Borel Rinkes[2], Menno R Vriens[2] & Gerlof D Valk[1]
[1]University Medical Center Utrecht, Endocrine Oncology, Utrecht, Netherlands; [2]University Medical Center Utrecht, Endocrine Surgical Oncology, Utrecht, Netherlands; [3]UMC Utrecht, Radiology, Utrecht, Netherlands; [4]Radboud University Medical Center, Endocrinology, Nijmegen, Netherlands; [5]Erasmus MC, Internal Medicine, Rotterdam, Netherlands; [6]Leiden University Medical Center (LUMC), Endocrinology and Metabolism and Clinical Epidemiology, Leiden, Netherlands; [7]University Medical Center Groningen, Endocrinology, Groningen, Netherlands; [8]Amsterdam UMC, locatie VUmc, Internal Medicine, Section of Endocrinology, Amsterdam, Netherlands; [9]Amsterdam UMC, locatie AMC, Endocrinology and Metabolism, Amsterdam, Netherlands; [10]Maastricht UMC, Internal Medicine, Division of Endocrinology, Maastricht, Netherlands

Background
Pancreatic Neuroendocrine Tumors (PanNETs) are highly prevalent in Multiple Endocrine Neoplasia type 1 (MEN1) and one of the main causes of mortality. Conventional imaging is the mainstay of PanNET screening/surveillance in MEN1. This study aims to assess the diagnostic accuracy of conventional pancreatic imaging studies and to determine the added value of pancreatic fine needle aspirations (FNA) for the diagnosis of MEN1-related PanNETs.
Methods
Patients were included from the population-based MEN1 database of the DutchMEN Study Group from 1990–2017 ($n=445$). Magnetic resonance imaging (MRI), computed tomography (CT), endoscopic ultrasound (EUS), FNA, and surgical resection specimens were obtained. For diagnostic accuracy assessment patients with a PanNET diagnosis >1990 were included if both index and reference test were available. To assess diagnostic accuracy, the first imaging (CT, MRI or EUS) of the pancreatic head and the first imaging of the pancreatic body/tail were considered the index test. For specific comparison of diagnostic accuracy between MRI and CT in the modern era, the first MRI or CT between 2010 and 2017 was the index text. The reference standard was a composite of surgical histopathology and if histopathology was unavailable radiological follow-up.
Results
413 patients underwent 3477 imaging studies. Median radiological follow-up was 8.4 yrs. Time trends show an increasing number of scans/patient, and a preference for MRI in the last decade. Overall diagnostic accuracy of the combined conventional imaging was good with a positive (PPV) and negative predictive value (NPV) of 88.9% (76.0-95.6) and 92.8% (89.4-95.1) for PanNET located in the pancreatic head and 92% (85.3-96.0) and 85.3% (80.5-89.1) in the body/tail. For comparison of MRI vs CT, PPV and NPV for tumors located in the head were 100%(76.0-100) and 87.1%(76.3-93.6) (MRI) vs 60%(22.9-88.4) and 70.4%(51.3-84.3) (CT). PPV and NPV for tumors located in the body/tail were 91.3%(72.0-98.8) and 87.0%(75.3-93.9) (MRI) vs 100%(74.9-100) and 77.8%(54.3-91.5) (CT). FNA was performed of 34 lesions in 33 patients. FNA diagnosis was PanNET in 24 (all confirmed PanNET by histology (10) or follow-up (14)), normal/cyst/unrepresentative in 6 (all confirmed PanNET by follow-up), and adenocarcinoma in 4 (2 confirmed, 2 PanNET).
Conclusion
Diagnostic accuracy for the diagnosis of PanNET was higher for MRI compared to CT and MRI should be the preferred (non-invasive) imaging modality for PanNET screening/surveillance in MEN1. The high diagnostic accuracy of pancreatic imaging and the sporadic occurrence of pancreatic adenocarcinoma question the need for routine (EUS-guided) FNA.

DOI: 10.1530/endoabs.81.YI11

YI12

Role of the transcription factor HHEX in inner adrenal cortex homeostasis and response to progesterone signaling

Typhanie Dumontet[1], Kaitlin Basham[2], Antonio Lerario[1], Christina Bothou[3], Bjoern Brixius[1], Adina F Turcu[1], Felix Beuschlein[3] & Gary D Hammer[1]
[1]University of Michigan, Arbor Arbor, United States; [2]University of Utah, Salt Lake City, United States; [3]University of Zurich, Zurich, Switzerland

The adrenal glands serve as central organs of the endocrine system by producing steroid hormone essential for organismal homeostasis. Mechanisms ensuring proper adrenal homeostasis and function are therefore crucial for maintaining human life. ACTH, released by the pituitary corticotrope, is required for the differentiation of the inner part of the adrenal cortex (the zona fasciculata) and the resultant stimulation of cortisol production. Perturbation of ACTH signaling can lead to diverse pathologic manifestations such as adrenal hyperplasia, hypertrophy, hormone overproduction or adrenal insufficiency. For example, elevated ACTH is a characteristic of patients suffering from Congenital Adrenal Hyperplasia (CAH), a set of defects in cortisol synthesis due to autosomal recessive mutations in genes encoding steroidogenic enzymes. To study the complexity of the ACTH-responsive cell population in the adrenal cortex, we performed single-cell RNAseq of the steroidogenic lineage in the adult mouse adrenal. We identified *Hhex* as a transcription factor with a restricted expression to the ACTH-responsive zona fasciculata. Although the role of HHEX in adrenal biology is completely unknown, a meta-analysis identified a germ-line variant of uncertain significance near the gene *HHEX* associated with increased adrenal androgen production in humans. Interestingly, we have also observed an increase in Hhex expression in a mouse model of CAH. Together with our scRNAseq data, we hypothesized that HHEX contributes to the unique function of the ACTH-responsive inner cortex. To define the role of HHEX in adrenal homeostasis, we generated Hhex knockout mouse models. KO mice exhibited progressive adrenomegaly by 15 weeks of age, accompanied by hypertrophy, most prominent in the inner cortex. Expression of the transcription factor *Nr5a1/Sf1* and steroidogenic enzymes involved in corticosterone production were significantly upregulated at 6 weeks old, prior to adenomegaly. For insights into the signaling pathways controlled by HHEX, we analyzed global transcriptional changes during loss of *Hhex* and found dramatic downregulation of members of the membranous progesterone receptor family (PAQR). PAQR signaling has been implicated in the downregulation of cAMP, a primary mediator of ACTH signaling. Thereby, we speculate that down-regulation of PAQR and subsequent increased ACTH sensitivity could drive the increase in steroidogenesis in *Hhex* KO mice. These findings suggest that HHEX provides a unique autocrine/paracrine intra-adrenal feedback to ACTH-driven cAMP signaling by upregulating PAQR in a unique progesterone-responsive cell population in the inner cortex. As a result, we are currently assessing the implication of HHEX in contributing to the hypertrophy and steroidogenic phenotype observed in CAH.

DOI: 10.1530/endoabs.81.YI12

Rapid Communications

Diabetes, Obesity, Metabolism and Nutrition 1

RC1.1

Predictors of missing postpartum reclassification OGTT in women with gestational diabetes

Catarina Cidade-Rodrigues[1], Filipe Cunha[1], Catarina Chaves[1], Catarina Pereira[2], Silvia Paredes[1], Margarida Vieira[1], Anabela Melo[3], Odete Figueiredo[3], Ana Morgado[3], Mariana Martinho[1] , M. Ceu Almeida[4] & Margarida Almeida[1]

[1]Centro Hospitalar do Tamega e Sousa, Endocrinology, Penafiel, Portugal; [2]Centro Hospitalar de Tras-os-Montes e Alto Douro, Endocrinology, Vila Real, Portugal; [3]Centro Hospitalar do Tamega e Sousa, Gynaecology and Obstetrics, Penafiel, Portugal; [4]Maternidade Bissaya Barreto, Centro Hospitalar e Universitário de Coimbra, Obstetrics, Coimbra, Portugal

Introduction
Women with gestational diabetes (GD) have an increased risk of developing future type 2 diabetes *mellitus* (T2DM). A reclassification oral glucose tolerance test (OGTT) is currently recomended in the postpartum period. However, most studies report a compliance rate below 50% and as low as 23%.
Objectives
We aimed to study predictors of missing postpartum OGTT in women with GD.
Materials and Methods
Retrospective study based on the national register of GD. Included women followed between 2012 and 2017. Excluded women with fetal losses and missing data on age, educational level, BMI, previous history of GD, abortion or arterial hypertension, family history of T2DM, treatment, delivery and obstetric/neonatal complications. Women with and without OGTT were compared. A logistic regression model was used to study factors associated with absence of OGTT: variables with different distribution between groups were included in the analysis.
Results and Conclusions
We studied a total of 14081 women, 4324 (30.7%) had missed postpartum OGTT. Women without OGTT were younger, more frequently foreigners, had higher BMI, more often had had previous GD, multiparity, twin pregnancies and preterm deliveries and they were less frequently diagnosed in the 1st trimester. Newborns from women without OGTT were more often macrossomic and had neonatal hypoglycemia. In the multivariate analysis, age [OR 0.96 (IC 95%: 0.95-0.96), $P<0.001$], BMI ≥ 30 kg/m^2 [1.13 (1.04-1.23), $P=0.004$], preterm delivery [1.35 (1.18-1.54), $P<0.001$], foreign nationality [1.33 (1.18-1.49), $P<0.001$], having a college degree [0.90 (0.83-0.97), $P=0.01$], multiparity [1.91 (1.73-2.12), $P<0.001$], twin pregnancy [1.39 (1.08-1.78), $P=0.009$], pharmacological treatment [0.68 (0.63-0.73), $P<0.001$], previous GD [1.16 (1.04-1.29), $P=0.01$], previous abortion [1.21 (1.12-1.32), $P<0.001$], diagnosis in the 1st trimester [0.86 (0.79-0.92), $P<0.001$] and neonatal hypoglycemia [1.21 (1.01-1.45), $P=0.04$] were associated with missing postpartum OGTT. Women with higher BMI, multiparity, foreigners, with twin pregnancies, previous history of GD, abortion, preterm delivery and neonatal hypoglycemia have an increased risk of missing OGTT. On the other hand, older women and those who needed pharmacological treatment, who have a college degree and who are diagnosed in the 1st trimester have lesser risk of missing OGTT.

DOI: 10.1530/endoabs.81.RC1.1

RC1.2

Glucose alterations, insulin resistance, hypertension, and activation of the renin-aldosterone system are strictly associated in pediatric obesity

Valentina Antoniotti[1], Martina Amore[1], Simonetta Bellone[1], Roberta Ricotti[1], Roberta De Grandi[1], Marina Caputo[2], Daniele Spadaccini[2], Valentina Mancioppi[1], Gianluca Aimaretti[2] & Flavia Prodam[2]

[1]University Of Piemonte Orientale, SCDU of Pediatrics, Department of Health Sciences, Novara, Italy; [2]University of Piemonte Orientale, Department of Health Science, Novara, Italy

Background
The increase of global childhood obesity has led to an increase of associated co-morbidities also at a young age. The pro-inflammatory state and insulin resistance are two master regulators of several complications, including hypertension and pre-diabetes frequently connected in a complex cross-talk.
Aim
To evaluate the relationship between glucose alterations and blood pressure and the pathogenetic involvement of the renin-aldosterone system (RAAS) in pediatric obesity.
Methods
We retrospectively evaluated 800 paediatric subjects (11.4 $\pm$ 3.1 years) with overweight or obesity at the first visit with a complete clinical and metabolic screening (BMI, BMI-SDS, blood pressure, glucose, and insulin levels during an OGTT). Aldosterone and renin were measured with chemiluminescence, and their ratio (ARR) was calculated.
Results
774 patients had all the parameters. 11.5% of patients were with overweight and 88.5% with obesity. Blood pressure has been characterized following the last American Academy of Pediatrics guidelines: 679 patients (87,6% 88.0%) had hypertension (HTN). Of them, 38 (5%) had elevated blood pressure, 226 (29.2%) were classified as HTN stage 1, and 414 (53.4%) stage 2. Regarding glucose levels, 41 subjects had impaired glucose levels, (IFG), 52 impaired glucose tolerance (IGT), 3 type 2 diabetes (T2DM), and a totally 80 subjects had one or more glucose alterations (IFG/IGT/T2DM). Patients with IFG ($P<0.01$), IGT ($P<0.02$), or T2DM/glucose alterations ($P<0.02$) were more frequently with HTN. Blood pressure levels were higher in subjects with glucose alterations ($P<0.04$) than those with normal glucose levels (NGT). OGTT glucose levels and HOMA-IR ($P<0.002$) were higher in subjects with the three HTN stages than those with normal levels. Subjects with glucose levels $>$ 155 mg/dl after 60' at OGTT had more frequent HTN ($P<0.001$) and higher diastolic blood pressure levels ($P<0.002$) than NGT. We also found increased activation of the renin-angiotensin-aldosterone system (RAAS), positively correlated with BMI and female gender, that mainly characterized subjects in HTN stage 2. Aldosterone levels were higher in subjects with glucose levels $>$ 155 mg/dl after 60' at OGTT than those without it ($P<0.003$).
Conclusions
Already in childhood obesity, there is a close relationship between insulin resistance, glucose alterations, hypertension, and RAAS. The identification of specific risk categories, such as the presence of altered blood glucose or hypertension, could provide risk indicators to close clinical surveillance for the prevention and identification of complications and follow-up of organ damage.

DOI: 10.1530/endoabs.81.RC1.2

RC1.3

Plasma amino acid profile in women with polycystic ovary syndrome and its correlation with metabolic disturbances

Katarzyna Paczkowska[1], Dominik Rachon[2], Andrzej Berg[3], Marta Siomkajlo[1], Jacek Rybka[4], Katarzyna Kapczynska[4], Marek Bolanowski[1] & Jacek Daroszewski[1]

[1]Wroclaw Medical University, Department of Endocrinology, Diabetes and Isotope Therapy, Wroclaw, Poland; [2]Medical University of Gdansk, Department of Clinical and Experimental Endocrinology, Gdansk, Poland; [3]Medical University of Gdansk, Department of Enviromental Toxicology, Gdansk, Poland; [4]Polish Academy of Sciences, Laboratory of Medical Microbiology, Hirszfeld Institute of Immunology and Experimental Therapy, Wroclaw, Poland

Background
Polycystic ovary syndrome (PCOS) is a heterogenous endocrinopathy commonly diagnosed in reproductive age women, predisposing to the development of metabolic disturbances. However, the mechanisms underlying the connection between PCOS and metabolic disorders are still not well understood. The aim of the study was to investigate amino acid (AA) profile in women with PCOS and to assess its relation with metabolic disturbances.
Methods
326 women: 209 diagnosed with PCOS and 117 healthy controls participated in the study. Anthropometrical, biochemical and hormonal parameters were assessed. A subgroup of patients with abdominal obesity (defined as the waist circumference $\geq$ 80 cm) was separated and included 143 PCOS patients and 74 controls. The gas–liquid chromatography combined with tandem mass spectrometry was used to assess amino acids levels – branched chain amino acids (BCAAs): leucine, isoleucine, and valine, and the aromatic amino acids (AAAs): phenylalanine, tryptophan and tyrosine.
Results
Statistical analysis showed significantly higher plasma levels of the BCAAs (540.4 ± 97.0 nmol/ml vs 501.0 ± 85.7 nmol/ml; $P<0.001$) and AAAs (162.8 ± 22.6 nmol/ml vs 153.1 ± 20.5 nmol/ml, $P<0.001$) in women with PCOS. Significant correlations ($P<0.05$) were also found in PCOS patients between both BMI and HOMA-IR and BCAAs ($rs=0.34$ for BMI and $rs=0.39$ for HOMA-IR) and AAAs ($rs=0.15$ for BMI and $rs=0.23$ for HOMA-IR). In the analysis of women with abdominal obesity, there were significant differences between PCOS subjects and controls in BCAAs (560.2 ± 99.2 nmol/ml vs 513.5 ± 78.1 nmol/ml; $P<0.001$) and AAAs (163.1 ± 21.4 nmol/ml vs 156.7 ± 20.1 nmol/ml, $P=0.01$).
Conclusions
Plasma amino acid profile is altered in women with PCOS and it is correlated with BMI and HOMA-IR. Additionally, in women with abdominal obesity BCAAs

and AAAs concentrations are more severe altered in PCOS group. Derangement in the plasma amino acid profile might be an important connection between PCOS and metabolic disturbances, however, further studies are needed.

DOI: 10.1530/endoabs.81.RC1.3

RC1.4

Exploring the role of skeletal muscle Mineralocorticoid Receptor in glucose metabolism and insulin signaling

Alessandra Feraco[1,2], Stefania Gorini[1,2], Vincenzo Marzolla[1], Caterina Mammi[1], Andrea Armani[1,2] & Massimiliano Caprio[1,2]
[1]IRCCS San Raffaele Rome, Laboratory of Cardiovascular Endocrinology, Roma, Italy; [2]Università Telematica San Raffaele, Department of Human Sciences and Promotion of the Quality of Life, Roma, Italy

Mineralocorticoid Receptor (MR) is able to regulate the transcription of a number of genes in the myotube, nevertheless the role of this steroid hormone receptor in skeletal muscle (SM) metabolism needs to be clarified. SM represents a major site for glucose uptake and local metabolic derangements play a pivotal role in the development of insulin resistance (IR). The aim of this study was to investigate the contribution of MR in mediating SM metabolic alterations in a mouse model of diet-induced obesity. We observed that mice fed a high fat diet (HFD mice), showed impaired glucose tolerance compared to mice fed a normal diet (ND mice). Mice fed a HFD treated with the MRA spironolactone (HFD + spiro mice) revealed an improvement in glucose tolerance, compared with HFD mice. In addition, MRA-treated obese mice showed brown adipose tissue activation, which was expected to contribute to the improved glucose metabolism. To investigate if MR blockade in SM could contribute to the observed MRA-mediated metabolic effects, we analyzed MR expression in gastrocnemius, observing that MR protein abundance was downregulated by HFD compared to ND mice, whereas administration of spiro was able to partially revert this effect in HFD + spiro mice. Interestingly, SM MR expression profile was opposite to that observed in adipose tissue (AT), showing increased protein abundance in HFD group, thus suggesting a different metabolic function of MR in AT and SM. Upregulated levels of mineralocorticoids, as well as up-regulated MR activation, are associated with impaired glucose metabolism. In our experimental model, downregulated expression and function of MR in SM of HFD mice with altered glucose tolerance, suggests that SM MR has a completely different role in regulation of glucose metabolism. To confirm this hypothesis, we investigated the effect of MR blockade on insulin signalling in a cellular model of myocytes (C2C12) with IR, which was obtained by treatment with palmitate, in the presence or absence of spiro. We confirmed MR protein downregulation in insulin resistant myotubes. We also analysed Akt phosphorylation, upon insulin stimulation, and we did not observe any difference between palmitate- and palmitate + spiro-treated cells. These results were confirmed by in vitro glucose uptake analysis. Taken together our data indicate that MR does not regulate insulin signaling in mouse myocytes, excluding any protective effect of SM MR pharmacological blockade upon local and systemic insulin sensitivity.

DOI: 10.1530/endoabs.81.RC1.4

RC1.5

Sex steroids regulate liver fat content and body fat distribution in both men and women: a study in transgender persons

Marieke Tebbens[1], Moya Schutte[1], Marian Troelstra[2], Eveline Bruinstroop[3], Renée de Mutsert[4], Aart Nederveen[2], Martin den Heijer[1] & Peter H. Bisschop[3]
[1]Amsterdam UMC, Vrije Universiteit Amsterdam, Endocrinology, Amsterdam, Netherlands; [2]Amsterdam UMC, University of Amsterdam, Radiology, Amsterdam, Netherlands; [3]Amsterdam UMC, University of Amsterdam, Endocrinology, Amsterdam, Netherlands; [4]Leiden University Medical Center (LUMC), Clinical Epidemiology, Leiden, Netherlands

Objective
Visceral adipose tissue (VAT) and liver fat content are associated with insulin resistance and cardiovascular disease and show clear sex differences. Our objective is to determine the effect of estradiol and testosterone on VAT and liver fat content in trans women (assigned male at birth, identify as female) and trans men (assigned female at birth, identify as male).
Design
Open-label partly randomized intervention study in 8 trans women and 18 trans men, receiving hormone treatment.
Methods
Trans women were treated with triptorelin for 6 weeks, followed by triptorelin and estradiol for 52 weeks. VAT, abdominal subcutaneous adipose tissue (SAT) and liver fat content were quantified by magnetic resonance imaging (MRI) and magnetic resonance spectroscopy (MRS) at baseline, 6, 8, 18 and 58 weeks. Trans men were randomized to receive triptorelin and testosterone with or without anastrozole for 12 weeks, followed by only testosterone until week 52. VAT, SAT and liver fat content were determined at baseline, 6, 12 and 52 weeks.
Results
In trans women, after 58 weeks, VAT did not change (+1% (95% CI -14 to 17), SAT increased by 33% (21 to 44), the VAT/SAT ratio decreased by 0.19 (-0.28 to -0.10) and liver fat content decreased by 37% (-65 to -10), compared to week 6 (start of estradiol). In trans men with anastrozole, SAT increased by 9% (2 to 17) after 12 weeks, while VAT, VAT/SAT ratio and liver fat content did not change. In trans men without anastrozole, after 52 weeks, VAT increased by 34% (16 to 51), SAT by 15% (8 to 21), VAT/SAT ratio by 0.06 (0.03 to 0.10) and liver fat by 1% (0 to 2).
Conclusions
Sex steroids regulate liver fat content and body fat distribution in both men and women.

DOI: 10.1530/endoabs.81.RC1.5

RC1.6

Evidence for three superimposed components, via which metformin affects blood glucose in obese mice

Mairam Kaplanian[1], Cecile Philippe[2], Marianna Beghini[1], Matthaeus Metz[1], Sameer Abu Eid[1], Alexandra Kautzky-Willer[1], Thomas Scherer[1] & Clemens Fürnsinn[1]
[1]Medical University of Vienna, Department of Medicine III, Division of Endocrinology & Metabolism, Vienna, Austria; [2]Medical University of Vienna, Department of Biomedical Imaging and Image-Guided Therapy, Division of Nuclear Medicine, Vienna, Austria

Introduction
Despite a plethora of suggested targets and pathways, the mechanism of anti-hyperglycaemic metformin action is still unknown. The present study critically re-analysed protocols broadly applied in preclinical rodent studies.
Methods
Obese male C57BL/6J mice on high fat diet were treated with metformin in the form of a single dose, daily intraperitoneal injections, admixture to drinking water, or continuous infusion via intraperitoneal minipumps. Glucose tolerance tests (GTT) were performed to evaluate effects on blood glucose homeostasis.
Results
Thirty min after intraperitoneal injection of 50mg/kg metformin, the plasma concentration of metformin was 56 ± 22µmol/l and glucose tolerance was improved (AUC, min*g/dl: 40.4 ± 1.8 vs 34.0 ± 1.2, $P = 0.008$). The beneficial effect on glucose tolerance was gone 3 h after drug administration, when plasma metformin was down to 2.8 ± 0.7µmol/l (AUC, min*g/dl: 39.0 ± 1.4 vs 36.4 ± 1.7, n.s.). Rapid clearance of metformin accompanied by fading of its action suggests that mice under typical long-term treatment regimens (daily dosing; admixture to food or water) are not permanently exposed to effective drug concentrations. In mice under long-term treatment, we therefore found effects on glucose tolerance to depend on the time span between the preceding metformin dose and measurement of blood glucose. Under regular treatment, however, metformin also affected glucose tolerance indirectly via reduced appetite and blunted weight gain (g gained in 7 weeks on metformin 50 mg/kg/d: +6.7 ± 1.0 vs +3.1 ± 0.5, $P = 0.005$). When dosing shortly before the GTT was avoided and weight-mediated actions were eliminated by restricted feeding of the control mice, counterintuitive worsening of glucose tolerance by metformin was unmasked (after 6 weeks with 4.1g/kg metformin in drinking water: AUC, min*g/dl: 32.2 ± 0.8 vs 38.5 ± 1.2, $P = 0.0003$). In mice continuously infused with the drug (13mg/kg/d), plasma metformin was intra-individually associated with less weight gain ($r = 0.81$) and lower blood glucose ($r = 0.78$).
Conclusions
Our results suggest three superimposed components of metformin action on blood glucose in mice: (i) Glucose lowering shortly after dosing, which fades rapidly with the clearance of plasma metformin - we hypothesise that this component accounts for antidiabetic action in the clinic. (ii) Indirect action via reduced appetite and weight gain - we suspect that this component is not sufficiently considered in many rodent studies. (iii) Deterioration of glucose homeostasis by prolonged treatment - this component is unmasked by exclusion of weight-mediated effects in combination with avoidance of dosing shortly before glucose measurements. Dependent on the specific experimental protocol, the net effect of these components can be decreased, increased, or unchanged blood glucose.

DOI: 10.1530/endoabs.81.RC1.6

RC1.7

The role of chemokines in type 1 diabetes-associated neuropathy

Evangelia Baldimtsi[1,2], Nektaria Papadopoulou-Marketou[3], Maria Jenmalm[4,5] & Jeanette Wahlberg[1,2,6]
[1]Linköping University, Department of Health,Medicine and Caring Sciences, Linköping, Sweden; [2]Linköping University Hospital, Department of Endocrinology, Linköping, Sweden; [3]National and Kapodistrian University of Athens, 1st Department of Propaedeutic and Internal Medicine, Medical School, Athens, Greece; [4]Linköping University, Department of Biomedical and Clinical Sciences, Linköping, Sweden; [5]Linköping University, Division of Inflammation and Infection, Linköping, Sweden; [6]Örebro University, Faculty of Medical Sciences, Örebro, Sweden

Background and aims
Diabetic neuropathy is a common complication in patients with type 1 diabetes mellitus (T1D). In this study, we explore the importance of circulating chemokines for the development of diabetic neuropathy (DN) in T1D.
Materials and methods
This study was a cross-sectional analysis of patients with childhood onset T1D followed prospectively in a long-term longitudinal cohort study. Fifty-two patients (20 women/32 men; mean age 28 ± 4 yrs.; diabetes duration 19.5 ± 5.5 yrs.), and 19 control subjects (11 women/8 men; mean age 26.5 ± 4.5 yrs.) were included. Plasma levels of Th1- (CXCL9, CXCL10, CXCL11), Th2- (CCL17, CCL22) and Th17-associated (CXCL8, CCL20) chemokines were assessed in all subjects. Clinical examination and electroneurography tests with bilateral measurements of peroneal MCV and CMAP and sural SCV and SNAP were performed in the TID patients.
Results
Patients with diabetic neuropathy had higher levels of CXCL9 (Th1) than patients without DN. Both patients with and without neuropathy had significantly higher CXCL9 levels compared to controls, $P=0.002$ and $P=0.05$, respectively. The levels of the other chemokines were similar in patients and controls. In T1D patients with peripheral DN, the CXCL8 (Th17) levels correlated negatively with cold perception threshold (rho -0.645, $P=0.032$), while the CXCL10 (Th1) levels were positively correlated with the vibration perception threshold (rho 0.639, $P=0.034$).
Conclusions
The Th1 associated chemokine CXCL9 was increased in patients with T1D, both in patients with and without neuropathy. Increased Th1 and Th17 associated chemokines showed possible associations to an impaired peripheral sensory nerve function and nerve conduction tests for the suralis nerve.

DOI: 10.1530/endoabs.81.RC1.7

Adrenal and Cardiovascular Endocrinology 1

RC2.1

A rapid genetic diagnosis for >80% individuals with non-CAH Primary Adrenal Insufficiency is achievable by candidate gene sequencing combined with WES

Chris Smith[1], Jordan Read[1], Charlotte Hall[1], Avinaash Maharaj[1], Lucia Marroquin Ramirez[1], Younus Qamar[1], Claire Hughes[1,2], Adrian Clark[1], Rathi Prasad[1], Li Chan[1], Salwa Musa[3] & Louise Metherell[1]
[1]William Harvey Research Institute, United Kingdom; [2]Royal London Hospital, United Kingdom; [3]Gaafar Ibn Auf Children Hospital, Pediatric Endocrinology Unit, Sudan

Primary adrenal insufficiency in children can be due to mutations in >20 genes, most commonly *CYP21A2*, giving rise to 21-hydroxylase deficiency. Phenotypically these disorders overlap and present with conditions ranging from isolated (or familial) glucocorticoid deficiency (FGD) to syndromic disorders involving multiple tissues. Distinguishing between them can be problematic, especially where biochemical testing is not possible or not undertaken. Over the last 30 years 400 individuals with suspected FGD, from 31 different countries, have been referred to our centre for genetic testing. All cases had low/undetectable serum cortisol and, where measured, elevated plasma ACTH levels. Using a combined, two-step protocol we have sequenced 369 of the 400 individuals. In the first step we sequenced the small, frequently mutated, candidate genes; *MC2R, MRAP, STAR* and *CYP11A1*, by Sanger sequencing (CGS) before proceeding to whole exome sequencing (WES) if these were mutation free. For CGS, sequences were aligned to reference sequences using BioEdit software and WES variant call files were analysed using Ingenuity Variant Analysis package and/or examination of BAM files, using the Integrative Genomics Viewer, to detect exonic deletions. Rare, synonymous or predicted benign variants were subjected to an in vitro splicing assay using the pET01 vector (MoBiTec). In 308/369 individuals we found a definitive diagnosis in a causative gene for adrenal insufficiency, a success rate of 81%, and identified many novel mutations. The findings also highlighted a number of causal synonymous and predicted benign variants resulting in splice defects. The aetiologies of cases with a gene defect were as follows; *MC2R* (22%), *MRAP* (17%), *NNT* (15%), *STAR* (9%), *CYP11A1* (7%), with the remaining 30% due to a further 13 genes. Previous founder effects were reinforced e.g S74I in *MC2R* and rs6161 in *CYP11A1* in the UK population, P24Rfs*4 in *MCM4* in Ireland and R188C in *STAR* in Canada, with new associations being discovered for T731= in *NNT* in Sudan and R222Q in *SGPL1* in Saudi Arabia. In contrast, common MRAP splice mutations seen at the exon 3/intron 3 junction were present in individuals from many countries. The use of CGS/WES now permits a rapid genetic diagnosis for >80% individuals and is an invaluable, cost-effective tool to improve tailored patient management. For patients without a genetic diagnosis, it is unclear whether they have unconventional mutations in known genes or if there are further gene defects to be discovered.

DOI: 10.1530/endoabs.81.RC2.1

RC2.2

FKBP5 methylation in adrenal insufficiency: looking at a new tool for assessing the quality of glucocorticoid replacement?

Irina Chifu[1], Scheuermann Carolin[1], Burger-Stritt Stephanie[2], Juliane Lippert[1], Sabine Herterich[3] & Stefanie Hahner[1]
[1]University Hospital Würzburg, Endocrinology and Diabetes, Würzburg, Germany; [2]Uppsala University Hospital, Endocrinology and Diabetes, Uppsala, Sweden; [3]University Hospital Würzburg, Clinical Chemistry and Laboratory Medicine, Würzburg, Germany

Available glucocorticoid (GC) replacement regimens in adrenal insufficiency (AI) only roughly correspond to physiological steroid profiles. Control of substitution quality is therefore difficult but significant, as even mild chronic over- or under-replacement may be clinically relevant. FKBP5 regulates GC receptor sensitivity by reducing its affinity to cortisol when bound to the receptor complex. FKBP5 methylation has been inversely correlated with cortisol levels both in healthy controls and in patients with endogenous hypercortisolism. We analyzed FKBP5 gene methylation (DNAm) within introns containing GC responsive elements as well as promoter and proximal enhancer regions by bisulfite pyrosequencing in a cohort of 86 patients with primary (PAI, $n=57$) and secondary (SAI, $n=29$) AI. Results were correlated with GC dose, salivary and 24-hour urinary cortisol, prevalence of adrenal crises (AC) per patient-year and 24-hour blood pressure (BP) levels. GC dose and DNAm were negatively correlated for the majority of the investigated regions (intron 1 $r_s=-0.45$, $P<0.01$, intron 5 $r_s=-0.35$ $P<0.01$, intron 7 $r_s=-0.23$ $P=0.034$, promoter A1 $r_s=-0.35$ $P<0.01$, proximal enhancer A2 $r_s=-0.38$ $P<0.01$). Intronic DNAm correlated negatively with 24-hour urinary cortisol (intron 2, $r_s=-0.25$, $P=0.032$) and positively with bedtime salivary cortisol (intron 7, $r_s=0.3$, $P<0.01$). We observed a positive correlation between the prevalence of AC and intronic DNAm (intron 2 and 5, $r_s=-0.29$ $P<0.01$ for each). Systolic 24-hour and day-time BP, systolic and diastolic night-time BP and noctural dipping correlated negatively with DNAm within several intronic, promoter and proximal enhancer regions. GC replacement was higher, whereas intronic DNAm was lower in PAI compared to SAI (GC: 22 (10-60) vs 20 (10-37,5) mg $P=0.032$, intron 5: 11% vs 15% $P=0.028$). FKBP5 methylation analysis may provide helpful further insight regarding the evaluation of GC replacement and might help improving assessment of GC load in AI, as it correlates with replacement doses, cortisol levels and 24-hour BP. Our observations warrant further analyses in larger cohorts.

DOI: 10.1530/endoabs.81.RC2.2

RC2.3

Diagnostic accuracy of basal cortisol level to predict secondary adrenal insufficiency in patients with pituitary disease

Campbell Mathieson[1], Razan Ali Rashid[2], Christopher S Boot[2], Andy James[2] & Yaasir Mamoojee[2]
[1]Medical Student, Newcastle University, Newcastle Upon Tyne, United Kingdom; [2]The Newcastle upon Tyne Hospitals, Endocrinology and Metabolic Medicine, Newcastle upon Tyne, United Kingdom

Objective
The 250 µg short Synacthen stimulation test (SST) is the most commonly used dynamic assessment to diagnose adrenal insufficiency (AI). There are challenges to the use of the SST in routine clinical practice, including staff and resource

limitation in the current COVID-19 pandemic and Synacthen cost. We aimed to investigate the value of basal cortisol level for predicting AI in our selected cohort of patients at risk of secondary adrenal insufficiency from pituitary disease, pituitary surgery or pituitary irradiation.
Methods
A ten-year retrospective review was performed in our tertiary unit. SSTs were performed before midday. AI was defined as peak serum cortisol level of <550 nmol/l on Roche Cortisol I assay or <420 nmol/l on Roche Cortisol II assay. Conversion of baseline cortisol level from Roche I to Roche II equivalent measurement was done using validated regression equation. Diagnostic performance was evaluated by Receiver Operating Curve (ROC) analysis.
Results
595 SSTs performed from 2010 to 2020 were included. 51 (8.6%) were positive for AI. The ROC analysis showed an overall area under the curve (AUC) for basal cortisol of 0.975 (95% CI 0.959 to 0.986). If a basal cortisol level cut-off of ≤ 237 nmol/l was implemented to predict AI, no failed SST would be missed, hence the negative predictive value to rule-out AI was 100% (95% CI 93 to 100%). By using a cut-off value of 237 nmol/l, 399 out of 544 (73%) SSTs could be eliminated. With a lower basal cortisol cut-off of ≤ 165 nmol/l, 5 out of 51 failed SSTs would be missed but 503 out of 544 (92%) normal SSTs would be avoided.
Conclusion
In our cohort of patients at risk of secondary adrenal insufficiency, basal morning serum cortisol concentration can be utilised as a convenient screening test, with high diagnostic performance, to identify patients requiring confirmatory dynamic testing using SST. Further prospective studies are required to validate the cut-off values proposed.

DOI: 10.1530/endoabs.81.RC2.3

RC2.4

Diagnostic value of basal cortisol level to predict adrenal insufficiency in patients treated with glucocorticoids during COVID-19: a single centre observational cohort study

Mojca Jensterle[1,2], Matej Rakusa[1,2], Gaj Vidmar[2,3,4], Andrej Janez[1,2] & Tomaž Kocjan[1,2]
[1]Department of Endocrinology, Diabetes and Metabolic Diseases, University Medical Centre Ljubljana, Ljubljana, Slovenia; [2]Faculty of Medicine, University of Ljubljana, Ljubljana, Slovenia; [3]University Rehabilitation Institute, Ljubljana, Slovenia; [4]FAMNIT, University of Primorska, Koper, Slovenia

Objective
During the current pandemic of COVID-19, many therapeutic protocols adopted high dose systemic glucocorticoids (GC) for treatment of moderate to severe respiratory insufficiency. The suppression of the hypothalamic–pituitary–adrenal axis by synthetic GC, even after a short treatment period, cannot be reliably predicted due to pathophysiological changes in cortisol dynamics in critically ill, inter-individual pharmacokinetic differences, and sensitivity variations in glucocorticoid receptors. Moreover, the revealed pathological adrenal changes in Covid-19 patients make prior estimates even less reliable.
Aim
We aimed to estimate percentage of patients with adrenal insufficiency (AI) at the end of acute phase of COVID-19 after tapering GC toward replacement dose of hydrocortisone for at least 1 week and to investigate for the first time the basal cortisol level for prediction of AI in this population.
Methods
We retrospectively analysed 287 consecutive patients (median 65 years, range 26-91 years); 113 (39.4%) female and 174 (60.6%) male) who had low-dose (1 μg) cosyntropin testing. Site-specific cut-off levels for AI were <500 nmol/l. The overall potential of cortisol at baseline to classify patients into adrenal (in) sufficiency was assessed using receiver-operating-characteristic (ROC) curve analysis.
Results
The average cortisol level at baseline was 419 nmol/l (median 429, range 36-953 nmol/l), and at 30' 617 nmol/l (median 623, range 114-1092 nmol/l); Overall, 65 (22.6%) showed an insufficient increase of cortisol and were categorized as AI. ROC showed an overall area under the curve (AUC) for basal cortisol of 0.84, with 95% confidence interval 0.79-0.89. If basal cortisol level was below 100 nmol/l, which was the case in 7 patients (2.4%), the positive predictive value (PPV) to predict AI was 100%. If basal cortisol was at least 450 nmol/l, which was the case in 125 patients (43.6%), the negative predictive value (NPV) to predict no AI was 96.0%; if it was at least 400 nmol/l (158 patients, 55.1%), NPV was 93.0%; and if it was at least 460 nmol/l (113 patients, 39.4%), NPV was 99.1%. PPV sharply declines after the threshold of 100 nmol/l. On the other hand, PPV increases approximately linearly over the threshold range from 350 to 460 nmol/l, where it practically reaches 100%.
Conclusion
Basal cortisol levels ≤ 100 and ≥ 460 nmol/l in patients tested for possible AI were found in 41.2% and had sufficient diagnostic accuracy to safely abolish the need for cosyntropin testing. The data may help guide clinicians when testing for AI can be simplified.

DOI: 10.1530/endoabs.81.RC2.4

RC2.5

Treatment of adrenal insufficiency in the netherlands from a patient perspective in the recent past. Lessions learned for europe

Anton Franken[1], Roselinda van der Vlugt[2] & Johan Beun[3]
[1]Isala Hospital Zwolle, Endocrinology, Zwolle, Netherlands; [2]Ace Pharmaceuticals, Manager Quality Assurance and Regulatory Affairs, Zeewolde, Netherlands; [3]Manager AdrenalNET, Netherlands

In 2015 AdrenalNET organized a roundtable conference with patient representatives, prescribers and pharmaceutical industry. The cause of this meeting was complaints of patients about the problematic hydrocortisone market in the Netherlands, characterized by frequent availability issues (shortage) of the hydrocortison tablets/capsules and frequent changes in manufacturers (compounding companies) leading to quality issues. All parties at the roundtable meeting agreed to join forces to achieve hydrocortisone tablets with the following requirements:
1. Immediate release hydrocortisone tablets for both children and adults. Conventional IR-released hydrocortison remains the gold standard (EndoERN position paper 2021).
2. Various strengths ranging from 1 to 10 mg.
3. Colour coded tablets with no bad taste and no need for splitting anymore4. Permanent availability which will be increased by obtaining marketing authorization and by production of hydrocortison tablets in the EU from preferable European raw materials. In 2018 one of our partners, a small Dutch pharmaceutical company, started the development of new hydrocortison tablets based on the above requirements. Despite a lot of regulatory struggles, in March 2020 registration was approved in the Netherlands for the 1,5 and 10 mg tablets, followed by recent registration (2021) of the 2 and 3 mg hydrocortison. The different strengths make it possible to mimic the individual patient's cortisol pattern during the day most closely. The introduction of the new tablets was followed by a fast-uptake in the market. At the moment expansion of these hydrocortison tablets to other European countries will take place. This project is a good example of fruitfull collaboration between patients, doctors and pharmaceutical companies which deserves a rollout over the rest of Europe. AdrenalNET and Endo-ERN may serve a important role in achieving this.

DOI: 10.1530/endoabs.81.RC2.5

RC2.6

Modified release hydrocortisone capsules (MRHC, Efmody) improve control of congenital adrenal hyperplasia (CAH) on a lower glucocorticoid dose than standard treatment

Aled Rees[1], Deborah P Merke [2], Wiebke Arlt[3], Aude Brac De La Periere[4], Angelica Linden Hirschberg[5], Anders Juul[6], Ashwini Mallappa[7], John D. C. Newell-Price[8], Colin Graham Perry[9], Alessandro Prete[3], Nicole Reisch[10], Monica Stikkelbroeck[11], Philippe A Touraine[12], Helen Coope[13], John Porter[13] & Richard John M Ross[8]
[1]Cardiff University, United Kingdom; [2]NIH Clinical Center, Bethesda, United States; [3]University of Birmingham, United Kingdom; [4]Louis Pradel Hospital, Bron, France; [5]Karolinska Institute, Sweden; [6]Rigshospitalet, København, Denmark; [7]AstraZeneca, Gaithersburg, United States; [8]The University of Sheffield, United Kingdom; [9]University of Glasgow, United Kingdom; [10]Endokrinologie, Nephrologie und weitere Sektionen - Medizinische Klinik und Poliklinik IV - Campus Innenstadt, München, Germany; [11]Radboud University Nijmegen, Nijmegen, Netherlands; [12]University Hospitals Pitié Salpêtrière - Charles Foix, Paris, France; [13]Diurnal Ltd, United Kingdom

Background
The therapeutic goal in CAH is androgen control on the lowest achievable glucocorticoid dose, preferably an adrenal replacement dose (15-25 mg hydrocortisone a day)[1]. However, the glucocorticoid dose required to control androgens frequently exceeds that required for adrenal replacement[2]. Modified-release hydrocortisone (MRHC) capsules, (Efmody, Diurnal Ltd, Cardiff, UK), replicate cortisol diurnal rhythm and improve CAH control compared to standard

therapy[3]. We have examined whether MRHC can improve CAH control in patients receiving high dose standard treatment.
Methods
We reviewed the data of patients in the randomised study of standard treatment versus MRHC and selected those on >25 mg/day hydrocortisone dose equivalent (HDE=prednisolone dose 5 & dexamethasone 80)[3] at study entry. Patients were assessed at 24 weeks after blinded dose titration aimed to bring 17OHP into the optimal range (<36 nmol/l) and A4 into the reference range. After 24 weeks, patients participated in an ongoing MHRC single arm extension study. Control of CAH was defined as 0900h 17OHP <36 nmol/l.
Results
At baseline 41% (n=43/105) of patients were on >25mg HDE/day standard treatment; 21/43 were female, mean baseline 0900h 17OHP was 106 nmol/l and 48% were uncontrolled. At 24 weeks 95% (n=21/22) of patients on MRHC were controlled on median 40 mg/day (mean 17OHP 10 nmol/l) and for standard treatment 81% were controlled on median 40 mg HDE/day (mean 17OHP 49 nmol/l). In the full cohort, there were no adrenal crises in the MRHC group and three in the standard treatment group (10.7/100 patient years). After 24 weeks 27 of the 43 patients entered the clinician-titrated, MRHC single-arm extension study. At the 18-month interim analysis 76% patients were in control with a median dose of 25 mg (52% ≤25 mg/day) and mean 17OHP 24 nmol/l. In the ongoing extension study of all patients on MRHC (221 patient years), there were 12 adrenal crises in 5 patients (5.4/100 patient years).
Conclusions
It is common in CAH patients for the glucocorticoid dose to exceed the recommended adrenal replacement dose and still ~50% of patients remain uncontrolled. MRHC controlled 17OHP in 95% patients who were previously on high dose standard therapy and over time it was possible to reduce the MRHC dose to an adrenal replacement dose in ~50% of patients and retain control in 75%.
References
1. Speiser P., *JCEM* 2018 **103** 4043-4088.
2. Prete A., *EJE* 2021 **186** R1-R14.
3. Merke DP., *JCEM* 2021 **106** e2063-e2077.
DOI: 10.1530/endoabs.81.RC2.6

RC2.7

Improved biochemical control with modified-release hydrocortisone overturns the impaired fludrocortisone effect in salt-wasting CAH patients

Lea Tschaidse[1], Nicole Reisch[2], Wiebke Arlt[3] , Aude Brac De La Perriere[4], Angelica Linden Hirschberg[5], Anders Juul[6], Ashwini Mallappa[7], Deborah P Merke[8], John DC Newell-Price[9], Colin Graham Perry[10], Alessandro Prete[3], Aled Rees[11], Monica Stikkelbroeck[12], Phillippe A Touraine[13], Helen Coope[14], John Porter[14], Richard John M Ross[14] & Marcus Quinkler[15]
[1]Klinikum der Universität München, Standort Großhadern, München, Germany; [2]Endokrinologie, Nephrologie und weitere Sektionen - Medizinische Klinik und Poliklinik IV - Campus Innenstadt, München, Germany; [3]University of Birmingham, United Kingdom; [4]Louis Pradel Hospital, Bron, France; [5]Karolinska Institute, Sweden; [6]Rigshospitalet, København, Denmark; [7]AstraZeneca, Gaithersburg, United States; [8]NIH Clinical Center, Bethesda, United States; [9]The University of Sheffield, United Kingdom; [10]Queen Elizabeth University Hospital, United Kingdom; [11]Cardiff University, United Kingdom; [12]Radboud University Nijmegen, Nijmegen, Netherlands; [13]University Hospitals Pitié Salpêtrière - Charles Foix, Paris, France; [14]Diurnal, United Kingdom; [15]Endocrinology in Charlottenburg, Berlin, Germany

Background
Patients with salt-wasting congenital adrenal hyperplasia (CAH) due to classic 21-hydroxylase deficiency require glucocorticoid (GC) and mineralocorticoid (MC) replacement therapy. Recently, it was shown that twice daily modified-release hydrocortisone hard capsules (MRHC, Efmody®, Diurnal Ltd) improved control of CAH with most patients showing good disease control versus standard GC therapy. However, no data has been reported on the renin-angiotensin-aldosterone (RAA) system in these patients. This is of clinical relevance because 17-hydroxyprogesterone (17-OHP) is a known MC-receptor antagonist, and poorly controlled salt-wasting CAH patients often require higher fludrocortisone doses than patients with primary adrenal insufficiency. The aim of this study was to investigate the RAA system in patients on MRHC.
Methods
Data was analyzed from the 6-month, phase 3 study1. Patients with salt-wasting CAH (5 excluded; 83 included; 34.9% male, median age 35.3 yrs) were randomized to either MRHC twice daily (n=42) or standard GC (n=41; 4.9% dexamethasone, 39% prednisolone, 56.1% HC). MC replacement therapy with fludrocortisone remained stable and unchanged throughout the study. Blood pressure, potassium, sodium, plasma-renin-activity (PRA) serum androgen precursors 17-OHP and androstenedione were analyzed at baseline, 4, 12 and 24 weeks.
Results
Both groups improved hormonal control (17-OHP and androstenedione) on intensive monitoring and with stable GC doses on MRHC (median 25.0 to 25.0 mg/d, P= 0.062) and increased doses on standard GC (25.0 to 31.3 mg/d, P= 0.001) at 24 weeks. However, the serum 17-OHP was significantly lower on MRHC compared to standard GC at 24 weeks (2,5 nmol/l vs 10,5 nmol/l, P= 0.001). PRA decreased significantly from baseline to 24 weeks in patients on MRHC (0.83 ng/l/s to 0.48 ng/l/s, P=0.012) but not in patients on standard GC therapy (0.53 ng/l/s to 0.52 ng/l/s, P=0.613). In line with these changes, serum sodium concentrations increased from baseline to 24 weeks in patients on MRHC (138.8±1.9 mmol/l to 139.3±1.8 mmol/l, P=0.047), but remained unchanged on standard GC (139.8±1.6 mmol/l to 139.3±1.9 mmol/l, P=0.135). No significant changes were seen in systolic and diastolic blood pressure and serum potassium levels.
Conclusion
Six months of MRHC therapy decreased PRA and increased sodium levels indicating a better MC effect of the unchanged fludrocortisone dose. This might be due to the significantly decreased levels of the MC-receptor antagonist 17-OHP owing to the improved control of precursor excess by MRHC, indicating lower fludrocortisone efficacy in poorly controlled salt-wasting CAH patients.
References
Merke DP. *JCEM* 2021 **106** e2063-e2077.
DOI: 10.1530/endoabs.81.RC2.7

RC2.8

Fertility in congenital adrenal hyperplasia (CAH) patients on modified release hydrocortisone capsules (MRHC, Efmody)

Lea Tschaidse[1], Marcus Quinkler[2], Wiebke Arlt[3], Aude Brac De La Perriere[4], Angelica Linden Hirschberg[5], Anders Juul[6], Ashwini Mallappa[7], Deborah P Merke[8], John DC Newell-Price[9], Colin Graham Perry[10], Alessandro Prete[3], Aled Rees[11], Monica Stikkelbroeck[12], Philippe A Touraine[13], Helen Coope[14], John Porter[14], Richard John M Ross[14] & Nicole Reisch[1]
[1]Endokrinologie, Nephrologie und weitere Sektionen - Medizinische Klinik und Poliklinik IV - Campus Innenstadt, München, Germany; [2]Endocrinology in Charlottenburg, Berlin, Germany; [3]University of Birmingham, United Kingdom; [4]Louis Pradel Hospital, Bron, France; [5]Karolinska Institute, Sweden; [6]Rigshospitalet, København, Denmark; [7]AstraZeneca, Gaithersburg, United States; [8]NIH Clinical Center, Bethesda, United States; [9]The University of Sheffield, United Kingdom; [10]Queen Elizabeth University Hospital, United Kingdom; [11]Cardiff University, United Kingdom; [12]Radboud University Medical Center, Nijmegen, Netherlands; [13]University Hospitals Pitié Salpêtrière - Charles Foix, Paris, France; [14]Diurnal, United Kingdom

Background
Fertility in CAH women is impaired: 0.25 live births vs 1.8 in the UK population and 45% have irregular menses vs 13.6% in healthy women[1]. Male fertility is also impaired in CAH with oligospermia reported in 48%[2]. Treatment of infertility usually involves increasing the glucocorticoid dose to normalise adrenal androgens and progesterone to facilitate ovulation and implantation, respectively. Modified-release hydrocortisone (MRHC) capsules, (Efmody, Diurnal Ltd, Cardiff, UK), replicate the physiological cortisol diurnal rhythm and improve CAH control compared to standard therapy. In the phase 3 randomised study of MRHC versus standard treatment[3]; 4 women had restoration of menses on MRHC versus 1 on standard treatment but seeking fertility was an exclusion criteria. We have examined fertility in the ongoing MHRC single arm extension study.
Methods
Review of fertility in the ongoing MHRC single arm extension study. Standard therapy dose is given as hydrocortisone dose equivalent (HDE=prednisolone dose 5 & dexamethasone 80).
Results
Twenty-seven of 49 premenopausal women were not using oral or intrauterine contraception. Of these women, 10/27 (37%) reported evidence of improved fertility: 5 reported menstrual regularisation and 5 women reported 6 pregnancies (3 healthy live births, 1 ongoing, 2 miscarriages). In these women the mean(SD) HDE on standard treatment before the study and pregnancy was 29(12) mg and then on MRHC at time of interim analysis or withdrawal due to positive pregnancy test the dose was 28(8) mg. In the 29 men (contraception data not collected), 4 pregnancies occurred in 3 female partners resulting in healthy live

births; the baseline mean(SD) HDE dose was 28(3) mg before the study and at time of pregnancy 32(10) mg. Two men had a dose increase from baseline, the 3rd subject had a dose decrease at time of first partner pregnancy, and increase to baseline dose at 2nd same partner pregnancy. 1 man had spermatograms with severe oligospermia and scarce mobile sperm on standard treatment and moderate oligospermia and 45% mobile sperm on MRHC.
Conclusions
Fertility is impaired in women and men with CAH and treatment usually aims to increase glucocorticoid dose. In the MRHC single arm extension study patients reported improved fertility with no increase in glucocorticoid dose in women.
References
1. Reisch N. *Endocrinol Metab Clin North Am* 2019 **48** 619-641.
2. King TF. *Clin Endocrinol (Oxf)* 2016 **84** 830-836.
3. Merke DP. *JCEM* 2021 **106** e2063-e2077.
DOI: 10.1530/endoabs.81.RC2.8

Thyroid 1

RC3.1

Usefulness of the EU-TIRADS score on sparing thyroid nodules cytology: a retrospective study
Francisca Puga, André Carvalho & Cláudia Freitas
Centro Hospitalar Universitário do Porto, Endocrinology, Portugal

Introduction
Incidental diagnosis of thyroid nodules has increased in recent years, leading to thyroid cancer diagnosis inflation. Nonetheless, mortality rate for thyroid malignancies remains very low, suggesting that its treatment is unlikely to affect the overall prognosis in the majority of cases. Several thyroid imaging scores have been proposed to reduce unnecessary invasive diagnostic procedures. Our aim was to verify the usefulness of the EU-TIRADS score on sparing thyroid nodules cytology.
Methods
We conducted a retrospective and observational study of thyroid nodules submitted to fine-needle aspiration biopsy (FNAB) between January 2016 and October 2021 at our center. Each nodule was classified as whether having an indication for FNAB (group A) or not (group B), according to the EU-TIRADS score. We then compared cytology results between the two groups, using Bethesda diagnostic categories.
Results
FNAB were performed in 1935 thyroid nodules from 1308 patients. Using the EU-TIRADS score, 766 (39.6%) nodules had no cytology indication (group B). Of these, 40.2% ($n=308$) were EU-TIRADS 2, 35.4% ($n=271$) EU-TIRADS 3 $\leq$20 mm, 20.2% ($n=155$) EU-TIRADS 4 $\leq$15 mm and 4.2% ($n=32$) EU-TIRADS 5 $\leq$10mm. In group B, a suspicious or malignant category was reported only in 7 (0.9%) nodules. Suspicious follicular neoplasm was reported in 13 (1.7%) nodules. Group A presented a higher prevalence of suspicious or malignant categories (2.8% vs 0.9%, $P<0.01$), a higher prevalence of suspicious follicular neoplasm category (4.1% vs 1.7%, $P<0.01$) and a higher prevalence of nondiagnostic categories (45.1% vs 36.5%, $P<0.01$). Notably, nondiagnostic categories were found in 279 (36.5%) of nodules submitted to cytology in group B, leading to repetition of cytology and consequent avoidable visit to the clinic in 63 individuals. Interestingly, when comparing avoidable cytology rate per year, we observed a lower rate in the more recent year (26.8% vs 41.3%, $P<0.01$), suggesting a greater adherence to the EU-TIRADS system for decision making.
Conclusion
In the context of a common disease, such as thyroid nodules, application of the EU-TIRADS system score can avoid unnecessary cytologies, reducing over-diagnosis and consequent overtreatment.
DOI: 10.1530/endoabs.81.RC3.1

RC3.2

Performance of a raman fingerprint in thyroid nodules with indeterminate cytology: a prospective blinded monocentric study
Andrea Palermo[1], Armida Sodo[2], Anda Mihaela Naciu[1], Michael Di Gioacchino[2], Alessio Paolucci[2], Alessandra Di Masi[2], Daria Maggi[1], Pierfilippo Crucitti[3], Filippo Longo[3], Eleonora Perrella[4], Chiara Taffon[4], Martina Verri[4], Maria Antonietta Ricci[2] & Anna Crescenzi[4]
[1]Fondazione Policlinico Universitario Campus Bio-Medico, Unit of Metabolic bone and thyroid disorders, Rome, Italy; [2]Università Roma Tre, Dipartimento di Scienze,, Rome, Italy; [3]Fondazione Policlinico Universitario Campus Bio-Medico, Unit of Thoracic Surgery, Rome, Italy; [4]Fondazione Policlinico Universitario Campus Bio-Medico, Unit of Pathology, Rome, Italy
Background
Molecular analysis of thyroid fine-needle aspiration biopsy (FNA) was proposed to improve indeterminate nodules management. However, sensibility and specificity as well as the cost of molecular diagnostics require to be improved to increase their cost-effectiveness for medical practice setting. Raman spectroscopy (RS) demonstrated ability in separating benign from malignant thyroid lesions in surgically removed tissues, based on specific RS profile. This study aimed to investigate the diagnostic performance of RS on cytological samples obtained by thyroid FNA.
Methods
In this prospective, blinded monocentric study, we enrolled 123 patients with indeterminate or worse cytological diagnosis, candidate to surgery according to international guidelines, and submitted to RS analysis of FNA samples. Cytology specimens were evaluated in agreement to Italian Reporting System for Thyroid Cytology[1] as follows: TIR1 (non-diagnostic), TIR1C (non-diagnostic-cystic), TIR 2 non-malignant/benign, TIR3A (low-risk indeterminate lesion), TIR3B (high-risk indeterminate lesion), TIR 4 (suspicious of malignancy), or TIR 5 (malignant). As previously published[2], the two diagnostic subcategories referred to indeterminate nodules with low (TIR3A) and high risk (TIR3B) of malignancy, may be respectively compared to the class III and Class IV of The Bethesda System for Reporting Thyroid Cytopathology. We compared RS, cytology and final histology, as reference standard, using various statistical approaches.
Findings
Our study population included 37 TIR3A, 32 TIR3B, 16 TIR4 and 38 TIR5; the 30.9% of patients had benign histological diagnosis after surgery. In particular, 72.9% of patients classified TIR3A and 31.3% TIR3B had benign histological diagnosis. RS analysis of FNA samples had overall specificity of 86.8% in predicting thyroid malignancy. In indeterminate cytological categories, RS specificity was 86.5%. In patients with TI-RADS score four or five, the specificity of RS increased to 87.5% for TIR3A and reached 100% in TIR3B.; if considering RS positive test, unnecessary surgery was reduced to 7.4% in the whole sample, 33.3% in TIR3A, and 6.7% in TIR 3B.
Interpretation
We demonstrated for the first time that RS represents a valuable tool for thyroid cytology and a valid alternative to molecular analyses, able to improve management and reduce unnecessary surgery in indeterminate nodules.
Funding
This study was supported by Ministero della Salute, through TIRAMA project (RF-2018-12366568).
References
1. *J Endocrinol Invest*. 2014; **37** (6):593-599. doi:10.1007/s40618-014-0062-0.
2. *Cytopathology*. 2021;**32** (6):714-717.
DOI: 10.1530/endoabs.81.RC3.2

RC3.3

Tailoring the diagnostic indication to radioactive iodine treatment in differentiated thyroid cancer- novel biomarkers
Angelika Buczyńska[1], Maria Kościuszko[2], Iwona Sidorkiewicz[1], Agnieszka Adamska[2], Katarzyna Siewko[2], Adam Krętowski[1,2] & Anna Popławska-Kita[2]
[1]Clinical Research Centre, Medical University of Bialystok, Białystok, Poland; [2]Department of Endocrinology, Diabetology and Internal Medicine, Medical University of Bialystok, Białystok, Poland

Differentiated thyroid cancer (DTC) is the most common malignant neoplasm arising from the thyroid parenchymal cells. DTC incidence is steadily increasing worldwide and there are approximately 1700 new cases/per year in Poland. The biopsy with subsequent thyroid resection plays a central role in the diagnosis and treatment of this malignancy. After surgery, radioactive iodine (RAI) treatment is recommended to eradicate potential residual disease and improve prognosis. Due to the fact that RAI application is associated with oxidative stress formation, this treatment may exert an important impact on homeostasis. From the other hand, it was proved that protein 53 (p53), nuclear factor kappa B (NF-kB), forkhead box protein 01 (FOXO) and sirtuin 1 (SIRT1) play a crucial role in oxidative stress as well as cancer progression. Therefore, the determination of their role may be useful in DTC clinical management. In our study, we evaluated the total oxidative status (TOS), total antioxidant capacity (TAC), and p53, NF-kB, FOXO, SIRT1 concentrations to assess diagnostic usefulness of these parameters as indication markers for RAI therapy. For the purpose of this study 60 patients diagnosed with different stages of DTC after total thyroidectomy with an indication to RAI therapy and 20 pT1a DTC patients after total thyroidectomy without any recommendation to RAI therapy were enrolled as study and control groups, respectively. Serum TOS status and SIRT1 concentration were significantly higher (both $P<0.001$), when TAC status and p53, NK-kB, FOXO concentrations were significantly lover (all $P<0.05$) in the study group

compared to the control group. All the parameters were tested for their diagnostic utility as indicators for RAI treatment. The diagnostic usefulness as RAI indication markers was demonstrated for TAC (AUC=0.99), FOXO (AUC=0.78), TOC (AUC=0.76), SIRT1 (AUC=0.74), p53 (AUC=0.71) and NK-kB (AUC=0.68). Furthermore, our study revealed increased oxidative stress and decreased antioxidant capacity in DTC patients qualified for RAI treatment. This may indicate a worse prognosis and advanced neoplastic process.

DOI: 10.1530/endoabs.81.RC3.3

RC3.4

Are BRAF-TERT mutated differentiated thyroid cancers similar to other double mutated?

Alessandra Colapinto[1], Cristina Basso[1], Valentina Vicennati[1], Ottavio Cavicchi[2], Elisa Lodi Rizzini[3], Arber Golemi[4], Elena Tabacchi[4], Margherita Nannini[5], Dario De Biase[6], Antonio De Leo[7], Giovanni Tallini[7], Uberto Pagotto[1] & Andrea Repaci[8]

[1]IRCCS Azienda Ospedaliero-Universitaria di Bologna, Alma Mater Studiorum University of Bologna, Department of Medical and Surgical Sciences (DIMEC), Division of Endocrinology and Diabetes Prevention and Care, Bologna, Italy; [2]IRCCS Azienda Ospedaliero-Universitaria di Bologna, Otolaryngology Head and Neck Surgery Unit; [3]IRCCS Azienda Ospedaliero-Universitaria di Bologna, Radiotherapy Unit, Bologna, Italy; [4]IRCCS Azienda Ospedaliero-Universitaria di Bologna, Nuclear Medicine Unit, Bologna, Italy; [5]IRCCS Azienda Ospedaliero-Universitaria di Bologna, Oncology Unit, Bologna, Italy; [6]Alma Mater Studiorum University of Bologna, Department of Pharmacy and Biotechnology (FaBit), Molecular Diagnostic Unit, Bologna, Italy; [7]Alma Mater Studiorum University of Bologna, Department of Experimental, Diagnostic and Specialty Medicine, Anatomic Pathology and Molecular Diagnostic Unit,, Bologna, Italy; [8]IRCCS Azienda Ospedaliero-Universitaria di Bologna, Division of Endocrinology and Diabetes Prevention and Care, Bologna, Italy

Introduction

Differentiated thyroid cancers (DTCs) carrying BRAF and TERT mutations are associated with high-risk clinicopathological features and poor prognosis. However, there are currently no studies comparing BRAF-TERT tumors to other double mutated DTCs.

Aim

To verify whether BRAF-TERT mutated DTCs differ from other double mutated DTCs in terms of clinicopathological characteristics and outcome.

Materials and Methods

168 DTCs consecutively operated between 2017 and 2021 were analyzed by Next Generation Sequencing. Based on the number of mutant genes, patients were first classified into single or double mutated groups. Multiple mutated DTCs were further subclassified on the basis of the presence or absence of the BRAF-TERT mutation in two groups and finally compared each other regarding clinicopathological characteristics, persistent disease one year after the initial treatment and at the end of the follow-up, respectively.

Results

In our population 25/168 DTCs (14,8%) had a double mutation, which in more than 50% (14/25 – 56%) was BRAF-TERT positive. The other double mutated tumors were subdivided as: 5/25 RAS-TERT (20%), 2/25 BRAF-P53 (8%), 2/25 BRAF-PI3KCA (8%), 1/25 RAS-PI3KCA (4%) and 1/25 TERT-PI3KCA (4%). From the comparison with single mutated DTCs, double mutated DTCs were more associated with older age, larger tumor, more advanced TNM stage (OR 8,88; 95% CI 2,68 to 29,36), greater risk of structural persistence (OR 13,39; 95% CI 5,06 to 35,41), increased progression of disease (OR 7, 00; 95% CI 2.04 to 23,93) and death. Compared to other double mutated, BRAF-TERT DTCs do not differ in age, sex, aggressive histotype, tumor size, extrathyroidal extension, lymph node involvement, distant metastases, stage (AJCC 8 ed), ATA risk, post-therapeutic I-131 whole body scan and PET uptake (*P*-value > 0.05). Although 3 of the 14 patients carrying BRAF-TERT mutated DTC died from disease progression, this data was not statically significant and no differences were observed in terms of disease persistence rates at 12 months and at the last follow-up. The two groups differ from each other only in the value of thyroglobulin at the time of ablation, which was statistically significant lower in the BRAF-TERT subgroup (median 2,2 ng/dl vs 54,10 ng/dl *P*-value 0.010).

Conclusions

Double mutated DTCs showed similar clinicopathological features, regardless the pair of gene involved. Furthermore, lower thyroglobulin at ablation in BRAF-TERT mutated DTCs should not be considered as a valid predictor of remission. Further prospective studies with longer follow-up and wider population are necessary to confirm our results.

DOI: 10.1530/endoabs.81.RC3.4

RC3.5

Impact of stimulated thyroglobulin and BRAF status in Stage I and ATA intermediate risk DTC

Cristina Basso[1], Alessandra Colapinto[1], Valentina Vicennati[1], Uberto Pagotto[1], Giovanni Tallini[2,3], Antonio De Leo[2,3], Dario De Biase[3,4], Elisa Lodi Rizzini[5], Ottavio Cavicchi[6], Margherita Nannini[7], Elena Tabacchi[8], Arber Golemi[8] & Andrea Repaci[9]

[1]IRCCS Azienda Ospedaliero-Universitaria di Bologna, Department of Medical and Surgical Sciences (DIMEC), Alma Mater Studiorum, University of Bologna, Division of Endocrinology and Diabetes Prevention and Care, Bologna, Italy; [2]S.Orsola-Malpighi Hospital, University of Bologna, Department of Experimental, Diagnostic and Specialized Medicine, Bologna, Italy; [3]Anatomic Pathology and Molecular Diagnostic Unit-University of Bologna Medical Center, Bologna, Italy; [4]University of Bologna, Department of Pharmacy and Biotechnology (FaBit), Bologna, Italy; [5]IRCCS Azienda Ospedaliero-Universitaria di Bologna, Radiotherapy Unit, Bologna, Italy; [6]IRCCS Azienda Ospedaliero-Universitaria di Bologna, Department of Otolaryngology, Bologna, Italy; [7]IRCCS Azienda Ospedaliero-Universitaria di Bologna, Division of Oncology, Bologna, Italy; [8]IRCCS Azienda Ospedaliero-Universitaria di Bologna, Nuclear Medicine Unit, Bologna, Italy; [9]IRCCS Azienda Ospedaliero-Universitaria di Bologna, Division of Endocrinology and Diabetes Prevention and Care, Bologna, Italy

Introduction

There is no clear indication for radioiodine treatment (RAI) in patients affected by differentiated thyroid cancer (DTC) in Stage I and ATA intermediate risk, according to American Thyroid Association (ATA) guidelines.

Purpose

Our aim is to evaluate whether integration of BRAF status and thyroglobulin TSH-stimulated at the time of RAI (A-HTg) could further improve accuracy of stratification, and therefore therapeutic management, in DTC patients with Stage I AJCC and ATA intermediate risk.

Materials and Methods

This retrospective study involved 372 patients affected by DTC with Stage I AJCC 8th ed. and ATA intermediate risk, followed at the Endocrinology and Diabetes Prevention and Treatment Department from 2000 to 2020. For each patient we analyzed persistence of the disease one year after the initial treatment and at the end of the follow up (median: 8 years), BRAF status and A-HTg levels, respectively. By ROC curve we calculated the A-HTg cutoff of 5.9 ng/ml (sensitivity 64%, specificity 75%, AUC 0.725).

Results

In our population, 265/372 (68.8%) patients had BRAFV600E mutation, 121/372 (32.5%) A-HTg levels $>$ 5.9 ng/ml, 91/372 (24.5%) persistent disease after one year and 75/372 (20.2%) at the end of the follow up. The presence of A-HTg levels $>$ 5.9 ng/ml, regardless of BRAF status, was associated with a higher risk of disease persistence after one year (BRAFwt: RR 7.615, p-value $<$ 0.001; BRAFV600E: RR 5.535, p-value $<$ 0.001) and at the end of the follow up (BRAFwt: RR 3.004, p-value 0.038; BRAFV600E: RR 4.776, p-value $<$ 0.001). Our population was further divided in 4 groups: A-HTg $<$ 5.9 ng/ml and BRAFwt, A-HTg $<$ 5.9 ng/ml and BRAFV600E, A-HTg $>$ 5.9 ng/ml and BRAFwt, A-HTg $>$ 5.9 ng/ml and BRAFV600E. In these subpopulations we observed a progressive increase of persistent disease after one year, respectively of 8.3%, 15.6%, 40.9% and 50.6% (*P*-value $<$ 0.001), and at the end of the follow up, respectively of 9.7%, 15.1%, 24.4% and 46.2% (*P*-value $<$ 0.001).

Conclusions

Among patients with Stage I and ATA intermediate risk DTC, those with high A-HTg and BRAFV600E had the maximum rate of persistent disease. Therefore, radioiodine treatment could be proposed only to this subpopulation, rather to the entire cohort of Stage I and ATA intermediate risk. Prospective studies with longer follow-up and wider population are necessary to confirm our results.

DOI: 10.1530/endoabs.81.RC3.5

RC3.6

The mRNA of fibronectin 1 and of the integrin subunit alpha V are powerful prognostic indicators in papillary thyroid carcinoma

Mario Vitale[1], Vincenzo Marotta[2], Anna Tortora[2], Giulia Izzo[2] & Domenico Rocco[1]

[1]University of Salerno, Department of Medicine, Surgery and Dentistry, Italy; [2]UOC Clinica Endocrinologica e Diabetologica, AOU S. Giovanni e Ruggi D'Aragona, Italy

Integrins are cell-extracellular matrix adhesion molecules considered functionally related to the development of cancer metastasis. Starting from the dataset of

mRNA-seq of papillary thyroid carcinoma (PTC) from the TCGA, we determined the expression of fibronectin 1 (FN1) and fibronectin-binding integrins in PTC. We then analyzed the association of the expression of these two genes with the driver genes, the stage of the disease and its outcome. 355 PTCs and 58 normal thyroid (NT) tissues with the corresponding mutations of the driver genes, the pathological characteristics and the outcome of the disease entered the analysis. FN1 mRNA was increased 60-fold in PTC compared to NT. The integrin heterodimers that bind FN are 41, 51, V1, V3 and V6. The mRNA of V, 1 and 6 were all overexpressed. Flow cytometric analysis with specific antibodies confirmed in two PTC cell lines (BCPAP and TPC1) that the integrins V1, V3 and V6 were highly expressed. BRAFV600E positive PTCs showed the greatest expression of FN1 and integrin subunits, while the RAS positive PTC expression profile was much lower and similar to that of NT. FN1 expression was positively correlated with lymph node metastases, advanced stage and extrathyroidal extension ($P < 0.0001$) and with poor disease outcome (odds ratio 8.2: $P < 0.001$). The expression of V mRNA also correlated positively with an advanced disease and a worse outcome (odds ratio 4.05; $P < 0.002$). In conclusion, PTCs with BRAFV600E have a higher expression of FN1 and V mRNA. The expression of these genes correlates positively with an advanced disease and an unfavorable outcome, representing a powerful prognostic indicator.

DOI: 10.1530/endoabs.81.RC3.6

RC3.7

Immune-related thyroid dysfunctions during PD-1/PD-L1 inhibitors and their association to the oncological outcome: new evidence

Matteo Ferrari[1], Alice Anna Nervo[1], Sara Basile[1], Enrica Migliore[2], Valentina D'Angelo[1], Giovanni Gruosso[1], Daniela Rosso[1], Francesca Retta[1], Alessandro Piovesan[1] & Emanuela Arvat[1]
[1]Azienda Ospedaliero-Universitaria Città della Salute e della Scienza di Torino, Oncological Endocrinology Unit, Torino, Italy; [2]Azienda Ospedaliero-Universitaria Città della Salute e della Scienza di Torino, Cancer Epidemiology Unit, Torino, Italy

Background
Immune checkpoint inhibitors (ICIs) showed impressive results in several malignancies; however, a large spectrum of immune-related adverse events (IRAEs) may occur, including thyroid dysfunction (DYSTHYR). IRAEs seem to be associated with better cancer outcome; limited data suggested that thyroid toxicity could be a predictor of response to ICIs.
Patients and methods
We retrospectively evaluated all patients who started treatment with the programmed cell death protein-1 (PD-1) and its ligand (PD-L1) inhibitors between 2017 and 2020 at the Città della Salute e della Scienza Hospital (Department of Oncology). Patients with central hypothyroidism were excluded from the analysis. Both the new onset and the worsening of pre-existing DYSTHYR were recorded; hypothyroidism was categorized as grade (G) 1 or 2 according to TSH levels ($< \text{or} \geq 10$ mU/l) similarly to thyrotoxicosis (G1 or 2 in case of TSH $>$ or ≤ 0.1 mU/l). Radiological tumor response was defined according to RECIST criteria. Progression free survival (PFS) and overall survival (OS) were assessed and compared among different groups.
Results
Among 324 patients (median age 67 years, 70.7% males, 95.4% treated with anti-PD-1, 49.4% affected by lung cancer), DYSTHYR was observed in the 24.7% of the population, after a median time of 3.3 (1.8-6.2) months. The most recorded event was hypothyroidism (85%); DHYSTHYR was G2 in 70% of cases. No statistically significant benefit in terms of PFS was observed in patients with DYSTHYR. However, the development of DISTHYR was associated with a significantly longer OS (87.3% vs 73.5% at 12 months, $P = 0.03$) and lower mortality (HR 0.61; 95% CI 0.39-0.95). Considering only patients without pre-existing thyroid dysfunction at baseline (277, 85.5% of the sample), a better OS was observed in case of DYSTHYR G2 in comparison to cases with DYSTHYR G1 or without DYSTHYR ($P = 0.03$), with a decreased risk of death (HR 0.47; 95% CI 0.24-0.91).
Conclusions
DYSTHYR is a common IRAE during anti PD-1/PD-L1 treatment. We detected a better clinical outcome in patients with DISTHYR during ICIs, in terms of improved OS and reduced mortality. In subjects without pre-existing thyroid alteration, the benefit was observed especially in case of detection of higher TSH levels during ICIs.

DOI: 10.1530/endoabs.81.RC3.7

Pituitary and Neuroendocrinology 1

RC4.1

Immunotherapy in a non-functioning metastatic pituitary neuroendocrine tumor. An encouraging case report

Tiziana Feola[1,2], Francesca Gianno[3,4], Monica Verrico[4], Felice Giangaspero[3,4], Silverio Tomao[4], Claudio Colonnese[4], Vincenzo Esposito[5,6], Andrea Isidori[2], Giuseppe Minniti[7,8] & Marie-Lise Jaffrain-Rea[1,9]
[1]Neuromed IRCCS, Neuroendocrinology, Pozzilli, Italy; [2]Sapienza University of Rome, Department of Experimental Medicine, Rome, Italy; [3]Neuromed IRCCS, Neuropathology, Pozzilli, Italy; [4]Sapienza University of Rome, Department of Radiological, Oncological and Pathological Sciences, Rome, Italy; [5]Neuromed IRCCS, Neurosurgery, Pozzilli, Italy; [6]Sapienza University of Rome, Department of Neurology and Psychiatry, Rome, Italy; [7]Neuromed IRCCS, Neuroncology, Pozzilli, Italy; [8]University of Siena, Department of Medicine, Surgery, and Neurosciences; [9]University of L' Aquila, Department of Biotechnological and Applied Clinical Sciences, Italy

Introduction
Metastatic pituitary neuroendocrine tumors (PitNETs) or pituitary carcinomas are rare and challenging conditions. We present a recent and encouraging observation of a temozolomide (TMZ)-resistant clinically non-functioning metastatic PitNET showing a remarkable response to the anti-PDL1 drug Pembrolizumab.
Case presentation
A 57-years-old man had transsphenoidal surgery in November 2012 for a large non-functioning intra/suprasellar mass revealed by visual defects, and invasive into the left cavernous sinus. A diagnosis of "null cell" PitNET (Ki-67 10%, p53 5%) was made and in June 2013 the surgical resection was completed transcranially. One year later he received stereotactic radiotherapy on the left cavernous remnant with a good response. However, delayed infrasellar regrowth was observed, first presenting as nasal pseudopolyps and leading to re-operation in March 2018. The pathological diagnosis was consistent with the aggressive clinical behavior (Ki67 20%, p53 10%) and two small pre-pontine nodules revealed metastatic progression. Further immunohistochemical characterization of the tumor indicated a PIT1 lineage. The patient started TMZ with a standard schedule for 5 cycles, followed by a metronomic schedule in association with stereotactic radiotherapy on pre-pontine nodules and additional small multiple asymptomatic brain and spinal metastases indicative of disease progression. The primary tumor also progressed with nasal obstruction and visual loss. Searching for alternative therapeutic options, a high expression of PDL-1 was found and suggested immunotherapy. TMZ was withdrawn and in March 2021 the patient started Pembrolizumab. Encouraging results were noticed after 4 cycles of treatment. After 8 cycles of treatment, a remarkable clinical, radiological and metabolic response was documented, with a significant shrinkage of the primary lesion, a regression of metastatic nodules, and a decrease of SUV values at 18-FDG PET-CT. Moderate cutaneous and renal toxicities (G1-G2) and mild eosinophilia were observed and successfully managed by systemic steroid therapy and transient drug withdrawal. Pembrolizumab is currently continued as a maintenance therapy.
Discussion
To the best of our knowledge, no such remarkable response to anti-PDL1 monotherapy in a Pit1-positive metastatic PitNET has been reported so far. Interestingly, in few reports of other aggressive or metastatic PitNET treated by immunotherapy, PDL-1 expression – if available - was low ($<1\%$) or negative. This case supports recent data suggesting that PIT1-positive PitNETs may express more PDL-1 than other phenotypes.
Conclusion
This observation suggests a promising role of immunotherapy for metastatic PitNETs, refractory to standard therapy. In addition to the potential role of PDL-1 expression, further predictors of response should be searched for.

DOI: 10.1530/endoabs.81.RC4.1

RC4.2

Macro-GH – a novel clinical entity causing a diagnostic challenge – a case report

Maria Stelmachowska-Banas[1], Magdalena Ostrowska[1], Tomasz Goszczyński[2], Konrad Kowalski[3], Marta Korbonits[4], Renata Kapuścińska[1], Wojciech Zgliczyński[1] & Piotr Glinicki[1]
[1]Centre of Postgraduate Medical Education, Department of Endocrinology, Warsaw, Poland; [2]Hirszszfeld Institute of Immunology and Experimental Therapy, Polish Academy of Science, Wrocław, Poland; [3]Masdiag Laboratory, Warsaw, Poland; [4]William Harvey Research Institute, Barts and the London School of Medicine, Queen Mary University of London, Department of Endocrinology, London, United Kingdom

Introduction
Hormone macromolecules are complexes of hormones with other compounds, most often with IgG immunoglobulin. They show variable immunoreactivity in immunochemical tests (IRMA, ELISA, CLIA, ECLIA) and usually have a weak biological effect. They can interfere with immunological assays of various hormones. Some known hormone macrocomplexes are: BB-PRL (24% - 34%), macro-TSH (0.6% - 1.2%) and very rare macromolecules of various hormones: calcitonin, PTH, insulin (single reports). Presentation of a new hormone macromolecule – macro-GH (GH- growth hormone), that may interfere with different GH assays leading to false-high results in serum samples.
Case presentation
A 61-year-old female was admitted to our department with suspected acromegaly. Laboratory test showed increased fasting GH level without suppression on oral glucose tolerance test and normal IGF-1. A trial 3-month treatment with the long-acting somatostatin analogue was initiated. Despite the treatment, elevated GH with normal IGF-1 levels persisted. No visible decrease in pituitary adenoma size on MRI was detected. Finally, the patient underwent a transsphenoidal resection of a pituitary tumor. After the surgery, laboratory tests remained unchanged with elevated GH level and normal IGF-1. Interference in the determination of GH level was suspected.
Methods and results
We found a different immunoreactivity (different results) in the determination of GH by routine immunochemical methods: ECLIA, CLIA and IRMA. A serial dilution test showed non-linearity. Rheumatoid factor (RF) was absent. The test for the presence of heterophile antibodies was performed. GH recovery after incubation was 95%, indicating no interference from heterophile antibodies. In the penultimate stage, a sample of the patient's serum was incubated with the serum of an acromegalic patient with a high concentration of GH. The GH recovery after incubation was 98%. Next the sample was precipitated with 25% PEG. The GH recovery was 12%, which means that 88% of growth hormone was in the form of macrocomplex (macro-GH). The last step in confirming the presence of the macrocomplex GH (macro-GH) was the use of the reference method - size-exclusion chromatography (SEC).
Conclusions
In the analyzed case, we confirmed a very rare type of interference - a presence of macro-GH. In each case of suspected inconsistency of laboratory test results with the clinical picture and/or other tests, it is advisable to start the procedure of excluding/looking for various types of interference that may impede the diagnosis and/or treatment of patients with various endocrine diseases.

DOI: 10.1530/endoabs.81.RC4.2

RC4.3

Pre-treatment GH levels and number of therapeutic interventions for acromegaly management are predictive of altered MRI bone shape and severity of arthropathy in acromegaly

Nikolaos Kyriakakis[1,2], Michael Bowes[3], Julie Lynch[1], Sarah R Kingsbury[4], Steve M Orme[1], Robert D Murray[1,2] & Philip G Conaghan[4]
[1]Leeds Teaching Hospitals NHS Trust, Department of Endocrinology, Leeds, United Kingdom; [2]University of Leeds, Leeds Institute of Cardiovascular and Metabolic Medicine (LICAMM), Leeds, United Kingdom; [3]Imorphics Ltd, Manchester, United Kingdom; [4]University of Leeds, Leeds Institute of Rheumatic and Musculoskeletal Medicine, Leeds, United Kingdom

Introduction
Emerging research in 3D-bone shape has provided new insights into the pathogenesis of osteoarthritis (OA). OA patients have increased subchondral bone area, associated with higher prevalence of cartilage loss. Higher B-score, a novel, machine learning-derived OA bone biomarker, is associated with increased OA symptom severity and structural progression. Arthropathy, despite being the commonest cause of morbidity amongst acromegaly patients, remains one of the under-investigated areas in acromegaly and currently, data based on modern imaging modalities are limited.
Design/Methods
Cross-sectional study, in which bilateral knee MRI scans were obtained from 60 patients with acromegaly. Knee bone shape, 3D-joint space width (3DJSW), cartilage thickness, B-score and bone area were measured based on automated segmentation of MR images using active appearance models.
Results
Thirty-nine acromegaly patients (65%) had B-score <2 (Group 1), indicating absence of significant arthropathy on knee MRI, with the remaining 21 patients (Group 2) having B-score ≥ 2. There was no difference in age, male:female ratio, height and weight between the two groups. Following adjustment for these variables, Group 2 patients had increased mean femoral, tibia and patella bone areas compared with Group 1. Both mean medial and lateral femorotibial cartilage thickness were increased in Group 2 [Medial cartilage thickness, Group 1: 5.35mm (95% CI 5.0-5.7) vs Group 2: 6.12 mm (95% CI 5.66-6.59), $P=0.01$; Lateral cartilage thickness, Group 1: 6.48 mm (95% CI 6.17-6.79) vs Group 2: 7.78 mm (95% CI 7.36-8.2), $P<0.001$], leading to increased 3DJSW medially. Patients with B-score ≥ 2 had higher median pre-treatment GH levels [Group 1: 6.6 (4.1-17) mg/l vs Group 2: 39 (5.4-57.8) mg/l, $P=0.015$] and required significantly higher number of pituitary surgeries than patients with B-score <2. Multiple linear regression analysis showed that higher number of pituitary surgeries, radiotherapy and use of GH-lowering medications were independently correlated with higher B-scores. 3DJSW was positively associated with higher pre-treatment GH levels, height, weight and male gender. Regarding clinical outcomes, Group 2 patients had significantly longer median duration of knee pain [4 years (1.75-10)] than Group 1 [1.5 years (0-5)], $P=0.01$. Additionally, 47.6% of Group 2 patients had undergone previous joint replacement surgery compared with 12.8% in Group 1 ($P=0.009$).
Conclusions
Patients with B-score ≥ 2 had higher pre-treatment GH values and required higher number of therapeutic interventions for the management of acromegaly, suggesting that the risks of more profound changes to the bone shape and increased severity of arthropathy are dependent on the degree of overall GH excess.

DOI: 10.1530/endoabs.81.RC4.3

RC4.4

KLB gene mutations - a rare cause of hypogonadotropic hypogonadism

Catarina Cidade-Rodrigues, Catarina Chaves, Filipe Cunha, Mariana Martinho & Margarida Almeida
Centro Hospitalar do Tamega e Sousa, Endocrinology, Penafiel, Portugal

Introduction
Congenital hypogonadotropic hypogonadism (CHH) is a rare disease. Mutations in various genes have been implicated in its pathophysiology, the most frequent being *ANOS1*, *FGFR1* and *GNRHR* genes. FGFR1 is essential for cell proliferation, differentiation and migration during embryonic development and is involved in GnRH neuron development and maintenance. Klotho-*beta* protein (KLB) is expressed in the postnatal hypothalamus and is the co-receptor for FGF21 binding to his receptor FGFR1. Recent evidence suggests that FGF21/KLB/FGFR1 pathway is implicated in approximately 17% of CHH cases.
Case report
Male, 19 years old, diagnosed with hypogonadism at the age of 16 because of pubertal delay and anosmia. He had no history of testicular/head trauma. No family history of hypogonadism or congenital malformations. He was treated with testosterone with complete pubertal development and stopped for no apparent reason. He had normal libido and no erectile dysfunction. Physical examination: no congenital abnormalities, weight 69.9 Kg, height 180.5 cm, BMI 21.45 kg/m^2, arm-span 178 cm, waist-circumference 98 cm. Testicular volume: 12 ml(left) and 10 ml(right). He had secondary sexual characteristics and gynecomastia. No synkinesis. His total testosterone without treatment was <0.1 ng/ml, FSH 1.5 mUI/ml, LH 0.6 mUI/ml, TSH 1.33 uUI/ml, free T4 0.84 ng/dl, 8h 00 cortisol 10.01 ug/dl, prolactin 10.2ng/ml, IGF-1 357ng/ml, total cholesterol 201mg/dl, HDL-cholesterol 47 mg/dl, LDL-cholesterol 123mg/dl, triglycerides 150 mg/dl, insulin 23.4 µUI/ml, glucose 87 mg/dl, HbA1c 5.0%. Pituitary MRI: normal-sized gland, no sellar/parasellar masses and olfactory bulbs and tracts were present. Normal renal ultrasound. Karyotype: 46,X,inv (Y) (p11.2 q11.2). Genetic next-generation sequencing identified the variant NM_175737,3:c,2443A$>$G p.(Lys815Glu) in *KLB* gene and the variant NM_000406.2:c,937_947del p.(Phe313Metfs*3) in *GNRHR* gene, both in heterozygosity. He was diagnosed with congenital hypogonadotropic hypogonadism due to heterozygous mutations in *KLB* and *GNHRHR* genes and started on testosterone treatment.
Discussion
The mechanism involved in CHH caused by loss-of-function *KLB* mutations is not well understood, however it appears to be related to the inability of GnRH neurons to release GnRH in response to FGF21. The phenotypic spectrum is wide. Most patients have metabolic defects consistent with the metabolic role of the FGF21/KLB/FGFR1 pathway. This was present in our patient, who had hypercholesterolemia, insulin resistance and increased waist circumference. The *KLB* gene variant presented was described only once in literature, however, this is the first case ever associated with a *GNRHR* gene mutation. The *GNRHR* gene normally cause autosomal recessive CHH but the presence of a heterozygous *GNRHR* mutations in a patient with a *KLB* mutations might have act synergically in the pathogenesis and phenotype of this disease.

DOI: 10.1530/endoabs.81.RC4.4

RC4.5

Validation of the ICD-codes for acromegaly – strategies to reduce false positive cases and improve estimation of the incidence in Sweden

Erika Tsatsaris[1], Jonas Robèrt[2], Katarina Berinder[3], Lorenza Bonelli[4], Pia Burman[4], Per Dahlqvist[3], Charlotte Höybye[3], Oskar Ragnarsson[6], Konstantina Vouzouneraki[5] , Anna-Karin Åkerman[7], Bertil Ekman[2] & Britt Eden Engstrom[1]

[1]Department of Medical Sciences, Endocrinology and Mineral Metabolism, Uppsala University, Department of Endocrinology and Diabetes, Uppsala University Hospital, Uppsala, Sweden; [2]Department of Health, Medicine and Caring Sciences, Linköping University, Linköping, Sweden; [3]Department of Molecular Medicine and Surgery, Karolinska Institutet, Department of Endocrinology, Karolinska University Hospital, Stockholm, Sweden; [4]Department of Endocrinology, Skåne University Hospital Malmö, University of Lund, Malmö, Sweden; [5]Department of Public Health and Clinical Medicine, Umeå University, Umeå, Sweden; [6]Institute of Medicine at Sahlgrenska Academy, University of Gothenburg, Department of Internal Medicine and Clinical Nutrition, Gothenburg, Sweden; [7]Department of Internal Medicine, Örebro University Hospital, Örebro, Sweden; *Erika Tsataris and Jonas Robèrt are joint first authors

Purpose
We aimed to validate the diagnosis and estimated national incidence of acromegaly reported in the Swedish National Patient Register (NPR), based on clinically reported International Classification of Diseases (ICD-codes), in comparison with the Swedish Pituitary Register (SPR).
Methods
All patients in NPR or SPR between 1991-2018 with the ICD-9 or ICD-10 diagnosis of acromegaly and age >18 years at diagnosis were included. The diagnosis was assumed correct if found in both registers. Medical records were reviewed in two of Sweden's six healthcare regions in patients only found in one of the registers. An algorithm aiming to correctly identify most patients with acromegaly in the NPR was constructed from validated data and applied to the remaining four health care regions. The algorithm was based on at least two registrations in the NPR of diagnostic codes E220 or 253A or the diagnostic code alone in combinations with codes for pituitary tumour and/or pituitary surgery, giving the highest functional diagnosis sensitivity and high positive predictive value (PPV).
Results
A total of 1868 patients were found, 938 reported in both registers and 930 patients only in one register (908 only in the NPR and 22 only in the SPR). Internal validation of the algorithm was performed in the SPR and captured 98.9% (928 of 938) of the patients. All 22 patients only reported in the SPR were validated, and 14 patients were confirmed with acromegaly. Applying the diagnostic algorithm to the NPR-search reduced the number of patients only found in NPR to 347, of which 85 have confirmed acromegaly after review of medical records. Thus, 1023 of the total 1846 patients with acromegaly codes in the NPR were confirmed to have acromegaly (PPV 55.4%). The most common reasons for misclassification were acromegaly initially suspected but later ruled out, hyperprolactinemia/prolactinoma, non-functioning pituitary adenoma, other/unknown pituitary tumours or cysts. Among the 1037 confirmed cases, 952 patients were already in the SPR, which gave a coverage rate of 91.8%. Based on this validation, the annual incidence of acromegaly in Sweden during 1991-2018 was calculated to 5.1 per million.
Conclusion
By using the diagnostic code for acromegaly alone to identify patients with the disease in NPR is not sufficiently specific for epidemiological research. However, the usage of an algorithm including combinations of diagnostic, tumour and surgical codes increased the probability of correct diagnosis and provided an improved estimate of the incidence of acromegaly in Sweden.

DOI: 10.1530/endoabs.81.RC4.5

RC4.6

Impact of diabetes on morbidity and mortality in patients with acromegaly

Daniela Esposito[1], Daniel S Olsson[1], Stefan Franzén[2], Soffia Gudbjörnsdottir[3], Mervete Miftaraj[3], Jonatan Nåtman[3] , Ann-Marie Svensson[3] & Gudmundur Johannsson[1]

[1]Institute of Medicine, Sahlgrenska Academy, University of Gothenburg and Sahlgrenska University Hospital, Department of Internal Medicine and Clinical Nutrition and Department of Endocrinology, Gothenburg, Sweden; [2]Sahlgrenska Academy, University of Gothenburg, Health Metrics Group, Gothenburg, Sweden; [3]National Diabetes Register, Centre of Registers, Gothenburg, Sweden

Background
Diabetes is an important risk factor for cardiovascular morbidity and mortality but its impact on outcome in acromegaly is unknown.
Methods
This was a nationwide, observational, matched-cohort study. Adult patients with acromegaly due to a pituitary adenoma were identified in the Swedish National Patient Registry between 1987 and 2020 and those with coexistent type 2 diabetes in the National Diabetes Registry and Drug Registry. Overall mortality, and cardiovascular mortality and morbidity were estimated in acromegalic patients with diabetes (ACRO-DM group) in comparison with those without diabetes (ACRO group) using Cox regression adjusted for multiple confounders with propensity score.
Results
The study included 786 patients with acromegaly, 254 in the ACRO-DM group and 532 in the ACRO group. Mean follow-up was 9.2 years. At baseline, mean age (SD) was 62.6 (11.4) and 60.0 (12.1) years ($P=0.004$) and mean duration of acromegaly was 6.8 (8.1) and 6.0 (6.2) years ($P=0.098$) in the ACRO-DM and ACRO group, respectively. Mean income and level of education were lower in patients with coexistent diabetes while the frequency of pre-existing cardiovascular diseases was higher (61% vs 37%, $P<0.001$). The use of pituitary surgery (71% vs 68%, $P=0.62$) and radiotherapy (16% vs 16%, $P=1.00$) was similar among the two groups. Overall, 466 (59%) patients received pharmacotherapy in the entire study cohort. The use of somatostatin analogues (37% vs 30%, $P=0.055$) and GH receptor antagonists (10% vs 6%, $P=0.063$) was somewhat more frequent in the ACRO-DM group. The unadjusted overall mortality rate per 1000 person-years was 35.1 (95% CI 27.2–44.7) for the ACRO-DM group and 20.1 (16.5–24.3) for the ACRO group, with a hazard ratio (HR) of 1.58 (1.12–2.23) after adjustment for multiple confounders. The ACRO-DM group had increased cardiovascular mortality (HR 2.11, 1.09–4.10) and increased risk of cardiovascular diseases (HR 1.49, 1.21–1.82). Risk factor for cardiovascular diseases were age [HR 1.03 (95% CI 1.02–1.04)], diabetes duration [HR 1.09 (1.05–1.13)], diastolic blood pressure [HR 1.02 (1.00–1.04)], body mass index [HR 1.05 (1.01–1.09)], and treatment with antihypertensive drugs [HR 2.1 (1.21–3.64)] or lipid-lowering medication [HR 1.60 (1.08–2.36)].
Conclusions
Diabetes in patients with acromegaly was associated with excess overall and cardiovascular mortality and increased risk of cardiovascular diseases. These findings are novel and emphasize the need of optimizing management of acromegaly to prevent the development of diabetes since it might improve survival.

DOI: 10.1530/endoabs.81.RC4.6

RC4.7

The burden of pain in patients with acromegaly

Ilonka Kreitschmann-Andermahr[1], Annalena Kahl[1], Timo Deutschbein[2], Jürgen Honegger[3], Nicole Unger[4], Mario Detomas[5,6], Sabrina Giese[3], Bernadette Schroeder[1], Witold Chmielewski[1] & Sonja Siegel[1]

[1]University Hospital Essen, Neurosurgery and Spine Surgery, Essen, Germany; [2]MEDICOVER Oldenburg MVZ, Oldenburg, Germany; [3]University of Tübingen, Neurosurgery, Tübingen, Germany; [4]University Hospital Essen, Endocrinology, Diabetes and Metabolism, Essen, Germany; [5]Würzburg, Würzburg, Germany; [6]University Hospital Würzburg, Endocrinology and Metabolism, Würzburg, Germany

Introduction
The aim of the present study was to explore pain prevalence, pain locations and its impact on everyday activities and health-related quality of life (QoL) in a large cohort of patients with acromegaly.
Methods
We conducted a survey at three major centers specialized on the treatment of pituitary diseases. 124 patients with acromegaly (mean age 56.6y ± 13.5) filled in a self-constructed questionnaire on acromegaly symptoms, pain including a pain location diagram and interference with daily life. Additionally, joint pain, physical functioning and stiffness were queried with the Western Ontario and McMaster Universities Arthritis Index (WOMAC), and health-related QoL was assessed with the Short Form (SF)-36. Prevalences (in valid %), comparison of means by *t*-tests and Pearson correlation coefficients (r) are reported.
Results
62% of the patients reported pain they attributed to acromegaly. Of these 78% reported pain located in the joints, predominantly in knees and hips. 59% of them had headache and 47% had back pain. Of those patients with pain 84% reported daily pain, 81% had pain during work, 80% while sitting or lying down and 62% in stressful situations. 60% of them avoided certain activities to reduce pain. Pain prevalences did not differ between men and women (n.s) and were unrelated to age (n.s). Patients with pain had significantly lower physical (34.6±11.0 vs

48.7±10.3, $P=0.000$) and mental QoL (48.9±10.5 vs 42.0±11.5, $P=0.002$). Physical QoL was negatively correlated to the WOMAC subscales pain ($r=$-0.723), stiffness ($r=$-0.499) and functional limitation ($r=$-0.777) as well as to the number of different pain locations ($r=$-0.599, all $P=0.000$). The impact on psychological QoL was less pronounced (r ranging from -.279 to -.360), but still highly significant (all $P<0.005$).

Discussion

The results indicate that the majority of acromegaly patients suffers from pain with a detrimental effect on their daily living and QoL. This underlines the importance of addressing joint pain and other painful conditions in the diagnostic and therapeutic management of acromegaly.

DOI: 10.1530/endoabs.81.RC4.7

RC4.8

Impaired insulin secretion without changes in insulin sensitivity explains hyperglycemia in patients with acromegaly treated by pasireotide LAR

Peter Wolf[1], Alexandre Dormoy[2], Luigi Maione[2], Sylvie Salenave[2], Jacques Young[2], Peter Kamenicky[2] & Philippe Chanson[2]
[1]Medical University of Vienna, Internal Medicine III, Division of Endocrinology and Metabolism; [2]Université Paris-Saclay, Hôpital Bicêtre, Service d'Endocrinologie et des Maladies de la Reproduction, Le Kremlin Bicetre, France

Background

Pasireotide is a second line treatment for acromegaly. Besides the growth hormone (GH) lowering efficacy, clinical use is limited by side effects on glycemic control. The aim of this study was to evaluate longitudinal changes in beta-cell function and insulin sensitivity induced by pasireotide therapy in patients with acromegaly.

Methods

We performed a retrospective study in 33 patients. Efficacy (GH and IGF-I concentrations; tumor size) and effects on glycemic control were analyzed in all patients. In 14 patients longitudinal data on oral glucose tolerance tests were available before, shortly (mean±SD: 6.1±3.8 months) and on long term (mean±SD: 24.4±11.1 months) after initiation of pasireotide therapy. Insulin secretion (Insulinogenic index; Disposition index) and insulin sensitivity were calculated by validated indices.

Results

Hyperglycemia induced by pasireotide was mediated by impaired insulin secretion, which occurred shortly after initiation of treatment and then remained stable on long term (median (min; max): Insulinogenic index: 80 (12; 542) vs 16 (6.4; 101) vs 25 (3.7; 396) pmol/mmol, respectively; $P=0.028$; Disposition index 1.45 (0.42; 4.88) vs 0.53 0.17; 2.63) vs 0.60 (0.22; 1.71), respectively; $P=0.024$). No significant changes in insulin sensitivity were observed, despite a marked reduction of GH/IGF-I concentrations. Older age and a worse glycemic control at baseline were the strongest predictors for hyperglycemia and the need for an antidiabetic treatment.

Discussion

Worsening of glycemic control during pasireotide therapy is caused by an impaired insulin secretion, whereas insulin sensitivity is not affected. These findings might be important for the choice of the anti-diabetic treatment for pasireotide induced hyperglycemia.

DOI: 10.1530/endoabs.81.RC4.8

Diabetes, Obesity, Metabolism and Nutrition 2

RC5.1

Vascular cellular adhesion molecules are high during one year after acute COVID-19 infection in patients with type 2 diabetes

Anna Alieva, Feruza Khaydarova, Khurshida Sultonova, Khurshida Kamalova, Vasila Talenova & Iroda Tajieva

Background

Molecules of adhesion is a group of glycoproteins which expressed in cell surface and play pivotal role in inflammatory and oncological processes, and new studies show increasing of adhesion molecules within 6-12 hours after COVID-19 contamination, peaking in 24 hours. High level of adhesion molecules is a predictor of disease severity and mortality rate.

Aim

Of our study was to evaluate the level of VCAM-1 in patients with type 2 diabetes mellitus in one year after COVID-19 infection.

Materials and methods

We studied 166 type 2 diabetes patients who had COVID-19 in 2020 in 3-15 months (average, one year) after the acute infection. VCAM-1 was tested using Human ELISA Kit assay (Elabscience) in the laboratory of the Republican centre of Endocrinology. Statistic analysis was performed using STATA v.16.0.

Results

The level of VCAM-1 stayed increased up to 15 months after the COVID-19 onset. It was significantly lower in patients regularly taking rivaroxaban (174.65, 95%CI 134.2-215.1 vs 618.12, 95%CI 542.04-694.19), beta-blockers (466.39, 95% CI 373.91-558.87 vs 676.35, 95% CI 578.15-774.56), ACE inhibitors (417.76, 95% CI 314.72-520.81 vs 674.82, 95% CI 586.86-762.77), statins (318.65, 95% CI 238.54-398.75 vs 717.02, 95% CI 630.12-803.91), and fibrates (235.35, 95% CI 133.96-336.75 vs 902.53, 95% CI 812.43-992.63) and had no difference depending on glucose lowering therapy, aspirin or clopidogrel, or coagulogram. Interestingly, VCAM-1 level was significantly lower in those patients who received dexamethasone (423.76, 95% CI 332.37-515.14 vs 664.26, 95% CI 572.79-755.72) and remdesivir (244.29, 95% CI 160.25-328.32 vs 666.07, 95% CI 586.89-745.25), but not favipiravir during the acute COVID-19. Patients who had arterial hypertension and did not take regular antyhypertensive therapy had significantly higher levels of VCAM-1 (851.09, 95% CI 597.77-1104.42 vs 527.93, 95% CI 461.99-593.86).

Conclusion

Endothelial dysfunction may be preserved up to one year after COVID-19, and patients with type 2 diabetes should be monitored closely for post-COVID vascular complications.

Key words: Diabetes, COVID-19, vascular adhesion molecules, endothelial dysfunction

DOI: 10.1530/endoabs.81.RC5.1

RC5.2

Association between lipoprotein(a) concentrations and atherosclerotic cardiovascular disease risk in patients with familial hypercholesterolemia: an analysis from the HELLAS-FH

Panagiotis Anagnostis[1], Christos Rizos[2], Ioannis Skoumas[3], Loukianos Rallidis[4], Konstantinos Tziomalos[5], Emmanuel Skalidis[6], Vasileios Kotsis[7], Michalis Doumas[8], Genovefa Kolovou[9], George Sfikas[10], Anastasia Garoufi[11], Vaia Lambadiari[12], Ioanna Dima[6], Estela Kiouri[4], Dimitrios Agapakis[13], Evangelos Zacharis[6], Christina Antza[7], Vana Kolovou[9], Charalambos Koumaras[10], George Bantouvakis[6], George Liamis[2] & Evangelos Liberopoulos[14]
[1]Police Medical Centre of Thessaloniki, Department of Endocrinology, Thessaloniki, Greece; [2]Department of Internal Medicine, Medical School, University of Ioannina, Ioannina, Greece; [3]Cardiology Clinic, Hippokration General Hospital, Athens, Greece; [4]Department of Cardiology, Medical School, National and Kapodistrian University of Athens, Attikon University General Hospital, Athens, Greece; [5]Aristotle University of Thessaloniki, 1st Propedeutic Department of Internal Medicine, Medical School, Thessaloniki, Greece; [6]Cardiology Clinic, University General Hospital of Heraklion, Heraklion, Greece; [7]Department of Internal Medicine, Medical School, Aristotle University of Thessaloniki, Papageorgiou General Hospital Thessaloniki, Thessaloniki, Greece; [82]nd Propedeutic Department of Internal Medicine, Medical School, Aristotle University of Thessaloniki, Hippokration General Hospital, Thessaloniki, Greece; [9]Cardiometabolic Center, Lipid Clinic, LA apheresis Unit, Metropolitan Hospital, Athens, Greece; [10]Department of Internal Medicine, 424 General Military Training Hospital, Thessaloniki, Greece; [11]Department of Pediatrics, Medical School, National and Kapodistrian University of Athens, B' Pediatrics Clinic, General Children's Hospital "Pan. & Aglaia Kyriakou", Athens, Greece; [122]nd Propedeutic Department of Internal Medicine, Medical School, National and Kapodistrian University of Athens, Attikon University General Hospital, Thessaloniki, Greece; [13]Department of Internal Medicine, General Hospital of Goumenissa, Goumenissa, Greece; [141]st Propedeutic Department of Medicine, School of Medicine, National and Kapodistrian University of Athens, Athens, Greece

Aims

Lipoprotein(a) [Lp(a)] is an independent risk factor for atherosclerotic cardiovascular disease (ASCVD) in the general population. However, such a role in patients with familial hypercholesterolemia (FH) is less documented. The purpose of this study was to evaluate the association between Lp(a) concentrations and ASCVD prevalence in adult patients with FH.

Methods
This was a cross-sectional study from the Hellenic Familial Hypercholesterolemia Registry (HELLAS-FH). Patients were categorized into 3 tertiles according to Lp(a) levels.
Results
A total of 541 adult patients (249 males) with possible/probable/definite FH heterozygous FH (HeFH) were included (mean age 48.5 ± 15.0 years at registration, 40.8 ± 15.9 years at diagnosis). Median (interquartile range) Lp(a) concentrations in the 1st, 2nd and 3rd Lp(a) tertile were 6.4 (3.0-9.7), 22.4 (16.0-29.1) and 77.0 (55.0-102.0) mg/dl, respectively. There was no difference in lipid profile across Lp(a) tertiles. The overall prevalence of ASCVD was 9.4% in the first, 16.1% in the second and 20.6% in the third tertile ($P = 0.012$ among tertiles). This was also the case for premature ASCVD, with prevalence rates of 8.5%, 13.4% and 19.8%, respectively ($P = 0.010$ among tertiles). A trend for increasing prevalence of coronary artery disease (8.3%, 12.2% and 16.1%, respectively; $P = 0.076$ among tertiles) was also observed. No difference in the prevalence of stroke and peripheral artery disease was found across tertiles.
Conclusions
Elevated Lp(a) concentrations are significantly associated with increased prevalence of ASCVD in patients with possible/probable/definite HeFH.

DOI: 10.1530/endoabs.81.RC5.2

RC5.3

Microvascular assessment of diabetes mellitus patients by nailfold capillaroscopy

Genessis Maldonado[1], Zineb Aouhab[2], Madalina Ionescu[3], Amala Chacko[1], Diana Franco[1], Lydia Robles[1] & Deyger Navarrete[1]
[1]Loyola MacNeal Hospital, Internal Medicine, Berwyn, United States; [2]Loyola University Medical Center, Rheumatology, Maywood, United States; [3]Loyola Macneal Hospital, Endocrinology, Berwyn, United States

Introduction
Diabetes mellitus (DM) is frequently associated with vascular complications including diabetic microangiopathy. Nailfold capillaroscopy is a useful non-invasive diagnostic tool to identify changes in the microvascular architecture. Published literature hints at the presence of nailfold circulatory morphologic changes in diabetic patients.
Objective
The purpose of the study was to identify by nailfold capillaroscopy microvascular changes in patients with type II diabetes mellitus.
Materials and methods
Observational, descriptive and prospective study which included patients with diabetes type II. Capillaroscopy was performed in the fourth and fifth digit of the non-dominant hand, by a 200x magnification capillaroscope (Dino-Lite). Data was analized using SPSS v.23.
Results
We included 36 diabetic patients, 58% [21] male and 42% [15] female, with a mean age of 36 ± 18, race included hispanic 56% [20], white 39% [14], African American and asian in 3% respectively. The mean of years of diagnosis was 16 ± 10 [1-40] years. The mean of hemoglobin A1c was 7.96 ± 1.6 [5.3-12.3] and mean of latest glucose level was 159 ± 65 [83-427]. The majority had an uncontrolled disease 64% [23] and 36% [13] controlled diabetes mellitus. Capillaroscopy was performed in the fourth and fifth digit of the non-dominant hand. The visibility of the patients studied was good in 58% [21], poor 39% [14] and none in 3% [1]. The architecture was altered in 70% [25] and normal in 31% [11]. Capillary density was reduced 29% [14], very reduced in 6% [2], good in 42% [15] and very good in 14% [5]. The presence of giant capillaries was seen in 44% [16], avascular areas in 36% [13], ramified capillaries 25% [9], ectasia 67% [24], microhemorrhages 6% [2], tortuous capillaries 83% [30] and cross linked capillaries 83% [30]. SD pattern was seen in 11% [4]. The mean of apical capillary diameter was 41.59 ± 8.7μm [32-71]. It was seen a significance correlation between the presence of decrease density and increased HgbA1c. Between groups of controlled and uncontrolled diabetes, it was seen that the architecture was more altered in the uncontrolled group than the controlled, density was reduced in 23% and 42% in the uncontrolled group.
Conclusion
The overall architecture was altered in 70%, the characteristic pattern was the presence of ectasias, tortuous and cross linked with increased presence of ramified capillaries and reduced density. It was evident that patients with uncontrolled diabetes had more capillaroscopic changes than the controlled disease group. Further studies will need to be performed to correlate these findings.

DOI: 10.1530/endoabs.81.RC5.3

RC5.4

Empagliflozin induces endocan expression and alleviates NAFLD through regulation of NF-κB pathway

Narjes Nasiri-Ansari[1], Georgios Kyriakopoulos[1,2], Ioannis Kyrou[3,4,5,6,7], Christina-Maria Flessa[1,3], Maria Lianou[1], Angeliki Karapanagioti[1,8], Gregory Kaltsas[8], Athanasios G Papavassiliou[1] & Eva Kassi[1,8]
[1]National and Kapodistrian University of Athens, Medical School, Department of Biological Chemistry, Athens, Greece; [2]Evangelismos General Hospital, Department of Pathology, Athina, Greece; [3]University Hospitals Coventry and Warwickshire NHS Trust, Warwickshire Institute for the Study of Diabetes, Endocrinology and Metabolism (WISDEM), Coventry, United Kingdom; [4]Aston University, Aston Medical Research Institute, Aston Medical School, College of Health and Life Sciences, Birmingham, United Kingdom; [5]Agricultural University of Athens, Department of Food Science and Human Nutrition, Athens, Greece; [6]Coventry University, Centre for Sport, Exercise and Life Sciences, Research Institute for Health & Wellbeing, Coventry, United Kingdom; [7]University of Warwick, Medical School, Coventry, United Kingdom; [8]National and Kapodistrian University of Athens, Medical School, 1st Department of Propaedeutic Internal Medicine, Laiko General Hospital, Athens, Greece

Introduction
Nonalcoholic fatty liver disease (NAFLD) is the leading cause of chronic liver disorders. Endocan is a novel molecule of endothelial dysfuction which is expressed in liver. SGLT2i have been reported to improve NAFLD through amelioration of inflammation. While there are contradictory results regarding the serum endocan levels in NAFLD patients, data regarding endocan expression in liver tissue are limited.
Aim
Herein, we aimed to investigate the effect of SGLT2i empagliflozin on the expression of endocan in liver tissues as well as in hepatocyte cells and to delineate the underlying mechanism.
Material and methods
ApoE(-/-) mice fed a western high-fat diet were used as NAFLD model. At the age of 5 weeks, ApoE(-/-) male mice were switched from normal diet to HFD. After 5 weeks, mice were divided into two groups: Control-groups (HFD + vehicle), Empa-group (HFD + empagiflozin 10 mg/kg/day) for 5 further weeks. At the end of intervention, mice were sacrificed, whole blood was drawn by cardiac puncture and liver tissues were harvested. H&E staining was performed in all liver sections for histomorphometric analysis and IHC was performed to evaluate endocan levels. The mRNA levels of endocan, ICAM-1,VCAM-1,LFA-1,SGLT2, and IL-6 were measured by qRT-PCR and the protein levels of p65 and phospho-p65, were evaluated by immunoblotting. HepG2 cells were cultured in media supplemented with low(1 g/l), intermediate(2.25 g/l) and high(4.5 g/l) glucose concentrations. The expression of the abovementioned genes were evaluated after 24 and 48 h of treatment with empagliflozin (10^{-6}, 2×10^{-6},10^{-7}, 5×10^{-7} M).
Results
Biochemical tests revealed reduction in blood glucose, total cholesterol, LDL-cholesterol, and triglycerides after empagliflozin intervention for 5 weeks as compared to the Control-group. Additionally, empagliflozin administration resulted in reduced hepatic lipid accumulation and NA score (NAS). Empagliflozin significantly increased the endocan mRNA and protein levels while reduced IL-6 mRNA levels. Western blot analysis revealed that empagliflozin also regulates NF-κB pathway through phosphorylation of p65 subunit. Moreover, our in vitro data confirmed the in vivo results since 48 hours incubation of HepG2 cells with empagliflozin (10^{-6}M,2×10^{-6}M) at the presence of low and intermediate glucose levels, but not high glucose levels, increased endocan expression ($P < 0.01$ and $P < 0.05$,respectively). Interestingly, SGLT2 mRNA expression was detected in liver and HepG2 cells.
Conclusions
Our in vitro and animal study results indicate that empagliflozin ameliorates NAFLD through –among others- induction of endocan expression. Regulation of NF-κB pathway and IL-6 expression may mediate these effects.

DOI: 10.1530/endoabs.81.RC5.4

RC5.5

Very Low Calorie Ketogenic Diet combined with interval training for preserving muscle mass during weight loss in sarcopenic obesity: a pilot study

Elisabetta Camajani[1,2], Alessandra Feraco[2,3], Sabrina Basciani[1] & Massimiliano Caprio[2,3]
[1]Sapienza University of Rome, Department of Experimental Medicine, Rome, Italy; [2]San Raffaele Roma Open University, Department of Human

Sciences and Promotion of the Quality of Life, Rome, Italy; [3]IRCCS San Raffaele Pisana, Laboratory of Cardiovascular Endocrinology, Rome, Italy

The prevalence of sarcopenic obesity (SO) is increasing worldwide, posing important challenges to public health and national health care system, especially during the COVID pandemic. In subjects with SO, it is essential to reduce body weight preserving lean mass, in order to avoid a worsening of muscle function. Lifestyle modification with adequate nutrition and proper physical activity is essential to counteract SO progression. In accordance with the Position Statement of the Italian Society of Endocrinology, Very Low Calorie Ketogenic Diet (VLCKD), a well established nutritional intervention in the context of obesity, has been promoted also for the treatment of SO. To date, the effects of physical training during VLCKD have not been studied.

Aim

This pilot study aims to determine the efficacy of VLCKD combined with interval training, compared to a VLCKD alone, on weight-loss, body composition and physical performance in patient with SO.

Materials and methods

Twenty-six patients with SO, aged between 50 and 70 years, who met the inclusion criteria, accepted to adhere to a VLCKD nutritional program ($<$ 800 Kcal/die) and gave informed consent, were enrolled in the study. Thirteen patients followed a structured VLCKD protocol (VLCKD group) and thirteen patients followed a structured VLCKD protocol combined with interval training (IT), two times a week (VLCKD+IT group). Data were collected at baseline and after 45 days. Anthropometric indexes, body composition by Bioelectrical Impedance Analysis, muscle strength measurement by Chair Stand Test and physical performance analysis by Short Physical Performance Battery were assessed at baseline and at the end of treatment.

Results

At the end of the study, Body Mass Index, body weight and waist circumference were significantly reduced both in the VLCKD group and in the VLCKD+IT group. Moreover, significant improvement of muscle strength and physical performance was found in all groups. A significant reduction in hip circumference was observed only in the VLCKD+IT group. A multiple comparisons of delta variations in the measured parameters between groups was performed. No differences were observed for the majority of parameters, with the exception of FFM and FM: the individuals fed with VLCKD combined with IT preserved their FFM ($P<0.0001$) and reduced their FM ($P=0.0006$) to a greater extent than in the VLCKD group.

Conclusions

Our pilot study showed that a VLCKD was effective in terms of body weight reduction, particularly of FM; moreover, we conclude that the combination of VLCKD and interval training determines a better preservation of FFM.

DOI: 10.1530/endoabs.81.RC5.5

RC5.6

Effects of bariatric surgery and dietary intervention on changes in insulin resistance and appetite hormones over the period of 3 years

Malgorzata Brzozowska[1,2,3], Michelle Isaacs[2,4], Dana Bliuc[2,3], Paul Baldock[2,3,5], John Eisman[2,3,4,5], Chris White[2,6,7], Jerry Greenfield[2,3,4] & Jacqueline Center[2,3,4,5]

[1]The Sutherland Hospital, Endocrinology, Caringbah, Australia; [2]UNSW Sydney, Faculty of Medicine, Sydney, Australia; [3]Garvan Institute of Medical Research, Healthy Ageing Theme, Darlinghurst, Australia; [4]St Vincent's Hospital Sydney, Endocrinology, Darlinghurst, Australia; [5]The University of Notre Dame Australia, School of Medicine, Darlinghurst, Australia; [6]Prince Of Wales Hospital, NSW Health Pathology, Randwick, Australia; [7]Prince Of Wales Hospital, Endocrinology, Randwick, Australia

Objectives

Little is known about the mechanisms responsible for improvement in insulin resistance after bariatric surgery. We examined the impact of three types of bariatric surgery, in comparison with dietary intervention (DIET) on concurrent changes in Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) and appetite hormones over the period of 3 years. We also investigated the weight loss independent hormonal effects on insulin resistance.

Methods

Fifty-five adults undergoing weight-loss interventions, Roux-en-Y gastric bypass RYGB ($n=$ 7), gastric sleeve GS ($n=$ 21), laparoscopic adjustable gastric banding surgery LAGB ($n=$ 11) and DIET ($n=$ 16) were studied at baseline and at 1, 3, 6, 12, 24 and 36-months post intervention. Measurements of glucose (BSL), HbA1c, insulin levels, fasting and postprandial PYY and GLP1, adiponectin, C-reactive protein (CRP), retinol-binding protein 4 (RBP4), fibroblast growth factor-21 (FGF21) and dual-Xray absorptiometry were performed throughout the study. Two separate, random, intercept mixed-effects models examined the HOMA-IR changes within individual groups and in comparison with DIET during the initial phase of rapid weight loss (0-12 months) and during the stage of weight stability (12-36 months).

Results

During the first 12 months, RYGB, GS and DIET, but not LAGB, led to significant reductions in HOMA-IR. However, after controlling for the lost weight, postoperative HOMA-IR values were no longer different to the DIET group. During the phase of weight stability, all three bariatric procedures, achieved significant reductions in HOMA-IR, with the greatest difference in the RYGB group (-3.7; 95% CI: -5.4, -2.1; $P=0.001$). After controlling for the weight loss procedure, weight and body composition changes, HOMA-IR level decreased by 1.1 (95% CI: -2.1, -0.06; $P=0.045$) for every 2-fold increase from baseline in postprandial PYY. Fasting insulin declined by 3.4 mU/l (95% CI: -7.2, 0.09; $P=0.06$) for every 2-fold increase in adiponectin level. Initial, non-sustained changes in RBP4 and FGF21 had no significant association with HOMA-IR values.

Conclusions

An initial rapid weight loss after bariatric surgery is a major contributing factor to the decline in HOMA-IR score. The exaggerated secretions of the PYY hormone and adiponectin are associated with weight-independent improvements in HOMA-IR during weight stability. The metabolic roles of RBP4 and FGF21 may be related to rapid fluctuations in weight or changes in nutritional intake. Further mechanistic studies involving larger numbers of subjects are needed to fully understand the complex neuroendocrine regulation of weight, appetite, and glucose homeostasis in bariatric patients.

DOI: 10.1530/endoabs.81.RC5.6

RC5.7

How do people with type 2 diabetes compare with type 1 diabetes in their outcomes of diabetes-related ketoacidosis?

Amy Birchenough[1], Senthil Krishnasamy[2], Sanjay Saraf[3], Megan Owen[2], Dineshwaran Rajendran[3], Gobeka Ponniah[4] , Wai Nga Alice Yip[4], Emily Warmington[4], Meghnaa Hebbar[4] & Haaziq Sheikh[5]

[1]Sandwell and West Birmingham Hospitals NHS Trust, United Kingdom; [2]Walsall Manor Hospital, United Kingdom; [3]Good Hope Hospital, Birmingham, United Kingdom; [4]University of Birmingham, United Kingdom; [5]Haberdashers' Adams' Grammar School, United Kingdom

Introduction

Diabetes-related ketoacidosis (DKA) is an acute endocrine emergency requiring immediate diagnosis and management. Common misconception is that DKA is associated with type 1 diabetes only. We explored the proportion of people with type 2 diabetes, and compared the management, complications and outcome of DKA between people with type 1 and type 2 diabetes.

Methods

We conducted a retrospective study on people admitted with DKA across six hospitals in the United Kingdom from January to November 2021. DKA was diagnosed as serum glucose $\geq$ 11 mmol/l or known history of diabetes, ketones $\geq$ 3 mmol/l and pH $\leq$7.3 or bicarbonate $\leq$ 15 mmol/l. Data on demographics, use of fixed-rate insulin infusion (FRIII) and intravenous fluid infusion (IVI), blood glucose and ketone monitoring, DKA duration and length of stay were collected. We also collected data on hypoglycaemia and potassium derangement during DKA treatment.

Results

A total of 418 people admitted during this period with biochemically-proven DKA were included. 287 (68.7%) of people had type 1 diabetes; 131 (31.3%) had type 2 diabetes. There was no significant difference in duration of DKA between people with type 1 vs type 2 diabetes (13.2 hours vs 15 hours, $P=$ 0.137), however, those with type 2 diabetes had a significantly longer length of stay (3 days vs 8 days, $P=0.000$). There was no significant difference in the proportion of hourly glucose (99.9% vs 98.6%, $P=0.633$) and ketone measurement (71.5% vs 68.6%, $P=0.731$), or use of FRIII (100% vs 100%, $P=0.376$) and IVI (100% vs 93.3%, $P=0.681$) There was no significant difference in the prevalence of hypoglycaemia (12.2% vs 12.2%, $P=0.959$), hypokalaemia (31.7% vs 36.6%, $P=0.36$) or hyperkalaemia (33.4% vs 36.6%, $P=0.345$).

Conclusions

Nearly a third of DKA cases are in people with type 2 diabetes, debunking the myth DKA is synonymous with type 1 diabetes. There was no significant difference in the complications or outcomes associated with DKA between people with type 1 vs type 2 diabetes mellitus, suggesting the current guidelines are appropriate for either type of diabetes. However, further research is needed to study if revised guidelines may result in better outcomes in DKA in type 2 diabetes. People with type 2 diabetes had significantly longer hospital stays; this

finding may support earlier discharge planning and allocation of resources in those with type 2 diabetes who present with DKA.

DOI: 10.1530/endoabs.81.RC5.7

RC5.8

Attitude of Italian endocrinologists towards obesity management. Results of a survey with 534 respondents

Marco Chianelli[1], Olga Eugenia Disoteo[2], Borretta Giorgio[3], Roberto Attanasio[4], Agnese Persichetti[5], FRANCO GRIMALDI[6], Agostino Paoletta[7], Irene Samperi[8], Enrico Papini[1], Rinaldo Guglielmi[1] & Alessandro Scoppola[9]
[1]Regina Apostolorum Hospital, Endocrinology Department, Italy; [2]ASST Grande Ospedale Metropolitano Niguarda, SC Diabetologia, Milan, Italy; [3]Santa Croce & Carle Hospital, Department of Endocrinology, Diabetes and Metabolism, Cuneo, Italy; [4]AME, Scientific Committee, Milan, Italy; [5]IRCCS-Regina Elena National Cancer Institute, Service of Pharmacovigilance, Rome, Italy; [6]University Hospital S. Maria della Misericordia, Endocrinology, Metabolic Disease and Clinical Nutrition Unit, Udine, Italy; [7]ULSS 6 Euganea, Padova, Italy; [8]Azienda Sanitaria Locale Novara, SSD of Diabetology, Novara, Italy; [9]Santo Spirito Hospital, Endocrinology Unit, Rome, Italy

Background
Obesity represents a threatening worldwide epidemic but, beyond the guidelines recommendations, its modalities of treatment in the medical community appear as variable and not clearly defined. Aim of our survey was to assess the present real-world approach to obesity management in Italy.
Methods
Online anonymous survey among the 2248 members of the Italian Association of Clinical Endocrinologists (AME). The survey included 8 questions about demographics and 26 questions about obesity management.
Results
Response rate was 23.7% (534/2248 endocrinologists). The survey sample was representative of the Italian endocrinologist population, because sex, age, regional distribution, and professional experience of respondents were not different from the overall figures of the AME members. 38.0% of respondents worked in a hospital setting and 31.0% in private practice only. Obesity was managed by dedicated professionals in half of professional settings. 76.0% of patients seeking an endocrine consultation resulted affected by obesity as the main reason for referral or as a coexisting clinical condition. 47.0% of endocrinologists referred their obese patients to specialists with specific experience, while 39.0% of respondents directly managed their patients. Pharmacologic treatments were directly employed in addition to lifestyle modifications by 58.0%, 33.0% and 10.0% of respondents in patients with first-, second-, and third-degree obesity, respectively. Metformin, orlistat, naltrexone/bupropion, and liraglutide were employed by 36.0%, 6.5%, 4.8%, and 20.0% of respondents, respectively. Over half of respondents claimed that the drugs cost was the main factor that limited the use of anti-obesity drugs and that this factor impacted unfavorably on the adherence to long-term treatment. Metabolic surgery was considered for obese patients resistant to medical treatment in 9.0%, 20.0%, and 37.0% of first-, second-, and third-degree cases, respectively. According to 34% of respondents, psychological support should be offered to all obese patients. Finally, 44% of respondents stated that the availability of new drugs with greater efficacy, lower cost and less side-effects would increase the number of obese patients eligible for anti-obesity medical treatment and would improve their adherence to therapy.
Conclusions
The results of this large-scale, obese-centered, survey demonstrate that obesity is widely impacting on the clinical activity of Italian endocrinologists. The use of pharmacologic treatment is considered as an appropriate therapeutic support in 10.0–58.0% of cases, and metformin and liraglutide appear as the most used drugs. The availability of drugs with greater efficacy and lower side-effects could markedly improve the clinical approach to these patients and their long-term management.

DOI: 10.1530/endoabs.81.RC5.8

Endocrine-Related Cancer

RC6.1

Clinical relevance of body composition measurement at L3 level in gastroenteropancreatic neuroendocrine tumors

Fernando Sebastián Valles[1], Nuria Sánchez de la Blanca Carrero[1], Víctor Rodríguez Laval[2], Carolina Knott Torcal[1], Ana Serrano-Somavilla[3], Rebeca Martínez-Hernández[1], Elena Martín-Pérez[4], Jose Luis Muñozde Nova[4], Mónica Marazuela[3] & Miguel Sampedro-Nuñez[3]
[1]Hospital de La Princesa, Endocrinología, Madrid, Spain; [2]Hospital de La Princesa, Radiología, Madrid, Spain; [3]Hospital de La Princesa, Endocrinología y Nutrición, Madrid, Spain; [4]Hospital De La Princesa, Cirugía General y del Aparato Digestivo, Madrid, Spain

Introduction
Nutritional status in patients with neuroendocrine tumors (NETs), especially with gastroenteropancreatic origin, may be affected and have an impact on prognosis and survival. Different techniques are currently available to assess nutritional status, but not all of them are accessible in routine clinical practice. In this context, Body composition of NET patients was calculated by computed tomography (CT) at L3 level to evaluate its importance on clinical prognosis.
Materials and Methods
We collected gastroenteropancreatic NET patients with L3 level CT images at diagnosis since 2004 at Hospital Universitario La Princesa (Madrid). L3 CT images were analyzed using NIH ImageJ protocol and R version 4.0. The following measures were obtained: body area, visceral fat tissue, subcutaneous fat, total fat, intermuscular fat, very low density muscle, low density muscle, normal density muscle (NDM), high density muscle and total muscle. All of them were normalized by the squared height of each patient. We used normality Shapiro-Wilk test and Mann-Whitney-U or Kruskal-Wallis tests and one-way t test or ANOVA/ANCOVA for group differences in those with non-normal and normal distribution respectively. We applied Spearman correlation to establish possible relationships between age and biochemical parameters and body composition measures. All the statistical analysis was performed using R 4.0 version.
Results
The sample is composed of 61 gastroenteropancreatic NET patients classified according to: 1) their NET primary location in small intestine (44.26%), pancreatic (37.70%) and large intestine (24.59%); and 2) tumor type: nonfunctioning (70.49%), functioning carcinoid (24.59%), gastrinoma (4.92%) and insulinoma (6.56%). Patients' mean age was 63.19 +/-10.97 years, and 53.73% were females. NDM was positively correlated with albumin ($r=0.3655$, $P=0.0084$) and lymphocyte number ($r=0.3749$, $P=0.0100$). On the other hand, NDM was inversely correlated with age ($r=$-0.5185, $P=0.0012$), myosteatosis ($r=$-0.7065, $P<0.0001$) and inflammation parameters such as ferritin ($r=$-0.3038, $P=0.0349$) and fibrinogen ($r=$-0.3119, $P=0.0481$). Low levels of NDM and total muscle were associated with any type ($P-=0.0007$, $P=0.0029$) and tumor-specific mortality ($P=0.0149$, $P=0.0113$), regardless of sex and age in multivariable analysis. Patients with metastasis have less total fat (pvalue=0.0187) and myosteatosis was more frequent in insulinoma ($P<0.05$) than in non-functioning tumors, carcinoids and gastrinomas. There were no differences according to tumor location.
Conclusion
Body composition analysis is feasible using CT data acquired in routine clinical practice in patients with NETs. Low levels of NDM seem to be independently associated with a worse analytical profile and with mortality.

DOI: 10.1530/endoabs.81.RC6.1

RC6.2

Reciprocal interactions between fibroblast and pancreatic neuroendocrine tumor cells: putative impact of the tumor microenvironment

Thomas Cuny[1], Gregoire Mondielli[1], Peter van Koetsveld[2], Wouter de Herder[2], Anne Barlier[1] & Leo Hofland[2]
[1]Aix Marseille University, INSERM, U1251, Marseille Medical Genetics, Marseille, France; [2]Division Endocrinology, Erasmus Medical Center, Department of Internal Medicine,, Rotterdam, Netherlands

Introduction
Pancreatic neuroendocrine neoplasms (PNEN) present with a fibrotic stroma which constitutes the tumor microenvironment (TME). The role played by stromal fibroblasts over the growth of PNEN and their sensitivity to the mTOR inhibitor, RAD001, are as yet unestablished.
Methods
We investigated reciprocal interactions between 1) human PNEN cell lines (BON-1/QGP-1) or primary cultures of human ileal neuroendocrine neoplasm (iNEN) or PNEN, and 2) human fibroblast cell lines (HPF/HFL-1). Proliferation was assessed in transwell co-culture (HFL-1tw, HPFtw, BON-1tw, QGPtw) or in the presence of serum-free conditioned media (BON-1cm, QGP-1cm, HFL-1cm, HPFcm), with and without RAD001. Migration of BON-1/QGP-1 was evaluated when incubated with HPFcm.
Results
Proliferation of BON-1 and QGP-1 increased in the presence of HFL-1cm, HPFcm, HFL-1tw and HPFtw (BON-1: +46 to +70% and QGP-1: +42 to

+55% $P < 0.001$ vs controls for both), whereas this stimulatory effect was reversed in presence of RAD001. Likewise, proliferation of human iNEN and PNEN primary cultures increased in presence of HFL-1 or HPF. Reciprocally, BON-1cm and BONtw stimulated the proliferation of HPF (+90 +/- 61% and +55 +/- 47% respectively, $P < 0.001$ vs controls), an effect less pronounced with either QGP-1cm or QGPtw (+19 to + 27%, $P < 0.05$ vs controls) and unmodified by RAD001. RAD001 resulted in a decrease of colony number of BON-1 and QGP-1, while colony size remained the same in presence of the drug. Finally, a higher migration potential of BON-1 and QGP-1 occurred in presence of HPFcm ($P < 0.001$ vs basal).

Conclusions

Fibroblasts, in the TME of PNEN, represent a target of interest to control escape from mTOR inhibitors tumor growth and dissemination.

DOI: 10.1530/endoabs.81.RC6.2

RC6.3

New epigenetic and functional features in pheochromocytoma

Jacopo Manso[1], Loris Bertazza[1], Susi Barollo[2], Simona Censi[2], Sofia Carducci[2] & Caterina Mian[2]
[1]Padua University, Department of Medicine (DIMED), Padova, Italy; [2]Padua University, Department of Medicine (DIMED), Padua, Italy

Background

Pheochromocytoma (Pheo) is a tumor deriving from chromaffin cells. It can be studied using ^{18}F-dihydroxyphenylalanine (DOPA) - positron emission tomography (PET) due to its overexpression of L-type amino acid transporters (LAT1 and LAT2). The oncogenic pathways involved are still poorly understood. This study examined the relationship between ^{18}F-DOPA-PET uptake and LAT1 expression, and explored the role of miR-375 and putative target genes.

Methods

A consecutive series of 58 Pheo were retrospectively analyzed, performing ^{18}F-DOPA-PET in 32/58 patients. qRT-PCR was used to assess the expression of LAT1, LAT2, phenylethanolamine N-methyltransferase (PNMT), miR-375, and the major components of the Hippo and Wnt pathways. 24 h-urinary metanephrine, normetanephrine, epinephrine and norepinephrine were analyzed for diagnostic purposes prior to surgery. Principal germline mutations associated with hereditary Pheo were also studied.

Results

Pheo tissues had significantly higher LAT1, LAT2 and PNMT mRNA levels than normal adrenal tissues. MiR-375 was strongly overexpressed. YAP1 and TNKS1 were upregulated, while beta-catenin, axin2 and MCT8 were downregulated. A positive relationship was found between ^{18}F-DOPA-PET SUVmean and LAT1 gene expression, as was for 24 h-urinary norepinephrine and LAT1.

Conclusion

The present study confirms in a larger population that LAT1 and LAT2 are upregulated in Pheo. It provides the first experimental proof of a quantitative correlation between ^{18}F-DOPA uptake and LAT1 expression levels, and the first evidence of miR-375 overexpression in Pheo, with a consensual downregulation of the Wnt signaling. The present report also pave the way to studies on the Hippo pathway as a possible new oncogenic driver in Pheo

DOI: 10.1530/endoabs.81.RC6.3

RC6.4

Glucose-coated superparamagnetic iron oxide nanoparticles prepared by metal vapor synthesis can target GLUT1 overexpressing tumors: in vitro tests and in vivo preliminary assessment

Daniele Barbaro[1,2], Lorenzo Dibari[3,3], Valentina Gandin[4], Cristina Marzano[4] & Claudio Evangelisti[5]
[1]U.O. Endocrinology, ASL Nord Ovest Toscana, Livorno, Italy; [2]USL Tuscany Northwest, Pisa, Italy; [3]University of Pisa, Pisa, Italy; [4]University of Padua, Padova, Italy; [5]CNR PISA, Pisa, Italy

Background

It is well known that one of the basic characteristics of tumor cells is that they are greedy for glucose. Delivering Glucose Coated Superparamagnetic iron oxide nanoparticles (Glc-SPIONs) to tumor cells by i.v. administration could represent "the magic bullet" for detecting and treating cancer,

Materials, methods and results

Glc-SPIONs were prepared by a new approach called Metal Vapor Synthesis (MVS) and their structural features were investigated by transmission electron microscopy and dynamic light scattering. Our Glc-SPIONs are homogeneous, with a mean diameter of 2.7 nm, and surrounded by a thick layer of glucose, reaching an apparent hydrodynamic diameter of 13 nm (30). From 4 mg/ml onwards, there was a constant level of positive contrast in a T1-weighted sequence at MRI. In vitro experiments were performed in three cell lines: pancreatic cancer (PSN-1), human papillary thyroid cancer (BCPAP), and human embryonic kidney non-tumor cells (HEK293). Concentration of the Glc-SPIONs we used did not affect cell viability. Glc-SPIONs were internalized in all the cancer cells in a time-dependent manner. PSN-1 cells were the most effective at internalizing Glc-SPIONs. Although significantly higher than the control cells, a lower Fe content was detected in human BCPAP cells treated with Glc-SPIONs. We evaluated GLUT1 expression in each cell line and demonstrated that the exposure time Glc-SPION uptake in the two different cancer cells correlated well with the detected GLUT1 levels, thus suggesting the involvement of GLUT1 in the cellular internalization of Glc-SPIONs. To confirm the involvement of GLUT1 in Glc-SPIONs internalization, cellular uptake experiments were also conducted by pre-treating cancer cells for 1 h with specific GLUT1 inhibitors, namely a polyclonal anti-GLUT1, WZB117, Fasentin, BAY-876, and STF-31. *In vivo* tests were performed on mice inoculated with Lewis lung carcinoma. Our results showed a great bioavailability to the malignant tissue by the i.v. administration of Glc-SPION while a substantial number of Glc-SPIONs were excreted in the urine 6 h after injection, thus supporting the hypothesis that Glc-SPIONs can be efficiently eliminated by the kidney. Regarding nefrotoxicity treatment with Glc-SPIONs led to a 24 h excretion of uTP, which was three times lower than the one recorded with cisplatin.

Conclusion

To the best of our knowledge, our study demonstrates for the first time that Glc-SPIONs prepared with MVS can be electively internalized by tumor cells both *in vitro* and *in vivo* by exploiting one of the most universal metabolic anomalies of cancer.

DOI: 10.1530/endoabs.81.RC6.4

RC6.5

Granin family peptides and INSM-1 (Insulinoma-associated protein 1) in the biochemical diagnosis of pheochromocytoma

Piotr Glinicki[1], Magdalena Ostrowska[1], Maria Stelmachowska-Banas[1], Lucyna Papierska[1], Alicja Szatko[1], Konrad Kowalski[2] & Wojciech Zgliczyński[1]
[1]Centre of Postgraduate Medical Education, Department of Endocrinology, Warsaw, Poland; [2]Masdiag Laboratory, Warsaw, Poland

Introduction

Pheochromocytoma is a rare, usually benign tumor composed of neuroendocrine (chromaffin) cells of the adrenal medulla. It is the cause of secondary arterial hypertension. The biochemical diagnosis of a pheochromocytoma is based on the determination of concentration/excretion of catecholamine metabolites in blood or urine. The most sensitive biomarkers in the biochemical diagnosis of pheochromocytoma are plasma free methanephrines (metanephrine, normetanephrine and 3-methoxytyramine) assayed with chromatography tandem mass spectrometry (LC-MS/MS). Neuroendocrine cells have the ability to produce various proteins and neuropeptides, which, together with catecholamines, are released into the blood and can be designated as so-called circulating tumor markers.

Purpose

The aim of the study was to assess the usefulness of the determination of levels of selected Granin family proteins and INSM-1 (Insulinoma-associated protein 1) in the diagnosis of patients with pheochromocytoma.

Material and methods

Patients were divided into 4 groups:
1. Patients with pheochromocytoma ($n = 39$),
2. Patients with incidentaloma ($n = 20$),
3. Patients with primary arterial hypertension ($n = 20$),
4. Control group – healthy volunteers ($n = 40$).

The following biochemical determinations were performed in all patients: plasma levels of metanephrine, normetanephrine and 3-methoxytyramine, concentration of chromogranin B (CgB), proSAAS, INSM-1, chromogranin A (CgA) and derivates peptides: Pancreastatin/chromogranin A (250-301), Serpinin/prepro-chromogranin A (429-454), WE-14/prepro-chromogranin A (342-355) and Catestatin. Biochemical determinations were made using the LC-MS/MS technique with various immunochemical techniques (RIA, IRMA, ELISA).

Results

In patients with adrenal pheochromocytoma levels of: CgA, WE-14 and Catestanin were significantly different ($P < 0.001$) compared to control groups (adenoma, hypertension and healthy subjects). The concentration of INSM-1 was significantly higher ($P < 0.001$) in patients with pheochromocytoma compared to

the group of healthy people. In the group of patients with pheochromocytoma, the following indicators of the diagnostic value of the analyzed biomarkers were obtained: CgA: 82% sensitivity and 100% specificity (AUC 0,930); CgB: 87% sensitivity and 77% specificity (AUC 0,885); WE-14: 90% sensitivity and 95% specificity (AUC 0,959); Catestatin: 80% sensitivity and 92% specificity (AUC 0,903); Pancreastatin: 80% sensitivity and 95 specificity (AUC 0,913); proSAAS: 82% sensitivity and 67% specificity (AUC 0,760); INSM-1: 97% sensitivity and 100% specificity (AUC 0,976).
Conclusion
Determination of biomarkers: CgA, WE-14, Catestatin and INSM-1 had the highest diagnostic value in patients with pheochromocytoma.

DOI: 10.1530/endoabs.81.RC6.5

RC6.6

The clinical and molecular evaluation of the GIP/GIPR axis in Medullary Thyroid Cancer (MTC)

Gianluca Occhi[1], Loris Bertazza[2], Susi Barollo[2], Eva Galletta[1], Alberto Mondin[2], Stefania Zovato[3], Maurizio Iacobone[4], Eleonora Zilio[1], Serena Avallone[2], Konstantions Lefkimmiatis[5,6], Giulietta Di Benedetto[6,7], Caterina Mian[2], Carla Scaroni[2] & Daniela Regazzo[2]
[1]University of Padova, Department of Biology, Padova, Italy; [2]Padova University Hospital, Department of Medicine - Endocrinology Unit, Padova, Italy; [3]Veneto Institute of Oncology-IOV-IRCCS, Hereditary Tumors Unit, Padova, Italy; [4]Padova University Hospital, Department of Surgery, Oncology and Gastroenterology - Endocrine Surgery Unit, Padova, Italy; [5]University of Pavia, Department of Molecular Medicine, Pavia, Italy; [6]Foundation for Advanced Biomedical Research, Veneto Institute of Molecular Medicine (VIMM), Padova, Italy; [7]National Research Council, Neuroscience Institute - Padova Section, Padova, Italy

The glucose-dependent insulinotropic polypeptide receptor (GIPR) is a 7-transmembrane class B G-protein coupled receptor that mediates the incretin response after nutrient stimulation. Although mostly involved in metabolic disorders, in the last years an improper activation of the GIP/GIPR axis has been increasingly recognized in endocrine tumors, with a potential diagnostic and prognostic value. In Medullary Thyroid Cancer (MTC), a neuroendocrine tumor of the parafollicular C cells, a high tumor-to-normal tissue ratio (T/N ratio) of GIPR was reported both in human and in rat. In this latter, a direct link between the neoplastic transformation and the mechanism of receptor overexpression has been proposed. In this work, we aimed at evaluating the potential diagnostic and prognostic significance of GIPR expression in a large cohort of MTC by correlating GIPR mRNA steady-state level with patients' clinical features. Moreover, given the paucity of data on the GIP/GIPR axis in this tumor type, an additional aim of this study was to molecularly dissect the signaling pathways associated with GIPR stimulation in MTC-derived cells with particular attention to cell proliferation and calcitonin secretion. By Droplet Digital PCR (ddPCR) technology, we observed a GIPR positive expression (GIPR+) of nearly 80% (38/49) of MTC tumoral specimens and more frequently in larger, advanced-stage cancer with higher Ki-67 values and sporadic rather than familial manifestation. In MTC-derived cells (i.e., MZ-CRC-1, and a primary culture originating from a regional metastatic lymph node of a GIPR+ MTC patient), GIPR stimulation induced cAMP elevation – with the consequent activation of the PKA cascade – and a small but significant fluctuation in Ca^{2+}, both likely associated with increased calcitonin secretion. GIP has instead no effects on cell viability nor on PI3K-Akt and MAPK-ERK1/2 signalling pathways. The data emerging from this study confirmed the high T/N GIPR ratio in MTC tumors and demonstrate for the first time that it may represent an index of the degree of advancement of the malignant process. The observation that GIP stimulated the adenylyl cyclase and activate the downstream cAMP pathway in MTC-derived cellular models confirms the correct coupling of GIPR to Gas which was ultimately related to an increased CT secretion. Further studies with specific provocative tests, however, will be mandatory to establish the real involvement of GIP/GIPR axis in regulating calcitonin secretion in MTC.

DOI: 10.1530/endoabs.81.RC6.6

RC6.7

Oncological patients with endocrine complications after immunotherapy with checkpoint inhibitors present longer progression free and overall survival

Stavroula A Paschou[1], Michael Liontos[2], Evangelos Eleftherakis-Papaiakovou[2], Katerina Stefanaki[1], Christos Markellos[2], Konstantinos Koutsoukos[2], Flora Zagouri[2], Theodora Psaltopoulou[2] & Meletios-Athanasios Dimopoulos[2]
[1]Endocrine Unit and Diabetes Center, Department of Clinical Therapeutics, Alexandra Hospital, School of Medicine, National and Kapodistrian University of Athens, Athens, Greece; [2]Hematology and Oncology Unit, Department of Clinical Therapeutics, Alexandra Hospital, School of Medicine, National and Kapodistrian University of Athens, Athens, Greece

Aim
To investigate the association of endocrine complications after ICIs immunotherapy with progression free survival (PFS) and overall survival (OS) in a large single-center oncological cohort.
Patients and methods
In total, 351 patients were included in the analysis, 248 men (70.7%) and 103 women (29.3%). The median age was 66 years. Patients had a variety of cancer types, namely bladder cancer (131, 37.3%), renal cancer (89, 25.4%), lung cancer (74, 21.1%), ovarian cancer (22, 6.3%) and other types of cancer (35, 10%). The majority (314, 89.4%) were classified as stage IV, while 10.6% (37) were classified as stage III. Most of the patients received immunotherapy with anti-PD1 agents (262, 74.6%) and the rest with anti-PD-L1 agents (89, 25.4%). Kaplan-Meier estimates were used to describe and visualize the effect of categorical variables on OS and PFS. Survival analysis was performed by Kaplan-Meier curves and survival differences between groups were estimated using the log-rank test. The estimation of the prognostic value of several variables with patients' survival was made by Cox regression models.
Results
In total, 68 (19.4%) of patients presented an endocrine complication after immunotherapy with ICIs. Specifically, 66 (18.8%) had thyroid dysfunction, 1 patient presented hypophysitis (0.3%) and 1 patient had combination of thyroid dysfunction and hypophysitis (0.3%). Patients with an endocrine complication had mPFS of 15 months (95% CI 11.0-18.9 months), while in those without endocrine complication mPFS was 7 months (95% CI 6.1-7.9 months, $P<0.001$). Similarly, median OS (mOS) was statistically significant lower in the patients' group without endocrine complication. In fact, mOS was 51 months (95% CI 39.3-62.7 months) for these patients. These results retained significance in terms of longer PFS (1.812, 95% CI 1.270-2.586) and OS (1.805, 95%CI 1.088-2.994) after multivariate analysis.
Conclusions
ICIs endocrinopathies may be a positive predictor of immunotherapy response.

DOI: 10.1530/endoabs.81.RC6.7

RC6.8

Unveiling the role and contribution of CELF4 to the malignant features of PanNETs

Víctor García Vioque[1,2,3,4], Emilia Alors-Pérez[1,2,3,4], Sergio Pedraza Arévalo[1,2,3,4], Antonio Agraz-Doblas[1,2,3,4], Ricardo Blázquez-Encinas[1,2,3,4], Ricardo Blázquez-Encinas[1,2,3,4], María Trinidad Moreno Montilla[1,2,3,4], Aura D Herrera-Martínez[5,6], Elena María Yubero Serrano[5,6], Rosa Ortega Salas[1,7], Raquel Serrano Blanch[1,8], María Ángeles Gálvez Moreno[1,6],, Manuel D Gahete[1,2,3,4],, Alejandro Ibañez Costa[1,2,3,4], Raul M Luque[1,2,3,4] & Justo P Castaño[1,2,3,4]
[1]Maimónides Institute for Biomedical Research of Córdoba (IMIBIC), Córdoba, Spain; [2]University of Córdoba (UCO), Cell Biology, Physiology and Immunology, Córdoba, Spain; [3]CIBER Fisiopatología de la Obesidad y Nutrición (CIBERobn), Madrid, Spain; [4]Reina Sofia University Hospital (HURS), Córdoba, Spain; [5]Maimónides Institute for Biomedical Research of Córdoba (IMIBIC), Córdoba, Spain; [6]Reina Sofia University Hospital (HURS), Endocrinology and Nutrition Service, Córdoba, Spain; [7]Reina Sofia University Hospital (HURS), Pathology Service, Córdoba, Spain; [8]Reina Sofia University Hospital (HURS), Medical Oncology Service, Córdoba, Spain

Pancreatic neuroendocrine tumors (PanNETs) are heterogeneous neoplasms with a relatively low but increasing incidence, mainly due to the difficulty in diagnosing this disease in its early stages. This notably complicates the treatment of this pathology and leads to a poor prognosis. One of the main reasons for this problem is the lack of adequate diagnostic biomarkers as well as effective therapeutic targets. In this sense, there is still a limited knowledge about alternative splicing, a key process emerging as a transversal hallmark of cancer, as its frequent dysregulation influences most tumor cell features. In a pilot study, we discovered that *CELF4*, — a member of the CELF/BRUNOL family, which is involved in the regulation of RNA splicing, editing, and translation in the central nervous system —, may be altered in PanNETs. Therefore, we aimed at evaluating the role of *CELF4* as a biomarker and/or therapeutic target in PanNETs. To this end, *CELF4* expression levels were determined using a microfluidic based technology, comparing tumor and adjacent non-tumor tissue,

in a cohort of 20 PanNETs patients. This revealed a clear overexpression of *CELF4* in tumor tissue compared to adjacent non-tumoral tissue. Then, an RNA-seq dataset was used to investigate the associations between *CELF4* expression, patient clinical parameters, and splicing event patterns. We observed that *CELF4* is linked to critical features of malignancy, the expression of key genes in tumors (*TP53* or *CDKN2B*) and different splicing events profiles. Likewise, the functional relevance of this factor was determined *in vitro* with several functional assays (cell proliferation and drug response) in two PanNETs cell models (BON-1 and QGP-1), including an mTOR phospho-antibody array to determine the mechanism of action of *CELF4*. Remarkably, the modulation of *CELF4* expression levels in the cell lines resulted in a significant change in proliferation as well as in the response of these cells to the mTOR inhibitor everolimus. In particular, *CELF4* silencing resulted in a disruption of several crucial intermediaries in the mTOR signaling pathway. Finally, we carried out *in vivo* studies using BON-1-xenografted mice, observing a significant reduction of tumor growth by silencing *CELF4*. These results demonstrate that the splicing factor *CELF4* is dysregulated in PanNETs, and its alteration can contribute to tumor development and a more aggressive phenotype, impacting the mTOR signaling pathway. Altogether, these findings provide original evidence that encourage further study of this factor as a novel potential target in PanNETs.

DOI: 10.1530/endoabs.81.RC6.8

Pituitary and Neuroendocrinology 2

RC7.1

Does the postoperative dose of hydrocortisone influence the health-related quality of life in patients with cured Cushing syndrome?

Ivana Kraljevic[1,2], Anja Barac[3], Mirsala Solak[1], Tanja Skoric Polovina[1], Annemarie Balasko[1], Karin Zibar Tomsic[1], Tina Dusek[1,2] & Darko Kastelan[1,2]
[1]University Hospital Center Zagreb, Dpt of Endocrinology, Zagreb, Croatia; [2]Zagreb University School of Medicine, Zagreb, Croatia; [3]General Hospital Dubrovnik, Division of Internal Diseases, Dubrovnik, Croatia

Objective
Patients with Cushing syndrome (CS) have impaired health-related quality of life (HRQoL) before and after surgery. The data on the optimal hydrocortisone dose after surgical cure of CS is scarce. Therefore, we investigated the influence of hydrocortisone dose on HRQoL after surgical treatment of CS. We hypothesized that patients who receive higher hydrocortisone doses after surgery would have better HRQoL and fewer cortisol withdrawal symptoms.
Methods
The study population comprised 38 patients with CS, 18 with adrenal, and 20 with pituitary origin. After surgical remission of CS, patients were randomized to 15 mg or 30 mg of hydrocortisone. All patients completed the EQ-5D questionnaire at baseline, one month, and three months after surgery. In addition, data on symptoms related to cortisol withdrawal and the consequent need for hydrocortisone dose escalation were collected.
Results
The HRQoL did not differ between patients receiving 15 mg (22 patients) or 30 mg (16 patients) of hydrocortisone, at baseline, after one month, or three months after curative surgery. Total EQ-5D scores in patients on 15 mg and 30 mg of hydrocortisone were 60(1-90) vs 60(0-100), 70(3-85) vs 45(2-95), and 80(20-100) vs 52.5(20-100), respectively ($P=0.934$, $P=0.308$, and $P=0.544$). Three patients needed a temporary increase of hydrocortisone dose during follow-up due to acute illness or worsening of symptoms.
Conclusions
This prospective randomized study showed no difference in HRQoL between patients receiving 15 or 30 mg of hydrocortisone replacement therapy in the first three months after the surgical remission of CS.

DOI: 10.1530/endoabs.81.RC7.1

RC7.2

Development and internal validation of a predictive score for the diagnosis of central adrenal insufficiency when morning cortisol is in the grey zone

Fabio Bioletto, Alessandro Maria Berton, Emanuele Varaldo, Daniela Cuboni, Chiara Bona, Mirko Parasiliti Caprino, Nunzia Prencipe, Ezio Ghigo, Silvia Grottoli, Mauro Maccario & Valentina Gasco
University of Turin, Department of Medical Sciences, Turin, Italy

Background
When evaluating a patient for central adrenal insufficiency (CAI), there is a wide range of morning cortisol values for which no final conclusion on hypothalamus-pituitary-adrenal (HPA) axis function can be drawn; in these cases, a stimulation test is required. Aim of this study was to develop an integrated model for the prediction of CAI when morning cortisol is in the grey zone, here defined as 40.0-160.0 μg/l.
Methods
Overall, 119 patients with history of sellar tumour which underwent insulin tolerance test (ITT) for the evaluation of HPA axis were enrolled; a peak cortisol value $\geq$ 180.0 μg/l at ITT was adopted for the definition of CAI. Supervised regression techniques were used for model development. Model calibration was evaluated by the Hosmer-Lemeshow test. A ten-fold cross-validation algorithm was adopted for internal validation.
Results
After a stepwise backward selection, the variables retaining a statistically significant association with the outcome were morning cortisol values, the presence of $\geq$ 3 other pituitary deficits, and male sex. Based on these predictors, a multivariable predictive model was developed, and showed a significantly better diagnostic performance in the prediction of CAI than morning cortisol alone (AUC 0.811 vs 0.699, $P=0.003$). The Hosmer-Lemeshow test did not reveal any significant miscalibration ($P=0.54$). At ten-fold cross-validation, the final estimation of the model performance on unseen data was equal to 0.769, thus reassuring about a small overfitting effect. In order to simplify the use of the model in clinical practice, a novel predictive score (CAI-score) is proposed, on a 5.5-point scale, by considering morning cortisol (0 points if 130.1-160.0 μg/l, 1 point if 100.1-130.0 μg/l, 1.5 points if 70.1-100.0 μg/l, 2.5 points if 40.0-70.0 μg/l), other pituitary deficits (2 points if $\geq$3 deficits), and sex (1 point if male). A diagnostic algorithm integrating CAI-score and ITT is finally presented, with an overall accuracy of 99.2%, and the possibility to avoid the execution of a stimulation test in 25.2% of patients.
Conclusion
This was the first study that formally proposed and internally validated a multivariable predictive score for the diagnosis of CAI when morning cortisol is in the grey zone. This score might be helpful to reduce the number of patients who need a stimulation test for the assessment of HPA axis function.

DOI: 10.1530/endoabs.81.RC7.2

RC7.3

Pituitary microadenoma vs macroadenomas in cushing's disease: does size matter?

Amit Akirov[1,2], Ilan Shimon[1,2], Manisterski Yosi[3], Nirit Aviran-Barak[3], Varda Nadler[3], Sandra Alboim[3], Vered Kopel[3], Gloria Tsvetov[3] & Dania Hirsch[1,2,3]
[1]Tel Aviv University, Sackler School of Medicine, Tel Aviv-Yafo, Israel; [2]Beilinson Medical Center, Petah Tikva, Israel; [3]Maccabi Healthcare Services, Tel Aviv-Yafo, Israel

Background
The majority of adrenocorticotropic hormone (ACTH)-secreting pituitary adenomas are less than 10 mm in diameter and are described as microadenomas, while corticotroph macroadenomas ($\geq$10 mm) are a less common cause of Cushing's disease. Prior reports on the differences of clinical and biochemical behavior of corticotroph microadenomas and macroadenomas were inconsistent.
Objective
Describe the clinical and biochemical characteristics of patients with corticotroph macroadenomas and microadenomas.
Methods
Retrospective charts review of patients with Cushing's disease treated at Rabin Medical Center between 2000 and 2017, or at Maccabi Healthcare Services in Israel between 2005 and 2017. Tumors in which the largest diameter was $\geq$10 mm were considered to be macroadenomas. When no visible tumor was seen on MRI, the tumor was considered to be a microadenoma. Epidemiologic, clinical and biochemical factors were compared between patients with corticotroph macroadenomas and microadenomas.
Results
The cohort included 105 patients (82 women, 78%; mean age $\pm$ SD, 41.5 $\pm$ 14.5 years), including 68 patients (64.8%) with a pituitary microadenoma (mean size, 5.2$\pm$2.2 mm), 25 patients (23.8%) with a macroadenoma (mean size, 18.0$\pm$7.7 mm), and 12 patients with no visible adenoma. Baseline characteristics were similar between the groups, including age, gender, body mass index, and comorbidities. Most common reasons for completing an investigation for Cushing's syndrome among patients with microadenomas and macroadenomas were weight gain (46.3% vs 52.0%, $P=$NS) and Cushingoid features (27.5% vs 20.0%, $P=$NS). While mean urinary free cortisol levels (5.2 $\pm$ 5.4 ULN vs 7.8

± 8.7 ULN) and mean serum cortisol levels following low-dose dexamethasone suppression test (487.6 ± 329.8 vs 372.0 ± 324.5 nmol/l, respectively), were higher among patients with macroadenomas, the differences were not statistically significant and there was considerable overlap between the two groups. Concentrations of ACTH were greater in patients with macroadenoma than in those with microadenoma (1.9 ± 1.2 ULN vs 1.3 ± 0.8 ULN, respectively, $P = 0.01$). Most patients in both groups underwent transsphenoidal surgery, and rates of recurrent or persistent disease were similar in patients with microadenomas and macroadenomas (35.2% vs 28.6%, respectively; P=NS). The rate (83.9% vs 83.3%, respectively) and duration (9.4 ± 8.3 vs 9.7 ± 11.9 months, respectively) of post-operative glucocorticoid treatment were similar in both groups.
Conclusions
While ACTH-secreting macroadenomas exhibit higher plasma ACTH levels than microadenomas, there was no correlation between tumor size with cortisol secretion values or clinical characteristics in patients with Cushing's disease.

DOI: 10.1530/endoabs.81.RC7.3

RC7.4

Evaluation of the impact of covid-19 on the hypothalamic-pituitary-adrenal axis and the hypothalamic-pituitary-thyroid axis

Juliette Andre[1], Abdallah Al-Salameh[1], Noemie Scherman[1], Claire Andrejak[2] & Rachel Desailloud[1]
[1]CHU Amiens Picardie, Department of Endocrinology, Diabetes Mellitus and Nutrition, Amiens, France; [2]CHU Amiens Picardie, Department of Pulmonary Diseases, Amiens, France

Context
The long-term consequences of Covid-19 are unknown. Most patients experience persistent symptoms more than a month after the acute illness, including fatigue, dyspnea, memory loss, concentration disorder. The pituitary, the thyroid and the adrenal gland express the ACE-2 receptor, which is the cellular receptor for SARS-CoV-2, and could therefore be affected by the virus. However, the effect of Covid-19 on the hypothalamic-pituitary-adrenal-axis and hypothalamic-pituitary-thyroid-axis are unclear.
Objective
Our objective was to evaluate the impact of the SARS-CoV-2 infection on the hypothalamic- pituitary-adrenal-axis and hypothalamic-pituitary-thyroid-axis in the medium term.
Methods
A prospective, observational study conducted from May 2020 to March 2021 at Amiens University Hospital, including 318 adult patients hospitalized for Covid-19. Participants attended a medical consultation 3 month after hospital admission. They had serum cortisol, TSH and FT4 analyzed, and the persistence of symptoms after hospitalization was evaluated. Adrenal insufficiency was defined by a morning cortisol <5 g/dl. Possible central hypothyroidism was defined by FT4 below the laboratory range and low or normal TSH levels.
Results
The post-COVID-19 consultation took place 112 [97-144] days after hospital admission. Basal morning serum cortisol was available for 232 patients. 2 patients had secondary adrenal insufficiency, with basal cortisol levels respectively of 1.4 and 2.1 g/dl, and adrenocorticotropin levels of 3.3 et 7.6 pg/ml. No patient had primary adrenal insufficiency. The median of basal cortisol level was 13.1 g/dl [10.1-16.9] in the group of patients who received Dexamethasone during hospitalization, and 14.7 g/dl [11.5-18.3] in the group of patients who didn't receive Dexamethasone, there was no statistical difference between the two groups. TSH and FT4 were available for 219 patients. 8 patients had results compatible with central hypothyroidism. One patient had both central adrenal insufficiency and central hypothyroidism, due to a pituitary apoplexy following Covid-19 infection. 113 patients presented with persistent symptoms. There was no difference in basal cortisol level between patients who experienced persisting symptoms and those who didn't, the median of cortisol levels were respectively 14.1 and 13.9 g/dl. The FT4 levels were not different between patients with persisting symptoms and those without.
Conclusion
The pituitary- adrenal axis function was preserved 3 months after hospitalization in patients who survived the infection. 3% of the patients had results in favour of central hypothyroidism and <1% had secondary adrenal insufficiency. 35% of the participants had persistent symptoms after the infection but these symptoms were not related to either hypothalamic-thyroid-axis or hypothalamic-adrenal-axis dysfunction.

DOI: 10.1530/endoabs.81.RC7.4

RC7.5

Osilodrostat therapy improves physical manifestations of hypercortisolism in patients with cushing's disease: findings from the phase III LINC 3 study

Rosario Pivonello[1], Maria Fleseriu[2], Shimatsu Akira[3], John Newell-Price[4], Richard Auchus[5], Richard Feelders[6], Alberto Pedroncelli[7], Andrea Piacentini[8] & Beverly MK Biller[9]
[1]Universitá Federico II di Napoli, Dipartimento di Medicina Clinica e Chirurgia, Sezione di Endocrinologia, Naples, Italy; [2]Oregon Health & Science University, Pituitary Center, Departments of Medicine and Neurological Surgery, Portland, OR, United States; [3]Omi Medical Center, Kusatsu, Japan; [4]The Medical School, University of Sheffield, Department of Oncology and Metabolism, Sheffield, United Kingdom; [5]University of Michigan, Ann Arbor, Division of Metabolism, Endocrinology and Diabetes, Departments of Internal Medicine and Pharmacology, Ann Arbor, MI, United States; [6]Erasmus Medical Center, Department of Internal Medicine, Endocrine Section, Rotterdam, Netherlands; [7]Recordati AG, Basel, Switzerland; [8]Recordati SpA, Milan, Italy; [9]Massachusetts General Hospital, Neuroendocrine and Pituitary Tumor Clinical Center, Boston, MA, United States

Background
Improving physical manifestations of hypercortisolism is an important treatment goal for patients with Cushing's disease (CD). In the Phase III LINC 3 study (NCT02180217), osilodrostat therapy, a potent oral 11β-hydroxylase inhibitor, rapidly normalised mean urinary free cortisol (mUFC) in most patients with CD and sustained control of mUFC over a median treatment period of 130 weeks (W). Here we describe concomitant improvements in physical manifestations of hypercortisolism.
Methods
137 adults with CD and mUFC >1.5 times the upper limit of normal were enrolled in the published 48W core phase. 106 patients opted to enter the extension phase, which ended when all patients had received ≥72W of treatment. Photographs from the shoulders up (frontal and lateral) and of the trunk with the patient standing (frontal and dorsal) were taken by investigators at baseline, every 12W during the core phase, and at W72; manifestations were rated subjectively on a semi-quantitative scale: 0=absent; 1=mild; 2=moderate; 3=severe. Body weight and waist circumference were also measured. Data are presented descriptively for all patients with an assessment at baseline and the given visit.
Results
At baseline, most patients had mild, moderate or severe physical features of hypercortisolism: dorsal fat pad (73.7%), supraclavicular fat pad (68.6%), central obesity (71.5%), facial rubor (63.5%), hirsutism (58.5% [females only; n=62/106]), proximal muscle atrophy (51.8%), striae (48.9%) and ecchymosis (38.7%). At W48 (n=97) and W72 (n=86), respectively, improvements in physical features scores from baseline were noted in 52.6% and 57.0% of patients for dorsal fat pad, 51.5% and 53.5% for supraclavicular fat pad, 42.3% and 39.5% for central obesity, 46.4% and 52.3% for facial rubor, 34.2% (n=26/76) and 34.4% (n=22/64) for hirsutism, 38.1% and 34.9% for proximal muscle atrophy, 32.0% and 30.2% for striae, and 35.1% and 31.4% for ecchymosis. Mean weight improved from 80.8 kg at baseline to 75.5 kg (–4.6%) at W48 and 74.1 kg (–5.8%) at W72. Mean waist circumference decreased from 103.5 cm at baseline to 97.4 cm (–4.2%) at W48 and 95.6 cm (–5.8%) at W72. Mean body mass index improved from 30.3 kg/m^2 at baseline to 28.4 kg/m^2 (–4.6%) at W48 and 27.9 kg/m2 (–5.8%) at W72.
Conclusions
Most patients in LINC 3 had physical manifestations of hypercortisolism at baseline. Osilodrostat therapy provided long-term mUFC control and clinical improvements, with reductions in patient weight and the severity of physical manifestations, including hirsutism, that were sustained through to W72.

DOI: 10.1530/endoabs.81.RC7.5

RC7.6

Long-term results from the Phase III LINC 4 study: Osilodrostat maintained normal mean urinary free cortisol in patients with Cushing's disease, with a favourable safety profile

Monica Gadelha[1], Peter J Snyder[2], Przemysław Witek[3], Marie Bex[4], Zhanna Belaya[5], Adina F Turcu[6], Richard Feelders[7], Anthony Heaney[8], Michaela Paul[9], Alberto Pedroncelli[10] & Richard Auchus[11]

[1]Medical School and Hospital Universitário Clementino Fraga Filho, Universidade Federal do Rio de Janeiro, Neuroendocrinology Research Center, Endocrinology Section, Rio de Janeiro, Brazil; [2]Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, United States; [3]Medical University of Warsaw, Department of Internal Medicine, Endocrinology and Diabetes, Warsaw, Poland; [4]University Hospitals Leuven, Department of Endocrinology, Leuven, Belgium; [5]Endocrinology Research Centre, Department of Neuroendocrinology and Bone Disease, Moscow, Russian Federation; [6]University of Michigan, Ann Arbor, Division of Metabolism, Endocrinology and Diabetes, Ann Arbor, MI, United States; [7]Erasmus Medical Center, Department of Internal Medicine, Endocrine Section, Rotterdam, Netherlands; [8]David Geffen School of Medicine, University of California, Los Angeles, Division of Endocrinology, Diabetes and Metabolism, Department of Medicine, Los Angeles, CA, United States; [9]Novartis Pharma AG, Basel, Switzerland; [10]Recordati AG, Basel, Switzerland; [11]University of Michigan, Ann Arbor, Division of Metabolism, Endocrinology and Diabetes, Department of Pharmacology, Ann Arbor, MI, United States

Background
Osilodrostat (potent oral 11β-hydroxylase inhibitor) provided rapid normalisation of mean urinary free cortisol (mUFC) in Cushing's disease (CD) patients during the 48-week (W) core period of LINC 4 (NCT02697734) and was well tolerated. We report long-term efficacy and safety results from the LINC 4 core and extension phases.
Methods
73 adults with CD and mUFC >1.3 upper limit of normal (ULN) were enrolled. LINC 4 comprised a 12W, randomised, double-blind, placebo-controlled period followed by 36W of open-label osilodrostat. At W48, patients could continue receiving open-label osilodrostat during an optional extension. Dose adjustments were permitted based on efficacy/tolerability (open-label range, 1–30 mg bid). Efficacy/safety are reported for all patients unless otherwise stated (excludes W1–12 data for placebo recipients).
Results
65/73 patients completed the core phase; 60 entered the extension. Median (range) osilodrostat exposure from core baseline to study end was 87.1 (2–127) W; median (IQR) average dose was 4.6 (3.7–9.2) mg/day. 15 patients discontinued osilodrostat, 7 after W48 (6 because of adverse events [AEs]). The proportion of patients with normal mUFC ($\leq$138 nmol/24 h) was 68.5% ($n=50/73$) at W48, 61.5% ($n=40/65$) at W72 and 72.4% ($n=42/58$) at extension end-of-treatment (EOT). Median mUFC decreased from 2.5ULN (core baseline) to 0.5ULN (W48 and W72) and 0.4ULN (EOT). Median late-night salivary cortisol decreased from 2.8ULN (core baseline) to 1.2ULN (W48 and W72) and 1.1ULN (EOT). Most common AEs overall were decreased appetite (46.6%), arthralgia (45.2%), fatigue (39.7%), nausea (37.0%), headache (34.2%) and dizziness (30.1%). AEs related to hypocortisolism and accumulation of adrenal hormone precursor occurred in 28.8% (21/73) and 61.6% (45/73) of patients overall, less frequently in the extension than the core. Most were grade 1/2 and resolved with dose reduction/interruption and/or concomitant medication. After W48, one patient experienced an AE of hirsutism. Median adrenocorticotropic hormone increased from 1.1ULN (core baseline) to 3.0ULN (W48), 3.6ULN (W72) and 3.5ULN (EOT). Median change (95%CI) in pituitary tumour volume (by MRI) from core baseline to last assessment was 4.0 (-24.1, 169.8) mm^3; AEs related to pituitary tumour enlargement led to discontinuation in 2 and 0 patients during the core and extension. No trend was observed between tumour volume change and osilodrostat dose.
Conclusion
Osilodrostat provided long-term control of cortisol production during LINC 4. Fewer AEs related to hypocortisolism and accumulation of adrenal hormone precursors occurred during the extension than the core. Osilodrostat is an effective and well-tolerated long-term treatment option for CD patients.

DOI: 10.1530/endoabs.81.RC7.6

RC7.7

Outcome in repeat transsphenoidal surgery in patients with persistent and recurrent Cushing's disease

Isabella Nasi-Kordhishti & Jürgen Honegger
Eberhard Karls Univerity Tübingen, Department of Neurosurgery, Tübingen, Germany

Objective
Transsphenoidal surgery is the treatment of choice for Cushing's disease (CD). Surgery is challenging due to the often very small adenomas. In experienced pituitary centers a high remission rate is reported. Nevertheless, endocrinologists and neurosurgeons face cases with persistent or recurrent CD .These patients must be referred to an experienced pituitary center. In addition to medical treatment, radiation therapy and bilateral adrenalectomy, repeat TSS must also be evaluated. The aim of this study is to analyse the outcome of repeat surgery and to compare persistent and recurrent CD.
Methods
We retrospectively analysed 52 patients with confirmed CD, who underwent repeat TSS in our department. Both persistence of CD after unsuccessful first surgery ($n=24$) and recurrence of CD ($n=28$) were the indications for repeat TSS. Thirty-two patients underwent their first surgery externally, 20 patients had both TSS in our pituitary center. All surgeries were performed by a single experienced pituitary surgeon through a microscopic transsphenoidal approach.
Results
The time range between the first and the repeat TSS was between 0 – 93 months (median 7.5 months) in the case of persistent CD, and between 3 – 219 months (median 64.5 months) in the cases of recurrent CD ($P<.0001$). A high-quality MRI was performed preoperatively in all cases. A clear adenoma was found in 65.4% of cases (66.7% persistent CD, 64.3% recurrent CD). A remission rate of 71% ($n=17/24$) was achieved in the group with persistent CD, and of 82% ($n=23/28$) with recurrent CD. The complication rate was 5.7% (8.3% in persistent CD, 3.6% in recurrent CD). There was no mortality rate in either group.
Conclusion
Persistent and recurrent CD pose a greater challenge for further treatment. If repeat surgery is an option, it should be offered to the patient at an experienced pituitary center. A higher remission rate is achieved in recurrent CD compare to persistent CD. With high surgical experience, there is still a low complication rate of repeat TSS with a satisfactory probability of remission.

DOI: 10.1530/endoabs.81.RC7.7

Calcium and Bone

RC8.1

Growth hormone excess in fibrous dysplasia and mccune albright syndrome (FDMAS)

Oana O Dănilă[1,2], Raya ES Geels[1], Kim Claessen[3], Maartje E Meier[1,4], Elizabeth M Winter[1], Nienke Biermasz[3] & Natasha M Appelman-Dijkstra[1]
[1]Leiden University Medical Center, Department of Medicine, Division of Endocrinology & Center for Bone Quality, Leiden, Netherlands; [2]National Institute of Endocrinology C.I. Parhon, Bucharest, Romania; [3]Leiden University Medical Center, Department of Medicine, Division of Endocrinology & Center for Endocrine Tumors, Leiden, Netherlands; [4]Leiden University Medical Center, Department of Orthopedic Surgery, Leiden, Netherlands

Introduction
Fibrous dysplasia (FD)/McCune Albright Syndrome (MAS) is a rare disorder affecting bone and hormonal glands. In FDMAS patients, autonomous GH hypersecretion (GH+) is the most common endocrinopathy after Precocious Puberty and has a great impact on the morbidity and complication rate in patients with craniofacial fibrous dysplasia. However clinical and biochemical features of GH over secretion can be subtle and awareness is warranted. We aimed to explore the GH/IGF-I axis in FDMAS.
Methods
We included 163 patients with measurements of GH/IGF-1. Patients with MAS and GH+ were compared with MAS-patients without GH-. Growth hormone excess was diagnosed by Growth Hormone suppression Test (GST) with 75 grams of glucose, cut off value of 1.45 mU/l. GST is performed in our center in case of progressive Craniofacial FD (CFD), phenotypic changes or IGF-1 levels >1.0SD as typical complaints of acromegaly are often lacking in FDMAS.
Results
38 (68.4% females) MAS patients were included,10 had GH excess. In the GH+ group, 7 had prolactin co-secretion. All 10 subjects had precocious puberty and CFD, 7 had skull base involvement. Patients with GH+ were diagnosed with FDMAS at a younger age, 3.5 (0-14 yrs) vs 12 years (1-51 yrs) than GH- patients, $P<0.01$. Median age of GH+ diagnosis was 36 years (7-43 yrs). GH+ was more frequent in males, 7 vs 3. A pituitary microadenoma could be detected in 3

patients (30%). GH+ correlated with visual impairment ($P<0.001$, $r=0.267$), $n=7$ subjects (70%) resulting in blindness in 4. IGF1 levels at time of GH+ diagnosis were within the normal range in 60% of FDMAS GH+ subjects, 48 nmol/l (24.3-88.3) SD 1.95, albeit significantly higher than FDMAS GH- patients, $P=0.007$. Alkaline phosphatase-(ALP) at first presentation was higher in FDMAS GH+ ($P<0.01$), also after correction for disease severity. All GH+ patients were started on medical treatment as surgery was not feasible. After 12 months IGF-1 levels dropped to 37.3 nmol/l (17.30-50.60), SD 0.5 ($P=0.04$). In addition, ALP decreased as well from 1131.5 U/l to 598.5 U/l, $P=0.034$.
Conclusion
In this cohort of FDMAS patients, GH excess was observed in 26% of patients. 60% had IGF-1 levels < 2.5 SD and could only be diagnosed with GST. GH excess was associated with more visual impairment and higher bone turnover. Early diagnosis using GST should be performed as in 60% of subjects IGF-1 levels were within the normal range as treatment is of upmost importance to prevent complications in the future.

DOI: 10.1530/endoabs.81.RC8.1

RC8.2

Temporal effects of encaleret (CLTX-305) on mineral physiology in autosomal dominant hypocalcemia type 1 (ADH1): results from a phase 2B, open-label, dose-ranging study [NCT04581629]

Rachel Gafni[1], Iris Hartley[1], Kelly Roszko[1], Karen Pozo[1], Edward Nemeth[2], Ramei Sani-Grosso[3], Arun Mathew[3], Ananth Sridhar[3], Mary Scott Roberts[3], Jonathan Fox[3] & Michael Collins[1]
[1]National Institutes of Health, Skeletal Diseases and Mineral Homeostasis Section, Bethesda, United States; [2]MetisMedica, Toronto, Canada; [3]Calcilytix Therapeutics, Inc, San Francisco, United States

Autosomal dominant hypocalcemia type 1 (ADH1), caused by gain-of-function variants in the calcium-sensing receptor (CaSR, gene: *CASR*) and is characterized by hypocalcemia, hyperphosphatemia, low parathyroid hormone (PTH), and hypercalciuria. Calcilytics (negative allosteric modulators of the CaSR) decrease the sensitivity of activated receptors to extracellular calcium and normalize blood and urine abnormalities in ADH1 rodent models. Encaleret is an oral calcilytic under investigation as a treatment for ADH1. Data on the encouraging effects of encaleret on PTH and blood and urine calcium (Ca) were previously reported. Here we expand on those data and describe the temporal and relative changes in PTH, nephrogenous cAMP (NcAMP), tubular reabsorption of phosphate (TRP), blood phosphate (Pi) and Ca, fractional excretion of Ca (FECa), 1,25-dihydroxyvitamin D ($1,25(OH)_2$ D), and intact FGF23 (fibroblast growth factor 23) after encaleret administration. Six adults (22-60 years) with ADH1 due to 4 *CASR* variants were studied in Period 1 of a Phase 2b, open-label, dose-ranging study. Subjects received sequential, increasing daily doses of encaleret for 3d (30 mg, 90 mg, 180 mg) followed by 180mg bid on day 4 and 120 mg or 180 mg bid on day 5, while undergoing frequent blood and urine sampling. The temporal changes in the mean$\pm$SD values over 24 hr on day 4 are compared to baseline (blood volume limitations only allowed for collection of the mineral panel parameters through day 4). PTH was low at baseline (3.4 ± 4.5 pg/ml, normal 10-65), rose rapidly, peaked at 2 hr (65.0 ± 49.2), and remained normal through the 24 hrs measured. NcAMP rose by 4hr and was significantly increased through the 24 hrs measured. TRP and Pi decreased rapidly and remained significantly decreased through 24 hrs. FECa was 0.03 ± 0.02 at baseline, was significantly decreased by 4hr, which was maintained through 24 hrs. Blood albumin-corrected Ca was below normal prior to 0hr dosing (7.6 ± 0.6 mg/dl, normal 8.4-10.2), was normal by 4hr and remained significantly increased from 8-24 hrs. $1,25(OH)_2$ D was below normal at 0hr, increased and remained in the normal range from 4-24 hrs. Intact FGF23 was above normal at time 0hr and surprisingly remained unchanged over the 13hrs monitored, despite the reported changes in Pi, PTH and $1,25(OH)_2$ D. Bone turnover markers CTX and P1NP were unchanged compared with day 1. Encaleret was well-tolerated, with no serious adverse events reported. The observed temporal changes of key mineral homeostasis factors and normalization of blood Ca and FECa in encaleret-treated subjects with ADH1 shed light on mineral physiology and potential utility of encaleret in ADH1.

DOI: 10.1530/endoabs.81.RC8.2

RC8.3

What is the most efficient way to fortify food items with vitamin D? A randomised, multiple crossover study

Rasmus Espersen[1,2], Lene Ring Madsen[3,4,5], Caroline Nebel[6,7], Marianne Danielsen[6,7], Trine Dalsgaard[6,7] & Lars Rejnmark[1,2]
[1]Aarhus University, Department of Clinical Medicine, Denmark; [2]Aarhus University Hospital, Department of Endocrinology and Internal Medicine, Aarhus, Denmark; [3]Regional Hospital West Jutland, Department of Internal Medicine, Herning, Denmark; [4]Steno Diabetes Center Aarhus, Aarhus, Denmark; [5]Danish Diabetes Academy, Odense, Denmark; [6]Aarhus University, Department of Food Science, Aarhus, Denmark; [7]Aarhus University, iFood, Centre for Innovative Food Research, Aarhus, Denmark

Introduction
Vitamin D insufficiency (25-hydroxy vitamin D <50 nmol/l) is a global health problem. Vitamin D food fortification might be the solution, but knowledge is sparse on whether fortification of various food items affects the bioavailability differently. It is generally assumed that ingesting vitamin D with a fatty meal improves the bioavailability of vitamin D. Furthermore, complex formation with whey protein isolate (WPI) may enhance the stability of vitamin D and thereby improve bioavailability. We studied the efficiency of fortifying different food items with vitamin D_3.
Materials and methods
In a randomised, multiple (5-periods), crossover trial, we enrolled 30 postmenopausal women with vitamin D insufficiency aged 60-80 years. We measured immediate changes in plasma concentrations of cholecalciferol (D_3) in response to intake of different food matrices with 200 µg D_3 added i.e., 1) 500 mL of water, 2) 500 mL of milk, 3) 500 mL of juice, 4) 500 mL of juice with D3 complex-bound to WPI, and 5) 500 mL of water without D_3 (placebo). The different food matrices were provided in a randomised order with at least ten days washout period in-between study days. On each study day, blood samples were collected at 0 h, 2 h, 4 h, 6 h, 8 h, 10 h, 12 h and 24 h.
Results
Complexation D_3 -WPI in apple juice did not enhance maximum concentration (Cmax) of serum D_3 compared to juice without WPI (25 nmol/l vs 24 nmol/l; $P=0.61$), nor the area under the time-D_3 curve (AUC) (370 nmol/l *24 h vs 357 nmol/l *24 h; $P=0.93$). However, compared to juice, Cmax and AUC of serum D_3 were significantly higher in response to intake of milk (30 nmol/l and 452 nmol/l *24 h) and water with D_3 added (32 nmol/l and 479 nmol/l *24 h) ($P<0.05$, all). No difference in serum D_3 was observed between milk and water ($P=0.29$, Cmax; $P=0.33$, AUC).
Conclusion
The bioavailability of D_3 assessed by Cmax and AUC was superior in water and milk compared to juice, independent of whether complexation D_3 -WPI was added to juice.

DOI: 10.1530/endoabs.81.RC8.3

RC8.4

Accuracy, costs and radiation exposure of current preoperative localization procedures in patients with primary hyperparathyroidism, a retrospective cohort study in a Swiss tertiary referral center

Martin Siegenthaler[1], Ole Christopher Maas[2], Frida Renström[1], Thomas Clerici[3], Flavio Forrer[2], Walter Kolb[3], Stefanie Sinz[3] & Stefan Bilz[1]
[1]Cantonal Hospital of St. Gallen, Clinic for Endocrinology, Diabetology, Osteology and Metabolic Diseases, St. Gallen, Switzerland; [2]Cantonal Hospital of St. Gallen, Clinic for Radiology and Nuclear Medicine, St. Gallen, Switzerland; [3]Cantonal Hospital of St. Gallen, Clinic for Endocrine Surgery, St. Gallen, Switzerland

Background
Focused parathyroidectomy has become the standard procedure for patients with sporadic primary hyperparathyroidism (pHPT) fulfilling the criteria for surgical therapy and requires preoperative localization procedures. Ultrasound imaging (US) and ^{99m}Tc-sestamibi-scintigraphy with/without SPECT/CT (SC) are established first line procedures. ^{18}F-choline PET/CT (PET) has emerged as a novel sensitive and specific method. However, current reimbursement policy in Switzerland limits its use to patients with negative or equivocal first line imaging.

The aim of this study was to compare the accuracy, costs and radiation exposure of SC and PET in patients with negative or equivocal US imaging.
Methods
We retrospectively evaluated all US, SC and PET images performed in patients with sporadic pHPT referred for surgery at our institution between March 2017 and June 2021. US imaging was reported diagnostic, equivocal or negative, SC and PET were reported as positive or negative. Parathyroidectomy was considered successful if normal serum calcium levels were observed six months postoperative.
Results
The study included 239 patients of which all underwent US imaging, 164 (68.6%) received SC and 70 (29.3%) PET imaging. The final diagnostic accuracy of a diagnostic preoperative US ($n=66$) was high with a sensitivity of 100% and a PPV of 95.5%. In patients with equivocal ($n=130$) or negative ($n=42$) US, the accuracy of PET was increased when compared to SC (negative US: sensitivity 38.9% vs 87.5%, PPV 77.8% and 91.3%; equivocal US: sensitivity 70.7% vs 95.0%, PPV 92.1% and 90.5%). The estimated total costs per patient with PET as immediate second line imaging following equivocal US would have been 32% higher compared to a stepwise approach, but comparable in patients with initially negative US. Immediate PET imaging would have reduced radiation exposure by approximately 3.6 mSv (41.8%) and 2.4 mSv (32.4%) in patients with negative and equivocal US results, respectively.
Conclusions
The results confirm the superior accuracy of PET vs SC for the localization of parathyroid adenomas in patients with sporadic pHPT and negative or equivocal US imaging. In patients with negative US immediate PET imaging reduces radiation exposure at comparable costs and should be recommended without previous SC.
DOI: 10.1530/endoabs.81.RC8.4

RC8.5

Estradiol is the major sex steroid regulating bone marrow fat in both men and women: a study in transgender persons

Marieke Tebbens[1], Moya Schutte[1], Marian Troelstra[2], Aart Nederveen[2], Martin den Heijer[1] & Peter H den Heijer[3]
[1]Amsterdam UMC, Vrije Universiteit Amsterdam, Endocrinology, Amsterdam, Netherlands; [2]Amsterdam UMC, University of Amsterdam, Radiology, Amsterdam, Netherlands; [3]Amsterdam UMC, University of Amsterdam, Endocrinology, Amsterdam, Netherlands

Background
Bone marrow fat is a unique fat depot that is regulated independently of other fat depots. Estradiol is an important regulator of bone marrow fat. This is illustrated by an increase in marrow fat fraction after menopause and a decrease following estradiol replacement. We hypothesize that estradiol is the major sex steroid that regulates bone marrow fat not only in women, but also in men.
Methods
This is an open-label partly randomized intervention study in trans women (assigned male at birth, identify as female) and trans men (assigned female at birth, identify as male) receiving hormone treatment. Trans women were treated with triptorelin for 6 weeks, followed by triptorelin and estradiol for 52 weeks. Measurements were performed at baseline, 6, 8, 18 and 58 weeks. Trans men were randomized to receive triptorelin and testosterone with or without anastrozole for 12 weeks, followed by only testosterone until week 52. Measurements were performed at baseline, 6, 12 and 52 weeks. The marrow fat fraction was quantified by magnetic resonance imaging (MRI). The bone mineral density (BMD) was estimated by dual-energy X-ray absorptiometry (DXA) at baseline and after 12 months.
Results
In trans women, the marrow fat fraction increased by 0.09 (95% CI 0.05 to 0.12) after 6 weeks, compared to baseline. Compared to week 6, the marrow fat fraction decreased by 0.06 (0.01 to 0.11), 0.09 (0.04 to 0.14), 0.08 (0.03 to 0.13) at 8, 18, and 58 weeks, respectively. In trans men without anastrozole, the marrow fat fraction did not change at week 6 and 52, but was slightly higher at week 12 (0.05 (0.01 to 0.08)), compared to baseline. In trans men with anastrozole, compared to baseline, the marrow fat fraction increased by 0.06 (0.03 to 0.09) and 0.06 (0.03 to 0.09) at week 6 and 12, respectively. BMD did not change in response to hormone treatment in any of the groups.
Conclusion
The results of this study indicate that estradiol and not testosterone is the major sex steroid regulating bone marrow fat in both men and women.
DOI: 10.1530/endoabs.81.RC8.5

RC8.6

Health related quality of life in adults with hypoparathyroidism in an exploratory analysis of the phase 2 PaTH forward trial of TransCon PTH

Andrea Palermo[1], Tamara J Vokes[2], Aliya Khan[3], Mishaela Rubin[4], Peter Schwarz[5], Bart L Clarke[6], Erik Eriksen[7], Claudio Marcocci[8], Uberto Pagotto[9], Elena Tsourdi[10], Tanja Sikjaer[11], Meryl Brod[12], Lori Mcleod[13], Denka Markova[14], Wahidullah Noori[14] , Walter Frank Eng[14], Aimee Shu[14] & Alden Smith[14]
[1]Campus Bio Medico University of Rome, Selcetta, Italy; [2]The University of Chicago, Chicago, United States; [3]McMaster University, Department of Endocrinology and Metabolism and Geriatrics, Hamilton, Canada; [4]Columbia University, New York, United States; [5]Rigshospitalet, Department of Endocrinology, København, Denmark; [6]Mayo Clinic, Rochester, United States; [7]Oslo University Hospital, Institute of Clinical Medicine, Oslo, Norway; [8]University of Pisa, Pisa, Italy; [9]Alma Mater Studiorum - Università di Bologna, School of Medicine and Surger, Bologna, Italy; [10]Dresden University of Technology, Department of Medicine III and Center for Healthy Aging, Dresden, Germany; [11]University of Aarhus, Department of Endocrinology and Diabetes, Aarhus, Denmark; [12]The Brod Group, Mill Valley, United States; [13]RTI Health Solutions, Durham, United States; [14]Ascendis Pharma, Inc, Palo Alto, United States

Background
Patients with hypoparathyroidism experience significant physical and cognitive symptoms and reduced health-related quality of life (HRQoL). Conventional therapy for hypoparathyroidism does not fully alleviate diminished HRQoL. The Hypoparathyroidism Patient Experience Scales (HPES) were developed to assess disease-specific physical and cognitive symptoms as well as the impact of hypoparathyroidsm on HRQol. TransCon PTH, an investigational long-acting prodrug of parathyroid hormone (PTH[1-34]), is in development as a potential hormone replacement therapy for adults with hypoparathyroidism.
Methods
The phase 2, randomized, double blind placebo controlled 4-week PaTH Forward trial was followed by an open label extension period and enrolled 59 participants. HRQoL was assessed at Week 4 and Week 26 in an exploratory ad-hoc analysis using HPES and the 36-Item Short Form Survey (SF-36) to assess the role of HPES in measuring the impact of TransCon PTH on HRQoL
Results
Improvements in HPES scores were significantly greater for participants treated with TransCon PTH ($n=44$) compared with placebo ($n=15$) from baseline to Week 4 of the trial for both HPES-Total Symptom score (Mean difference [standard error] in scores -20.0 [4.6], $P < 0.01$; 84% of treated patients had improved scores versus 47% of placebo, $P=0.013$) and HPES-Total Impact Score (Mean difference [standard error] in scores -15.7 [5.0], $P< 0.01$; 75% of treated patients had improved scores versus 40% of placebo, $P =0.025$). All HRQoL assessments demonstrated continued score improvements in patients treated with TransCon PTH at Week 26 of the trial compared with baseline. Participants treated with TransCon PTH who had higher (worse) HPES (Impact & Symptom) scores at baseline demonstrated a greater magnitude of improvement at Week 26 as did participants with lower (worse) SF-36 scores at baseline. The Pearson correlation analysis showed that HPES results diverged from SF-36 results over time, with a greater number of domain scores having a correlation of -0.40 or larger at Week 4 compared with Week 26.
Conclusions
This exploratory ad-hoc analysis of the PaTH Forward trial demonstrated improved HRQoL and symptom scores in participants treated with TransCon PTH compared with placebo. In addition, correlation analyses identified the distinct value and dynamic range of HPES as disease-specific assessment tools in hypoparathyroidism. The decreased correlation between HPES and SF-36 over time in the trial indicates that HPES and SF-36 are not redundant.
DOI: 10.1530/endoabs.81.RC8.6

RC8.7

The resorption status of magnesium screws for surgical treatment of ankle fractures assessed by HRpQCT – 2.5 years follow-up data of a first-in-human study

Ines Föß[1], Victor Labmayr[2], Ulrike Wittig[2], Annelie Martina Weinberg[2], Patrick Holweg[2] & Barbara Obermayer-Pietsch[1]
[1]Medical University of Graz, Division of Endocrinology, Department of Internal Medicine, Graz, Austria; [2]Medical University of Graz, Department of Orthopedics and Traumatology, Graz, Austria; I.F. and V.L. equally contributed as first authors; P.H. and B.O-P. equally contributed as last authors

Background
Bioresorbable screws for surgical fracture treatment are of great interest for the orthopaedic community. Such implants are designed to provide stability and compression of the fracture and should dissolve after healing, thereby making removal of surgical material obsolete. Magnesium implants are a new material option. So far, long-term follow-up of fracture healing and material decay has not been studied in human. Here, we present the results of the 2.5 year follow-up of 6 patients with medial malleolus fractures after surgical stabilization with magnesium screws.
Design and Methods
6 patients with isolated, bimalleolar or trimalleolar ankle fractures were surgically treated using bioresorbable screws (magnesium 99.1%, calcium 0.45%, zinc 0.45%) with an initial volume of 243,3 mm3 (+/- 5). Fracture healing was assessed clinically after one year. Implant resorption was studied after 2.5 years with HR-pQCT (high resolution peripheral quantitative computed tomography). Screw residues were carefully evaluated in a binary approach for every slice (residual present vs not present). Zones of degradation without visible bone were contoured manually and the volume was evaluated.
Results
All patients showed clinical evidence of fracture healing confirmed by plain radiographs, with full weight bearing and absence of pain in the fractured ankle after 1 year. After 2.5 years, resorption of the implant material was almost complete. Of the 11 implants in 6 patients, 3 were dissolved without visible residuals whereas at 8 implantation sites minimal residuals were observed, as assessed by HR-pQCT. In 10% of slices (min. 0%; max. 33%) residuals were observed at implant sites. The degradation zones lacked visible ingrowth of new bone for the most part. Mean volume of degradation zones was 504.8 mm^3 (min. 239.2 mm^3; max. 1109.1 mm^3).

	male, 32 years	female, 51 years	female, 58 years	male, 59 years	male, 33 years	male, 23 years
Slices with residuals (ventral implant)	175/532 (33%)	102/610 (17%)	41/541 (8%)	68/557 (12%)	27/525 (5%)	0/596 (0%)
Slices with residuals (dorsal implant)	133/495 (27%)	13/541 (2%)	35/555 (6%)	0/531 (0%)	N/A	0/558 (0%)

Conclusion
Considering the successful fracture healing and excellent clinical outcome after one year, bioresorbable magnesium screws are a viable option for fracture fixation. Implant removal is not necessary and the 2.5 year follow-up showed the screw material largely resolved. However, enlarged degradation zones and the lack of new bone in these zones were observed.

DOI: 10.1530/endoabs.81.RC8.7

Diabetes, Obesity, Metabolism and Nutrition 3

RC10.1

Insulin resistance as indexed by the estimated glucose disposal rate and liver fat content are correlated in type 1 diabetes

Jonathan Mertens[1,2,3], Maarten Spinhoven[4], Eveline Dirinck[1,2], Luisa Vonghia[3], Sven Francque[1,3] & Christophe De Block[1,2]
[1]University of Antwerp, Laboratory of Experimental Medicine and Paediatrics, Antwerpen, Belgium; [2]Antwerp University Hospital, Endocrinology, Diabetology and Metabolism, Edegem, Belgium; [3]Antwerp University Hospital, Gastroenterology and Hepatology, Edegem, Belgium; [4]Antwerp University Hospital, Radiology, Edegem, Belgium

Introduction
The prevalence of metabolic syndrome is increasing in individuals with T1D, which could potentiate the development of NAFLD. The pathophysiology of NAFLD in T1D is still unclear, due to the co-existence of predisposing and protective factors. Insulin resistance (IR) is theorized as a key driver of NAFLD.
Aim
We investigated the association between liver fat content (LFC), NAFLD, and IR in individuals with T1D. Subjects underwent magnetic resonance spectroscopy (MRS) to determine LFC. The estimated glucose disposal rate (eGDR) was calculated in two ways based on: (1) the presence of hypertension, waist circumference (cm), and HbA1c (%), and (2) the presence of hypertension, body mass index (BMI, kg/m^2) and HbA1c (%). An eGDR <8 mg/kg/min is considered insulin resistant. A mean LFC $\geq$ 6.0 % on MRS was considered diagnostic for NAFLD.
Results
Seventy-eight subjects were included. Age was 59 $\pm$ 17 years, BMI was 27.6 $\pm$ 5.0 kg/m2, waist circumference was 87 $\pm$ 13 cm in females and 99 $\pm$ 12 cm in males, and hypertension was present in 63%. LFC based on MRS was 4.3 $\pm$ 4.0 %, NAFLD was present in 11 (14%) subjects. HbA1c was 7.4 $\pm$ 1.2 % indicating good glycaemic control. The eGDRwaist measured 6.4 $\pm$ 2.5 mg/kg/min, and $eGDR^{BMI}$ was 6.4 $\pm$ 2.2 mg/kg/min. Correlation between eGDR methods was excellent ($r = 0.96$, $P < 0.001$). Kappa between eGDR methods was 0.87, $P < 0.001$. Prevalence of IR was 27% ($eGDR^{BMI}$) and 30 % ($eGDR^{waist}$). All 11 cases of NAFLD were in the IR group, regardless of eGDR method. Linear regression showed a weak correlation between $eGDR^{waist}$ and LFC (r: -0.277, B: -0.442, 95% CI: -(0.792 - 0.091), $P=0.014$), and between $eGDR^{BMI}$ and LFC (r: -0.270, B: -0.480, 95% CI: -(0.872 – 0.089, $P=0.017$). NAFLD was associated with the $eGDR^{waist}$ as a continuous variable (OR: 0.62, 95% CI: 0.39 - 0.99, $P=0.049$) in a logistic model including BMI, age, and gender. $eGDR^{BMI}$ was not significantly associated in a model including waist, age and gender.
Conclusions
These data show that IR, as indexed by the eGDR based on waist circumference, is associated with LFC and the presence of NAFLD in individuals with T1D. More studies are needed to elucidate the role of IR in the etiology of NAFLD in individuals with T1D.

DOI: 10.1530/endoabs.81.RC10.1

RC10.2

Weight changes and all-cause mortality in patients with prediabetes and diabetes

Jia Li[1], Gyorgy Simon[2], M. Regina Castro[3] & Pedro Caraballo[4]
[1]University of Minnesota, Department of Computer Science and Engineering, Minneapolis, United States; [2]University of Minnesota, Department of Medicine and Institute of Health Informatics, Minneapolis, United States; [3]Mayo Clinic, Department of Medicine, Rochester, United States; [4]Mayo Clinic, Department of Medicine and Department of Quantitative Health Sciences, Rochester, United States

Introduction
Weight loss is a cornerstone in the management of prediabetes and diabetes mellitus. The association between weight and all-cause mortality is controversial and even paradoxical. Studies usually assess baseline weight. Studies assessing weight changes over time are limited. We present preliminary results of our attempt to model weight changes in patients with prediabetes and diabetes assessing the relationship with all-cause mortality.
Methods
We evaluated a retrospective cohort of Olmsted county residents with prediabetes ($n=15868$) and diabetes ($n=10744$) seen at Mayo Clinic. They had vital signs before and after 01-01-2005 and were alive by 01-01-2011. Body mass index (BMI) was calculated to assess weight changes and classified as Low or High using 32 as cutoff. The study period, 01-01-2000 to 01-01-2011 was divided in 3 stages: Baseline from 01-01-2000 to 12-31-2004 (5 years), Follow-up 1 from 01-01-2005 to 12-31-2007 (3 years) and Follow-up 2 from 01-01-2008 to 01-01-2011 (3 years). For each patient we defined six 3-step BMI trajectories by using BMI Low (L), High (H) or any value (X): 1) L-L-L: always low BMI. 2) H-H-H: always high BMI. 3) L-H-L: start and end with Low but had a High BMI at some point. 4) H-L-H: start and end with High but had a Low BMI at some point. 5) H-X-L: start with High but end with Low BMI. 6) L-X-H: start with Low but end with High BMI.

Results
As expected, diabetes mortality rates were higher than prediabetes, but their overall distribution by BMI trajectories was similar (Table). Subjects with high BMI (H-H-H) had lower mortality rate compared with low BMI (L-L-L). Subjects that ended with Low BMI, regardless of initial BMI level (L-H-L and H-X-L), had higher mortality than subjects ending with high BMI (H-L-H and L-X-H).
Conclusion
Our preliminary results evaluating BMI trajectories suggest elevated mortality in subjects with BMI below 32 when compared with BMI above 32, and subjects that lost weight when compared with those that gained weight. These results are contrary to our expectation and against our conceived pathophysiological interaction between obesity, diabetes and its complications. The fact that similar findings have been described for other clinical conditions, impose the need for additional research to find a suitable explanation related to methodology or clinical cause.

Table. Mortality rates by BMI Trajectory

	L-L-L	H-H-H	L-H-L	H-L-H	H-X-L	L-X-H
Diabetes	19.79%	12.65%	15.87%	13.59%	21.78%	13.15%
PreDiabetes	11.98%	5.87%	10.53%	5.60%	11.91%	6.34%

DOI: 10.1530/endoabs.81.RC10.2

RC10.3

Primary bile acids differentially regulate differentiation of human abdominal and gluteal pre-adipocytes

Rugivan Sabaratnam[1], Ismael da Conceição[1], Nellie Loh[1], Constantinos Christodoulides[1], Fredrik Karpe[1], Jeremy Tomlinson[1] & Nikolaos Nikolaou[1,2]
[1]University of Oxford, Oxford Centre for Diabetes, Endocrinology and Metabolism, Oxford, United Kingdom; [2]University of Cambridge, Department of Pathology, Cambridge, United Kingdom

Bile acids (BAs) are synthesised from cholesterol in the liver and promote lipid digestion. An emerging body of evidence, however, suggests that BAs are also key signaling molecules with potent metabolic and endocrine functions, exerting their effects through activation of BA receptors, including the farnesoid-X- (FXR) and the G-protein-coupled- (TGR5) receptors. Disturbed BA synthesis has been associated with type 2 diabetes mellitus and insulin resistance, and recent studies have revealed expression of BA receptors in adipose tissue. However, the potential role of BAs to regulate human adiposity is poorly described. We have hypothesised that BAs play an important role in human adipose tissue differentiation and function. Human abdominal and gluteal pre-adipocytes were differentiated into mature-like adipocytes in the presence of vehicle (DMSO), cholic acid (CA) or chenodeoxycholic acid (CDCA) (primary BAs, 50uM) for 12 days. Adipocyte differentiation was determined by qPCR and AdipoRed staining. Intracellular triglyceride accumulation, glucose concentration, and adipokine secretion were determined by ILab biochemistry analyser and ELISA. CDCA treatment of human abdominal and gluteal pre-adipocytes significantly impaired adipogenic differentiation, as demonstrated by AdipoRed staining. However, CA had no impact. Endorsing these data, intracellular triglyceride levels were significantly lower in CDCA-, but not CA-treated, mature-like adipocytes compared to vehicle-treated cells [vehicle: 2388 ± 448.3 vs 126.1 ± 25.41 nmol/mg protein, $P = 0.04$]. In addition, intracellular glucose concentrations were elevated in CDCA-, but not CA-treated, cells compared to vehicle-treated ones (vehicle: 0.11 ± 0.03 vs CDCA: 0.34 ± 0.08 nmol/mg protein ($n = 3$)]. Supporting these findings, expression of the key adipogenesis gene markers *PPARG2*, *CEBPA*, *PLIN1* and *ADIPOQ* were significantly reduced in mature-like abdominal and gluteal cells following CDCA treatment, but were unchanged following CA treatment. Consistent with decreased *ADIPOQ* expression, cell media adiponectin levels were significantly lower in CDCA-treated cells. The effect of CA on adiponectin formation was not significant. In conclusion, we have demonstrated the differential effect of primary BAs on human adipocyte differentiation. Whilst CA had no effect, CDCA treatment resulted in marked repression of adipogenesis in human abdominal and gluteal adipocytes. Our data suggest that alterations in BA levels and/or composition of the BA pool can have a detrimental effect on adipogenesis, potentially contributing to abnormal lipid storage in non-adipose tissues, downstream leading to insulin resistance and hypertriglyceridemia. Additional studies are now required to elucidate the exact mechanisms through which BAs underpin their effects on adipose tissue function.

DOI: 10.1530/endoabs.81.RC10.3

RC10.4

Adequate metabolic control at early stages of childhood onset type 1 diabetes prevent diabetic neuropathy: a 30 year follow up study

Evangelia Baldimtsi[1,2], Salvador Amezcua[3], Håkan Olausson[3], Johnny Ludvigsson[4,5], Lars Hyllienmark[6] & Jeanette Wahlberg[1,2,7]
[1]Linköping University, Department of Health,Medical and Caring Sciences, Linköping, Sweden; [2]Linköping University Hospital, Department of Endocrinology, Linköping, Sweden; [3]Linköping University, Center for Social and Affective Neuroscience, Linköping, Sweden; [4]Linköping University, Department of Biomedical and Clinical Sciences, Linköping, Sweden; [5]Crown Princess Victoria Children's Hospital, Division of Pediatrics, Linköping, Sweden; [6]Karolinska University Hospital, Clinical Neurophysiology, Stockholm, Sweden; [7]Örebro University, Faculty of Medical Sciences, Örebro, Sweden

Background and aims
Diabetic neuropathy is a common complication of type 1 diabetes. In this study we investigated the importance of long-term metabolic control for the development of diabetic neuropathy in patients with type 1 diabetes diagnosed in childhood.
Materials and methods
Longitudinal cohort study. Twenty-five patients (9 women 16 men) were studied three times with neurophysiological measurements and clinical examinations. At baseline the patients were 15.7 ± 3.7 yrs. (range 7-22) and had diabetes duration of 7.7 ± 3.3 yrs. (range 4-15). At the first follow up 2007-2009 the patients were 29 ± 3.9 yrs. (range 20-35), and had a diabetes duration of 21.6 ± 4.3 yrs. (range 10-31). At the second follow up 2017-2018, the patients were 38.6 ± 3.7 yrs. (range 31-4) and had a diabetes duration of 31.2 ± 4.7 yrs. (range 20-39). The assessment of neurological symptoms followed a standardized process. A neuropathy impairment assessment (NIA) was used to evaluate the signs of diabetic neuropathy. Nerve conduction tests were carried out according to standard techniques. The presence of clinical diabetic neuropathy was determined by a staged approach according to established criteria. Subclinical neuropathy is defined as an electrophysiological abnormality of nerve function without clinical symptoms or signs.
Results
At the initial examination, all patients were free of clinical or subclinical neuropathy. At the first follow up, ten patients 10/25 (40%) had developed clinical ($n = 5$) or subclinical neuropathy ($n = 5$) and they had significantly higher HbA1c, 77.4 ± 16.2 mmol/mol, than the 15 patients without neuropathy, 60.3 ± 8.6 mmol/mol, $P = 0.022$. At the second follow up fifteen patients15/25 (56%) fulfilled the criteria of clinical ($n = 9$) or subclinical neuropathy ($n = 6$). At the second follow up, HbA1c in the ten patients with diabetic neuropathy decreased from 77.4 ± 16.2 mmol/mol at the first follow up to 64.2 ± 16.5 mmol/mol at the second follow up, $P = 0.013$. The additional group of five patients who developed neuropathy between the first and second follow up reduced their HbA1c from 72.0 ± 10.8 mmol/mol to 57.8 ± 14.1 mmol/mol, $P = 0.006$. Taken together, at the second follow up, the difference in HbA1c levels between the 15 patients with neuropathy, 61.4 ± 10.5 mmol/mol, and the 10 patients without neuropathy, 59.6 ± 13.6 mmol/mol, was no longer significant.
Conclusion
The prevalence of diabetic neuropathy in the patient cohort increased with longer diabetes duration and progressed to clinical neuropathy in several cases despite a better metabolic control at the last follow up. The study indicates that an inadequate glycaemic control at early stages of the disease is a risk factor for developing diabetic neuropathy.

DOI: 10.1530/endoabs.81.RC10.4

RC10.5

GLP-1RAs and glucagon can reshape adipose differentiation in vitro by activating the "browning process"

Giulia Cantini[1], Martina Trabucco[1], Laura Fei[1], Arianna Propato[1], Daniele Guasti[2], Giovanni Quartararo[3], Mario Maggi[1], Edoardo Mannucci[1] & Michaela Luconi[1]
[1]University of Florence, Experimental and Clinical Biomedical Sciences - Endocrinology Unit, Florence, Italy; [2]University of Florence, Experimental

and Clinical Medicine, Florence, Italy; [3]Santa Maria Nuova Hospital, General, Bariatric and Metabolic Surgery Unit, Florence, Italy

Obesity is associated with increased and dysfunctional white adipose tissue (WAT). Pharmacological approaches of obesity are still far from obtaining a stable weight loss. Glucagon-like peptide-1 receptor agonists (GLP-1RAs) have been proposed as anti-obesity drugs due to their effects on weight loss. Furthermore, dual agonists engaging both GLP-1 and glucagon are currently under investigation for their marked effects on weight loss, although their mechanisms of action is still unclear. Compared to WAT, brown adipose tissue (BAT) is specialized in energy dissipation by heat production resulting from the specific expression of the mitochondrial enzyme uncoupling protein-1 (UCP-1). There is growing interest for new therapeutic strategies aimed at stimulating BAT to increase energy expenditure and counteract the dysfunctional expansion of WAT in obesity. Our group has previously demonstrated that liraglutide, GLP-1 and glucagon impair the proliferative and differentiation ability of an *in vitro*-model of primary human adipose-derived stem cells (ASCs), supporting a peripheral action of GLP-1RAs on weight loss. In this study, we compared the effect of these three molecules in reshaping adipogenesis toward brown adipogenesis by stimulating the "browning process" in ASCs. Glucagon, liraglutide and GLP-1 (10nM) added during in vitro-stimulated adipogenesis significantly reduced intracellular triglyceride accumulation evaluated by Adipored staining (-24%,-40%,-23%, $P<0.001$) associated with a decreased expression in the white-adipocyte marker FABP4 (-48%,-94%,-78%, $P<0.05$), while the functional marker adiponectin was upregulated (+34%,65%,72%, $P<0.05$). These findings suggest a differentiation reshape towards a more functional adipocyte phenotype. Moreover, adipogenesis in the presence of the three molecules resulted in a significant upregulation of the brown phenotype marker UCP-1 (fold-increase 2.13, 2.48, 2.14-fold versus adipogenesis alone, $P<0.05$). Mitochondrial functional analysis through Seahorse technology of the adipocytes differentiated in the presence glucagon, liraglutide and GLP-1 revealed a significant increase in the maximal respiration (+15%,25%,29%, $P<0.05$) and a similar reduction (-17%,-14%,-18%, $P<0.001$) in ATP production, supporting a stimulation of the browning process. Finally, morphological analysis of the differentiated adipocytes revealed that liraglutide, GLP-1 and glucagon addition to the adipogenic media associated with an increase in the number and surface of mitochondria and an increase in the number of lipid droplets with decreased diameter, coherently with the typical feature of brown adipocytes. In conclusion, we demonstrated a direct effect of glucagon and GLP1RAs in inducing a significant improvement of the in vitro-derived adipocytes, determining a metabolic shift towards the brown phenotype, coherently with a peripherical action exerted by these molecules directly on the adipose tissue.

DOI: 10.1530/endoabs.81.RC10.5

RC10.6

Differences in prevalence of, and precipitating factors for, diabetes related ketoacidosis in type 1 and type 2 diabetes mellitus

Dengyi Zhou[1], Haaziq Sheikh[2], Dineshwaran Rajendran[3], Shamanth Soghal[4] , Wai Nga Alice Yip[1], Anjitha Anilkumar[1], Meghnaa Hebbar[1], Lakshmi Rengarajan[5], Senthil Krishnasamy[6] & Parth Narendran[4]

[1]University of Birmingham, College of Medical and Dental Sciences, Birmingham, United Kingdom; [2]Haberdashers' Adams' Grammar School, Birmingham, United Kingdom; [3]Good Hope Hospital, Sutton Coldfield, United Kingdom; [4]Queen Elizabeth Hospital Birmingham, Birmingham, United Kingdom; [5]Birmingham Heartlands Hospital, Birmingham, United Kingdom; [6]Walsall Manor Hospital, Walsall, United Kingdom

Introduction

Diabetes related ketoacidosis (DKA) is usually associated with type 1 diabetes mellitus (T1DM). However, DKA is increasingly being recognised in type 2 diabetes mellitus (T2DM). We studied the differences in prevalence and precipitating factors of DKA between T1DM and T2DM.

Methods

This retrospective study included all DKA episodes from January to November 2021 in six hospitals in the West Midlands, UK. DKA was diagnosed as serum glucose $\geq$ 11 mmol/l or known history of diabetes, ketones $\geq$ 3 mmol/l and pH $\leq$7.3 or bicarbonate $\leq$ 15 mmol/l as per Joint British Diabetes Societies guidelines. People admitted with DKA were classified as having T1DM or T2DM based on established diagnosis, autoantibody status, and/or phenotypic features. We compared the differences in prevalence and precipitating factors between these two groups.

Results

465 episodes of DKA were identified. 47 were excluded from analysis due to unclear diabetes type. 68.7% ($n=287/418$) had T1DM and 31.3% ($n=131/418$) had T2DM. The differences in precipitating factors for DKA in T1DM vs T2DM were significant ($P=0.006$). The most common precipitating factor in both groups was intercurrent illness (T1DM: $n=107/287$, 37.3%; T2DM: $n=57/131$, 43.5%). More DKA episodes were precipitated by suboptimal compliance to treatment in T1DM compared to T2DM (T1DM: $n=99/287$, 34.5%; T2DM: $n=20/131$, 15.3%). 9 (6.9%) episodes of DKA were related to SGLT2 in T2DM compared to none in T1DM. 19 (6.6%) episodes of DKA were new diagnoses of T1DM. Other precipitating factors included COVID-19 (T1DM: $n=14/287$, 4.0%; T2DM: $n=16/131$, 12.2%), sepsis (T1DM: $n=10/287$, 3.5%; T2DM: $n=11/131$, 8.4%), alcohol (T1DM: $n=12/287$, 4.2%; T2DM: $n=3/131$, 2.3%), drug induced (T1DM: $n=2/287$, 0.7%; T2DM: $n=3/131$, 2.3%) and trauma (T1DM: $n=2/287$, 0.7%; T2DM: $n=0/131$, 0.0%).

Conclusion

DKA is no longer synonymous with T1DM and we are now seeing significant DKA case numbers in T2DM. The precipitating factors differed between the two types of diabetes and these results can help allocate resources for improved education and individualised clinical care appropriately to minimise morbidity and mortality associated with an eminently preventable condition.

DOI: 10.1530/endoabs.81.RC10.6

RC10.7

Knowledge about Diabetic Ketoacidosis in Patients with Type 1 Diabetes mellitus – Data of a Patient-centered Questionnaire

Matthias Hepprich[1,2,3], Sebastian Stiebitz[1], Bernd Schultes[4], Daniela Schmitz[5], Barbara Felix[6], Jonas Rutishauser[7], Sabine Schubert[8], Pia Roser[9], Jens Aberle[9] & Gottfried Rudofsky[2]

[1]University Hospital Basel, Department of Endocrinology, Diabetes and Metabolism,, Basel, Switzerland; [2]Kantonsspital Olten, Olten, Switzerland, Stoffwechselzentrum, Olten, Switzerland; [3]Charité Universitätsmedizin, Medizinische Klinik für Endokrinologie, Berlin, Germany; [4]Stoffwechselzentrum St. Gallen - friendlyDocs AG, St. Gallen, Switzerland; [5]Gesundheitszentrum Fricktal, Endcrinology Rheinfelden, Rheinfelden, Switzerland; [6]Kantonsspital Basel-Land, Endocrinology, Bruderholz, Switzerland; [7]MedCenter Volta, Basel, Switzerland; [8]Diabetespraxis Buxtehude, Buxtehude, Germany; [9]University Hospital Hamburg-Eppendorf, Section Endocrinology and Diabetology, Hamburg, Germany

Background/Introduction

Diabetic ketoacidosis (DKA) is a severe complication of diabetes mellitus type 1 (T1DM) with potentially life-threatening course. Data on patient knowledge about DKA in German-speaking countries is rare. Thus, we aimed to gather data about T1DM patients' knowledge in terms of DKA.

Methods

Together with two T1DM patients and an experienced diabetes counselor, we developed an anonymous questionnaire covering general knowledge about DKA, as well as baseline health and social characteristics. First, health care professionals rated patient's knowledge about their management of diabetes and DKA from 0 (no idea) to 10 (best knowledge) and patients were then asked to fill out the questionnaire at the end of their outpatient clinic appointment. Filling out the questionnaire was fully voluntary.

Results

5 Swiss and 1 German endocrine outpatient clinics participated in the study. In total, 333 questionnaires were collected. Patients had a mean diabetes duration of 22 years (SD 15), and 109 (33.5%) patients used insulin pumps and the remainder basal/bolus insulin therapy. 176 patients (54%) stated that they were male and 148 (45%) female. Mean age was 47 years (SD 16). 78 patients (24%) were not familiar with the term "diabetic ketoacidosis" and 25 (7.7%) were unsure about it. The patients' personal knowledge on DKA was rated significantly lower by themselves (mean 4.33, SD 3.11 vs 5.60, SD 2.34; $P<0.0001$) compared to their physicians' assessment but correlated significantly ($r=0.268$, 95% CI [0.1253; 0.3992]; $P=0.0002$). 46% of patients were not able to name any symptom and 44% could not spontaneously think of possible causes of DKA. When presented with multiple answers to choose from, thirst (74%), polyuria (66%), sleepiness (66%) and nausea/vomiting (51%) were among the most frequently picked. As causes of DKA, 61% stated "missed insulin injection" and 54% "illness". 185 (64%) patients do not test for ketone bodies at all. About 40% of all patients felt secure in treating DKA with 206 patients (67%) wanting more information about the condition.

Conclusion
Patient knowledge about DKA is insufficient, especially symptoms and causes are not well understood. However, most patients would like to have more information about DKA, making it a good point to start from in the attempt to reduce DKA prevalence.

DOI: 10.1530/endoabs.81.RC10.7

RC10.8

Long-term treatment with glucagon-like peptide-1 (GLP-1) receptor agonists: a real-life study

Sara Piccini[1,2], Giuseppe Favacchio[2], Gherardo Mazziotti[1,2], Andrea Lania[1,2] & Marco Mirani[2]
[1]Humanitas University, Biomedical Sciences, Pieve Emanuele (MI), Italy; [2]IRCCS Humanitas Research Hospital, Endocrinology, Diabetology and Andrology Unit, Rozzano, Italy

RCTs and real-life studies have shown the efficacy of GLP-1 RAs on weight loss, glycemic outcomes, and prevention of cardiovascular (CV) events, but long-term data are lacking. This was a retrospective cohort study of 253 patients with a first prescription of a GLP-1 RA between 2009 and 2016 and a minimum follow-up of 5 years. The endpoints of the study were weight and glycemic outcomes. Secondary endpoints were the occurrence of renal and CV events, comparing patients with GLP-1 RA treatment durations over 5 years and under 5 years. Median follow-up was 8.15 years (5.01 to 11.74 years). Mean duration of GLP-1 treatment was 5.4 years (SD 3.2). The mean proportion of follow-up time on GLP-1 RA treatment was 69.6%. The proportion of patients still taking the GLP-1 RA was 85.1% at 1 year, 76.7% at 2 years, 64.1% at 4 years, 56.9% at 6 years, 57.7% at 8 years, and 56.3% at 10 years. Younger age at baseline, higher baseline HbA1c, and being hospitalized for heart failure were associated with a shorter time to GLP-1 RA discontinuation. Switching from any other GLP-1 RA to dulaglutide or semaglutide, and greater decreases in HbA1c at 1 and 2 years were associated to longer time to treatment discontinuation. Comparing patients who had withdrawn GLP-1 RA therapy and those with ongoing GLP-1 RA at each time point, there were significant differences in mean HbA1c (7.81% vs 7.16% at 6 years, 8.08% vs 6.85% at 8 years, 8.26% vs 6.69% at 10 years respectively), and mean weight loss (-1.4 vs -5.6 kg at 6 years, -1.0 vs -6.8 kg at 8 years respectively), except for mean weight loss at 10 years. In the shorter treatment duration group (<5 years on GLP-1) there was a higher proportion of strokes/transient ischemic attacks (7.5% vs 1.3% in the group treated for over 5 years, $P=0.014$). Acute coronary syndromes were more frequent in the shorter treatment duration group, although not statistically significantly (6.5% vs 3.8% respectively, $P=0.37$). No differences in arterial revascularization procedures, no differences in renal outcomes or hospitalizations for heart failure were observed. There were no deaths for CV causes. The study showed that GLP-1 RA treatment maintains its favorable effects on HbA1c and weight over time. The reduction in atherosclerotic events, mainly driven by stroke protection, is consistent with RCT studies and therefore reinforces the long-term use of these antidiabetic medications in real life.

DOI: 10.1530/endoabs.81.RC10.8

Thyroid 2

RC11.1

Impact of Covid-19 disease on thyroid function: longitudinal study

Ilaria Muller[1,2], Matteo Varallo[3], Anita Daturi[3], Tiziana E Re[4], Davide Dazzi[5], Virgilio Longari[6], Andrea Gori[7,8], Giovanna Mantovani[1,2], Maura Arosio[1,2] & Mario Salvi[2]
[1]University of Milan, Department of Clinical Sciences and Community Health, Milan, Italy; [2]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico di Milano, Endocrinology, Milan, Italy; [3]University of Milan, Milan, Italy; [4]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico di Milano, Department of Medicine - Acute Medical Unit, Milan, Italy; [5]Casa di Cura Val Parma SRL; [6]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico di Milano, Nuclear Medicine; [7]University of Milan, Department of Pathophysiology and Transplantation; [8]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico di Milano, Infectious Diseases, Milan, Italy

Background
The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic disease (Covid-19) affects thyroid function with different mechanisms: non-thyroidal illness syndrome (NTIS), direct infection of thyroid gland and cytokine storm. We provided the first description of painless atypical thyroiditis coexisting with NTIS in patients hospitalised for moderate-to-severe Covid-19 disease. We aimed to: 1) correlate thyroid dysfunction with Covid-19 disease severity; 2) follow the evolution of thyroid function over time.
Methods
Baseline (at hospital admittance) and longitudinal study of patients hospitalised for moderate-to-severe Covid-19 disease, without known history of thyroid disfunction, assessing serum thyroid function and autoantibodies, inflammatory markers and thyroid ultrasound scan (US). Patients showing at US focal hypoechoic areas suggestive for thyroiditis (thyroiditis-areas) also underwent thyroid 99mTc or I123 uptake scan.
Results
183 Covid-19 patients were studied baseline, of whom 63 (34%) were already on steroid treatment before hospital admission, thus were not considered for TSH analysis. Decreased serum TSH positively correlated with albumin ($P=0.02$) and lymphocyte count ($P<0.01$) but not with C-reactive-protein ($P=0.12$) and interleukin-6 ($P=0.10$); TSH also progressively and inversely correlated to the need of oxygen support ($P=0.02$). Serum FT3 correlated positively with albumin ($P<0.01$) and inversely with D-dimer ($P=0.02$). Baseline thyroid US scan showed thyroiditis-areas in 18/65 (28%) patients, associated with reduced thyroid uptake at $^{99m}Tc/I^{123}$ scintigraphy in 14/17 (82%) cases. Thyroiditis-areas were more frequent among patients with baseline low TSH (6/10, 60%) compared with those with normal TSH (10/40, 25%, $P=0.034$). The patients with thyroiditis-areas also had higher baseline FT4 ($P=0.018$) and IL-6 ($P=0.016$) compared with those with normal thyroid US. Follow-up analysis was conducted in 75/183 (41%) patients; thyroid function and inflammatory markers normalized at all time-points in nearly all cases and no increase of thyroid autoantibodies positivity was observed. The thyroiditis-areas, even if often reduced in size, were still present after 6 and 12 months in 13/15 (87%) and 6/12 (50%) patients, respectively. After 9 months the thyroid uptake at $^{99m}Tc/I^{123}$ scintigraphy was still reduced in 4/6 (67%) patients, even if partially recovered (mean +28%) compared with baseline.
Conclusions
Thyroid dysfunction during moderate-to-severe Covid-19 disease is mild and transient, and thyroid hormones correlate with disease severity. Thyroiditis-areas at US occur frequently and may persist after one year, even if reduced in size; long-term consequences are unknown. The association of thyroiditis-areas with low TSH and high FT4 and IL-6 serum concentrations support the hypothesis of direct thyroid gland involvement in SARS-CoV-2 infection.

DOI: 10.1530/endoabs.81.RC11.1

RC11.2

Subacute thyroiditis (SAT) during the COVID-19 pandemic: preliminary data from the "ESE Covid Grant 2021" project

Simona Loiacono[1,2], Eleonora Zanni[1,2], Roberta Sueri[1,2], Sara De Vincentis[1,2], Maria Laura Monzani[1,2], Francesco Di Marco[3], Ilaria Muller[4,5], Manuela Simoni[1,2], Daniele Santi[1,2] & Giulia Brigante[1,2]
[1]Unit of Endocrinology, Department of Medical Specialties, Azienda Ospedaliero-Universitaria of Modena, Modena, Italy, Italy; [2]Unit of Endocrinology, Department of Biomedical, Metabolic and Neural Sciences, University of Modena and Reggio Emilia, Modena, Italy; [3]School of Specialisation in Endocrinology, University of Milan, Milan, Italy; [4]Department of Clinical Sciences and Community Health, University of Milan, Milan, Italy; [5]Department of Endocrinology, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy

Introduction
A possible association between the severe acute respiratory syndrome coronavirus (SARS-CoV)-2 pandemic, in terms of infection and/or vaccination, and subacute thyroiditis (SAT) has been recently reported. Although a higher SAT incidence in pandemic has been described, data are still conflicting.
Aim
To determine SAT incidence in Italy during the SARS-CoV-2 pandemic and to characterize clinical peculiarities and response to medical treatment of SAT cases, correlating them to virus exposure and/or vaccine.
Methods
We are performing a prospective, longitudinal, observational, 3-year, multicentre study. All subjects with clinical diagnosis of SAT since November 2020 are enrolled and followed-up for 12 months. During medical history collection, SARS-CoV-2 infection (defined as a positive *rhino*-pharyngeal *swab* obtained before SAT onset) and vaccination were recorded. In order to evaluate SAT course, patients were evaluated at 1, 3, 6 and 12 months after onset with thyroid ultrasonography and blood examinations. This is an interim analysis considering baseline visit performed in two centres (Modena and Milan).

Results
A total of 51 subjects (40 females, 11 males) with SAT have been enrolled so far (age: 50.1 + 11.6 years, BMI: 23.5 + 3.5 kg/m^2). Personal or familiar thyroid disease history was reported in 14 (28%) and 25 (50%) patients, respectively. One (2%) patient had familiar history of SAT. At SAT diagnosis, 36 patients were thyrotoxic (72%) and 5 hypothyroid (10%). TSH serum level was 2.3 + 7.3 microUI/ml, with mean fT4 20.0 + 14.0 pg/ml, and fT3 4.8 + 2.6 pg/ml. Moreover, 30 patients (60%) had elevated erythrocyte *sedimentation rate* (ESR), 27 (54%) elevated high-sensitivity C-reactive protein (hs-CRP), 12 (24%) high thyroglobulin (Tg) serum levels. The cohort was divided according to either SARS-Cov2 infection (9 patients – 18%) or vaccination (18 patients – 36%) . Considering patients with previous infection, the thyrotoxicosis rate raised up to 88.9%. However, the thyrotoxicosis rate ($P = 0.286$), ESR ($P = 0.520$), hs-CRP ($P = 0.585$) and Tg ($P = 0.178$) elevations were not significantly different between patients with or without SARS-Cov2 infection. Similarly, thyrotoxicosis rate (72.2 vs 64.9%, $P = 0.468$), ESR ($P = 0.268$), hs-CRP ($P = 0.173$) and Tg ($P = 0.712$) elevations were not different between patients with or without SARS-Cov2 vaccination.
Conclusion
Our preliminary data suggest that both SARS-CoV-2 infection and vaccination have no impact on the general clinical SAT presentation. Only high thyrotoxicosis rate at diagnosis, especially in patients with previous SARS-CoV-2 infection has emerged. SAT incidence during pandemic will be evaluated at the end of the study.

DOI: 10.1530/endoabs.81.RC11.2

RC11.3

Is the pre-conceptional TSH optimization useful in women submitted to assisted reproduction technology?

Guia Maria Vannucchi[1], Irene Campi[1], Serena Cagnina[2], Danila Covelli[3], Luca Persani[1], Mario Mignini Renzini[4] & Laura Fugazzola[1]
[1]Italian Auxological Institute San Luca Hospital Emergency Room, Milano, Italy; [2]Università Degli Studi Di Torino Dipartimento Scienze Mediche, Torino, Italy; [3]ASST Bergamo EST, Seriate, Italy; [4]Zucchi Monza Clinical Institute, Monza, Italy

Background
thyroid function (TSH levels) and thyroid autoimmunity are involved in the immunomodulation of early pregnancy stages and can affect assisted reproductive technology (ART).
Aims
1) to evaluate if pre-conceptional TSH is associated with an increased risk of miscarriage, 2) to identify a TSH cut-off significantly associated with risk of miscarriage, 3) to assess the impact of TSH levels on primary and surrogate outcomes.
Methods
We retrospectively studied 1484 infertile women (mean ± age 36.7 ± 4.1 years, mean ± SD BMI 22.7 ± 4) submitted to IVF in a single center from 2004 and 2014. 60,8% and 39.2% of cycles were performed in women affected with primary and secondary infertility, respectively. Primary outcomes were biochemical pregnancy, clinical pregnancy, miscarriage and delivery. Surrogate outcomes were the number of oocytes, the number of embryos and the transfer of embryos.
Results
In 86% of cycles an embryo transfer was performed. 369/1274 (29%) of patients had a biochemical pregnancy and 146 of them experienced a pregnancy loss. Moreover, among the 146 women with pregnancy loss, 52 (36%) were clinically pregnant and had a miscarriage in the first trimester, while in 94 patients (64%) a biochemical pregnancy without clinical evolution was documented. No significant differences in mean TSH levels were recorded between women with different time of miscarriage. By a ROC curve analysis we found that a TSH of 3 mU/l was significantly associated with miscarriage ($P = 0.001$), while a TSH of 2.3 mU/l was associated with a higher chance to have a biochemical pregnancy. We further studied the relationship between the two TSH thresholds (2.5 or 3 mU/l) with surrogate outcomes and we observed a weak association between TSH $<= 2.5$ mU/l with the number of retrieved oocytes ($P = 0.04$) while no significant correlation was found with the number of embryos either obtained or transferred ($P =$ NS).
Conclusion
In women undergoing IVF, lower pre-conceptional TSH levels seems to favor the embryo implantation and reduce the risk of early pregnancy loss. These data strongly indicate the need for TSH screening prior to IVF procedures and suggest LT4 treatment in order to optimize TSH before ovarian stimulation.

DOI: 10.1530/endoabs.81.RC11.3

RC11.4

The "real-life" thyroid function tests results during pregnancy in the longitudinal observation

Malgorzata Trofimiuk-Muldner[1], Andrzej Nowak[2], Grzegorz Sokolowski[1], Monika Buziak-Bereza[4], Andrzej Lewiński[3], Małgorzata Karbownik-Lewińska[4] & Alicja Hubalewska-Dydejczyk[1]
[1]Jagiellonian University Medical College, Chair and Department of Endocrinology, Kraków, Poland; [2]Medical University of Warsaw, Department of Gynecological Endocrinology, Warszawa, Poland; [3]Medical University of Lodz, Chair and Department of Endocrinology and Metabolic Diseases, Lodz, Poland; [4]Medical University of Lodz, Chair and Department of Oncological Endocrinology, Lodz, Poland

The reference ranges of thyroid function tests during pregnancy are still being debated, even in ethnically homogenous populations. The defining of the normal range is of importance, as it influences therapeutic decisions, particularly the use (or over-use) of levothyroxine in this vulnerable population. The study was aimed at the longitudinal assessment of thyroid function tests results in marginally iodine sufficient Polish population of pregnant women. The study was performed between 2007-2017 as a part of the Polish National Programme for Elimination of Iodine Deficiency. The study included 1405 pregnant women (222 – 1st trimester, 561 – 2nd trimester, 622 – 3rd trimester of pregnancy) of median age 29 years (IQR - 6 years). In each woman serum TSH, FT4, FT4 and aTPO, as well as urinary iodine concentration (UIC) in a urine spot sample, were measured.
Results
Median TSH was, respectively: 1st trimester – 1.22 mIU/l (IQR – 1.42 mIU/l; 2.5–97.5 percentile: 0.04–4.02 mIU/l); 2nd trimester – 1.63 mIU/l (IQR – 1.28 mIU/l; 2.5–97.5 percentile: 0.19–4.42 mIU/l), 3rd trimester – 1.61 mIU/l (IQR – 1.13 mIU/l; 2.5-97.5 percentile: 0.3–4.28 mIU/l). There was no significant yearly difference in TSH concentrations. Median FT4 was, respectively: 1st trimester 15.19 pmol/l (IQR-2.37 pmol/l; 2.5–97.5 percentile: 11.65-21.68 pmol/l), 2nd trimester - 12.69 pmol/l (IQR-2.61 pmol/l; 2.5p–97.5 percentile: 9.29-17.32 pmol/l), 3rd trimester – 11.95 pmol/l (IQR -2.97 pmol/l; 2.5-97.5 percentile: 8.56–17.26 pmol/l). ATPO positivity was found in 18%, 15%, and 9% of pregnant women in the 1st, 2nd and 3rd trimester, respectively. Median TSH in aTPO-negative women was, respectively: 1st trimester – 1.11 mIU/l (2.5-97.5 percentile: 0.03–3.75 mIU/l), 2nd trimester 1.57 mIU/l (2.5-97.5 percentile: 0.18-4.18 mIU/l), 3rd trimester 1.60 mIU/l (2.5-97.5 percentile: 0.35-4,23). ATPO negative and positive women in the 1st and 2nd trimester of pregnancy differed significantly in mean TSH concentrations (1st trimester: 1.31 vs 2.24 mIU/l, $P = 0.002$; 2nd trimester: 1.73 vs 2.25 mIU/l, $P = 0.001$; 3rd trimester 1.78 vs 2.02 mIU/l, $P = 0.230$). The significant difference in FT4 according to aTPO status was found only for the 3rd trimester ($P = 0.020$). No difference was found between those groups in FT3 and UIC concentrations. The stepwise regression model failed to find significant relation between TSH and pregnancy week, aTPO positivity, and UIC.
Conclusions
Our results support the view that the upper TSH range in pregnancy is only slightly lower than in a general population. Therefore, more caution is needed while diagnosing hypothyroidism and deciding on treatment with levothyroxine during gestation.

DOI: 10.1530/endoabs.81.RC11.4

RC11.5

Which factors can influence the occurrence of two nondiagnostic results in fine-needle aspiration cytology of the same thyroid nodule?

Ines Cosme, Catarina Silvestre & Maria João Bugalho
Centro Hospitalar Universitário Lisboa Norte, Serviço de Endocrinologia, Diabetes e Metabolismo, Portugal

Introduction
Fine-needle aspiration cytology (FNAC) of thyroid nodules can be associated with non-diagnostic (ND) results, despite the usage of ultrasound (US) guidance. It is recommended to repeat the FNAC because of the possible risk of malignancy in these nodules.
Aim
To evaluate the influence of demographic, clinical and echographic characteristics in the recurrence of ND FNAC in a thyroid nodule.
Methods
Retrospective review of ND thyroid FNAC performed between 2017-2020. Demographic and clinical data (age, gender, cervical radiotherapy, presence of *Hashimoto's* thyroiditis and TSH value) and US characteristics (nodules' size, echogenicity, composition and microcalcifications) were collected at the moment of the first ND FNAC.
Results
Of 230 nodules with a first ND FNAC (patients' mean age 60.2 ± 14.1 years, 83% women), 195 (84.8%) were submitted to another FNAC, 9 (3.9%) were submitted

to surgery (only 1 had a malignant histology) and 26 (11.3%) remained under US surveillance. The second FNAC result was: benign in 121 cases, non-diagnostic in 63, indeterminate in 9 and malignant in 2. Concerning demographic and clinical data, there was a higher risk of a second ND FNAC in patients treated with anticoagulant/anti-aggregating agents (OR 2.2, 1.1-4.7, $P=0.03$). Men had a reduced risk of a second FNAC (OR 0.4, 0.2-0.9, $P=0.016$). Patients who had a second ND FNAC were older (63.4 ± 14 vs 59 ± 14 years; $P=0.032$). Previous cervical radiotherapy and *Hashimoto's* thyroiditis did not influence the risk of a second ND FNAC. Regarding echographic characteristics, nodules' echogenicity differed between the ND and diagnostic FNACs (hypoechogenic 71.9% vs 52.4%, hyperechogenic 1.6% vs 6.6% and isoechogenic 26.6% vs 41.8%; $P=0.031$); however, nodules' composition was not significantly different between them. Nodules' microcalcifications increased the risk of ND FNAC (OR 2.2, 1.1-4.5, $P=0.03$). Nodules' size and TSH value were not significantly different between ND and diagnostic FNACs. Eight out of 63 cases with a second ND FNAC were submitted to surgery (all with benign histology), 17 were submitted to a third FNAC (8 benign, 6 ND and 3 indeterminate), in 21 was decided US follow-up and 17 patients dropped out of the study. No malignant diagnosis was found in the nodules with 3 ND FNAC.

Conclusion

In the current series, a second ND FNAC occurred in almost one third of cases. Female gender, older age, treatment with anticoagulant or antiaggregating agents, hypoechogenic nodules and the presence of microcalcifications are likely to influence results. In addition, these nodules were rarely malignant (1.3%).

DOI: 10.1530/endoabs.81.RC11.5

RC11.6

Association of thyroid hormones with clinical status and cardiovascular outcomes of HFpEF patients

Ana Rita Leite[1], Joao Sergio Neves[1,2], Francisco Vasques-Nóvoa[1,3], Francisca A Saraiva[1], Ana Cristina Oliveira[1], Madalena von Hafe[1,4], Catarina Vale[1,3], António Angélico-Gonçalves[1] & Adelino F Leite-Moreira[1]
[1]Department of Surgery and Physiology, Faculty of Medicine, University of Porto, Porto, Portugal; [2]Department of Endocrinology, Centro Hospitalar Universitário de São João, E.P.E, Porto, Portugal; [3]Department of Internal Medicine, Centro Hospitalar Universitário de São João, E.P.E, Porto, Portugal; [4]Department of Pediatrics, Centro Hospitalar Universitário de São João, E.P.E, Porto, Portugal

Introduction

Heart failure with preserved ejection fraction (HFpEF) is a clinical syndrome with high mortality, for which there are few disease modifying therapeutics. Thyroid axis dysfunction is common in heart failure (HF) and may contribute to the pathogenesis of HFpEF. However, the association of thyroid hormones (TH) with the clinical status of HFpEF patients and their prognostic impact in this syndrome are not clear.

Methods

We evaluated 93 participants with stable HFpEF followed in our centre. We categorized participants according to TH tertiles. A cross-sectional analysis was performed to analyse associations of TH with clinical parameters, and B-type natriuretic peptide (BNP) and high-sensitivity troponin I (hs-TnI) levels. Ordered logistic and linear regression models were used. Associations between TH and a composite endpoint of diuretic intensification, HF hospitalization or all-cause death were assessed using Cox proportional hazard models. These analyses were adjusted for clinically relevant variables.

Results

The mean age of the participants was 73.9 years and 46% were women. Half (51%) had a NYHA class II. In comparison to participants with free T3 (FT3) levels in the upper tertile (2.74 – 3.5 pg/ml), participants with FT3 levels in the lower tertile (1.86 - 2.44 pg/ml) had a higher prevalence of orthopnea (OR= 5.57 [1.14 - 27.16]; $P=0.034$) and higher levels of BNP (= 0.53 [0.02–1.03]; $P=0.041$). On the other hand, participants with free T4 (FT4) levels in the lower tertile (0.72 – 0.98 ng/dl) had a trend for a lower prevalence of orthopnea (OR= 0.28 [0.07 – 1.06]; $P=0.061$) and lower levels of hs-TnI (=-0.41 [-0.82 – 0.00]; $P=0.050$), comparing with participants with FT4 levels in the upper tertile (1.10–1.65 ng/dl). Over a median of 1037 days of follow-up, 48 persons had at least one of the events included in the composite endpoint. Participants with FT3/FT4 ratio levels in the lower tertile had a higher risk of the composite outcome (HR=2.19 [1.01 – 4.76]; $P=0.047$), comparing with participants with FT3/FT4 ratio levels in the upper tertile.

Conclusions

Lower levels of FT3 and higher levels of FT4 are associated with a worse clinical status. A lower FT3/FT4 ratio at baseline is associated with increased risk of a combined outcome of diuretic intensification, HF hospitalization or all-cause mortality. These results lead us to the hypothesis that FT4 to FT3 conversion might be impaired in patients with HFpEF. This impairment could be an important player in the progression of the disease.

DOI: 10.1530/endoabs.81.RC11.6

RC11.7

Altered expression profiles of miR-22-5p and miR-142-3p display Hashimotós disease and are associated with thyroid antibodies

Olivia Trummer[1], Ines Föß[1], Natascha Schweighofer[1,2], Edi Arifi[1], Christoph Haudum[1,2], Sharmaine Reintar[1,2], Stefan Pilz[1], Verena Theiler-Schwetz[1], Christian Trummer[1], Andreas Zirlik[3], Albrecht Schmidt[3], Caterina Colantonio[3], Ewald Kolesnik[3], Nicolas Verheyen[3], Thomas Pieber[1,2] & Barbara Obermayer-Pietsch[1]
[1]Medical University of Graz, Division of Endocrinology and Diabetology, Graz, Austria; [2]Center for Biomarker Research in Medicine, Graz, Austria; [3]Medical University of Graz, Department of Cardiology, University Heart Center Graz, Graz, Austria

Background

Hashimoto's thyroiditis (HT), the most prevalent autoimmune disorder of the thyroid (AITD) is characterized by the presence of circulating autoantibodies, induced by a not fully understood dysregulation of the immune system. MicroRNAs (miRNAs) are small noncoding RNAs, which can play a pivotal role in immune functions and the development of autoimmunity. The aim of the present investigation was to evaluate whether a panel of nine selected miRNAs differs in serum expressions of patients with HT and to analyse possible relations to thyroid antibody levels.

Methods

Participants of the BioPersMed cohort ($n=1022$), an ongoing single-centre, prospective, observational study to evaluate novel biomarkers for the assessment of cardiovascular and common metabolic diseases, were screened for previously diagnosed HT patients ($n=27$) as well as age and sex matched participants suitable as healthy controls ($n=22$). Thyroid function and common autoantibodies were evaluated by serum levels of thyroid stimulating hormone (TSH), free triiodothyronine (fT3), free thyroxine (fT4), thyroid peroxidase autoantibody (TPOAb) as well as thyroglobulin autoantibodies (TgAb), determined by luminescence immunoassays (Siemens, Erlangen, Germany). MiRNA profiles were analysed in the selected samples using quantitative reverse transcription polymerase chain reaction (qRT-PCR).

Results

Systemic expressions of miR-21-5p, miR-22-3p, miR-22-5p, miR-142-3p, miR-146a-5p and miR-451 were significantly upregulated in patients with HT ($P<0.01$, respectively) and indicate HT in receiver-operating characteristic (ROC) analysis with an area under the curve of at least 0.76 (95% confidence interval 0.61-0.91) for miR-22-5p. Subgroup analyses within HT patients showed significantly higher miRNA expression for miR-22-5p and miR-142-3p in HT patients with higher thyroid antibody levels (TgAb and/or TPOAb >60 U/ml, $n=13$) as compared to HT patients with lower thyroid antibody levels (TgAb and/or TPOAb <60 U/ml, $n=11$).

Conclusion

Upregulated systemic expression levels of miR-22-5p and miRNA-142-3p indicate HT and were related with higher levels of thyroid antibodies suggesting a contribution to the pathogenesis of HT.

References

1. Trummer, O.; Foessl, I. Schweighofer, N.; Arifi, E.; Haudum, C.W.; Reintar, S.; Pilz, S.; Theiler-Schwetz, V.; Trummer, C.;Zirlik, A.; et al. Expression Profiles of miR-22-5p and miR-142-3p Indicate Hashimoto's Disease and Are related to Thyroid Antibodies. *Genes* 2022, **13**, 171. https://doi.org/10.3390/genes13020171.

DOI: 10.1530/endoabs.81.RC11.7

Reproductive and Developmental Endocrinology

RC12.1

RS 2247911 polymorphism of GPRC6A gene and serum under-carboxylated-osteocalcin are associated with testis function

Kenda Jawich[1], Maria Santa Rocca[2], Sahar Al Fahoum[1], Marwan Alhalabi[3], Andrea Di Nisio[4], Carlo Foresta[4], Alberto Ferlin[4] & Luca De Toni[4]
[1]Damascus University, Department of Biochemistry and Microbiology, Faculty of Pharmacy, Syria; [2]Padova University Hospital, Department of Medicine, Italy; [3]Damascus University, Department of Embryology and

Reproductive Medicine, Faculty of Medicine, Syria; [4]University of Padova, Department of Medicine, Italy

Purpose
Undercarboxylated-OCN (ucOCN), acting on the receptor GPRC6A, was shown to stimulate of testosterone (T) production in Leydig cells in rodents, in parallel with the hypothalamus/pituitary/gonadal axis mediated by luteinizing hormone (LH). Hence, reduced serum ucOCN and/or inactivating gene variants of GPRC6A, are supposed to affect testis function in humans. The aim of this study is to evaluate the association among serum ucOCN, rs2247911 GPRC6A gene polymorphism and the endocrine/reproductive pattern in a cohort of Syrian infertile males, possibly confirming the role of ucOCN/GPRC6A axis on testis function.
Methods
A total of 172 males, including 62 oligozoospermic,51 azoosperminc patients and 59 age-matched normozoospermic controls, were prospectively recruited at the Orient Hospital for Assisted Reproduction Treatment (Syria) and evaluated for the hormonal pattern, serum OCN, glycemic and lipid profile. Screening for rs2247911 GPRC6A gene polymorphism was also performed.
Results
Serum ucOCN correlated positively with total sperm count, sperm morphology and motility, total T, E2 and HDL-cholesterol, and negatively with LH, FSH, and LDL-cholesterol. Patients bearing the GG genotype of rs2247911 polymophism had higher sperm count ($P=0.008$), progressive motility($P=0.05$), normal morphology($P=0.009$), T ($P=0.003$), HDL-cholesterol ($P=0.008$) and lower triglycerides levels ($P<0.001$) compared to patients bearing AG and AA genotypes. Aside of LH levels, rs2274911 gene polymorphism ($P=0.024$), and to a minor extent ucOCN, were major predictors of serum T at linear stepwise regression analysis.
Conclusions
The novel ucOCN/GPRC6A axis was confirmed to participate in the regulation of the endocrine and reproductive function of the testis through the production of T.

DOI: 10.1530/endoabs.81.RC12.1

RC12.2

Proteomic changes in response to electrical stimulations in skeletal muscle of women with PCOS

Gustaw Eriksson[1], Emma Nilsson[2], Roberto Boi[3], Jenny Nyström[3], Elisabet Stener-Victorin[1] & Anna Benrick[3]
[1]Karolinska Institute, Dept. of Physiology and Pharmacology, Stockholm, Sweden; [2]Lund University, Department of Clinical Sciences, Lund University Diabetes Centre, Malmö, Sweden; [3]University of Gothenburg, Inst. of Neuroscience and Physiology, Gothenburg, Sweden

Polycystic ovary syndrome (PCOS) is an endocrine and metabolic disorder affecting women of reproductive age. The main features of PCOS are hyperandrogenism and reproductive and metabolic dysfunctions. We have previously shown that muscle contractions induced by either electrical stimulations or exercise act through partially similar signaling pathways in the muscle to induce glucose uptake in the acute response. Long-term electrical stimulations decrease circulating testosterone, HOMA-IR, and HbA1c in overweight/obese women with PCOS, but the mechanism is largely unknown. Here, we used transcriptomic and proteomic analyses to provide new mechanistic explanations to the improved glucose homeostasis in response to 30 min of electrical stimulations, 3 times/week for 5 weeks. Skeletal muscle biopsies from 10 women with PCOS were subjected to global methylation, transcriptomics and proteomic analysis at baseline and after 5 weeks of treatment. Changes in protein expression between baseline and after treatment were based on Student's t-test ($P<0.05$) and a fold change $>50\%$. Changes in skeletal muscle DNA methylation and gene expression in response to electrical stimulation were based on linear regression analysis ($P<0.01$) and a fold change $>20\%$. 12 unique transcripts exhibited increased expression in skeletal muscle after 5 weeks of treatment. Four types of collagens were upregulated, and together with *VCAN* and *LUM*, these genes were confirmed by gene ontology analysis to play a role in extracellular matrix organization and skeletal system development. Next, we analyzed if the response to electrical stimulation involved DNA methylation changes in skeletal muscle. The absolute changes in methylation were small and ranged from -1.29% to $+0.72\%$ points. The vast majority of the 43 significant CpG sites (75%) displayed decreased DNA methylation in response to electrical stimulation. Since relatively few genes and methylation sites were regulated in response to repeated electrical stimulations, we investigated if the long-term effects were regulated at the protein level. More than 300 proteins changed expression after treatment. 97% of these were upregulated and enriched pathways involved exocytosis, extracellular matrix organisation, integrin-mediated signalling, transforming growth factor production, and protein metabolic processes. Collagen 1A1 and 1A2 were upregulated both at the gene and protein expression level after electrical stimulation. One can speculate that up-regulation of integrins, collagens, and transforming growth factor-beta-1 likely lead to ECM remodeling, which can provide protective adaptation to repeated stimulation, and improved muscle strength and function. In conclusion, changes at the protein level mediate the response to long-term electrically stimulated muscle contractions.

DOI: 10.1530/endoabs.81.RC12.2

RC12.3

Binding affinity affecting SHBG SNPs do not majorly affect calculated estimates of free testosterone

Joeri Walravens[1], Thiberiu Banica[1] , Tibbert Van Den Eynde[1], Gido Snaterse[1], Tim Reyns[2], Nick Narinx[3], Leen Antonio[3], Tom Fiers[2] , Jean-Marc Kaufman[1] & Bruno Lapauw[1]
[1]Ghent University Hospital, Department of Endocrinology, Ghent, Belgium; [2]Ghent University Hospital, Laboratory for Clinical Biology, Ghent, Belgium; [3]Leuven University Hospital, Department of Endocrinology, Leuven, Belgium

Introduction
According to the free hormone transport hypothesis, only free testosterone (FT) is considered biologically active. Due to low circulating levels and technical challenges of direct FT measurements, calculators have been developed to estimate FT from serum total T, sex hormone-binding globulin (SHBG) and albumin levels. However, genetic polymorphisms altering SHBG's binding affinity or capacity might result in calculation imprecisions with consequent incorrect diagnosis in these individuals.
Objective
Investigating the prevalence of SHBG single-nucleotide polymorphisms (SNPs) in healthy men and evaluating differences in SHBG, total T, calculated FT (cFT) and measured FT (mFT) levels in SHBG SNP-carriers.
Methods
Population-based sibling-pair study, comprising 999 healthy men aged 24-46 years in whom genotyping was performed (LGC Genomics) for SNPs suggested to affect binding affinity and/or concentration of SHBG (rs6258, rs6259, rs146779355, rs145273466, rs368589266, rs143269613, rs373769356, rs143521188). SHBG and total T concentrations were measured by immunoassay and LC-MS/MS, respectively. FT levels (cFT; using the Vermeulen-formula) and free T-ratio (FT/total T) were calculated. In a subset of participants (145, 10 and 40 individuals for WT/WT, WT/rs6258 and WT/rs6259, respectively) FT was measured directly using LC-MS/MS after equilibrium dialysis (mFT). The difference between cFT and mFT was calculated and expressed as percentage of mFT (delta%). Parameters were compared by t-test or Mann-Whitney test depending on normality; method-comparison was performed using Passing-Bablok regression.
Results
11/971 (1%) and 0/971 participants were hetero- and homozygote for rs6258; 135/681 (20%) and 9/681 (1%) were hetero- and homozygote for rs6259, respectively. No other SNPs were detected. Versus wild-type, heterozygote rs6258 carriers had lower SHBG (26.5 nmol/l vs 38.5 nmol/l) and total T levels (468.8 ng/dl vs 583.9 ng/dl) but higher free T-ratio (2.3% vs 2.0% for cFT; 2.2% vs 1.7% for mFT). Heterozygote rs6259 carriers had higher SHBG levels (42.8 nmol/l vs 38.5 nmol/l) and lower free T-ratio (1.9% vs 2.0% for cFT) than non-carriers. Comparing cFT and mFT showed a significant difference in heterozygote rs6258 carriers (delta% 5.1% vs 15.4% in wild-type). No other differences nor differences in homozygote rs6259 carriers vs wild-type were observed.
Conclusion
Genetic polymorphisms suggested to affect SHBG concentration or steroid-hormone binding affinity are relatively rare in this population-based cohort of healthy men. Although carriers did present with different SHBG levels and free T-ratios compared to non-carriers, our results do not disprove the calculators' accuracy in men heterozygous for rs6258 or rs6259, despite in vitro experiments suggesting a 1.8 reduced binding affinity and reduced clearance rate respectively compared to wild-type SHBG.

DOI: 10.1530/endoabs.81.RC12.3

RC12.4

Unraveling the link between metabolism and reproduction in obese men

Georgios Papadakis[1], Favre Lucie[1], Yassine Zouaghi[1], Nathalie Vionnet[1], Nicolas Niederlander[1], Michela Adamo[1], James Acierno[1], Federico Santoni[1], Dassine Berdous[1], Alexia Spoerl[1], Emmanuelle Paccou[1], Yasser Aleman[2], Olivier Salamin[3], Patrick Hagmann[2], Andrea Messina[1] & Nelly Pitteloud[1]

[1]Lausanne University Hospital - CHUV, Service of Endocrinology, Diabetes and Metabolism, Lausanne, Switzerland; [2]Lausanne University Hospital - CHUV, Service of Diagnostic and Interventional Radiology, Lausanne, Switzerland; [3]Romand University Center of Legal Medicine, Swiss Laboratory for Doping Analyses, Epalinges, Switzerland

Introduction
Obesity is a worldwide pandemic, and in men can often be associated with hypogonadotropic hypogonadism (HH), a finding consistent with a clear link between sex steroids and reproduction. In this study, we aimed to characterize the phenotypic spectrum of male obesity, focusing on the metabolic and reproductive effect of weight loss after bariatric surgery, as well as to explore the role of central inflammation.
Methods
We conducted an observational study on 32 morbidly obese men (BMI $>$ 35 kg/m^2) scheduled to undergo Roux-en-Y Gastric Bypass (RYGB) and prospectively followed for 12 months thereafter. Nine lean men with strictly normal metabolic and reproductive status were also recruited. Obese men were categorized as either HH (ObHH, $n=15$; testosterone $<$ 10.4 nmol/l) or non-HH (ObnHH, $n=17$; testosterone $\geq$ 10.4 nmol/l). In addition to standard metabolic and reproductive profiles, a deep phenotyping consisted of Dual X-ray absorptiometry, metabolomics and blood transcriptomics. We also performed brain MRI – Diffuse Tensor Imaging (DTI) in a subset of patients before and after RYGB.
Results
Despite comparable BMI, ObHH exhibited more severe insulin resistance (HOMA-IR, $P=0.01$), a trend for expanded visceral fat ($P=0.08$) and higher systemic (serum hs-CRP, $P=0.09$) and hypothalamic inflammation (lower fractional anisotropy and higher diffusivity at DTI, $P<0.05$) as compared to ObnHH. Blood transcriptomics revealed a distinct expression profile in ObHH related to overexpression of genes implicated in inflammation and mitochondrial function, especially oxidative phosphorylation. In addition to lower testosterone levels, higher FGF21 and lower morning cortisol in the cohort of obese men strongly correlated with the transcriptomic changes. Following RYGB, all men lost substantial weight (21-39% at month 12) independent of the baseline gonadal status. Longitudinal assessment in nine men revealed a rise in plasma FGF21 at day 28 post RYGB ($P=0.04$), concomitant to the early decrease in HOMA-IR. FGF21 subsequently returned to baseline levels and decreased by month 12 ($P=0.02$). A significant reduction in plasma isoleucine levels (day 2, $P=0.01$) preceded the FGF21 peak. The extent of the FGF21 peak at day 28 significantly correlated with the degree of HH reversal at month 12 ($P=0.04$).
Conclusions
HH is a marker of metabolic syndrome in obese men, accompanied by MRI signs of altered hypothalamic structure. Serum levels of cortisol and FGF21 are additional predictors of metabolic defects. Post RYGB, FGF21 showed a unique bimodal change, tightly associated with the metabolic improvement and the recovery of obesity-induced HH.

DOI: 10.1530/endoabs.81.RC12.4

RC12.5

Association of Early Adulthood Hyperandrogenemia With Hypertension and Cardiovascular Events in Women

Katri Tuorila[1] , Meri-Maija Ollila[1] , Marjo-Riitta Järvelin[2,3,4,5], Juha Tapanainen[1,6], Stephen Franks[7], Terhi Piltonen[1], Kari Kaikkonen[8] & Laure Morin-Papunen[1]
[1]Department of Obstetrics and Gynecology, University of Oulu and Oulu University Hospital, Medical Research Center, PEDEGO Research Unit, Oulu, Finland; [2]MRC-PHE Centre for Environment and Health, Department of Epidemiology and Biostatistics, School of Public Health, Imperial College London, London, United Kingdom; [3]Center for Life Course Health Research, Faculty of Medicine, University of Oulu, Oulu, Finland; [4]Unit of Primary Health Care, Oulu University Hospital, OYS, Oulu, Finland; [5]Department of Life Sciences, College of Health and Life Sciences, Brunel University London, London, United Kingdom; [6]Department of Obstetrics and Gynecology, University of Helsinki and Helsinki University Hospital, Helsinki, Finland; [7]Institute of Reproductive and Developmental Biology, Imperial College London, London, United Kingdom; [8]Division of Cardiology, Department of Clinical Medicine, Medical Research Center, University of Oulu and Oulu University Hospital, Oulu, Finland

Background
Cardiovascular diseases (CVD) present sex specific characteristics, suggesting sex-hormones playing a role in the pathophysiology of CVDs. Hyperandrogenemia (HA) is a common condition in fertile age women but whether HA is a risk factor for CVD is still controversial.
Aims
To clarify the association of HA with the development of hypertension and CVDs in women.
Study population and methods
A general population-based birth cohort ($n=5889$ women) followed at ages 1, 14, 31 and 46. We investigated the association of serum levels of testosterone (T, measured using LC-MS/MS) and free androgen index (FAI) at age 31 with blood pressure (BP), hypertension (HT, defined as B $P\geq$ 140/90 mmHg and/or use of antihypertensive medication) at age 31 and with CVD risk [angina pectoris (AP) and/or acute myocardial infarction (AMI), and transitory cerebral ischemia (TIA) and/or stroke] with 22-year follow-up. After excluding women being pregnant ($n=212$) and those with lacking data, the final study population included 2820 women at age 31.
Results
After adjusting for body mass index (BMI), there was an independent positive association of T and FAI with systolic BP (T:$\beta=1.93$, 95% CI:0.93–2.93, FAI:$\beta=1.68$, 95% CI:0.67–2.70) and diastolic BP (T:$\beta=1.80$, 95% CI:0.93–2.67, FAI:$\beta=1.96$, 95%CI:1.10–2.82) at age 31. The prevalence of HT was significantly higher among women with elevated T (cut-off 2.3 nmol/l defined in this population) compared to normoandrogenic women (27.1% vs 11.9%, $P=0.002$). Conversely, women with HT at age 31 had significantly higher T levels (1.12 [0.82; 1.47] vs 0.97 [0.73; 1.25] nmol/l, $P<0.001$) and FAI (2.92 [1.95; 4.72] vs 2.16 [1.50; 3.09], $P<0.001$) compared to normoandrogenic women after adjusting for BMI. In logistic regression analysis, T and FAI associated positively and independently of BMI with HT (Odds ratio (OR) for T: 1.81, 95% CI:1.37–2.39, OR for FAI: 1.87, 95% CI:1.42–2.47). HA at age 31 did not associate significantly with TIA and/or stroke. Sex hormone binding globulin (SHBG) associated inversely [crude Hazard ratio (HR):0.97, 95% CI: 0.95–0.99] and FAI positively (crude HR:1.16, 95% CI: 1.04–1.30) with increased risk of incident CV events (AP/AMI) during the 22-years follow-up. However, after adjusting for BMI at age 31, the significances disappeared.
Conclusions
Women with HA at reproductive age had elevated risk for HT. They had a significantly increased CVD event risk during the 22-years follow-up, but this risk seemed to be mainly driven by BMI. A longer follow-up of this cohort is needed to clarify the long-lasting metabolic risks linked to HA.

DOI: 10.1530/endoabs.81.RC12.5

RC12.6

Is Turner syndrome at risk for thyroid carcinoma?

Elisabetta Belardinelli, Paola Dionese, Carolina Cecchetti, Valentina Vicennati, Andrea Repaci, Uberto Pagotto & Alessandra Gambineri
IRCCS Azienda Ospedaliero-Universitaria di Bologna, Department of Medical and Surgical Sciences (DIMEC), Alma Mater Studiorum, University of Bologna, Division of Endocrinology and Diabetes Prevention and Care, Italy

Background
Many questions concerning Turner Syndrome (TS) remain unresolved, such as the long-term complications and, therefore, the optimal care setting for adults. Most controversials regard tumors. Very few data are available on thyroid carcinoma and no specific screening protocol of monitoring is advised in the current official guidelines. This long-term cohort study was primarily aimed at estimating the incidence and time to comorbid conditions along the life course, including thyroid carcinoma and tumors in general.
Methods
The study cohort consisted of 160 TS women, the vast majority recruited during childhood (mean age= 9.4 years, median=9 years, IQR 2-16) and followed up for a median of 27 years (IQR 12-42) at the S. Orsola University Hospital of Bologna using the same multidisciplinary monitoring protocol (including thyroid ultrasound every one to two years). The last follow-up was carried out for all patients in December 2019.
Results
Autoimmune diseases (such as Hashimoto's thyroiditis, celiac disease and autoimmune polyendocrine syndrome) were the comorbidities with the highest incidence (61.2%), followed by osteoporosis and hypertension (23.8% for both), then by type 2 diabetes (16.2%) and by tumors (15.1%). Median age of onset ranged from 22yrs for autoimmune diseases to 39yrs for type 2 diabetes. Malignant tumors (including thyroid carcinoma, renal cell cancer, skin cancer, breast cancer, ovarian cancer and central nervous system tumors) were the most prominent form of neoplasms, with a cumulative incidence of 11.9% and an incidence rate of 0.44 per 100 person-year. Thyroid carcinoma (histologically all papillary -PTC- in our cohort) was the most common form of cancer with a cumulative incidence of 5% and an incidence rate of 0.56 per 100 person-year

(incidence rate of 0.037 per 100 person-year in a cohort of Italian women of similar age range). Median age of onset of PTC was 28.9yrs. No association with a specific karyotype of the TS was observed.
Conclusions
These findings demonstrate that TS patients are at risk of developing thyroid carcinoma, particularly the papillary form, thus suggesting, differently from current practice, the need to include thyroid ultrasonography within the structured follow-up protocol of this syndrome.

DOI: 10.1530/endoabs.81.RC12.6

RC12.7

Pubertal induction in girls with hypogonadism: insight into estrogen replacement therapy outcomes and optimization of progesterone introduction

Giulia Rodari[1], Silvia Federici[2,3], Alessandro Cattoni[4], Tommaso Todisco[5], Graziamaria Ubertini[5], Federico Giacchetti[6], Eriselda Profka[6], Alberta Dall'Antonia[7], Biagio Cangiano[2,3], Maura Arosio[1,6], Marco Bonomi[2,3], Marco Cappa[5] & Claudia Giavoli[1,6]
[1]University of Milan, Department of Clinical Sciences and Community Health, Milan, Italy; [2]University of Milan, Department of Medical Biotechnology and Translational Medicine, Milan, Italy; [3]IRCCS Istituto Auxologico Italiano, Dept. of Endocrine and Metabolic Diseases and Lab. of Endocrine and Metabolic Research, Milan, Italy; [4]Fondazione MBBM, San Gerardo Hospital, Department of Pediatrics, Università degli studi di Milano-Bicocca, Monza, Italy; [5]University-Hospital Pediatric Department (DPUO), Bambino Gesù Children's Hospital, IRCCS, Endocrinology Unit, Rome, Italy; [6]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Endocrinology Unit, Milan, Italy; [7]University of Milan, Milan, Italy

Background
Pubertal induction in girls with hypogonadism through estrogen replacement therapy (ERT) aims at mimicking physiological puberty. To date, the best induction regimen is still to be established.
Aims
By setting up a multicentre clinical registry, we analysed longitudinal data on pubertal induction in girls with hypogonadotropic hypogonadism or premature ovarian insufficiency (congenital, acquired, isolated or associated with multiple pituitary hormone deficiency, either associated with Turner Syndrome or secondary to late effects of cancer treatment) in order to insight into auxological and uterine outcomes in the light of different underlying diagnosis and regimens used.
Methods
Out of 106 hypogonadal girls (chronological age > 10.9 years, Tanner stage $\leq$ 2) who received ERT for pubertal induction included in the register, we considered 95 girls (median age 13.5 years) treated with transdermal (TD) 17β-estradiol patches for at least one year (median 3.3 years). Induction was started at a median dose of 0.14 mg/kg/day TD 17β-estradiol, with a six-monthly increase. Auxological, biochemical (estradiol levels) and radiological (pelvic US) data were collected at baseline and during follow-up. In 61/95 girls, progesterone was introduced after a median of 2.2 years. Induction was considered completed for the 49/95 patients who were started on combined oral contraceptive (COC) or progesterone *plus* at least 50 mg/day or 1 mg/kg/day of TD 17β-estradiol.
Results
at the end of induction, 90.0% patients had achieved Tanner stage B4 and 41.0% B5, the latter being associated with 17β-estradiol dose at progesterone introduction ($P = 0.034$). Uterine longitudinal diameter (ULD) showed a gradual increase during ERT and a significant correlation with 17β-estradiol dosage ($P < 0.0001$) at any point of induction. Nonetheless, final ULD was > 65 mm in only 17/45 (38%). At multiple regression analysis, a history of pelvic irradiation represented the major determinant of reduced final ULD ($P = 0.034$). After correction for uterine irradiation and other clinical confounders, ULD was associated with 17β-estradiol dose at progesterone introduction ($P = 0.043$). Final ULD was not significantly different from the one assed after COC introduction.
Conclusions
reaching an appropriate 17β-estradiol dose at the end of the induction seems to play a crucial role in uterine development and Tanner stage 5 achievement. Indeed, progesterone should be started only in the presence of a concomitant adequate ERT dose and an appropriate uterus and breast development, given the evidence that progestins may hamper the subsequent changes in uterus volume or the achievement of the last Tanner stage. At present, we aim to confirm present results on a larger scale.

DOI: 10.1530/endoabs.81.RC12.7

RC12.8

Ethinyl estradiol in a combined contraceptive exerts greater effect on serum proteome than estradiol valerate – a randomized trial

Marika Kangasniemi[1], Riikka Arffman[1], Sakari Joenväärä[2,3], Annina Haverinen[4], Kaisu Luiro[4], Tiialotta Tohmola[2,3], Risto Renkonen[2,3], Oskari Heikinheimo[4], Juha Tapanainen[4] & Terhi Piltonen[1]
[1]Oulu University Hospital, University of Oulu, Department of Obstetrics and Gynecology, PEDEGO Research Unit, Medical Research Center, Oulu, Finland; [2]Haartman Institute, University of Helsinki, Transplantation Laboratory, Helsinki, Finland; [3]Helsinki University Hospital, HUSLAB, Helsinki, Finland; [4]University of Helsinki, Helsinki University Hospital, Department of Obstetrics and Gynecology, Helsinki, Finland

Background
Combined oral contraceptives (COC) are known to have multiple beneficial effects besides contraception, but also cause some unwanted health outcomes. They interfere, for example, with metabolism, inflammation, hepatic protein synthesis and blood coagulation. COCs containing natural estrogens have recently been developed, yet little is known about their non-contraceptive effects compared to conventional COCs with ethinyl estradiol (EE). The aim of this study was to compare the impacts of COCs containing EE or estradiol valerate (EV) and dienogest (DNG) alone on the serum proteome.
Methods and findings
Fifty-nine healthy women participated in a randomized, controlled clinical trial. They were allocated to use either EE + DNG, EV + DNG or DNG alone continuously for nine weeks. Serum samples were collected before and after nine weeks of exposure. Samples from 44 women were available for this analysis (EE + DNG $n = 14$, EV + DNG $n = 16$ and DNG $n = 14$). Changes in serum proteins were analyzed using quantitative label-free proteomics. Altogether, 514 different proteins were detected. Number of proteins that changed within the study groups were 145 for EE + DNG, six for EV + DNG and zero for DNG-only preparation. Significant change between the groups was detected in 70 proteins, of which 64 were detected between the EE + DNG and EV + DNG groups. Most affected pathways were the complement system, acute phase response signaling, metabolism related LXR&FXR/RXR activation, and the coagulation system.
Conclusions
The COC containing EE exerts a broader effect on serum proteome compared with EV combination or DNG-only preparation. These results signal a need for further studies comparing the clinical health outcomes between COCs containing EE and natural estrogens.
Trial Registration: ClinicalTrials.gov NCT02352090

DOI: 10.1530/endoabs.81.RC12.8

Adrenal and Cardiovascular Endocrinology 2

RC13.1

HPA axis modulation by a potent inhibitor indicates 11β-hydroxy-steroid dehydrogenase type 1 (HSD-1) is a main source of cortisol that can bind intracellular receptors

David Katz[1] & Mark Mortier[2]
[1]Sparrow Pharmaceuticals, Portland OR, United States; [2]Emanate Biostats, Carlsbad CA, United States

Background
HSD-1 converts cortisone to cortisol in tissues in which cortisol excess is associated with morbidity including liver, adipose, bone, and brain. SPI-62 is a potent HSD-1 inhibitor in clinical development for treatment of Cushing's syndrome and autonomous cortisol secretion, and as adjunctive therapy to prednisolone in polymyalgia rheumatica. In Phase 1 clinical trials SPI-62 was generally well tolerated and associated with maximal liver and brain HSD-1 inhibition.
Methods
We analyzed multiple dose trial[1] data to characterize the contribution of HSD-1 to cortisol that can bind to intracellular receptors and HPA/HPG axis modulation by SPI-62. Data from subjects who received SPI-62 doses that achieved maximal liver HSD-1 inhibition were combined for analysis. ANCOVA models with treatment effect and baseline covariate were conducted; statistics are least squares mean [standard error].
Results
Compared to placebo ($n = 10$), single SPI-62 doses ($n = 40$) were associated with 24-hour urinary tetrahydrocortisol (2.27[0.134] v 4.44[0.269] mmol) and allotetrahydrocortisol (2.98[0.146] v 4.80[0.291] mmol) decreases, and tetrahydrocortisone (32.71[1.149] v 9.19[2.300] mmol) increase. Serum cortisol was decreased at 2-hours (152.2[11.64] v 226.6[24.00] nM) but not 4- or 12-hours post-dose. ACTH was increased at 4- and 12-hours (45.6[1.64] v 32.1[3.29]; 38.5[1.67] v 26.3[3.33] pg/ml) but not 2-hours post-dose. After 14 daily doses, SPI-62 was

associated with 24-hour urinary tetrahydrocortisol (2.05[0.154] v 4.36[0.321] mmol), allotetrahydrocortisol (2.75[0.181] v 4.13[0.377] mmol), and tetrahydrocortisone (42.73[1.968] v 8.51[0.410] mmol) changes. ACTH was increased at predose and 2-, 4-, and 12-hours post-dose (45.6[1.71] v 27.0[3.61]; 45.3[1.79] v 35.2[3.72]; 34.4[1.71] v 18.8[3.57]; 47.3[2.13] v 30.4[4.45] pg/ml). No differences on urinary cortisol or cortisone, serum cortisone, or CRH were observed after single or multiple doses. After multiple doses, SPI-62 was associated with increased DHEA-S (342.2[9.94] v 155.0[20.52] mg/dl) and, in females, testosterone (2.1[0.11] v 1.4[0.25] nM). No differences on aldosterone, estradiol, FSH, LH, progesterone, or SHBG were observed.

Discussion

SPI-62 resulted in ~40-50% decreases of urinary cortisol metabolites which indicate similar decrease of hepatocellular cortisol. Following a corresponding decrease, circulating cortisol homeostasis was restored rapidly by ACTH increase. Urinary cortisol was unaffected. SPI-62 is associated with moderate androgen increases that, to date, appear not associated with adverse effects. As HSD-1 contributes much of the intracellular cortisol that can access intracellular receptors, we hypothesize that HSD-1 inhibitors are potential treatments for conditions of cortisol excess such as Cushing's syndrome and autonomous cortisol secretion.

Reference

1. *Clin. Transl. Sci.* 2019;**12**:291-301.

DOI: 10.1530/endoabs.81.RC13.1

RC13.2

Age- and gender-specific cut-off levels may improve DHEAS as a marker for suppressed HPA-axis

Shobitha Puvaneswaralingam[1] & Henrik Olsen[2]

[1]Department of Endocrinology, Skånes University Hospital, Lund, Sweden; [2]Department of Endocrinology, Clinical Sciences, Lund University, Lund, Sweden

Background

Low levels of DHEAS, such as <1.04 µmol/l, have been used as a criterion for autonomous cortisol secretion (ACS) in patients with adrenal incidentalomas. Age- and gender-specific cut-off levels could theoretically improve DHEAS as a marker of HPA-axis suppression and as a criterion for ACS.

Objective

We aimed to find cut-off levels of DHEAS that are best associated with HPA-axis suppression and determine whether they are correlated with clinical outcomes.

Methods

We studied 989 patients with adrenal incidentalomas, investigated between 2005 and 2015 at two hospitals in southern Sweden and followed up for 14 years. Patients were divided into 10 groups according to age, separated as age <50, 50-<60, 60-<70, 70-<80 or ≥ 80 years, and gender.

Results

In patients with ACTH <2.0 pmol/l, DHEAS was <1.04 µmol/l in 0, 14, 10, 22, and 33% of males and in 40, 26, 46, 50, and 100% of females in the described age groups. Therefore, the sensitivity for HPA-axis suppression may be low in males, and females <60 years. ACTH was not related to age in males or females. Therefore, we studied DHEAS levels below the 25th percentile as a marker of HPA-axis suppression. The levels for the different age groups were <2.50, <2.10, <1.20, <0.93, and <0.81 µmol/l in males and <1.10, <1.00, <0.81, <0.81, and <0.81 µmol/l in females and were termed "low DHEAS". The odds ratio for cortisolDST ≥ 50 nmol/l was higher for low DHEAS than DHEAS <1.04 µmol/l in males, 1.92 (1.17-3.14) vs 1.59 (0.92–2.76), but was similar in females, 1.73 (1.19-2.51) vs 1.67 (1.17-2.38), adjusted for age. Low DHEAS was associated with pre-existing cardiovascular disease, odds-ratio 1.63 (1.14-2.33) and mortality, relative risk 1.57 (1.14-2.18), both adjusted for gender, age, and smoking.

Conclusion

Age-specific DHEAS is a more appropriate marker of HPA-axis suppression in men but seems not to perform better in females. Furthermore, the proposed age- and gender-specific cut-off levels were associated with pre-existing cardiovascular disease and increased mortality.

DOI: 10.1530/endoabs.81.RC13.2

RC13.3

Steroidomic approach for the characterization of patients with non-alcoholic fatty liver disease

Mirko Parasiliti Caprino[1], Chiara Rosso[2], Federico Ponzetto[1], Gian Paolo Caviglia[2], Chiara Lopez[1], Angelo Armandi[2], Giorgio Maria Saracco[2], Ezio Ghigo[1], Elisabetta Bugianesi[2] & Mauro Maccario[1]

[1]University of Turin, Endocrinology, Diabetes and Metabolism, Turin, Italy; [2]University of Turin, Unit of Gastroenterology, Turin, Italy

Introduction

The onset and progression of liver damage in non-alcoholic fatty liver disease (NAFLD) is tightly associated with metabolic derangements. Steroids may affect lipid metabolism but their alterations in the setting of NAFLD remain to be fully explored.

Patients and Methods

We analyzed data from 121 patients with biopsy-proven NAFLD and 108 controls (CT). A panel of 26 steroids (including glucocorticoids, mineralocorticoids, androgens, and progestogens as well as representative glucuro- and sulphoconjugated metabolites) were measured on plasma samples by liquid chromatography coupled to mass spectrometry (LC-MS/MS). Severe hepatic fibrosis was defined by $F \geq 3$.

Results

Compared to CT, NAFLD patients were older (median age 51 vs 43, $P<0.001$) and were characterized by a higher rate of MS (47% vs 2%, $P<0.001$). More than a half of steroids were deregulated in patients compared to CT. At liver histology, the prevalence of absent/mild, moderate, and severe fibrosis was 50.4%, 10.8% and 38.8%, respectively. Circulating levels of 16 compounds showed a significant stepwise decrease according to the degree of hepatic fibrosis. At univariate analysis, testosterone, and its derivatives, androsterone metabolites, etiocholanolone metabolites and glicoandrogens metabolites were differentially expressed in patients with severe fibrosis compared to those with absent/moderate fibrosis. After multivariable logistic regression analysis adjusted for age, gender and type 2 diabetes, epitestosterone sulphate, 5α-androstan-3α,17β-diol-3-glucuronide and androsterone sulphate levels were significantly associated with $F \geq 3$. The diagnostic accuracy of the model for the identification of $F \geq 3$ was 0.91 with a sensitivity and specificity of 87% and 85 %, respectively, and with a positive and negative predictive value of 78% and 91%, respectively.

Conclusions

In NAFLD patients, alterations in androgens and their glucuro- and sulphoconjugated metabolites levels could be expression of compromised 1) liver steroidogenesis or 2) liver steroid homeostasis regulation and are strongly associated with severe fibrosis. This research has been supported by the Italian MIUR under the programme "Dipartimenti di Eccellenza 2018-2022", project code D15D18000410001.

DOI: 10.1530/endoabs.81.RC13.3

RC13.4

Analysis of the body composition and glucose metabolism in relation to bcli glucocorticoid receptor polymorphism in women with adrenal incidentalomas

Sanja Ognjanovic, Bojana Popovic, Dusan Ilic, Valentina Elezovic, Jadranka Antic, Milica Opalic[1], Lena Radic & Djuro P Macut

Clinic for Endocrinology, Diabetes and Metabolic Diseases, University Clinical Centre of Serbia, Department for Endocrine Tumors and Hereditary Cancer Syndromes, Belgrade, Serbia

Single nucleotide polymorphisms in the glucocorticoid receptor (GR) gene influence tissue sensitivity of GR. Several studies have shown different effects of *Bcl*I GR polymorphism on body composition and metabolic parameters. The objective of this study was to explore the effect of *Bcl*I GR polymorphism on the body composition and glucose metabolism. Biochemical tests and hormonal evaluation were performed in 106 consecutive women with adrenal incidentalomas (AIs). Non-diabetic patients underwent an oral glucose tolerance test with 75 g glucose. Body composition was measured with dual-energy X-ray absorptiometry. DNA was obtained from peripheral blood leucocytes. The polymorphism was detected using PCR, RFLP and DNA sequencing. We observed no differences in mean age (57 ± 9.6 vs 56.5 ± 11.8, $P=0.823$), percent of postmenopausal women (76% vs 7%, $P=0.550$), and prevalence of metabolic syndrome (31.9% vs 21.3%, $P=0.158$) between carriers of the C allele of *Bcl*I polymorphism and non-carriers. *Bcl*I carriers have lower prevalence of impaired glucose tolerance (2.6% vs 17.5%, $P=0.031$), type 2 diabetes mellitus (T2DM) (9.1% vs 26%, $P=0.034$), and reduced glucose area under the curve, the mean difference of 2.62 (95% CI, 1.11-4.14), $P=0.001$. *Bcl*I carriers have a tendency towards lower lean body mass (41.7 ± 6.9 vs 44.1 ± 5.7, $P=0.08$) and a significantly higher percentage of legs fat (43.36 ± 5.75 vs 39.84 ± 7.6, $P=0.020$). *Bcl*I polymorphism was significantly associated with sum of legs fat mass (FM) percentage ($\beta=0.327$, $P=0.048$). Also, subjects with greater legs/trunk FM ratio had higher odds to be *Bcl*I carriers, OR 1.046 (95% CI, 0.046-23.565, $P=0.045$). Logistic regression analysis showed that presence of T2DM was significantly negatively correlated with *Bcl*I polymorphism after adjusting for

possible confounding factors such as age, truncal FM, appendicular lean mass index, and legs fat sum (OR = 0.158, 95%CI 0.031-0.806, $P = 0.027$). *Bcl*I carriers predispose to increased legs fat mass and greater legs/trunk FM ratio indicating reduced sensitivity to GC, which could explain why some women with AIs preserve more gluteo-femoral subcutaneous adipose tissue with beneficial effects on glucose metabolism.

DOI: 10.1530/endoabs.81.RC13.4

RC13.5

Skeletal muscle mass in patients with adrenal incidentaloma

Giacomo Colombin[1,2], Giulio Vara[1,2], Flaminia Fanelli[2,3], Matteo Magagnoli[2,3], Lorenzo Tucci[1,2], Kimberly Coscia[1,2], Cristina Mosconi[1,2], Uberto Pagotto[1,2], Valentina Vicennati[1,2] & Guido Di Dalmazi[1,2]

[1]S. Orsola-Malpighi Polyclinic, Bologna, Italy; [2]Alma Mater Studiorum - Università di Bologna, Bologna, Italy; [3]CRBA, Bologna, Italy

Background and aim

The relationship between sarcopenia and overt cortisol excess as in Cushing's syndrome is well-known. However, only a few studies investigated the relationship between autonomous cortisol secretion (ACS) in adrenal incidentalomas and skeletal muscle mass. The aims of our study were to analyze the skeletal muscle mass in patients with adrenal incidentalomas and to investigate the correlations with hormonal data.

Methods

We enrolled 200 adult patients (>18 years) without clinical signs of Cushing syndrome, bearing monolateral and bilateral benign adrenal incidentaloma detected at CT scan. We classified the adrenal tumors as non-secreting (NS) or ACS according to cortisol levels after 1-mg dexamethasone suppression test (DST) < or >50 nmol/l, respectively. Skeletal muscle mass was evaluated by Skeletal Muscle index (SMI) through a threshold segmentation (-19HU – +150HU) of the Skeletal Muscle Area on an L3 slice of the basal acquisition, subsequently divided by the height squared. Subjects underwent measurement of an 11-steroid profile in serum by Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS).

Results

SMI was lower in ACS than NS subjects (40.6 ± 1.2 vs 44.2 ± 1.2; $P = 0.007$). Accordingly, the prevalence of sarcopenia was higher in ACS than NS patients (59.4% vs 39.6%; $P = 0.012$). Similar results were confirmed after analyzing the data separately by sex. Overall, we identified correlations between SMI and age ($r = -0.34$; $P < 0.001$), body mass index (BMI) ($r = 0.39$; $P < 0.001$), basal cortisol ($r = -0.155$; $P = 0.041$) and post-DST cortisol ($r = -0.180$; $P = 0.018$). When analyzed separately by sex, similar correlations were confirmed in males, whereas only the correlations between SMI and basal cortisol, age, and BMI were observed in post-menopausal women. Additionally, in post-menopausal women, SMI was associated positively with DHEAs levels ($r = 0.318$; $P = 0.004$) and negatively with corticosterone ($r = -0.259$; $P = 0.007$). Multivariable analysis by generalized linear model (GLM) showed a positive correlation between SMI and BMI (B = 0,009; 95% C.I. 0.005 - 0.013; $P < 0.001$), independently of age ($P = 0.205$) and post-DST cortisol ($P = 0.078$) in males. In post-menopausal females, GLM highlighted an independent correlation between SMI and DHEAs levels (B = 0.036; 95% C.I. 0.005-0.068; $P = 0.024$), with an independent contribution of BMI (B = 0.004; 95% C.I. 0.002-0.007; $P = 0.001$) and age (B = -0.002; 95% C.I. -0.004-0.000; $P = 0.017$).

Conclusions

ACS is associated with impaired skeletal muscle mass, despite patients may not report symptoms of sarcopenia. A differential hormonal contribution to impaired skeletal muscle mass has been identified according to sex.

DOI: 10.1530/endoabs.81.RC13.5

RC13.6

Mild autonomous cortisol secretion in patients with adrenal incidentalomas and raised cardiovascular risk

Rebecca Sagar[1], Sheila Fraser[2], Emma Collins[2], Russell Frood[2], Andrew Scarsbrook[2], Paul M Stewart[1,3] & Afroze Abbas[1]

[1]Leeds Teaching Hospitals Trust, Leeds Centre for Endocrinology and Diabetes, Leeds, United Kingdom; [2]Leeds Teaching Hospitals Trust, Leeds, United Kingdom; [3]University of Leeds, School of Medicine, Leeds, United Kingdom

Background

Adrenal incidentalomas are common and require investigation to exclude malignancy and evidence of hormone overproduction. Clinical guidelines recommend overnight dexamethasone suppression tests (ONDST) to assess for cortisol hypersecretion with cortisol levels of 50-138 nmol/l termed "mild autonomous cortisol secretion" (MACS). MACS may be associated with both cardiovascular and metabolic morbidity. We assessed cardiovascular risk in patients with MACS using QRISK3. This is a validated algorithm used in the UK to predict cardiovascular risk, calculating a predicted percentage risk of myocardial infarction (MI) or stroke over the next 10 years.

Methods

Data were collected retrospectively on patients over a two-year period, who had an adrenal incidentaloma with a cortisol between 50-138 nmol/l following ONDST. Presence of cardiovascular co-morbidities including hypertension, type 2 diabetes mellitus (T2DM), atrial fibrillation and ischaemic heart disease (IHD) was recorded. Relative Risk (RR) of cardiovascular disease (MI or stroke) was calculated using the QRISK3. Statistical analysis was conducted using PRISM v9.3.1.

Results

228 patients (50% male), mean age 69 years ± 11.4 (SD), mean BMI 30.5 kg/m^2 ± 15.1 were identified with MACS. 79.8% of patients had a diagnosis of hypertension with 62% on more than one anti-hypertensive medication. 73% of patients were on statin therapy. 34.5% of patients had a diagnosis of T2DM. 27.1% of patients had ischaemic heart disease and 8% had congestive cardiac failure. Mean QRISK3 score was 26.7 ± 13%, compared with 16.6 ± 10% in age/sex matched healthy controls as per the QRISK3 algorithm. Relative risk for MI or stroke was 2.2 compared to the healthy age/sex matched controls. 88% of the cohort had a relative risk >1. There was no clear correlation between radiological characteristics and QRISK.

Conclusions

Amongst our unselected cohort of patients with adrenal incidentalomas and biochemistry consistent with MACS, there was high prevalence of hypertension, T2DM and IHD compared with the background population. Additionally cardiovascular QRISK-3 demonstrated this patient cohort had >2 times the likelihood of having an MI or stroke within the next 10 years compared with healthy age and sex matched people. Although the data suggests an association, it is possible other confounders such as BMI may influence both ONDST results and CV risk. CV risk assessment should be considered in all patients with an adrenal incidentaloma and MACS.

DOI: 10.1530/endoabs.81.RC13.6

RC13.7

An observational retrospective study on the association of urine metanephrine levels with cardiometabolic risk in patients with nonfunctioning adrenal incidentaloma

Maria Chiara Di Carlo[1], Mirko Parasiliti Caprino[1], Chiara Lopez[1], Martina Bollati[1], Fabio Bioletto[1], Chiara Sola[1], Federico Ponzetto[1], Iacopo Gesmundo[1], Fabio Settanni[2], Ezio Ghigo[1], Giulio Mengozzi[2], Mauro Maccario[1] & Roberta GIORDANO[1]

[1]University of Turin, Endocrinology, Diabetes and Metabolism, Turin, Italy; [2]University of Turin, Clinical Biochemistry Laboratory, Turin, Italy

Background

Several studies argued that the cardiovascular evaluation of patients with nonfunctioning adrenal incidentaloma is of particular importance, even if a direct association seems difficult to underline.

Objective

We aimed to evaluate the possibility of stratifying cardiometabolic risk through metanephrine levels in patients with incidentally discovered nonfunctioning adrenal adenoma.

Design

In this retrospective cross-sectional study, we collected data of metanephrine levels in 828 patients with nonfunctioning adrenal incidentaloma, referred to the Division of Endocrinology, Diabetes and Metabolism of the University Hospital of Turin between September 2007 and September 2021.

Results

The univariate analysis showed associations between urine metanephrines and cardiometabolic variables/parameters, particularly considering the noradrenaline metabolite. At univariate regression, normetanephrine was associated with

metabolic syndrome (OR = 1.13, 95% CI 1.05-1.22; $P = 0.002$), hypertensive cardiomyopathy (OR = 1.09, 95% CI 1.01-1.18; $P = 0.026$), microalbuminuria (OR = 1.14, 95% CI 1.00-1.25; $P = 0.024$), and with eGFR < 60 ml/min/1.73 m^2 (OR = 1.11, 95% CI 1.02-1.19; $P = 0.013$), while metanephrine was associated with microalbuminuria (OR = 1.50, 95% CI 1.11-1.85; $P = 0.008$). At multivariate regression, considering all major cardiovascular risk factors as possible confounders, normetanephrine retained a significant association with metabolic syndrome (OR = 1.10, 95% CI 1.01-1.19; $P = 0.037$). Moreover, metanephrine retained a significant association with the presence of microalbuminuria (OR = 1.66, 95% CI 1.21-2.98; $P = 0.003$).

Conclusions

The present study demonstrated a further role for metanephrines in the cardiovascular risk stratification of patients with nonfunctioning adrenal incidentaloma. Individuals with high levels of these indirect markers of sympathetic activity should be carefully monitored and may benefit from an aggressive treatment to reduce their additional cardiometabolic burden.

DOI: 10.1530/endoabs.81.RC13.7

RC13.8

Gut dysbiosis in patients with cushing's syndrome in remission. relationship with cardiometabolic risk

Elena Valassi[1,2,3], chaysavanh Manichanh[4] , Luciana Maria Martel Duguech[5], Pedro González Fernández[6], Sonia Gaztambide[3,6], Manel Puig-Domingo[3,7,8] & Susan Webb Youdale[3,9,10]

[1]Hospital Germans Trias i Pujol and Research Institute, Endocrinology, Badalona, Spain; [2]Universitat Internacional de Catalunya (UIC); [3]Centro de Investigación Biomédica en Red (CIBERER); [4]Gut Microbiome Group, Vall d'Hebron Institut de Recerca (VHIR), Barcelona, Spain; [5]Hospital Sant Pau, Barcelona, Spain; [6]Hospital Cruces, Endocrinology, Bilbao, Spain; [7]Hospital Germans Trias i Pujol and Research Institute, Badalona, Spain; [8]Universitat Autònoma de Barcelona, Barcelona,; 9Hospital Sant Pau, Barcelona, Spain; [10]Universitat Autònoma de Barcelona, Barcelona, Spain

Background

Patients with Cushing's syndrome (CS) in remission show residual cardiometabolic derangements leading to increased cardiovascular risk. Impaired characteristics of gut microbiome (dysbiosis), such as richness, diversity and composition, have been associated with several cardiometabolic risk factors, including obesity, insulin resistance and atherosclerosis. Whether CS patients present with intestinal dysbiosis is currently unknown. Our study was aimed at evaluating the relationship between the characteristics of gut microbiome and both body composition indexes and cardiometabolic risk factors in "cured" CS.

Methods

Twenty-seven female non-diabetic patients with CS in remission [mean (±SD) age, 51±9 years, mean (±SD) BMI, 26±3.8, median (IQR) duration of remission, 11(4) years] and 27 gender-, age-, and BMI-matched controls were included. Genomic DNA was extracted from fecal samples. The V4 region of the bacterial 16S rDNA was amplified by PCR, and sequencing was applied to analyze microbial richness (alpha diversity; Chao 1 index, observed number of species, effective Shannon index) and microbial community structure (beta diversity analysis through the Principal Coordinates Analysis (PCoA) of weighted and unweighted UniFrac distances). Inter-group difference in microbiome composition was analysed using ANCOM (Analysis of Composition of Microbiomes), a plugin from the QIIME2 pipeline. Lipid and coagulation profiles, fasting glycemia and fasting insulin were assessed using standard assays. Body composition was measured using dual-energy x-ray absorptiometry (DXA).

Results

The Chao 1 index was significantly lower in CS patients as compared with controls (Kruskal-Wallis test, q = 0.002), indicating that the former had lower microbial richness. Beta diversity analysis showed that fecal samples from CS patients clustered together and separated from the control samples (Adonis test, $P < 0.05$). The Analysis of Composition of Microbiomes showed that several microbial groups at phylum, family, order and genus categories were associated with CS. In particular, *Collinsella*, a form genus of the Actinobacteria phylum, was present in all CS patients but not in controls. In CS, the Chao 1 index was associated with fibrinogen levels ($\rho = 0.44$; $P = 0.034$), and inversely correlated with both triglyceride concentrations ($\rho = -0.48$; $P = 0.035$) and the HOMA-IR index ($\rho = -0.45$; $P = 0.038$).

Conclusions

Patients with CS in remission have gut microbial dysbiosis with decreased microbiota richness and diversity, and specific variations in the bacterial community structure. Dysbiosis in CS may be one of the mechanisms whereby cardiometabolic dysfunctions persist after "cure".

DOI: 10.1530/endoabs.81.RC13.8

Late Breaking

RC14.1

Long-term thyroid complications in haematological cancer survivors following systemic chemotherapy, neck radiotherapy and/or haematopoietic stem cell transplantation

Francesco Carlomagno, Christopher Nardi, Alessandra Tomaselli, Carla Pandozzi, Paola Mazzotta & Daniele Gianfrilli

Sapienza University of Rome, Dept. of Experimental Medicine, Roma, Italy

Introduction

With the increasing survival rates from cancer the focus has been shifting towards the adverse sequelae, occurring both acutely, or developing as late effects, deriving from its multimodality treatment.

Aim

We investigated the occurrence of thyroid complications in patients with haematological malignancies treated with chemotherapy, radiotherapy involving the neck and/or haematopoietic stem cell transplantation (HSCT), referred to our endocrine sequelae clinic over the course of 20 years.

Patients and Methods

We prospectively enrolled 343 patients (172 females, 50.1%), with median age at diagnosis of 17 years (range: 1-76), and median follow-up of 12.4 years. Diagnoses were similarly distributed across: acute myeloid leukaemia, acute lymphoblastic leukaemia, chronic myeloid leukaemia, Hodgkin's lymphoma, non-Hodgkin's lymphomas, myelodysplastic syndromes and multiple myeloma. All patients underwent systemic chemotherapy, radiotherapy involving the neck was needed in 103 patients and 208 subjects received HSCT. We investigated the occurrence of: overall thyroid complications, transient and permanent thyroid dysfunction, low T3 syndrome, thyroid autoimmunity, benign and malignant thyroid nodules using Kaplan-Meier survival analyses and Cox proportional hazards models with bootstrapping.

Results

Overall 58.7% of patients experienced thyroid complications, with a median latency time of 3.7 years. Primary hypothyroidism was encountered in 15.6% and transient hypothyroidism in 6.3% of patients; Cox regression revealed female sex ($P = 0.008$), adult age ($P = 0.035$) and radiotherapy ($P < 0.001$) as independent predictors. Low T3 syndrome was diagnosed in 10.1% of patients, and female sex and radiotherapy were independent predictors ($P = 0.027$ and 0.009, respectively). Transient hyperthyroidism was found in 2.1%, mostly after neck radiotherapy. Thyroid autoimmunity was encountered in 32%, and adult age at diagnosis (> 18 years) was the only independent predictor ($P = 0.028$). Thyroid nodules were encountered in 41.1%, with adult age at diagnosis as the only independent predictor ($P = 0.032$); 5 patients were diagnosed with papillary thyroid carcinomas. With regards to overall thyroid complications, female sex and adult age at diagnosis were associated with the highest risk ($P < 0.001$ and 0.001, respectively). Neck radiotherapy was associated with an increased risk of complications after a median of 18 years, whereas HSCT was not, after multiple adjustments.

Conclusions

Thyroid comorbidities are highly prevalent among patients treated for haematological malignancies, with specific associations with treatment modality, requiring long-term endocrine follow-up.

DOI: 10.1530/endoabs.81.RC14.1

RC14.2

Prevention of glucocorticoid-induced adipose dysfunction and hepatic lipid deposition through cold acclimation in aged mice

Manuel Gado[1], Zahra Ghane[1], Annett Heinrich[1], Denise Wiedersich[1], Stefan R Bornstein[2,3,4,5], Martina Rauner[1,2], Lorenz C Hofbauer[1,2] & Holger Henneicke[1,2]

[1]Center for Regenerative Therapies Dresden, Technische Universität Dresden, Dresden, Germany, Dresden, Germany; [2]Medizinische Klink III, Universitätsklinikum Carl Gustav Carus, Technische Universität Dresden, Dresden, Germany; [3]Division of Diabetes & Nutritional Sciences, Faculty of Life Sciences & Medicine, King's College London, London, United Kingdom; [4]University Hospital Zurich, Department of Endocrinology and Diabetology, Zurich, Switzerland; [5]Paul Langerhans Institute Dresden (PLID) of the Helmholtz Center Munich at Universitätsklinikum Carl Gustav Carus and Faculty of Medicine at Technische Universität Dresden, Dresden, Germany

Glucocorticoids (GC) are one of the most potent anti-inflammatory pharmacological agents. However, owing to their pleiotropic nature, their clinical effectiveness is frequently limited by their deleterious off-target effects. Frequently, metabolic abnormalities arise from GC excess involving the

development of dyslipidaemia, insulin resistance and muscle atrophy as well as excessive fat accumulation in both white adipose tissue (WAT) and the liver. In addition, suppressed thermogenic capacity in brown adipose tissue (BAT) has been observed during GC excess in rodents. Cold exposure is an established activator of sympathetic innervation of BAT triggering adaptive thermogenesis and lipid utilisation in BAT as well as WAT. Therefore, our investigation aimed to characterize the interaction between cold-induced thermogenesis and systemic GC excess on the adipose organ. To this end, we treated 32-week-old mice with corticosterone at either 29°C (thermoneutrality) or 13°C (cold temperature). Following 6 weeks of treatment, mice housed at 29°C gained more weight than their temperature-matched controls, which was coupled with excessive accumulation of white fat and consecutive adipocyte hypertrophy. Interestingly, mice maintained in the 13°C environment were protected from GC-driven obesity as well as adipocyte hypertrophy in WAT. Interestingly, the thermogenic capacity, as well as the sympathetic innervation of BAT, was partially preserved in mice maintained at 13°C in spite of corticosterone treatment, whereas mice housed at 29°C showed a considerable reduction in BAT thermogenic capacity and number of sympathetic nerve endings following GC excess. Moreover, treatment with corticosterone at 29°C resulted in increased hepatic lipid accumulation, while livers from mice maintained in the cold showed markedly fewer lipid deposits. On the systemic level, cold adaptation of mice partially prevented the development of GC-induced hyperinsulinemia and hyperleptinemia, both of which were readily observed at 29°C. Taken together, our data demonstrate that prolonged cold exposure prevents the onset of not only GC-induced adipose dysfunction but also related metabolic comorbidities including steatosis of the liver and hyperinsulinemia. Thus, activation of adaptive thermogenesis may be a potential therapeutic target for the prevention of GC-induced metabolic dysfunction.

DOI: 10.1530/endoabs.81.RC14.2

RC14.3

Can early postoperative hypocalcemia be predicted preoperatively in patients operated with minimally invasive technique for primary hyperparathyroidism ?

Fatma Dilek Dellal Kahramanca[1], Esra Çopuroğlu[2], Beril Turan Erdogan[1], Husniye Baser[2], Didem Ozdemir[2], Oya Topaloglu[2], Reyhan Ersoy[2] & Bekir Cakir[2]
[1]Ankara City Hospital, Endocrinology and Metabolism, Ankara, Turkey; [2]Ankara Yildirim Beyazit University, Faculty of Medicine, Endocrinology and Metabolism, Ankara, Turkey

Aim
Postoperative hypocalcemia is seen in 26-42% patients after parathyroidectomy.There are quite a lot of studies investigating preoperative factors that might be used to predict postoperative hypocalcemia in thyroidectomized patients, however there are less studies in parathyroidectomized patients.In this study, our aim was to determine whether any preoperative clinical, laboratory or ultrasonographical feature anticipate hypocalcemia in parathyroidectomized patients due to primary hyperparathyroidism (PHPT).
Material and Methods
All patients operated for PHPT between 2019–2022 were retrospectively evaluated.Patients undergoing minimally invasive parathyroidectomy were enrolled.Demographic, clinical, ultrasonography and histopathology results were noted and compared in patients with and without hypocalcemia (Group-1 and Group-2,respectively) within two days after surgery.
Results
Of 179 parathyroidectomized patients, 93 were operated with minimally invasive procedure. Postoperative hypocalcemia was observed in 21 (22.6%) patients.Group-1 was younger compared to Group-2 ($P=0.036$).Gender distribution and presence of osteoporosis were comparable.Nephrolithiasis was less prevalant in Group 1 ($P=0.046$).Preoperative levels of corrected calcium, phosphorus, magnesium, parathyroid hormone, alkaline phosphatase, 25 OH vitamin D were similar in two groups. Fractional excretion of calcium (FECa) was lower in group-1 ($P=0.048$).The optimal cut-off level of FECa that was predictive for postoperative hypoprathyroidism was 0.0216 with a sensitivity of 61.9% and specificity of 54.9% (AUC 0.643 ± 0.062, $P=0.048$).Ultrasonographic and histopathologic diameters and volumes of parathyroid lesions were not different in both groups ($p>0.05$ for all).Histopathological diagnosis was parathyroid adenoma in 76 (64.5%) patients, parathyroid hyperplasia in 9 (9.7%) patients, and cell-rich parathyroid gland in 8 (8.6%) patients.The distribution of the histopathological results were similar in two groups($P=0.750$).
Conclusions
Younger patients, patients with lower FECa and without nephrolithiasis undergoing minimally invasive parathyroidectomy for PHPT might require closer follow-up for the development of postoperative hypocalcemia. FECa lower than 0.0216 might help to predict occurrence of postoperative hypocalcemia.

	Group-1 (Patients with postoperative hypocalcemia) ($n=21$, 22.6%)	Group-2 (Patients without postoperative hypocalcemia) ($n=72$, 77.4%)	P
	n(%),[median (Q_1-Q_3)]	n(%),[median (Q_1-Q_3)]	
Age (year)	45.4±11.8	51.9±12.4	**0.036**
Gender (women)	18 (85.7)	53 (73.6)	0.251
Corrected calcium (N:8.7-10.4 mg/dl)	10.5 (10.2-10.7)	10.7 (10.3-11.4)	0.127
Phosphorus (N:2.4-5.1 mg/dl)	2.9±0.6	2.7±4.6	0.055
Magnesium (1.3-2.7 mg/dl) ($n=83$)	2.1±0.1	2.0±0.2	0.091
Alkaline phosphatase (42-98 U/l) ($n=91$)	103 (95-128)	113 (86-144)	0.950
Parathyroid hormone (18.4-80.1 ng/ml)	188,5 (147.0-210.0)	191.0 (140.5-281.8)	0.443
25 OH Vitamin D3 (25-80 ng/ml) ($n=92$)	19.8 (11.2-23.5)	16.0 (11.0-22.0)	0.466
Fractional excretion of calcium	0.0213 (0.0146-0.0229)	0.0225 (0.0177-0.0279)	**0.048**
Presence of nephrolithiasis	4 (19.0)	31 (43.1)	**0.046**
Presence of osteoporosis	10 (47.6)	26 (36.1)	0.279
Number of removed parathyroid lesions	1 (1-2)	1 (1-3)	0.212

DOI: 10.1530/endoabs.81.RC14.3

RC14.4

Sequential primary adrenocortical culture system for genetic transformation and adrenocortical tumorigenesis using CRISPR/Cas9-mediated genome editing

Carmina Teresa Fuss[1], Oliver Hartmann[2], Michaela Reissland[2], Nikolett Pahor[2] , Laura-Sophie Landwehr[1], Martin Fassnacht[1] & Markus E Diefenbacherc[2]
[1]Division of Endocrinology and Diabetes, University Hospital, University of Würzburg, Germany; [2]Protein Stability and Cancer Group, Department of Biochemistry and Molecular Biology, University of Würzburg, Germany

Adrenocortical carcinoma (ACC) is a rare malignancy with an incidence of 0.7–2.0 per million per year. Prognosis of ACC is generally poor but variable and therapeutic approaches are scarce. While surgical resection presents the best option for definitive cure, mitotane remains the only approved drug for adjuvant therapy in ACC to date. Advancements regarding novel treatment strategies as well as fostered understanding of potential drivers of adrenocortical carcinogenesis have been limited by the lack of tumour models reflecting genetic disease heterogeneity. Currently available cell culture and mouse models for ACC only comprise single patient derived cell lines, corresponding mouse xenograft models and few conventional genetically engineered mouse models mainly targeting components of the Wnt-signaling pathway. To overcome this gap, we developed a workflow for culturing adrenocortical cells from C57BL/6-WT, and C57BL6/J$^{6Rosa26Sor\text{-}CAGG\text{-}SpCas9\text{-}IRES\text{-}eGFP}$ mice. After isolation and longitudinal

culture of murine adrenal cortices, we performed LC-MS/MS based steroid hormone analyses in supernatant showing sustained secretion of aldosterone (day 7: 1535 ± 697 ng/l), corticosterone (day 7: 1111 ± 123 µg/l), 11-deoxycorticosterone (day 7: 74 ± 14 µg/l) and progesterone (day 7: 9 ± 2 µg/l). Furthermore, qRT-PCR of adrenal targets showed mRNA expression of several steroidogenic enzymes e.g. HSD3B2, HSD11B1, CYP11A1, CYP11B1 and CYP11B2, as well as SF-1, StAR and SCARB1. After confirmation of adrenocortical origin, cultured cells were immortalized via CRISPR/Cas9-mediated targeting of *Trp53*. This *ex vivo* setup holds the potential to study adrenal cell homeostasis and biology, and will allow us to replicate oncogenic transformation of adrenocortical cells using CRISPR/Cas9-mediated genome editing. It presents starting point for the development of versatile and clinically relevant isogenic mouse models for adrenocortical tumours.

DOI: 10.1530/endoabs.81.RC14.4

RC14.5

Calcitonin washout in the diagnosis of medullary thyroid cancer

Berna Evranos Ogmen, Nurcan Ince, Leyla Akdogan, Aysegul Aksoy Altınboga, Cevdet Aydin[1], Oya Topaloglu, Reyhan Ersoy & Bekir Cakir
Ankara Şehir Hastanesi, Ankara, Turkey

Background
Medullary thyroid cancers (MTC) originate from parafollicular C cells and constitute 3-5% of all thyroid cancers. Calcitonin (CT) measurement is useful in the diagnosis of MTC. The sensitivity and specificity of CT are low in the measurement alone, and the sensitivity and specificity increase when used with pentagastrin and calcium stimulation tests. However, the difficulty of accessing pentagastrin, the uncertainty of the cut-off value in calcium stimulation tests, the differences in calcitonin assay and the costs complicate the use of serum CT and stimulation tests in the diagnosis. For this reason, guidelines do not offer opposing or supportive recommendations about the routine measurement of CT in patients with thyroid nodules. In this study, we aimed to investigate the contribution of CT washout of the nodule (WO) to routine CT measurement for MTC diagnosis.
Methods
In our clinic for the last three years, calcitonin values have been routinely measured in patients with nodular thyroid disease. CT-WO is performed for the nodules of patients whose calcitonin values are still above the laboratory cutoff levels in repeated measurements after excluding confounding factors. CT-WO was implemented after the thyroid fine-needle aspiration biopsy specimen was spread on a slide. The remaining material was washed with 1 mL of saline, and then the CT level was measured. In this study, the results of 33 patients who were operated on will be presented.
Results
Papillary thyroid cancer (PTC) was found in 12 (36.4%), MTC in 14 (42.4%) and benign pathology in 7 (21.2%) of the patients. CT washout was performed on 69 nodules of these patients before surgery. According to the pathology reports, eleven of these nodules were PTC, 13 were MTC, and 45 were benign. PTC and MTC were detected incidentally in two separate patients. In patients with MTC, serum CT and CT-WO values were significantly higher than the other two pathology groups ($P=0.001$). ROC analysis was performed for serum CT value, and the level 29.9 determined MTC with 100% sensitivity and 90% specificity (AUC=0.975 (0.932-1), $P<0.001$). Also, ROC analysis was performed for the CT-WO values of the nodules, and level 413.5 determined MTC with 100% sensitivity and 86% specificity (AUC=0.987 (0.965-1), $P<0.001$). The median MTC diameter in the thyroidectomy specimens was 1 cm (0.6-5.5). Micro MTC was detected in 8 (61.5%) of the patients.
Conclusion
CT-WO appears to be useful in diagnosing MTC early and accurately.

DOI: 10.1530/endoabs.81.RC14.5

RC14.6

Does the knowledge about type 2 diabetes mellitus is capable of interfering in adherence to self-care in patients?

Thielsen Cardoso da Silva[1], Laura Vilas Boas[1], Camila Alexandre Xavier[2], João Guilherme Bernart Sernajotto[3], Mariana Regina Rompkovski[4], Rafael Paulino Schuitek[5], Victória Chechetto Segalla[6] & Mirnaluci Paulino Ribeiro Gama[1]
[1]Evangelical Mackenzie Faculty of Parana, Brazil; [2]Universidade Federal do Paraná, Brazil; [3]Positivo University - Campus Ecoville, Brazil; [4]Federal University of Paraná, Brazil; [5]Positivo University, Brazil; [6]Pontifical Catholic University of Paraná, Curitiba Campus, Brazil

Introduction
Self-care plays a fundamental role in the treatment and prevention of complications of diabetes mellitus (DM). The patient knowledge about DM and its potential complications are among the factors that are associated with treatment adherence. The process of understanding the disease provides the patient better communication with professionals, better metabolic and psycho-social results which may influence on their emotional well-being and quality of life.
Objective
The present study aims to evaluate the patients' knowledge about DM 2 and adherence to self-care.
Methods
Analytical, observational, cross-sectional, descriptive study. Diabetic patients being monitored at the outpatient clinic were evaluated regarding their knowledge about DM and adherence to self-care through two questionnaires validated for the Brazilian population – Diabetes Knowlege Scale (DKN-A) and Self-Care Activity Questionnaire (QAD). The first is composed by 15 items about five major dimensions of knowledge in DM - basic pathophysiology, hypoglycemia, food groups and substitutions, complications, and general care with the disease. The second, has 6 dimensions and 15 assessment items related to self-care with diabetes (general diet, specific diet, physical activity, blood glucose monitoring, foot care, medication use, smoking).
Results
Sixty-one patients with DM2 participated in the study. In the QAD, patients' low adherence to daily self-care practices was observed, with the physical activity domain having the lowest adherence, followed by blood glucose monitoring. As for the results obtained in the DKN-A, it is noted that most reached a score equal to or greater than 8, suggesting satisfactory knowledge about the disease. The questions about food groups and substitutions were the ones with the lowest average of correct answers.
Conclusions
When analyzing the results obtained about the knowledge of diabetic patients about their disease, it is observed that the majority (67.2%) reached a score equal to or greater than 8, suggesting satisfactory knowledge about the disease. Despite this, the majority showed low adherence to the expected changes in lifestyle and self-care. Therefore, it is necessary to differentiate knowledge from the level of information - knowledge goes beyond the act of reproducing information, as it presupposes changes in attitudes, behaviors, and habits acquired throughout life. In this way, education about diabetes can be placed as one of the pillars for a satisfactory treatment, promoting a better quality of life for the patient and reducing the chances of complications.

DOI: 10.1530/endoabs.81.RC14.6

RC14.7

Prognostic value of contralateral suppression on eGFR after surgery in primary aldosteronism

Jesper Krogh[1], Nathalie Voss[1], Claus Larsen Feltoft[2], Sara Mørup[1], Caroline Clausen[3] & Mikkel Andreassen[1]
[1]Rigshospitalet, Department of Endocrinology and Metabolism, Copenhagen, Denmark; [2]Herlev Hospital, Herlev, Denmark; [3]Rigshospitalet, Department of Radiology, Copenhagen, Denmark

Adrenalectomy for primary aldosteronism has been associated with post-surgical kidney failure. It has been proposed that elimination of excess aldosterone demask an underlying failure of the kidney function. Contralateral suppression (CLS) is considered an indication of aldosterone excess and disease severity and the purpose of this study was to assess the hypothesis that CLS would predict change in kidney function after adrenalectomy in patients with primary aldosteronism. We included patients diagnosed with primary aldosteronism referred for adrenal venous between May 2011 and August 2021 and who were subsequently offered surgical or medical treatment. A total of 138 patients were included and after adrenal venous sampling 85/138 (61.6%) underwent adrenalectomy while 53/138 (38.4%) were treated with MR-antagonists. Among surgically treated patients, 59/85 (69.4%) were classified as having CLS. In this patient group, eGFR was reduced by 17.5 (SD 17.6) ml/min/1.73 m^2 compared to an increase of 1.8 (SD 12.8) mL/min/1.73 m^2 in patients without CLS ($P<0.001$). The association between contralateral suppression and the change in kidney function remained unchanged in multivariate analysis. Post-surgery, 16/59 (27.1%) patients with CLS developed hyperkaliemia compared to 2/26 (7.7%) in patients without CLS ($P=0.04$).This retrospective study found that CLS is a strong and independent predictor of a marked reduction of eGFR and

an increased risk of hyperkalemia after adrenalectomy in patients with primary aldosteronism.

DOI: 10.1530/endoabs.81.RC14.7

RC14.8

Insulin resistance prevents SHBG increase after VLCKD in non-diabetic obese male subjects

Valentina Annamaria Genchi, Angelo Cignarelli, Simona Di Leo, Fiorella Giordano, Eleonora Conte, Sebastio Perrini, Annalisa Natalicchio, Luigi Laviola & Francesco Giorgino
University of Bari, Department of Emergency and Organ Transplantation, Bari, Italy

Hepatocytes are both insulin sensitive and the primary site for synthesis of SHBG. Thus, it is possible that a condition of hepatic insulin resistance may impair hepatic synthesis of SHBG. In this study, we assessed SHBG circulating levels after 30 days of a very low-calorie ketogenic diet (VLCKD) based on high-biological value protein preparations diet (ISOMED) and natural food in a cohort of insulin-resistant obese male subjects. Moreover, we investigated the effects of exposure of different concentrations of glucose (5.5 mM, 10 mM, 30 mM) and human insulin (HI, 100 nM) on SHBG protein levels and analyzed the expression levels of insulin receptor (InsRec) in the hepatoma cell line HepG2. Twenty-two patients (mean age 39.3 $\pm$ 11.7 years, mean BMI 38.2 $\pm$ 6.4 kg/m^2) displayed fasting glycaemia within the normal range (77.5 $\pm$ 10.4 mg/dl), but elevated levels of insulin (29.3 $\pm$ 17.8 µIU/ml) and HOMA-IR (5.9 $\pm$ 3.7). Mean serum SHBG level was 20.3 $\pm$ 8.9 nmol/l at baseline. After VLCKD, a decrease of body weight (-9.3 $\pm$ 1.9 Kg), BMI (-3.0 $\pm$ 0.7 Kg/m^2), and fat mass (-6.4 $\pm$ 2.1 kg) ($P < 0.01$) was observed. A significant increase in serum SHBG levels ($+$ 7.7 $\pm$ 10 nmol/l) was also achieved after VLCKD, with a change of smaller magnitude in high ($+2.9$) vs low ($+12.4$) insulin resistance subjects. Interestingly, basal insulinemia (ß -0.6, $P<0.01$) and HOMA-IR (ß -3.2, $P<0.05$) appeared as negative predictors of SHBG variation at day 30, independently of BMI. *In vitro* results showed that 96-h treatment of HepG2 with high glucose concentrations (10 mM and 30 mM) resulted in higher SHBG protein levels (2-fold and 7-fold, respectively) and InsRec expression (1,5-fold and 2-fold, respectively) as compared to normal (5 mM) glucose. Conversely, the co-incubation with HI for 96 h blunted the augmentation of SHBG observed in the absence of insulin (-40% at 10 mM of glucose; -32% at 30 mM of glucose). Likewise, co-incubation with HI resulted in reduced InsRec expression by -67% and -60%, at 10 mM and 30 mM glucose respectively, compared to the absence of insulin. Altogether, these results suggest that high insulin levels may counteract the induction of SHBG during weight loss. *In vitro* data show that high insulin levels may favor hepatic insulin resistance by inhibition of insulin receptor expression and impair SHBG expression.

DOI: 10.1530/endoabs.81.RC14.8

Poster Presentations

Adrenal and Cardiovascular Endocrinology

P1

Familial hyperaldosteronism in a Singaporean kindred

Kevin Kwek & Eng Joo Phua
Khoo Teck Puat Hospital, Singapore, Singapore

Familial hyperaldosteronism type I (FH-I) is a rare subset of primary aldosteronism (PA) with an autosomal domintant pattern of inheritance. The molecular basis was determined to be from the unequal crossing over of the 11β-hydroxylase (CYP11B1) and aldosterone synthase (CYP11B2) genes, resulting in a chimeric gene duplication. This in turn leads to the ectopic synthesis of aldosterone in the zona fasciculata of the adrenal glands under the regulation of adrenocorticotropin along with hybrid steroids. While affected subjects typically have early onset hypertension, there is considerable phenotypic diversity. We describe the first ever series of three individuals with FH-I in a Singaporean kindred. The proband, an 18-year-old Chinese male, was initially diagnosed with primary aldosteronism during evaluation of normokalemic hypertension detected at health screening. A strong family history of early onset hypertension prompted further assessment of the proband's affected family members. His brother (aged 20) was diagnosed with essential hypertension, and his father (aged 50) had a personal history of early onset hypertension and coronary artery disease. Biochemical evaluation of both the proband and his brother revealed hyperaldosteronism, suppressed plasma renin activity with an elevated plasma aldosterone to renin ratio. Intravenous saline loading failed to suppress plasma aldosterone confirming primary aldosteronism. Computed tomographic imaging did not reveal any adrenal adenoma or hypertrophy. As FH-I was suspected, genetic analysis with long polymerase chain reaction was performed and all three subjects tested positive for the chimeric CYP11B1/B2 gene. The proband and his brother were initially treated with low-dose dexamethasone up to 0.5 mg/day and while this led to improvement in hypertension, blood pressure readings did not normalize. Due to the development of steroid-induced acne and weight gain, dexamethasone was switched to spironolactone with good effect. The proband's father was managed at another centre and declined a change in therapeutics as his blood pressure control was satisfactory. To our knowledge, this is the first report of FH-I in a Singaporean Chinese kindred and possibly the first in the region. This contributes to our local experience in managing this rare hereditary form of PA, and forms the basis for genetic screening and surveillance of this pedigree. In agreement with the Endocrine Society Clinical Practice Guidelines for PA, we recommend genetic testing for FH-I in subjects with young onset of PA (<20 years), in those with a family history of PA or strokes at a young age (<40 years).

DOI: 10.1530/endoabs.81.P1

P2

A rare ARMC5 mutation causing bilateral macronodular adrenal hyperplasia and Cushing's syndrome

Janki Panicker[1], Alison Waghorn[2] & David Ewins[3]
[1]Liverpool University Hospitals NHS Foundation Trust, Diabetes and Endocrinology Department, Liverpool, United Kingdom; [2]Liverpool University Hospitals NHS Foundation Trust, Endocrine Surgery Department, Liverpool, United Kingdom; [3]Countess Of Chester Hospital NHS Foundation Trust, Diabetes and Endocrinology Department, Chester, United Kingdom

Introduction
Primary bilateral macronodular adrenal hyperplasia (PBMAH) is a highly heterogeneous disorder and is the cause of $<2\%$ of cases of Cushing's syndrome. Around 20-25% of patients with primary bilateral macronodular adrenal hyperplasia (PBMAH) have a mutation in ARMC5.
Case report
47 year old gentleman was incidentally found to have bilateral adrenal lesions when he had a CT scan of his chest performed for chest and back pains. He had a past history of hypertension, diagnosed 8 years ago, on treatment. He had plethoric face but no striae or easy bruising, but had central obesity and thin legs. His BMI was 33 on presentation. CT scan of adrenals showed bilateral macronodular hyperplasia (right adrenal mass 5 cm and left adrenal mass 3.5 cm) not typical of adrenal adenoma. Random ACTH was suppressed. Overnight dexamethasone suppression test, low dose and high dose dexamethasone suppression tests failed to suppress cortisol with suppressed ACTH levels. Dexamethasone level, post dexamethasone suppression test showed adequate absorption/metabolism. 24 hour urinary cortisol was normal. MRI pituitary showed normal pituitary gland with no abnormal enhancement. He had slightly elevated mid night salivary cortisol and cortisone. His 17OHP level was normal. His urinary steroid profiling was normal (except low 5 alfa reductase level). His 24 hour urine catecholamines were negative and plasma renin and aldosterone level was normal. His DEXA scan was normal. All his investigations were in keeping with ACTH independent Cushing's disease. He underwent bilateral adrenalectomy and subsequently commenced on replacement dose of steroids. In view of radiological and histological diagnosis of bilateral macronodular adrenal hyperplasia, he was consented for screening for genetic mutations and this showed heterozygous ARMC5 mutation NM_001105247.1:c.2097_2099del p.(Phe700del) which was likely to be pathogenic and associated with ACTH independent macronodular adrenal hyperplasia Type 2. This particular variant has been reported in another case previously in 2015, but not reported in gnomAD database and so is only the second patient reported with such a variant in literature, as far as we know.
Conclusion
A significant proportion of what is thought to be sporadic cases of bilateral macronodular adrenal hyperplasia are due to ARMC5 genetic mutations and family history is not a reliable indicator. Patients with large multinodular adrenal gland and cortisol excess may be more likely to harbour ARMC5 germline mutation and there should be a low threshold for genetic testing.

DOI: 10.1530/endoabs.81.P2

P3

Long-term cardiometabolic morbidity in young adults wWith classic 21-hydroxylase deficiency congenital adrenal hyperplasia

Beatrice Righi[1], Salma Rashid Ali[1,2], Jillian Bryce[2], Jeremy Tolinson[3], Walter Bonfig[4,5], Federico Baronio[6], Eduardo C Costa[7], Guilherme Guaragna-Filho[8], Guy T'Sjoen[9], Martine Cools[10], Renata Markosyan[11], Tania A S S Bachega[12], Mirela C Miranda[12], Violeta Iotova[13], Henrik Falhammar[14,15], Filippo Ceccato[16], Eleni Daniel[17], Richard Auchus[18], Richard Ross[17] & Faisal Ahmed[1]
[1]Developmental Endocrinology Research Group, University of Glasgow, Royal Hospital For Sick Children, Yorkhill, Glasgow, UK; [2]Office for Rare Conditions, Royal Hospital for Children & Queen Elizabeth University Hospital, Glasgow, UK, United Kingdom; [3]Oxford Centre for Diabetes, Endocrinology & Metabolism, NIHR Oxford Biomedical Research Centre, Churchill Hospital, University of Oxford, Oxford, UK; [4]Department of Paediatrics, Technical University München, Munich, Germany; [5]Department of Paediatrics, Klinikum Wels-Grieskirchen, Wels, Austria; [6]Pediatric Unit, Department Hospital of Woman And Child, IRCSS S. Orsola-Malpighi University Hospital, Bologna, Italy; [7]Pediatric Surgery Service, Hospital de Clínicas de Porto Alegre, Porto Alegre, Brazil; [8]Department of Pediatrics, School of Medicine, Universidade Federal do Rio Grande do Sul (UFRGS), Porto Alegre, Brazil; [9]Department of Endocrinology - Center for Sexology and Gender, Ghent University Hospital, Ghent, Belgium; [10]Department of Internal Medicine and Paediatrics, Ghent University and Pediatric Endocrinology Service, Ghent University Hospital, Ghent, Belgium; [11]Endocrinology, Yerevan State Medical University Endocrinology Clinic, Yerevan, Armenia; [12]Unidade de Endocrinologia do Desenvolvimento, Laboratório de Hormônios e Genética Molecular/LIM42, Disciplina de Endocrinologia, Hospital Das Clinicas, Faculdade De Medicina, Universidade de São Paulo, São Paulo, Brazil; [13]UMHAT Sveta Marina, Medical University of Varna, Varna, Bulgaria; [14]Department of Molecular Medicine and Surgery, Karolinska Institute, Stockholm, Sweden; [15]Department of Endocrinology, Karolinska University Hospital, Stockholm, Sweden; [16]Endocrinology Unit, Department of Medicine DIMED, University-Hospital of Padua, Padua, Italy; [17]Department of Oncology and Metabolism, University of Sheffield, Sheffield, UK; [18]Division of Metabolism, Endocrinology and Diabetes, University of Michigan, Ann Arbor, MI, USA

Background
Congenital adrenal hyperplasia (CAH) and long-term glucocorticoid treatment may be associated with an increased risk of developing cardiometabolic sequelae such as abnormal glucose homeostasis, hyperlipidaemia, hypertension, cardiovascular (CV) disease, obesity and osteoporosis.
Objectives
To study the current practice amongst expert centres for assessing cardiometabolic outcomes in adult patients with 21-hydroxylase CAH and to assess the prevalence of cardiometabolic morbidity.
Methods
Data were collected using a structured questionnaire sent between January and August 2020 to 46 centres managing adults with CAH within three overlapping networks: International Congenital Adrenal Hyperplasia (I-CAH) Registry, CaH Adult Study Executive (CaHASE) Consortium UK and European Reference Network on Rare Endocrine Conditions (Endo-ERN). Information collected included current therapy and surveillance practice of adults with CAH particularly focusing on cardiometabolic conditions.

Results
Of the 31 (67%) centres from 15 countries that completed the survey, 30 (97%) screened for hypertension by measuring blood pressure, 30 (97%) screened for obesity by mainly using BMI (90%) and weight (83%), 26 (84%) screened for abnormal glucose homeostasis by mainly using Hb1Ac (73%) or fasting plasma glucose (50%), 25 (81%) screened for osteoporosis mainly by DXA (92%), 20 (65%) screened for hyperlipidaemia using fasting lipids and 6 (19%) routinely screened patients for additional CV disease. Of the 31 centres, 12 provided more information on 235 patients with a median age of 33 yrs (range 19,94). Of these, 121 (51%) were females and 165 (70%) took fludrocortisone in addition to glucocorticoids which included prednisolone (42%), hydrocortisone (34%), dexamethasone (9%) or a combination (13%). Of 235 adults, 73 (31%) were on therapy for at least one of the six cardiometabolic comorbidities; of these 73, 15 (21%) were treated for more than 2 comorbidities. Of 73, the number of patients who received therapy for osteoporosis/osteopaenia, hyperlipidaemia, type 2 diabetes/hyperinsulinaemia, hypertension, CV disease, obesity was 43 (59%), 17 (23%), 16 (22%), 10 (14%), 8 (11), 3(4%) respectively. The median age at start of these therapies was 34 (18, 63), 55 (19,79), 26 (14,78), 55(39,72), 65(55,72), 24(19,28) respectively. For some conditions such as hypertension there was a wide range of drugs used (6 drugs in 10 patients).
Conclusions
Cardiometabolic morbidities are not uncommon in adults with CAH. There is a need for greater standardisation of the screening for these morbidities from early adulthood and a need to explore optimal therapy through routine collection of standardised data.

DOI: 10.1530/endoabs.81.P3

P4

Patients with chronic kidney disease present HPA axis disregulation due to impaired glucocorticoid negative feedback

Laura Boswell[1,2,3], Miquel Blasco[4], Luis F. Quintana[4], Arturo Vega-Beyhart[2], Judith Viaplana[5], Gabriela Rodríguez[6], Daniela Díaz[2], Carme Vilardell[3], Mireia Mora[1,2,7,8], Irene Halperin[1,2,7], Antonio J. Amor[1], Gregori Casals[6] & Felicia A. Hanzu[1,2,7,8]
[1]Hospital Clínic de Barcelona, Endocrinology and Nutrition Department, Barcelona, Spain; [2]Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Barcelona, Spain; [3]Althaia, Xarxa Assistencial Universitària de Manresa, Endocrinology and Nutrition Department, Manresa, Spain; [4]Hospital Clínic de Barcelona, Nephrology Department, Barcelona, Spain; [5]Fundació Clínic per la Recerca Biomèdica, Barcelona, Spain; [6]Hospital Clínic de Barcelona, Biochemistry and Molecular Genetics Department, Barcelona, Spain; [7]Universitat de Barcelona, Barcelona, Spain; [8]Centro de Investigación Biomédica en Red de Diabetes y Enfermedades Metabólicas Asociadas (CIBERDEM), Carlos III Health Institute, Madrid, Spain

Aims
A few studies have shown disturbances in the hypothalamic-pituitary-adrenal (HPA) axis in chronic-kidney-disease (CKD), of unknown extent and clinical implications. We aimed to study the HPA axis in patients with CKD and its association with kidney impairment and metabolic disturbances.
Methods
Cross-sectional controlled study. Patients with CKD stages I-II (estimated glomerular filtration rate [eGFR] through CKD-EPI equation >60), stage III (eGFR 30-60) and stage IV (eGFR 15-30) CKD with preserved diuresis ($n=16$, 15 and 15, respectively) were included and paired with 17 healthy controls by age, sex and body mass index (BMI). Exclusion criteria were: active glucocorticoid, immunosuppressive or anti-inflammatory treatment, diabetes mellitus, morbid obesity, drugs interfering with the HPA axis or pseudo-Cushing states. Subjects underwent clinical and analytical assessment of metabolic comorbidities, body composition analysis using DEXA and a thorough evaluation of the HPA axis.
Results
We included 63 subjects (age 53 ± 12years, 52% women, BMI 26 ± 4kg/m^2). A stepped increase in hypertension and dyslipidaemia prevalence as well as increasing levels of glucose, triglycerides and 24h-urinary protein excretion were observed with worsening kidney function ($P<0.05$ for all). Both plasmatic insulin levels (7.3mIU/L in stages I-II, 11.3 in stage III, 11.4 in stage-IV-CKD, 6.3 in controls; $P<0.001$) and visceral adipose tissue volume measured using DEXA (663 cm^3 in stages I-II, 1042 in stage III, 1347 in stage-IV-CKD, 458 in controls; $P<0.001$) increased with worsening kidney function. A higher ACTH (23 vs. 17pg/ml, $P=0.048$) and less cortisol supression after 1 mg dexamethasone-suppression-test (DST) (1.2 vs. 0.9μg/dL, $P<0.001$) were seen in patients with CKD compared to controls. No differences in ACTH were observed according to CKD stage. 24h-urinary-free-cortisol was decreased in stages III-IV compared to CKD stages I-II and controls ($P<0.001$). Of all, 11 (24%) patients with CKD had a post-DST cortisol >2 mg/dL (2 [14%] in CKD stage III and 9 [60%] in the stage-IV-group); 45% of them persisted with cortisol >2 mg/dL after a low-dose 2-day-DST (2 mg/6h), all with stage IV ($P<0.001$ for all). No differences were observed in basal cortisol or cortisol-binding-globulin levels. In the whole cohort, cortisol after DST was lineally inversely correlated with eGFR (β -19.8, $P<0.001$). Cortisol after DST (OR 11.9, 95%CI 1.5-97, $P=0.021$) and glucose (OR 1.3, 95%CI 1.1-1.5, $P=0.003$) were independently associated with an eGFR <30 ml/min/m^2.
Conclusions
Negative feedback of the HPA axis is impaired in patients with CKD and correlates with disease stage. This should be taken into account when hypercortisolism is suspected and explored in this context.

DOI: 10.1530/endoabs.81.P4

P5

Group education programme for patients with adrenal insufficiency: evaluation based on patients experiences

Kirsten Davidse, Wanda Geilvoet, Lotte Brinkman, J.P. van Eck, Richard Feelders & Aart Jan Van der Lely
Erasmus University Medical Center, Internal Medicine, Division of Endocrinology, Rotterdam, Netherlands

Introduction
Adequate hormone replacement therapy in adrenal insufficiency is essential. Patients should have basic knowledge about their condition and what to do in situations which could trigger an adrenal crisis. Education on how and when hydrocortisone replacement therapy should be adjusted as well as instruction and practice an emergency injection are considered important measures to prevent an adrenal crisis. A standardized nurse-led group-based education programme (GEP) was developed based on a national guideline.
Methods
Sixty-seven patients, who attended the GEP from September 2018 until April 2020, were recruited to fill in a questionnaire in retrospect. The questionnaire categories assessed patients' experiences with the GEP on content, approach by the clinical nurse specialist and applicability in daily life. The questionnaire contained self-reported marks before and after the GEP, multiple choice questions and open questions. In addition to the questionnaire, electronic medical records for demographic data were studied.
Results
Of the 67 patients 48 responded, of whom 7 indicated they did not wanted to participate. Thirty-nine patients completed the part about the GEP-content. Three patients scored the content moderate, nine patients self-assessed the highest achievable score. On average, the patients scored a 8.6 on a scale of 10. The average reported score of 37 patients about the approach during the GEP was a 9.6 on a scale of 10. Twenty-six of the 37 patients gave the clinical nurse specialists the highest possible score. The part about applicability to apply the education in daily life was filled in by 38 patients. In this category the average score was above adequate, with a 7.7 on a scale of 10. Two patients scored below moderate, another seven patients scored average and 29 patients scored above average. Fifteen patients wrote additional comments. Strikingly, eight patients noted they would like the GEP to be given repeatedly. The greatest advantage of a group-based education reported by patients is sharing experiences and having contact with patients with the same condition. The self-reported marks were significantly improved after the GEP (p 0.003).
Conclusion
Overall, the patients who attended a two-hour group-based education programme were positive about the content of the education programme, the approach by the clinical nurse specialists and applicability of education in daily life. Repeated education and training was explicitly indicated by a large proportion of participating patients. Whether the results were affected by, for example, age or origin of adrenal insufficiency, needs to be further investigated.

DOI: 10.1530/endoabs.81.P5

P6

Primary aldosteronism and microprolactinoma: a new syndromic variant?

Chiara Parazzoli[1], Vittoria Favero[1], Valentina Morelli[2], Carmen Aresta[2], Iacopo Chiodini[1,2] & Alberto Falchetti[2]
[1]University of Milan, Department of Medical Biotechnology and Translational Medicine, Milan, Italy; [2]IRCCS Istituto Auxologico Italiano, Department of Endocrine and Metabolic Diseases, Milan, Italy

Introduction
Primary aldosteronism (PA) has been described in association with endocrine and non-endocrine neoplasms. Aldosterone-producing adenomas mainly associate with hyperparathyroidism, prolactinomas and pancreatic endocrine tumors, particularly in the context of multiple endocrine neoplasia type 1 MEN1 syndrome. Next-generation sequencing (NGS) studies have shown frequent somatic mutations underlying PA and, rarely, germline mutations of *CYP11B1/CYP11B2*, *KCNJ5*, *ATP1A1*, *ATP2B3*, *CACNA1D*, *CACNA1H*, *CLCN2* genes.
Case Report
We describe a 27-years-old PA female patient with microprolactinoma in whom we found a new variant at *KIF1B* gene. No other endocrine abnormalities have been detected, so far. She suffered for arterial hypertension and then was screened for secondary hypertension. In the context of this setting emerged a strong suspicion of PA (aldosterone-to-renin ratio 11.5). Therefore, a saline infusion test was performed confirming the diagnosis of PA. Subsequently, abdomen computed tomography revealed a left adrenal adenoma sized 14 mm in diameter. The patient was adrenalectomized with both biochemical and clinical remission. Twenty months after, she complained of oligomenorrhea, and further investigation showed a hyperprolactinemia and a microadenoma was detected on pituitary gland. Therapy with Cabergoline was initiated with remission of symptoms and normalization of prolactin levels. Considering the coexistence of an aldosterone-secreting adrenal adenoma and microprolactinoma in a young patient, an NGS genetic analysis was performed for genes linked to endocrine tumors and hereditary endocrine hypertension. The result of the genetic analysis revealed the rare heterozygous variant *c.782A > G* (p.Lys261Arg) at exon 8 of the *KIF1B* gene, classified as a variant of uncertain significance. Genetic analysis for the *KIF1B* mutation was also extended to patient's parent and her brother. The same mutation has been identified in the father, who suffers from hypertension too, and therefore we are going to screen him for PA.
Discussion
In literature, it has been suggested a direct role of hyperprolactinemia on aldosterone secretion, indicating a potential pathophysiological link between prolactin levels and PA when coexisting. However, the age of onset and the finding of hormone-secreting adenoma prompted us to perform a genetic evaluation, with the finding of the rare *KIF1B* variant. The tumor suppressor *KIF1B* gene is frequently deleted in neural-derived tumors, including neuroblastoma and pheochromocytoma, and non-neural tumors, such as hepatocellular carcinoma and lung adenocarcinoma. Considering the co-segregation of the variant with the phenotype in our family, *KIF1B* could likely play a role in tumorigenesis, possibly including also PA. Currently, the somatic genetic analysis on the adrenal adenoma is in progress.

DOI: 10.1530/endoabs.81.P6

P7

Waking salivary cortisone as screening test for adrenal insufficiency

Miguel Debono[1,2], Charlotte Elder[1], Jen Lewis[1], Jane Fearnside[1], Sharon Caunt[2], Simon Dixon[1], Richard Jacques[1], John Newell-Price[1], Brian Keevil[3] & Richard Ross[1]
[1]The University of Sheffield, Oncology and Metabolism, Sheffield, United Kingdom; [2]Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, United Kingdom; [3]The University of Manchester, Manchester, United Kingdom

Introduction
In many endocrine centres the 250μg Short Synacthen (Cosyntropin) Test (SST) is the reference standard for the diagnosis of adrenal insufficiency (AI) [1], but it is time consuming, expensive, and requires hospital attendance and venepuncture. The morning physiological peak of cortisol shortly after waking is a good predictor for a negative SST; however, a morning serum cortisol requires venepuncture. Serum cortisol and salivary cortisone correlate strongly[2], but salivary cortisone is far more convenient as can be collected at home, posted to the laboratory, and is stable at room temperature. We hypothesised that waking salivary cortisone (WSC) could predict a positive or negative SST in patients assessed for AI.
Methods
A prospective, diagnostic accuracy study of WSC was performed in 220 people at high risk of AI (majority on exogenous glucocorticoids). All patients collected a salivary cortisone sample on waking, and then attended the endocrine unit for a 250μg SST. AI was defined as a SST 30minute serum cortisol <430nmol/l. Baseline and 30minute serum cortisol was measured by LC-MS/MS and Roche Elecsys Cortisol II immunoassay, and WSC by LC-MS/MS. Questionnaires were used to assess patient views on home WSC vs SST in hospital. ROC curves were computed to assess diagnostic accuracy. Sensitivities, specificities, PPV and NPV (95%CI) were estimated.
Results
Insufficient salivary collection excluded 5.5% of samples. By SST the prevalence of AI in 208 subjects was 45% using LC-MS/MS and 44% using Immunoassay. Using the diagnostic thresholds in the table below with at least 95% sensitivity/specificity on valid WSC samples we achieved 96% NPV and 95% PPV, to exclude and confirm AI respectively. 82% of subjects preferred the home salivary cortisone.
Conclusion
Home WSC testing is a highly accurate screening tool for AI. We have shown that using WSC at 95% sensitivity/specificity avoids performing a SST in 76% (measured by LC-MS/MS) and 74% (measured by immunoassay) of patients at high risk for AI. WSC is also the preferred test by patients.
References
[1]Elder CJ, Arch Dis Child 2012 97:870-873;[2]Debono M, JCEM 2016 101:1469-1477

DOI: 10.1530/endoabs.81.P7

Table 1

WSC Threshold Predicts		Sensitivity	Specificity	PPV	NPV
SST 30 minute cortisol by LC-MS/MS					
Exclude AI	≥17 nmol/l	**96.81(90.96-99.34)**	68.42 (59.05-76.81)	71.65 (62.98-79.29)	**96.3 (89.56-99.23)**
Confirm AI	<8nmol/L	78.72 (69.07-86.49)	**96.49 (91.26-99.04)**	**94.87 (87.39-98.59)**	84.62 (77.24-90.34)
SST 30minute cortisol by Immunoassay					
Exclude AI	≥17nmol/L	**96.7 (90.67-99.31)**	66.67 (57.36-75.11)	69.29 (60.49, 77.17)	**96.3 (89.56-99.23)**
Confirm AI	<7nmol/L	75.82 (65.72-84.19)	**96.58 (91.48-99.06)**	**94.52 (86.56-98.49)**	83.7 (76.37-89.50)

P8

Pre-, peri- and post-operative characteristics of biochemically silent pheochromocytomas: a case series

Athanasios Fountas[1], Georgia Kanti[1], Spyridoula Glikofridi[1], Athanasia Kalantzi[1], Irini Giagourta[1], Athina Markou[1], Maria Christou[2], Stelios Tigas[2], Georgia Ntali[3], Chrysanthi Aggeli[4], Giorgos Zografos[4], Eleftheria Saoulidou[5], Antonia Dimakopoulou[5], Theodora Kounadi[1] & Labrini Papanastasiou[1]
[1]General Hospital of Athens 'G. Gennimatas' Unit of Endocrinology and Diabetes Center, Athens, Greece; [2]University Hospital of Ioannina, Department of Endocrinology, Ioannina, Greece; [3]'Evangelismos' General Hospital of Athens, Department of Endocrinology, Diabetes and Metabolism, Greece; [4]'G. Gennimatas' General Hospital of Athens, Third Department of Surgery, Athens, Greece; [5]'G. Gennimatas' General Hospital of Athens, Department of Anesthesiology, Athens, Greece

Introduction
Pheochromocytomas (PCs) and paragangliomas are rare tumours occurring in about 0.6 cases per 100,000 person-years. Biochemically silent PCs with normal catecholamine levels due to lack of catecholamine secretion or subtle secretion within the established normal levels are even rarer. Up to date, biochemically silent PCs are poorly investigated.
Aim
To assess the pre-, peri- and post-operative characteristics of patients with biochemically silent PCs
Design
Observational multicentre retrospective study between 2014-2021 in three tertiary hospitals.
Patients and methods
Records of patients diagnosed with biochemically silent PC and followed-up at each participating centre were reviewed and clinical, laboratory and imaging data, as well as treatment outcomes were recorded.
Results
Ten patients (5 men) with biochemically silent PC [median age 52.5 years (24-72) and BMI 25.26 Kg/m^2 (16-34.2)] were included. The adrenal masses were incidentally discovered in all patients except one who presented with paroxysmal hypertension, palpitations and postural hypotension. Twenty-four-hour urine

metanephrine and normetanephrine levels were found in the low-normal, normal and high-normal range in 4, 4 and 2 patients and in 1, 6 and 3 patients, respectively. Tumours were unilateral in all cases (7 on the right side) with a median size of 46 mm (17-125). High tumour density on pre-contrast CT imaging [median density 35 HU (22-45)] or high signal intensity on T2-weighted MRI scan was found in all cases; cystic and/or necrotic component was evident in 7 cases. ^{131}I-MIBG scan was performed in 4 cases and it was positive in all of them. Alpha-adrenergic receptors blockade with phenoxybenzamine at a median total daily dose of 70 mg (20-100) was offered in 5 patients. Intra-operatively, 4 patients developed hypertension requiring glyceryl trinitrate administration (2 of them had no pre-operative treatment with phenoxybenzamine) and 8 developed hypotension; vasoconstrictors were required in 5 cases (3 of them did not receive pre-operative alpha-adrenergic receptors blockade). One patient, not pre-operatively treated with phenoxybenzamine, developed Takotsubo cardiomyopathy requiring admission in the ICU. On histology, PASS score was $\geq$4 (2-9) in all but one cases. During a median 24-month (12-88) period of follow-up, one patient had disease progression (a right retroperitoneal paraaortic metastasis detected 88 months after surgery).

Conclusions

Patients with biochemical silent PCs were in the vast majority asymptomatic and had lesions suspicious for PC on CT or MRI scan. Despite these tumours being biochemically silent, hemodynamic instability could manifest during surgical management. A multidisciplinary approach with experienced endocrinologist, surgeon and anaesthesiologist is mandatory.

DOI: 10.1530/endoabs.81.P8

P9

Development and internal validation of a predictive model for the estimation of pheochromocytoma recurrence risk after radical surgery

Chiara Lopez[1], Mirko Parasiliti Caprino[1], Fabio Bioletto[1], Martina Bollati[1], Francesca Maletta[2], Marina Caputo[3], Valentina Gasco[1], Antonio La Grotta[4], Paolo Limone[5], Giorgio Borretta[6], Marco Volante[7], Mauro Papotti[2], Massimo Terzolo[8], Mario Morino[9], Barbara Pasini[10], Franco Veglio[11], Ezio Ghigo[1], Emanuela Arvat[12] & Mauro Maccario[1]

[1]Endocrinology, Diabetes and Metabolism; Department of Medical Sciences; University of Turin;, Turin, Italy; [2]Pathology Unit, Department of Oncology, University of Turin, Turin, Italy; [3], Endocrinology and Diabetes, University of Eastern Piedmont, Novara, Italy; [4]Endocrinology and Hypertension, Cardinal Massaia Hospital, Asti, Italy, Asti, Italy; [5]Endocrinology, Diabetes and Metabolism, A.O. Ordine Mauriziano, Turin, Italy; [6]Cuneo, Endocrinology and Metabolism, Santa Croce and Carle Hospital, Cuneo, Italy; [7]Pathology Unit; Department of Oncology; University of Turin;, Orbassano, Italy; [8]Internal Medicine, Department of Biological and Clinical Sciences, University of Turin, Orbassano, Italy; [9]Surgery, Department of Surgical Sciences, University of Turin, Turin, Italy; [10]Medical Genetics, Department of Medical Sciences, University of Turin, Turin, Italy; [11]Internal Medicine and Hypertension Unit, Department of Medical Sciences, University of Turin, Turin, Italy; [12]Oncological Endocrinology, Department of Medical Sciences, University of Turin, Turin, Italy

Objective

Various features have been identified as predictors of relapse after complete resection of pheochromocytoma, but a comprehensive multivariable model for recurrence risk prediction is lacking. The aim of this study was to develop and internally validate an integrated predictive model for post-surgical recurrence of pheochromocytoma.

Methods

The present research retrospectively enrolled 177 patients affected by pheochromocytoma and submitted to radical surgery from 1990 to 2016, in nine referral centers for adrenal diseases. Cox regression analysis was adopted for model development, and a bootstrapping procedure was used for internal validation.

Results

Variables independently associated with recurrence were tumor size (HR 1.01, 95%CI 1.00–1.02), positive genetic testing (HR 5.14, 95%CI 2.10–12.55), age (HR 0.97, 95%CI 0.94–0.99), and PASS (HR 1.16, 95%CI 1.04–1.29). The predictive performance of the overall model, evaluated by Somers' D, was equal to 0.594, and was significantly higher than the ones of any single predictor alone ($P=0.002$ compared to tumor size; $P=0.004$ compared to genetic testing; $P=0.048$ compared to age; $P=0.006$ compared to PASS). Internal validation by bootstrapping techniques estimated an optimistic bias of 6.3%, which reassured about a small tendency towards overfit.

Conclusions

We proposed a multivariable model for the prediction of post-surgical recurrence of pheochromocytoma, derived by the integration of genetic, histopathological and clinical data. This predictive tool may be of value for a comprehensive tailoring of post-surgical follow-up in radically operated pheochromocytoma patients.

DOI: 10.1530/endoabs.81.P9

P10

Comparison of assays for salivary cortisol and cortisone in the diagnosis of Cushing's syndrome

Nils Bäcklund[1], Göran Brattsand[2], Staffan Lundstedt[2], Elisabeth Aardal[3], Inga Bartuseviciene[4], Katarina Berinder[5,6], Pia Burman[7], Britt Eden Engstrom[8,9], Charlotte Höybye[6], Anders Isaksson[10], Oskar Ragnarsson[11], Ulrika Rüetschi[12], Jeanette Wahlberg[13], Tommy Olsson[1] & Per Dahlqvist[1]

[1]Umeå University, Department of Public Health and Clinical Medicine, Umeå, Sweden; [2]Umeå University, Department of Medical Biosciences, Umeå, Sweden; [3]Linköping University, Department of Clinical Chemistry, and Department of Biomedical and Clinical Sciences, Linköping, Sweden; [4]Karolinska University Hospital, Department of Clinical Chemistry, Stockholm, Sweden; [5]Karolinska institute, Department of Molecular medicine and surgery, Stockholm, Sweden; [6]Karolinska University Hospital, Department of Endocrinology, Stockholm, Sweden; [7]Skåne University Hospital, Department of Endocrinology, Malmö, Sweden; [8]Uppsala University, Department of Medical Sciences, Endocrinology and Mineral Metabolism, Uppsala, Sweden; [9]Uppsala University Hospital, Department of Endocrinology and Diabetes, Uppsala, Sweden; [10]Lund University, Department of Clinical Chemistry and Pharmacology, Lund, Sweden; [11]University of Gothenburg, Department of Internal Medicine and Clinical Nutrition, Gothenburg, Sweden; [12]Sahlgrenska University Hospital, Department of Clinical Chemistry, Gothenburg, Sweden; [13]Örebro University, Department of Internal Medicine, School of Health and Medical Sciences, Örebro, Sweden

Background & Objective

Late night salivary cortisol (LNSC) and 1 mg overnight dexamethasone suppression test (DST) are two of the three recommended screening tests for Cushing's syndrome (CS). The classical DST uses serum cortisol, but analysis of salivary cortisol and cortisone has shown high diagnostic accuracy at DST (1). Salivary cortisol can be analysed with immunoassays, which suffer from variable degree of cross reactivity with other steroids, or with LC-MS/MS, highly specific for cortisol but more time consuming and expensive. For optimal diagnostic accuracy the reference interval and diagnostic cut-off for CS should be determined for each analytical method. We aimed to establish reference intervals and compare diagnostic accuracy for late-night and post-DST salivary cortisol and cortisone analysed with clinical routine methods used in Sweden.

Design & Method

Saliva was collected at 23:00 and after DST at 08:00 in 155 reference subjects and 22 patients with CS. Samples were aliquoted and analysed with three immunoassays for salivary cortisol and three LC-MS/MS methods for salivary cortisol and cortisone. The upper reference limit (URL) was calculated as the 97.5th percentile of the reference population and sensitivity and specificity for CS was calculated. The diagnostic accuracy for each method was compared with our published LC-MS/MS using area under the curves (AUCs) for receiver operating characteristics (ROC) curves (1).

Results

The URL for LNSC with the LC-MS/MS methods were 3.4–3.9 nmol/L, and with the immunoassays; Roche 5.8 nmol/L; Salimetrics 4.3 nmol/L; and Cisbio 21.6 nmol/L. After DST, the URL for salivary cortisol were 0.7–1.0 nmol/L for LC-MS/MS, 2.4 nmol/L (Roche), 4.0 nmol/L (Salimetrics) and 5.4 nmol/L (Cisbio). The URL for salivary cortisone were 13.5 – 16.6 nmol/L in late night samples and 3.0 – 3.5 nmol/L after DST. ROC AUCs for CS diagnosis were high for all tested methods both for late night samples (0.974 – 0.986) and after DST (0.964 – 0.996). For late night samples salivary cortisol (Roche) and salivary cortisone (LC-MS/MS) showed a slightly, but significantly, higher diagnostic accuracy.

Conclusions

We present robust reference limits for salivary cortisol and cortisone in late night samples and after DST for six clinically used methods. Reference limits vary considerably for different methods. However, using method specific cut offs, all methods show high diagnostic accuracy for CS.

Reference

1. Bäcklund N, et al. Reference intervals of salivary cortisol and cortisone and their diagnostic accuracy in Cushing's syndrome. Eur J Endocrinol. 2020 Jun;182(6):569–582.

DOI: 10.1530/endoabs.81.P10

P11

Associations of age, BMI, and renal function to cortisol after dexamethasone suppression in patients with adrenal incidentalomas

Henrik Olsen[1,2], Shobitha Puvaneswaralingam[3] & Martin Olsen[4]
[1]Department of Endocrinology, Clinical sciences, Lund University, Lund, Sweden; [2]Department of Medicine, Ångelholm Hospital, Ängelholm, Sweden; [3]Department of Endocrinology, Skånes University Hospital, Lund, Sweden; [4]Department of Business Development and Technology, Aarhus University, Herning, Denmark

Introduction
The specificity of cortisol after 1 mg dexamethasone ($cortisol_{DST}$) $\geq$50 nmol/l as a criterion for mild autonomous cortisol secretion (MACS) is approximately 80% in patients with adrenal incidentalomas (AI). The aim was to study the associations of $cortisol_{DST}$to age, BMI, and renal function. We used machine learning models to uncover potential non-linear associations.
Methods
We studied 1129 patients with AI examined from 2005 to 2015 at Skåne University Hospital and Helsingborg Hospital. $Cortisol_{DST}$was ln-transformed in the analyses. The covariates studied were gender, age, BMI, eGFR, treatment with inhalation steroids, size of the AI, and size of the smallest AI in patients with bilateral AI (set to 0 in unilateral AI). Various machine learning models were trained to fit the data and examined using feature importance analysis and partial dependence plots. Partial dependence plots show the marginal effect on $cortisol_{DST}$of a covariate averaging over other covariates.
Results
$Cortisol_{DST}$ was strongly associated to the size of the AI but had weaker associations to age, BMI, and eGFR according to permutation importance. The partial dependence plots indicated relatively linear relationships for $cortisol_{DST}$to age (positively) and eGFR (negatively). There was a negative relationship to BMI at levels below 30 kg/m^2. Using linear regression, we found that $cortisol_{DST}$ increased 10% (95% CI, 7–14%) for each 10-year increase in age. In patients with BMI below 30 kg/m^2, $cortisol_{DST}$decreased 19% (95% CI, 14–23%) for each 5 kg/m^2 increase in BMI. We found no association at BMI levels above 30 kg/m^2. $Cortisol_{DST}$ increased 9% (95% CI, 6–11%) for each 10 ml/min/1.73m^2 decrease in eGFR.
Conclusions
$Cortisol_{DST}$ is positively associated to age, negatively to BMI if below 30 kg/m^2, and negatively to eGFR. These associations should be considered before diagnosing MACS.

DOI: 10.1530/endoabs.81.P11

P12

SIMBA for Students: teaching preclinical medical and pharmacy students endocrinology through online simulation - a pilot study

Isabel Allison[1], Tamzin Ogiliev[2], Jameela Sheikh[3], Georgia Morgan[4], Aditya Swaminathan[3], Alice Yip[3], Catherine Cooper[5], Fatema Rezai[3], Haaziq Sheikh[6], Harjeet Kaur[3], Kashish Malhotra[7], Eka Melson[8], Neil Gittoes[9], Kristien Boelaert[10], Alessandro Prete[11], Wiebke Arlt[11,12], Lynne Robinson[13], Justin Chu[13], Meri Davitadze[14], Paul Foster[11,12], Vivek Dhir[11], Punith Kempegowda[11,15] & Simba Team[11]
[1]Chelsea and Westminster Hospital NHS Foundation Trust, West Middlesex University Hospital, Isleworth, United Kingdom; [2]Lancaster Medical School, Bailrigg, United Kingdom; [3]University of Birmingham, College of Medical and Dental Sciences, Birmingham, United Kingdom; [4]Princess of Wales Hospital, Cwm Taf Morgannwg, United Kingdom; [5]Walsall Manor Hospital, Birmingham, United Kingdom; [6]Haberdashers' Adams' Grammar School, Newport, United Kingdom; [7]Dayanand Medical College, Punjab, India; [8]Ninewells Hospital, Dundee, United Kingdom; [9]Queen Elizabeth Hospital, Department of Endocrinology, Birmingham, United Kingdom; [10]Institute of Applied Health Research, Birmingham, United Kingdom; [11]Institute of Metabolism and Systems Research, Birmingham, United Kingdom; [12]Centre for Endocrinology, Diabetes, and Metabolism, University Hospitals NHS Trust, Birmingham, United Kingdom; [13]Birmingham Women's And Children's NHS Foundation Trust, Birmingham, United Kingdom; [14]Georgian-American Family Medicine Clinic, 'Medical House', Tbilisi, Georgia; [15]Queen Elizabeth Hospital, Birmingham, United Kingdom

Introduction
Simulation via Instant Messaging – Birmingham Advance (SIMBA) for Students is an online education model used to teach diabetes and endocrine topics to preclinical medical and pharmacy students using simulated clinical cases delivered over WhatsApp. It was developed in 2020 to provide an engaging alternative to online small group teaching (SGT). This study investigated the efficacy and acceptability of SIMBA for students compared with traditional SGT.
Methods
Each session included three 15-minute interactive clinical cases on a specific area of endocrinology, followed by a 30-minute Q&A session with an expert. All students were invited to participate in sessions relevant to their year-group curriculum. The sessions focused on the curriculum learning objectives and took place between the topic lecture and SGT. Students who attended SIMBA completed a post-SIMBA survey, including 15 multiple choice questions (MCQs). All students were asked to complete a post-SGT survey after the associated SGT, containing the same questions. Median MCQ score was compared between SIMBA only, SGT only and SIMBA + SGT groups using Wilcoxon signed rank test. The answers to Likert scale questions were expressed as percentages. Open-ended questions from surveys underwent thematic analysis.
Results
106 students attended 10 SIMBA sessions in 2020 and 2021 covering adrenal, metabolic bone, thyroid, diabetes, and reproductive endocrinology. All participants were year 1, year 2 medical, or year 1 pharmacy students. The median MCQ result was significantly higher in the SIMBA only group than both the SGT only group and SIMBA + SGT group ($P < 0.05$). There was no significant difference in score between the SGT only group and the SIMBA + SGT group ($P = 0.7103$). Most students agreed that SIMBA was well-structured (93%), engaging (76%), stimulated their interest in endocrinology (82%), promoted knowledge (91%) and an in-depth understanding (93%) and prepared them for exams (78%). Only 53% agreed that time for each case was sufficient. 80% enjoyed the session, and 85% would like to have SIMBA alongside SGT. Positive themes from thematic analysis were knowledge application through case-based learning, interaction, and instantaneous feedback. Benefits of SGT over SIMBA included peer-peer discussion and smaller group size for tutor interaction; however, tutor quality varied.
Conclusions
SIMBA is a good alternative model for SGT to teach endocrinology to pre-clinical medical and pharmacy students by providing engaging, interactive, and interesting sessions. A study is currently underway to assess improvements to the model and wider impacts on academic performance in a larger cohort.

DOI: 10.1530/endoabs.81.P12

P13

ARMC5 as a possible regulator of acetylation in the adrenal cortex in partnership with SIRT1

Annabel Berthon[1,2], Fabio Faucz[1], Benjamin Feldman[1], Ludivine Drougat[1], Stephanie espiard[3], Isadora Pontes Cavalcante[2], Bruno Ragazzon[2], Jerome Bertherat[2] & Constantine Stratakis[1,4,5]
[1]National Institutes of Health , Bethesda, United States; [2]Institut Cochin, Paris, France; [3]Institut National de la Santé et de la Recherche Médicale, U1190, European Genomic Institute for Diabetes (EGID), CHU Lille, Lille, France; [4]Human Genetics & Precision Medicine, IMBB, FORTH, Heraklion, Greece; [5]Research Institute, ELPEN, Pikermi, Athens, Greece

ARMC5 is a tumor suppressor gene responsible for 20 to 40% of Primary Bilateral Macronodular Adrenal Hyperplasia (PBMAH) with a function that remains unclear. Based on pathway analysis from RNAseq results obtained on zebrafish models of transient *Armc5* up- and down-regulation, we identified transcriptional alterations of several members of SIRT1 (sirtuin (silent mating type information regulation 2 homolog) 1) signaling in our models and hypothesized that ARMC5 can regulate SIRT1 and its signaling in adrenocortical cells. Accordingly, the expression of the desacetylase SIRT1 is significantly increased in PBMAH tissues mutated for *ARMC5* compared to tumors without mutations. However, this overexpression of SIRT1 is associated with an elevation of the profile of acetylated protein in the absence of *ARMC5* suggesting that SIRT1 activity is actually decreased and that SIRT1 expression could increase to maintain its activity. Consistently, the measurement of SIRT activity on PBMAH tissues demonstrate a decrease of its activity when *ARMC5*is mutated. Similar results are obtained in adrenal cells of 18-month-old $Armc5^{+/-}$ mice that are also hypercorticosteronemic. Altogether, these data support that ARMC5 could regulate SIRT1 expression and/or activity. *In vitro* measurement of purified SIRT1 activity in the presence of ARMC5-enriched protein extracts demonstrated that the presence of ARMC5 protein does indeed alter SIRT1 activity. We hypothesize, therefore, that ARMC5 may be a new regulator of SIRT1 function but the underlying mechanism and the consequences of abnormal acetylated proteins on adrenocortical function require further investigation.

DOI: 10.1530/endoabs.81.P13

P14

Profound changes of inflammatory and cardiovascular biomarkers in patients with autonomous cortisol secretion and Cushing syndrome

Grethe Åstrøm Ueland[1], Paal Methlie[1,2], Kristian Løvås[1], Åse Bjorvatn Sævik[2], Anette Heie[1] & Eystein Sverre Husebye[1,2]
[1]Haukeland University Hospital / Health Bergen, Norway; [2]University of Bergen, Bergen, Norway

Objective
Determine inflammatory and cardiometabolic biomarkers in patients with autonomous cortisol secretion (ACS), compared with healthy controls and patients with overt Cushing syndrome (CS).
Method
Serum from prospectively included patients with ACS ($n=65$), overt CS ($n=8$), and healthy subjects ($n=120$) were analysed for 92 different inflammatory biomarkers using proximity extension assay.
Results
ACS and CS patients revealed significant differences in levels of 49/92 inflammatory and cardiometabolic biomarkers (46 raised/3 decreased) compared with healthy subjects. No difference in biomarker levels were found between ACS and overt CS, and the biomarker levels did not correlated with the degree of hypercortisolsim. Among the 46 raised biomarkers, 20 were cardiometabolic, and 13 were inflammatory markers. Several of the biomarkers have previously been found to be elevated in patients with overt CS. The assays showed robustness, as only three biomarkers had one outlier each in healthy subjects. Seventeen patients delivered postoperative samples, median 24 months (range 6–40) after operation and hormonal cure. There was no significant normalisation of the biomarkers postoperatively.
Conclusion
We found a systemic rise in inflammatory and cardiometabolic biomarkers among patients with ACS and CS, unrelated to the degree of hypercortisolism. Curing ACS/CS did not lead to normalisation of these biomarkers after 24 (range 6–40) months.

DOI: 10.1530/endoabs.81.P14

P15

Decreased steroidogenic enzymes activity in benign adrenocortical tumors is more pronounced in bilateral lesions as determined by steroid profiling in HPLC-MSMS during ACTH stimulation test

Bonnet Fideline[1,2,3], Maxime Barat[3,4,5], Anna Vaczlavik[3,5,6], Anne Jouinot[3], Lucas Bouys[3], Christelle Laguillier-Morizot[1,5,7], Corinne Zientek[1], Catherine See[1], Etienne Larger[3,5,8], Laurence Guignat[6], Lionel Groussin[3,5,6], Guillaume Assié[3,5,6], Jean Guibourdenche[1,5,7], Ioannis Nicolis[5,9], Marie-Claude Menet[10] & Jerome Bertherat[3,5,6]
[1]Hôpital Cochin-APHP, UF d'Hormonologie, France; [2]Université de Paris, France; [3]Institut Cochin, INSERM U1016; [4]Hôpital Cochin-APHP, Radiologie, France; [5]Université de Paris; [6]Hôpital Cochin-APHP, Endocrinologie, France; [7]INSERM , Physiopathologie et pharmacotoxicologie placentaire humaine : Microbiote pré & post natal, Paris, France; [8]Hôpital Cochin-APHP, Diabétologie, France; [9]EUR 7537 BioSTM, Paris, France; [10]Institut de Chimie Physique, Université Paris-Saclay-CNRS, UMR8000, Orsay, France

Objective
Large response of steroids precursors, including 17-hydroxyprogesterone and 11-deoxycortisol, to ACTH has been described in adrenocortical tumors, suggesting the existence of intra-tumoral enzymatic deficiencies. This study aimed to compare steroidogenic enzymes activity in unilateral and bilateral benign tumors using serum steroid profiling in HPLC-MS/MS in basal state and after ACTH 1-24 stimulation.
Design and Methods
A serum profile of seven consecutive adrenal steroids (progesterone, 17-hydroxyprogesterone, 11-deoxycortisol, cortisol, deoxycorticosterone, corticosterone, androstenedione) was determined in HPLC-MSMS in basal state (T0) and after ACTH 1-24 stimulation (T60) in 35 patients with bilateral adrenocortical tumors (BL), 38 patients with benign unilateral tumors (UL) and 37 control subjects (CT). Response amplitude of each individual steroid was evaluated by T60/T0 ratio whereas enzymatic activity was assessed by downstream/upstream steroid ratio. Adrenal volume was precisely quantified by a semi-automatic segmentation method.
Results
For the seven steroids assayed, the amplitude of response to ACTH was higher in BL than in UL and in CT. As illustration, on glucocorticoids pathway, T60/T0 17-hydroxyprogesterone ratio was higher in BL (11.5 [1.6-24.9]) than in UL patients (5.2 [1.1-24.0], $P=0.0030$) and CT subjects (3.3 [0.8-14.6], $P=<0.0001$) as well as T60/T0 11-deoxycortisol ratio, also higher in BL patients (8.6 [2.1-23.3]) than in UL patients (5.3 [1.2-15.9], $P=0.0070$) and in CT subjects (3.7 [0.5-12.5], $P<0.0001$). Finally, T60/T0 cortisol ratio was higher in BL patients (2.8 [1.6-5.9]) than in UL patients (2.2 [0.8-8.1], $P=0.0046$) and CT subjects (1.8 [0.8-4.1], $P<0.0001$). The difference between BL and UL persisted even after matching patients on adrenal volume. On glucocorticoids pathway, enzymatic activity of CYP11B1, catalyzing the last step for cortisol biosynthesis, was significantly decreased in BL (78.3 [43.1-199.4]) in comparison to both UL (122.7 [13.8-228.4], $P=0.0002$) and CT (186.8 [42.1-1236.3], $P<0.0001$). This was responsible for a lower T0 cortisol (309.8 [167.2-585.2] nmol/L) in BL than in both UL (379.2 [88.5-1078.6] nmol/L; $P=0.0317$) and CT (404.1 [191.6-777.8] nmol/L; $P=0.0036$). On mineralocorticoids and androgens pathways, enzymatic activity of distal steroidogenic enzymes CYP11B2 and CYP17A1-17,20 lyase was also lower in BL than UL and CT.
Conclusions
Decreased activity of distal steroidogenesis enzymes CYP11B1, CYP11B2 and CYP17A1-17,20 lyase, is responsible for an explosive response to ACTH of upstream precursors in bilateral tumors. It also limits the synthesis of bioactive steroids, explaining the lower basal cortisol, despite the increase in adrenal mass in these bilateral forms of adrenocortical tumors.

DOI: 10.1530/endoabs.81.P15

P16

Prevalence and clinical features of ARMC5 mutations in a single centre cohort of patients with bilateral adrenal incidentalomas

Sofia Frigerio[1,2], Valentina Morelli[3], Francesca Marta Elli[1], Walter Vena[4], Maria Antonia Maffini[1], Camilla Lucca[1], Matteo Piu[1], Nicola Mora[1], Serena Palmieri[1], Giovanna Mantovani[1,2] & Maura Arosio[1,2]
[1]Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Endocrinology Unit, Milan, Italy; [2]University of Milan, Department of Clinical Sciences and Community Health, Milan, Italy; [3]IRCCS Istituto Auxologico Italiano, Unit for Bone Metabolism Diseases and Diabetes & Lab of Endocrine and Metabolic Research , Milan, Italy; [4]IRCCS Humanitas Research Hospital, Unit of Endocrinology, Diabetology and Medical Andrology, Rozzano, Italy

Introduction
Primary bilateral macronodular adrenal hyperplasia (PBMAH) is a rare cause of Cushing's syndrome (CS). Some familial forms have been associated to gene *ARMC5* (Armadillo repeat-containing protein 5) inactivating mutations. This study aimed to evaluate the prevalence and the complications of *ARMC5* mutations in our cohort of patients with bilateral adrenal incidentalomas (BAI).
Methods
72 patients, referred to our Center for BAI, were analysed to identify pathogenetic single nucleotide variants (SNVs) and/or structural rearrangements (duplications/deletions, termed as copy number variants, CNVs) involving *ARMC5* gene. We also evaluated the prevalence of glycometabolic complications, arterial hypertension (AH), nodules dimension and HPA axis parameters. Subclinical hypercortisolism (SH) was defined by cortisol levels after 1 mg overnight dexamethasone suppression (1 mgDST) $\geq$1.8 µg/dl.
Results
48/72 patients presented SH. A germline mutation of *ARMC5*was found in 9 SH patients (12.5% of the whole population), 7 SNVs and 2 CNVs (Group1). The remaining 39 SH patients were found to be wild type (*WT*) (Group2). No germline mutations were found among patients without SH (Group3; $n=24$). Moreover, we also looked for the presence of somatic *ARMC5* mutations in the tissue of 7 patients who had undergone adrenalectomy and we found that 100% presented CNVs (2 patients of Group1 and 5 patients of Group2). Age, gender and prevalence of obesity, AH, diabetes mellitus, dyslipidaemia and osteoporosis were comparable among the three groups. Patients of Group1 showed a larger diameter of the adenoma than patients of Group3 (5.77 $\pm$ 2.64 cm vs 3.40 $\pm$ 1.18 cm.; $P=0.000$), but comparable to Group2 (5.77 $\pm$ 2.64 cm vs 4.82 $\pm$ 1.62 cm, $P=0.124$). However, all the 4 patients who presented at least one nodule over 5 cm of diameter belonged to Group1. Basal ACTH levels were higher in Group3 compared to Group1 and Group2 (16.41 $\pm$ 7.50 ng/l, 10.61 $\pm$ 2.82 ng/l, 11.37 $\pm$ 6.50 ng/l respectively, $P<0.05$). Similarly, cortisol suppression after 1 mgDST was significantly lower in Group1 (7.06 $\pm$ 6.32 µg/dl) as compared to Group2 (3.97 $\pm$ 3.27 µg/dl) and Group3 (1.26 $\pm$ 0.35 µg/dl) ($P<0.01$).
Conclusion
Prevalence of germline *ARMC5* mutations in our BAI cohort was 12.5%, reaching up to 18.8% in subjects with SH. Mutation carriers seem to have poorer cortisol suppression to low dose DST and larger nodule diameter but similar metabolic comorbidities as compared to *WT* patients. Further studies are needed to elucidate

the meaning of the somatic CNVs observed in patients without germline mutations.

DOI: 10.1530/endoabs.81.P16

P17

Bilateral adrenal haemorrhages secondary to Rivaroxaban on a background of p-ANCA vasculitis

Mohammad Farhan Malik, Siva Sivappriyan, Jesse Kumar, Samantha Anandappa, Maliha Iqbal & Maha Khalid
Maidstone and Tunbridge Wells NHS Trust, United Kingdom

Background
A 73-year-old female presented to the hospital with a 3-day history of right upper quadrant abdominal pain and episodes of vomiting. Her past medical history included insulin treated Type 2 diabetes diabetes, deep venous thrombosis for which she was on rivaroxaban, COPD, right leg angioplasty and previous p-ANCA vasculitis. She also had flank tenderness and was noted to be hypertensive with a blood pressure of 225/93mmHg. A CT scan of the abdomen identified a new 4 cm right-sided indeterminate adrenal mass since her previous imaging where adrenal glands were reported normal in 2019. She became hypotensive and was treated with intravenous hydrocortisone for suspected unilateral adrenal haemorrhage. Two days later, she started to experience pain in the left flank. A dedicated MRI adrenal study showed the emergence of a new left adrenal lesion, similar in size, signal and characteristic to the lesion on the right adrenal gland. Synacthen test showed inadequate response, Aldosterone/renin ratio and adrenal androgens were not elevated. Whole body PET scan did not show any FDG avid lesions in the adrenal glands. Considering the acute history, rivaroxaban anticoagulation use, p-ANCA vasculitis, and new progressive bilateral adrenal lesions, the diagnosis was adrenal insufficiency secondary to bilateral adrenal haemorrhage. Rivaroxaban was replaced with warfarin after appropriate discussion with the haematology and adrenal MDT.
Discussion
Acute adrenal haemorrhage (adrenal apoplexy) is a rare, potentially life-threatening cause of adrenal crisis. Diagnosis can be challenging however needs to be considered especially with risk factors that include the use of anticoagulants as well as vasculitis. Abdominal CT can be useful in detecting haemorrhage within the adrenal glands. Management, after treatment of the adrenal insufficiency, often requires a multidisciplinary approach due to the complexity of the confounding risk factors. Surveillance imaging post haemorrhage can be used to monitor for resolution of the hematoma as well as investigating if there was any other underlying cause of adrenal enlargement.
Learning Points
1. Novel anticoagulant therapy can be a risk factor for developing the rare condition of bilateral adrenal haemorrhage especially in patients with a background of vasculitis. 2. Cortisol and catecholamines released by the expanding hematoma may initially precipitate hypertension and therefore adrenal insufficiency symptoms may be a late presenting feature. 3. Angiography and embolisation of adrenal haemorrhages may provide better outcomes compared with traditional surgical laparotomy and should be considered if the retroperitoneal bleeding is unresponsive to conservative management.

DOI: 10.1530/endoabs.81.P17

P18

Covid-19 infection: incidental diagnosis of pheochromocytoma in an adolescent bearing an uncommon mutation

Zoi Efstathiadou[1], Apostolos Gogakos[1], Paraskevi Komzia[1], Sophia Goulopoulou[1], Dimitrios Linos[2] & Marina Kita[1]
[1]"Hippokration" General Hospital of Thessaloniki, Endocrinology, Thessaloniki, Greece; [2]"Ygeia" Athens Medical Center, Athens, Greece, Surgery, Athens, Greece

Introduction
Chest computed tomography imaging in patients with Covid-19 infection often reveals incidental adrenal lesions, which are subsequently investigated, after recession of the infection.
Purpose
Description of a pheochromocytoma that was accidentally diagnosed in a teenager, during her hospitalization with Covid-19.
Case description
A 17-year-old girl, who was diagnosed with covid-19 infection, by molecular testing 6 days before, arrived at the emergency department, with tachycardia and dyspnea, during the first wave of the pandemic. Due to hypocapnia and tachycardia (heart rate = 110'), she underwent CT angiography to rule out pulmonary embolism. A right adrenal lesion formation of 3 cm in diameter was incidentally discovered, which showed intense enrichment with the contrast medium. The patient reported no symptoms other than emotional instability observed by the parents in recent years, which was attributed to adolescence. The girl had no personal medical history and was not on any medication. Family history was also free, negative for neoplasia. The recovery of acute covid-19 disease was followed by a complete clinical and hormonal control. On physical examination, the patient appeared with normal somatic and pubertal growth (tanner stage 5). Regular menstruation was reported. Blood pressure was normal (101/78mmHg), with a heart rate of 102'. On further MRI imaging, the tumor showed a high signal in the T2 sequences and increased enrichment. Additionally, an ^{18}F-FDG PET scan showed increased activity of the lesion (SUVmax of 21.5), with absence of other foci. The hormonal tests confirmed the diagnosis of pheochromocytoma with total metanephrines >3 times the upper normal limit. The posterior retroperitoneoscopic excision of the pheochromocytoma, after preparation of the patient with phenoxybenzamine, was uncomplicated. Histology confirmed the diagnosis of pheochromocytoma with a PASS score of zero. Genetic testing was negative for mutations in known genes associated with pheochromocytoma-paraganglioma. However, a mutation of unknown significance in the MSH6 gene (exon 4, p.K295R), which expresses a DNA mismatch-repair protein, and which is associated with Lynch syndrome, was detected in heterozygosity. The association of MSH6 gene mutations with pheochromocytoma has been reported in only 3 cases worldwide.
Conclusions
Owing to covid-19 infection, an early diagnosis and effective treatment of a potentially dangerous tumor was achieved. Furthermore, the extremely rare association of a mutation in a gene related to Lynch syndrome has also emerged, broadening the range of tumors attributed to these genes.

DOI: 10.1530/endoabs.81.P18

P19

The endocrine society practice guideline revisited: why do nowadays patients undergo screening for cushing' syndrome, and with which outcome?

Leah Braun[1], Frederick Vogel[1], Stephanie Zopp[1], Thomas Marchant Seiter[1], German Rubinstein[1], Christina M. Berr[2], Heike Künzel[1], Felix Beuschlein[3] & Martin Reincke[1]
[1]Endokrinologie, Nephrologie und weitere Sektionen - Medizinische Klinik und Poliklinik IV - Campus Innenstadt, München, Germany; [2]University Hospital Augsburg, Augsburg, Germany; [3]Klinik für Endokrinologie, Diabetologie und Klinische Ernährung USZ Campus, Zürich, Switzerland

Background
Cushing's syndrome (CS) is a rare but very severe condition with high morbidity and mortality. Patients are often diagnosed late in the course of the disease, many years after onset of symptoms. New approaches like extended screening of at risk populations, alternative biomarkers and clinical scores have been developed to improve diagnostic accuracy. However, there is still a debate, whether certain patient populations should be screened for CS outside the framework of current guideline recommendations.

Material and method
As part of the prospective German Cushing's registry, we studied 433 patients. They had suspected Cushing's syndrome or autonomous cortisol secretion. All patients underwent a standardized clinical examination including 20 clinical key items of CS. The main reason why they were referred to our department was documented. Finally, Cushing's syndrome was confirmed in 98 patients, autonomous cortisol secretion was diagnosed in 44 patients and CS was excluded in 291 subjects using the three standard screening tests urinary free cortisol, late-night salivary cortisol, the 1 mg-dexamethasone suppression-test and long-term clinical observation.
Results
Patients were referred for 18 different key presenting reasons. Five of them were more common in patients with Cushing's syndrome than in subjects in whom CS was excluded: osteoporosis (7% vs. 2%, $P=0.02$), adrenal adenoma (17% vs. 8%, $P=0.01$), metabolic syndrome (10% vs. 4%, $P=0.02$), myopathy (9% vs. 2%, $P=0.01$) and presence of multiple symptoms (16% vs. 1%, $P < 0.001$). Obesity was the single factor that was much more common in patients with exclusion of Cushing's syndrome (29% vs. 4%, $P < 0.001$). Obesity was also the most frequent reason to initiate a screening.
Conclusions
Obesity should not be a standard reason to screen a patient for CS. The results of our study confirm the current screening recommendations.

DOI: 10.1530/endoabs.81.P19

P20

Characterization of adrenal miRNA-based dysregulations in Cushing's Syndrome

Ru Zhang[1], Sharmilee Vetrivel[1], Deepika Watts[2], Andrea Osswald[1], Mareen Engel[3], Felix Beuschlein[4], Alon Chen[3,5], Silviu Sbiera[6], Ben Wielockx[2], Martin Reincke[1] & Anna Riester[1]
[1]Medizinische Klinik und Poliklinik IV, LMU Klinikum, Ludwig-Maximilians-University; [2]Institute of Clinical Chemistry and Laboratory Medicine, Technische Universität Dresden; [3]Max Planck Institute of Psychiatry; [4]Klinik für Endokrinologie, Diabetologie und Klinische Ernährung, Universitätsspital Zürich; [5]Weizmann Institute of Science; [6]Department of Internal Medicine I, Division of Endocrinology and Diabetes, University Hospital, University of Würzburg

Introduction
Transcriptional regulation of gene expression by miRNAs is critical for the fine-tuning of stress response. However, its role in hypercortisolism has not been explored well. After exploring circulating miRNAs in Cushing' Syndrome (CS) as biomarkers our aim was to investigate their origin and their role in adrenal tissue.
Methods
Next generation sequencing (NGS) based miRNA profiling was performed in adrenal samples from patients of German Cushing's registry: (1) Cortisol-Producing-Adenoma (CPA, $n=8$), (2) adrenals of patients with Cushing's Disease after adrenalectomy (CD, $n=8$) and (3) controls (adrenal samples of patients with pheochromocytoma ($n=8$). NGS data analysis and principal component analysis (PCA) clustering was performed by R (version 4.1). miRNAs were additionally validated by QPCR in other subtypes of ACTH independent CS (PBMAH, $n=10$) and ACTH dependent CS (Ectopic Cushing's syndrome, $n=3$). ACTH stimulation were done in 12 weeks-old female C57Bl6J mice according to protocol established previously. Adrenal glands were collected from the mice at 0 min (baseline), 10, 30, and 60 min upon ACTH stimulation for miRNA extraction and QPCR analysis.
Results
miRNA based NGS revealed miRNA profiles to be significantly different amongst the groups of Cushing's Syndrome (CD, CPA) and controls. Interestingly, 17 miRNAs significantly differ between the CS subtypes ($P<0.05$). Of these, four miRNAs were found to be significantly upregulated in CPA, in comparison to both CD and Controls. These upregulated miRNAs were taken for validation by QPCR. Upregulated expression of hsa-miR-139-3p ($P=0.01$, $l2fc>1.4$), hsa-miR-1247-5p ($P=0.02$, $l2fc>2.5$) in CPA compared to both CD and Controls could be confirmed by QPCR. Next, the validated miRNAs were analysed in other subtypes of CS. Hsa-miR-1247-5p was upregulated only in ACTH independent forms of CS (PBMAH ($l2fc>2.24$ $P=0.003$) and CPA ($l2fc>2.24$ $P=0.003$)). Incidentally, miR-1247-5p was not found in the previously characterized circulating miRNA profile in both CPA and CD. Finally, hsa-miR-1247-5p was found to show no differential expression in the murine adrenal tissues at different time points in comparison to the positive control of miR-96-5p.
Conclusion
This study identifies adrenal miRNAs to be regulated in ACTH dependent and independent manner in CS. ACTH independent upregulation of miRNA-1247-5p as a possible contributor to the hypercortisolism pathology in CPA and PBMAH was identified.

DOI: 10.1530/endoabs.81.P20

P21

Time from referral to definitive treatment in Cushing's syndrome

Amy Coulden[1,2,3], Simon Aylwin[4], Daniel Flanagan[5], Yaasir Mamoojee[6], Aparna Pal[7], Neil Gittoes[1,2,3] & Helena Gleeson[2,3]
[1]University Hospital Birmingham, Institute of Metabolism and Systems Research, Birmingham, United Kingdom; [2]Queen Elizabeth Hospital Birmingham, Endocrinology, Birmingham, United Kingdom; [3]Birmingham Health Partners, University of Birmingham, Centre for Endocrinology, Diabetes and Metabolism (CEDAM), Birmingham, United Kingdom; [4]Kings College Hospital NHSFT, Endocrinology, London, United Kingdom; [5]University Hospitals Plymouth NHSFT, Endocrinology, Plymouth, United Kingdom; [6]The Newcastle Upon Tyne Hospitals NHSFT, Endocrinology and Metabolic Medicine, Newcastle Upon Tyne, United Kingdom; [7]Oxford University Hospitals NHSFT, Endocrinology, Oxford, United Kingdom

Rapid diagnosis and treatment of Cushing's syndrome (CS) is essential for good outcomes. Current standards for appropriate timelines for referral are under review by NHSE. Data are required to substantiate standard setting. Knowledge of current referral pathways/processes are required to explore delays in accessing definitive surgical treatment. An audit of referral processes at Queen Elizabeth Hospital Birmingham was undertaken and further expanded to 4 additional tertiary centres in England. Data were collected on adult patients diagnosed with CS and referred for surgery at index hospitals between January 2018 and December 2019. Patients seen privately were excluded until seen in index hospital. Data were collected on demographics, initial referrer and referral pathway and dates of first clinic, subsequent referral to index hospital (if applicable), first index hospital clinic, MDT and definitive surgery. 72 patients were diagnosed with CS; 69 had definitive surgical treatment. 37 patients had pituitary CS, 34 adrenal CS, 1 had ectopic ACTH secretion. Demographics and referral pathways are outlined in table below. Results are given as median averages. Time from initial referral to secondary clinic (39.5 days in all patients, 45 days in pituitary and 35 days in adrenal patients) was shorter than those referred direct to index tertiary clinic (57 days in all-comers, 56 days in pituitary and 62 days in adrenal patients). However, total time from

Table 1

		All ($n=72$)	Pituitary ($n=31$)	Adrenal ($n=34$)
Median age (years)		49	44	48
M:F ratio		17:55	8:29	8:26
Initial referrer	GP	44(61.1%)	22(59.4%)	22(64.7%)
	Inpatient referral	25(34.7%)	13(35.1%)	12(35.3%)
Initial clinic	Secondary	44(61.1%)	20(54.1%)	24(70.6%)
	Index tertiary	22(30.6%)	14(37.8%)	7(20.6%)

referral to tertiary clinic via secondary pathway was significantly longer (158.5 days in all, 140 days in pituitary and 171 in adrenal patients). The number of diagnostic tests performed in secondary care was 6 in each group. Time from referral to index hospital to MDT was 32, 61 and 22.5 days for all, pituitary and adrenal patients respectively. Time to definitive surgical treatment was 183, 178 and 180 days for all, pituitary and adrenal patients respectively. By mapping average timeline from referral to definitive surgical treatment in CS patients, we've highlighted areas of national and hospital-specific delays which can be improved for better patient outcomes. Both secondary and tertiary centres should organise more rapid reviews of patients with a potential diagnosis of CS and minimal investigation criteria should be set before secondary centres involve tertiary centres in management of CS patients.

DOI: 10.1530/endoabs.81.P21

P22

Mesenchymal Stem Cells exposed to persistently high glucocorticoid levels develop insulin-resistance and altered lipolysis: a promising in vitro model to study Cushing's Syndrome

Mariangela Di Vincenzo[1], Marianna Martino[1], Vincenzo Lariccia[2], Giulia Giancola[1], Caterina Licini[1], Giovanni Maria Di Benedetto[3], Monia Orciani[1] & Giorgio Arnaldi[1]

[1]Università Politecnica delle Marche, Department of Clinical and Molecular Sciences (DISCLIMO), Ancona, Italy; [2]Università Politecnica delle Marche, Department of Biomedical Sciences and Public Health, Ancona, Italy; [3]Università Politecnica delle Marche, Department of Experimental and Clinical Medicine, Ancona, Italy

Objective

In Cushing's Syndrome, chronic glucocorticoid excess and their disrupted circadian rhythm lead to insulin-resistance, diabetes mellitus, dyslipidemia and cardiovascular comorbidities. As undifferentiated, self-renewing progenitors of adipocytes, mesenchymal stem cells may display the detrimental effects of glucocorticoid excess, thus revealing a promising model to study molecular mechanisms underlying metabolic complications of Cushing's Syndrome.

Design and methods

mesenchymal stem cells isolated from the abdominal skin of healthy subjects were treated thrice daily with glucocorticoids according to two different regimens: lower, circadian-decreasing (Lower, Decreasing Exposure, LDE) *vs* persistently higher (Higher, Constant Exposure, HCE) doses, aimed at mimicking either the physiological condition or Cushing's Syndrome, respectively. Subsequently, mesenchymal stem cells were stimulated with insulin and glucose thrice daily, resembling food uptake, and both glucose uptake/GLUT-4 translocation and the expression of *LIPE*, *ATGL*, *IL-6* and *TNF-α* genes were analyzed at predefined timepoints (T1 to T7) over three days.

Results

A LDE to glucocorticoids did not impair glucose uptake by mesenchymal stem cells, whereas a HCE significantly decreased glucose uptake by mesenchymal stem cells only when prolonged. Persistent signs of insulin-resistance occurred after 30 hours of HCE to glucocorticoids ($P < 0.05$ from T5 on). As compared to LDE, mesenchymal stem cells experiencing a HCE to glucocorticoids showed a significant down-regulation of lipolysis-related genes in the acute period ($P < 0.05$ for *LIPE*, *ATGL* and *TNF-α* at T2), followed by a significant overexpression once insulin-resistance had established ($P < 0.05$ for *LIPE*, *ATGL*, *IL-6* and *TNF-α* at T7).

Conclusions

Preserving circadian glucocorticoid rhythmicity is crucial to prevent the occurrence of metabolic alterations. Like mature adipocytes, mesenchymal stem cells suffer from insulin-resistance and impaired lipolysis due to chronic glucocorticoid excess: mesenchymal stem cells could represent a reliable model to track the mechanisms involved in glucocorticoid-induced insulin-resistance throughout cellular differentiation.

DOI: 10.1530/endoabs.81.P22

P23

Characterization of cytological assessments of adrenal lesions: A 12-year single center experience

Ana Maria Cristina Carasel[1,2], C Christofer Juhlin[3,4], Jan Calissendorff[1,2] & Henrik Falhammar[1,2]

[1]Karolinska Institutet, Department of Molecular Medicine and Surgery, Stockholm, Sweden; [2]Karolinska University Hospital, Department of Endocrinology, Stockholm, Sweden; [3]Karolinska Institutet, Department of Oncology-Pathology, Stockholm, Sweden; [4]Karolinska University Hospital, Department of Pathology and Cytology, Stockholm, Sweden

Background

The accuracy of the radiological and laboratory findings used to investigate adrenal masses are not optimal and therefore additional investigation methods, such as fine needle aspiration (FNA) are sometimes needed. Different methods are used for obtaining FNA such as endoscopic ultrasound (EUS), transabdominal ultrasound and computerized tomography (CT)-guided biopsy.

Methods

Using a search function incorporated in our institutional pathology database, patients who underwent FNAs of adrenal glands at Karolinska University Hospital, Stockholm Sweden between the years 2007-2019 were identified. Medical records for these patients were scrutinized from clinical, radiological, and cytological perspectives. Data included gender, age at time of FNAB, primary origin of the original tumor, uni- or bilateral disease, metastasis to other organs, tumor size, patient outcome during the observation time including survival, adequacy of the sample as well as subsequent histological diagnosis.

Results

A total of 139 adrenal FNAs were identified. Of those, 54 (38.8%) were obtained by EUS, 52 (37.4%) by transabdominal ultrasound and 26 (18.7%) were CT-guided. Preceeding radiological investigation suspected malignant lesions in 107 cases (77%). Adequate material for diagnosis was retrieved in 52 cases (96.3%) by EUS, 47 cases (90.4%) by transabdominal ultrasound and in 22 cases (84.6%) by CT-guided biopsies. By FNA adrenal lesions were diagnosed as distant metastasis in 82 cases (59%), adrenocortical cells were found in 54 cases (38.8%) and the diagnosis was unclear in 3 cases (2.2%). Of those in which adrenal cells were identified 5 were later diagnosed as adrenal cortical cancer (3.6%). Most metastases were from lung cancer (48 cases, 58.5%) followed by malignant melanoma (5 cases, 6.1%), renal cancer (4 cases, 4.9%), gynecological cancer (4 cases, 4.9%), and other malignancies (21 cases, 25.6%) (e.g., breast, prostate, hepatocellular, and gastrointestinal cancer). Complications due to the biopsy procedure such as bleeding and pneumothorax were reported in 10 cases (7.2%).

Conclusions

FNA of the adrenal glands is safe and provides useful information in diagnosis of adrenal tumors. Complications are rare regardless of method used. Overall adequacy rate for adrenal biopsy were high, with the EUS having the best results.

Keywords

fine needle aspiration, adrenal glands.

DOI: 10.1530/endoabs.81.P23

P24

Midnight ACTH vs morning ACTH levels in Cushing's syndrome diagnosis

Thibault BAHOUGNE[1], Sarah Homsi[1], Françoise Ortega[1], Marion Munch[1], Laurent Meyer[1], Nathalie Reix[2], Michel Vix[3], Helene Cebula[4], Bernard Goichot[1] & Nathalie Jeandidier[1]

[1]CHRU Strasbourg, Endocrinology, France; [2]CHRU Strasbourg, Hormonology Laboratory, France; [3]CHRU Strasbourg, Endocrine Surgery, France; [4]CHRU Strasbourg, Neurosurgery, France

Cushing's syndrome (CS) is a rare and complex condition. Once the diagnosis of CS is confirmed, repetitive morning ACTH measurement is indicated to assess whether CS is ACTH dependent or independent. ACTH under 2,2 pmol/l characterises ACTH-independent CS and above 4,4 pmol/l ACTH-dependent CS. Some groups recommend midnight ACTH measurement rather than the morning. The purpose of our work was to evaluate 12PM ACTH vs 8AM ACTH measurement in the etiological diagnostic of CS, based on 42 patients with CS (Cushing's disease, adrenal adenomas and adrenal carcinomas histologically proven) between 2004 and 2021. In Cushing's disease ($n=12$), patients are correctly categorised "ACTH-dependent" whether ACTH is measured at 8AM (92%) or at 12PM (93%) ($P=0,6$). In adrenal carcinomas ($n=6$), patients are correctly categorised "ACTH-independent" whether ACTH is measured at 8AM (100%) or at 12PM (100%). In adrenal adenomas ($n=24$), patients are more accurately classified "ACTH-independent" when ACTH is measured at 12PM (96%) rather than 8AM (58%) ($P=0,003$). In the non-classified cases, the classification is corrected when both ACTH 12AM and 8Pm are performed. We

observed that the particular interest of a 12AM dosage was observed in patients with "milder" hypercortisolism (defined as serum cortisol at 8 am under 138 nmol/l after dexamethasone 1 mg (overnight) suppression test). The main limits of our study are a small patient's sample (histology needed), a retrospective data collection, and a possible measurement bias for ACTH due to the use of 3 different kit assays. Possible inclusion of subclinical CS cannot be ruled out. To our knowledge, no other study has compared 8AM and 12PM ACTH in the etiological diagnosis of CS. In summary, assessing the cause of CS by 8AM ACTH measurement seems appropriate in first line. Additional midnight ACTH may contribute to the etiological diagnosis in mild CS ACTH independent but requires patient's night hospitalisation.

DOI: 10.1530/endoabs.81.P24

P25

Fibroblast growth factor 21 contributes to adrenal cortex renewal

Daniela Díaz Catalán[1], Arturo Beyhart[1], Mireia Mora[1,2,3], Maite Rodrigo[4], Laura Boswell[2], Gregori Casals[5] & Felicia Alexandra Hanzu[1,2,3,6]
[1]Institut d'Investigacions Biomèdiques August Pi Sunyer (IDIBAPS), Group of Endocrine Disorders, Barcelona, Spain; [2]Hospital Clínic de Barcelona, Endocrinology and Nutrition, Barcelona, Spain; [3]University of Barcelona, Barcelona, Spain; [4]Hospital Clínic de Barcelona, Pathology, Barcelona, Spain; [5]Hospital Clínic de Barcelona, Biochemistry and Molecular Genetics, Barcelona, Spain; [6]Centro de Investigación Biomédica en Red de Diabetes y Enfermedades Metabólicas Asociadas (CIBERDEM),, Madrid, Spain

Objective
After Cushing Syndrome (CS) is cured, up to 70% of patients develop chronic adrenal insufficiency (AI) and hypothalamus-pituitary-adrenal (HPA) axis dysfunction. A long-term treatment with glucocorticoids (GC) is mandatory to overcome AI. However, this treatment implies non-desired complications. Fibroblast growth factor (FGF21), a key regulator of metabolism, has a bidirectional relationship with GC that bypasses the negative feedback of the HPA axis. In this study, we aimed to investigate the potential effects of FGF21 treatment in the HPA axis in a mouse model with AI post-CS.
Methods
Male C57B6/J mice ($n = 10$/group) received corticosterone (CORT) (500μg/mL) or vehicle (VEH) in the drinking water for 5 weeks, followed by 3 days tapering period. After this period, the animals developed AI post-CS, and then they were injected daily intraperitoneally with recombinant FGF21 or VEH for 7 days. Plasma circadian and stimulated CORT and ACTH levels were assessed by immunoassay. Steroidogenic and stem/progenitor genes in the adrenal gland were determined by qPCR.
Results
AI mice during the nocturnal circadian cycle had decreased plasma CORT levels and down-regulated adrenal steroidogenic genes, whereas plasma ACTH levels remained similar to non-treated (CTL) mice. Three hours after FGF21 administration, CTL-FGF21 and CTL-VEH had similar plasma ACTH levels. However, plasma CORT levels in the CTL-FGF21 mice were significantly increased compared with CTL-VEH mice. As expected, AI groups showed lower plasma CORT levels than CTL mice. Remarkably, between the AI groups, at 1 h the FGF21 treated mice exhibited higher plasma CORT levels and maintained significantly higher ACTH levels during the 3 h after FGF21 administration compared with the VEH group. CTL mice treated with FGF21 for 7 days, increased their circadian and hypoglycemic stimulated plasma CORT levels compared to the CTL-VEH group. In line with this result, the expression of adrenal steroidogenic genes (*StAR*, *Cyp11a1*,and *Cyp11b1*) and stem/progenitor markers (*Gli*, *Wt1*, *Wnt4*, and *Dlk*) were upregulated in the CTL-FGF21 group. In agreement with CORT withdraw, AI groups maintained lower plasma CORT levels in circadian and hypoglycemic conditions, together with upregulated stem/progenitor markers compared with their respective treatment CTL groups. Interestingly, under hypoglycemic conditions, AI-FGF21 mice presented higher expression levels of adrenal Sonic hedgehog (Shh) than CTL-FGF21 and AI-VEH mice.
Conclusion
Our data describe that FGF21 contributes to maintaining a sustained CORT secretion and suggests that FGF21 accelerates and supports the adrenocortical cell renewal during AI.

DOI: 10.1530/endoabs.81.P25

P26

Prevalence of NCAH, defined by 17-hyroxyprogesterone levels after ACTH-stimulation test, in a population with adrenal incidentaloma

Fredrik Sahlander[1,2,3], Sophie Bensing[1,4] & Henrik Falhammar[1,4]
[1]Karolinska Institutet, Department of Molecular Medicine and Surgery, Stockholm, Sweden; [2]Falu hospital, Department of Medicine, Falun, Sweden; [3]Center for Clinical Research Dalarna, Falun, Sweden; [4]Karolinska University Hospital, Department of Endocrinology, Stockholm, Sweden

Background
Nonclassic congenital adrenal hyperplasia (NCAH) is a condition associated with adrenal masses and suggested by current European guidelines to be considered in case of bilateral adrenal lesions. NCAH is caused by different mutations in the *CYP21A2* gene coding for the 21-hydoxylase enzyme in the glucocorticoid synthesis leading to mild cortisol deficiency and elevated androgen and steroid precursor levels. 17-hydroxyprogesterone (17OHP) is the most important steroid precursor and used to diagnose NCAH. Elevated ACTH levels lead to development of adrenocortical hyperplasia and adrenal masses. NCAH is one of the most common autosomal recessive disorders and with an estimated prevalence of around 0.1% in the general population but up to 2-4% in some ethnic groups. The prevalence of NCAH in a population with adrenal incidentaloma (AI) is unknown but assumed to be higher than in the general population. The main reason to exclude NCAH is that a correct diagnosis can enable glucocorticoid replacement that can improve quality of life for individuals with symptoms of hyperandrogenism. The aim of this study was to investigate the prevalence of NCAH in a population of adrenal incidentalomas (AIs).
Method
After overnight fasting serum cortisol and 17OHP were measured before and 30 and 60 minutes after an intravenous injection of 0.25 mg ACTH (Synacthen®) in subjects, >18 years with AI fulfilling ESE's definition of AI at a single centre in Regional Sweden. A 17OHP >30 nmol/l before or after ACTH-stimulation was classified as NCAH.
Results
An ACTH-stimulation test was performed in 222 subjects (median age 66 (25–87) years, 58.6% women). None of the subjects presented a basal 170HP >30 nmol/l. Eight subjects (3.6%) presented a 17OHP >30 nmol/l (median 38 nmol/l (33–62) which could be compatible with NCAH. Four subjects (50%) with 17OHP >30 nmol/l had bilateral lesions.
Conclusion
The prevalence of NCAH based on the level of 17HOP after ACTH-stimulation in a population of patients with AI was 3.6%. The prevalence based on genetic analysis is probably lower, as the secretion of 17OHP can be slightly increased even from lesions without CAH. However, the prevalence of NCAH appears to be significant higher in a population diagnosed with AI than in the general population. Thus, screening for NCAH in AI may be considered even without bilateral AIs.

DOI: 10.1530/endoabs.81.P26

P27

Multiplex serum steroid profiling using liquid chromatography mass spectrometry with post column infusion ammonium fluoride

Lina Schiffer[1], Fozia Shaheen[1], Lorna Gilligan[1], Karl Storbeck[2], James M Hawley[1,3], Brian Keevil[3], Wiebke Arlt[1] & Angela Taylor[1]
[1]Institute of Metabolism and Systems Research, University of Birmingham, Birmingham, United Kingdom; [2]Department of Biochemistry, Stellenbosch Univeristy, Stellenbosch, South Africa; [3]Wythenshawe Hospital, Biochemistry Department, Manchester, United Kingdom

Background
Development of multi-steroid profiling allows comprehensive investigation into the different branches of steroid metabolism. Immunoassays only allow analysis of a single steroid per assay and suffer from problems with specificity due to cross reactivity of similar steroids. Liquid-chromatography mass spectrometry has the specificity to analyse multiple steroids in a single experiment and the dynamic range to quantify steroids at high concentrations such as those observed for cortisol (50-600nM) and at low concentration such as DHT (0.07-2.5nM). Here,

we present the optimisation, validation and application of an ultra-high performance liquid chromatography-tandem mass spectrometry assay for the profiling of 25 steroids.
Methods and Results
Sensitivity in mass spectrometry can be enhanced by addition of mobile phase additives which aid ionisation. Typically for steroids this is an acidic additive such as formic acid. Ammonium fluoride significantly enhanced ionisation in a steroid structure-dependent fashion compared to the use of formic acid, with increases in average peak area ranging between 100% and 1280%. Therefore, we validated our method with ammonium fluoride as the additive. Quantification was performed on a Waters Xevo TQ-XS mass spectrometer using electrospray ionisation in positive ion mode. Steroids were extracted via liquid-liquid extraction (using 1ml tert-methyl butyl ether) from 200µL of serum after addition of an isotopically labelled internal standard mixture. Steroids were chromatographically separated using a Phenomenex Luna Omega C18 column (1.6µm, 100Å, 2.1 x 50mm) with a water-methanol gradient. To extend column lifetime ammonium fluoride was introduced via post-column infusion (6mmol/L at 5µL/min). This method was then clinically validated and applied to serum from a healthy control cohort (167 females and 125 males, aged 21-95 years) to obtain a reference range, 18 of the 25 steroids were quantifiable in serum. Lower limits of quantification ranged from 0.28 to 3.42nM. Extraction efficiencies ranged from 90-122% and matrix effects were -19 to + 19%. Imprecision and bias at four concentrations did not exceed 15% for the majority of analytes.
Conclusions
Ammonium fluoride used as a mobile phase additive significantly enhanced sensitivity for steroid multiplex analysis. Thus, allowing quantitative analysis of 25 steroids from glucocorticoid, mineralocorticoid and androgen biosynthetic pathways in a single assay- a comprehensive assessment of the steroid metabolome. This method can be applied to a variety of biological fluids, including serum, cell and tissue culture extracts.

DOI: 10.1530/endoabs.81.P27

P28

Comparison of plasma metanephrines in patients with cyanotic and acyanotic congenital heart disease

Mojca Jensterle[1], Ana Podbregar[2], Andrej Janez[1], Matej Rakusa[1], Katja Goricar[3] & Katja Prokselj[4]
[1]Department of Endocrinology, Diabetes and Metabolic Disease, Ljubljana, Slovenia; [2]University Rehabilitation Institute Republic of Slovenia,, Ljubljana, Slovenia; [3]University of Ljubljana, Faculty of Medicine, Institute of Biochemistry, Pharmacogenetics Laboratory, Ljubljana, Slovenia; [4]Department of Cardiology, University Medical Center Ljubljana, Ljubljana, Slovenia

Background
Pheochromocytomas (PHEO) and paragangliomas (PGL) are rare neuroendocrine tumors that can lead to life-threatening conditions. The diagnosis of PHEO/PGL is established by measuring normetanephrine and metanephrine. Biochemical detection usually precedes clinical diagnosis of PHEO/ PGL by several years. Co-occurrence of cyanotic congenital heart disease (CCHD) and PHEO/PGL has been reported but potential association remains unclear. We aimed to compare plasma metanephrine and normetanephrine between patients with CCHD and patients with acyanotic congenital heart disease (ACCHD).
Material and Methods
We designed cross sectional study of prospective cohort including 44 patients with CHD (13 (29.5%) males, 31 (70.5%) females) of median age 37.5 (31.0-55.6) years at the time of follow up. Thirty-two (73%) patients had CCHD and 12 (27%) patients had ACCHD. Morning blood samples for plasma metanephrine and normetanephrine were collected and measured using the radioimmunoassay. Intra-assay coefficient of variation (CV) was 6–14%, inter-assay CV was 10–15%.
Results
Levels of plasma normetanephrine were significantly increased in patients with CCHD compared to ACCHD ($P=0.002$); 31.3% (10) patients with CCHD had increased levels of plasma normetanephrine, whereas all ACCHD patients had normal levels. Patients with lower oxygen saturation had significantly higher normetanephrine levels ($\rho=-0.444$, $P=0.003$).
Conclusions
Levels of plasma normetanephrine in patients with CCHD are higher than in patients with ACCHD, suggesting that chronic hypoxemia in CCHD contributes to the risk of PHEO/PGL development in this patients population. Routine biochemical screening for PHEO/PGL should be considered in the management of patients with CCHD, to allow timely detection of clinically important PHEO/PGL in this higher risk population. Future research is needed to better understand the association between chronic hypoxia in CCHD and PHEO/PGL.

DOI: 10.1530/endoabs.81.P28

P29

The changing face of drug-induced adrenal insufficiency in the food and drug administration adverse event reporting system

Emanuel Raschi[1], Michele Fusaroli[1], Francesco Massari[2], Veronica Mollica[2], Andrea Repaci[2], Andrea Ardizzoni[1], Elisabetta Poluzzi[1], Uberto Pagotto[1] & Guido Di Dalmazi[1]
[1]Alma Mater Studiorum - Università di Bologna, Bologna, Italy; [2]S. Orsola-Malpighi Polyclinic, Bologna, Italy

Importance
Adrenal insufficiency is a life-threatening condition complicating heterogenous disorders across various disciplines, with challenging diagnosis and a notable drug-induced component.
Objective
To describe the spectrum and main features of drug-induced adrenal insufficiency through adverse drug event reports received by the Food and Drug Administration (FDA).
Design
We conducted a retrospective disproportionality analysis within one of the largest publicly accessible spontaneous reporting systems.
Setting
The FDA Adverse Event Reporting System (FAERS) collecting more than 15 million reports since 2004.
Participants
Adverse event reports extracted from FAERS over the past 2 decades, with a focus on the 2015-2020 period.
Main Outcomes and Measures
We assessed the reporting trend of drug-induced adrenal insufficiency through descriptive statistics. Cases were selected if they contained any of the preferred terms in the Medical Dictionary for Regulatory Activities describing adrenal hypofunctions. We computed the reporting odds ratio (ROR) with relevant 95% confidence interval (CI) using Bonferroni correction to identify signals of disproportionate reporting for drugs recorded in at least 10 cases as primary suspect.
Results
We identified 8496 cases of adrenal insufficiency, 97.5% serious and 41.1% requiring hospitalization. Adrenal insufficiency showed an exponential increase throughout the years, with 5282 (62.2%) cases in 2015-2020. Among 164 drugs, we identified 56 compounds associated with significant disproportionality within various pharmacological classes: glucocorticoids ($n=1971$), monoclonal antibodies ($n=1644$, of which 1330 associated with immune checkpoint inhibitors, reaching 76% in 2020), hormone therapy ($n=291$), anti-infectives ($n=252$), drugs used for hypercortisolism or adrenocortical cancer diagnosis and/or treatment ($n=169$), protein kinase inhibitors ($n=138$). Cases of adrenal insufficiency by glucocorticoids were stable in each 5-year period (22-27%), whereas those by monoclonal antibodies peaked from 13% in 2010-2015 to 33% in 2015-2020.
Conclusions and Relevance
Our study provides a comprehensive insight into the evolution of drug-induced adrenal insufficiency, highlighting the heterogeneous spectrum of culprit drugs classes, the consolidated role of topical and systemic corticosteroids, and the emerging increased reporting of immune checkpoint inhibitors. Our data claim for an urgent identification of predictive factors of drug-induced adrenal insufficiency, and the establishment of screening protocols and educational programs for patients and caregivers.

DOI: 10.1530/endoabs.81.P29

P259

Outcome of COVID-19 infections in patients with adrenal insufficiency

Hanna Nowotny[1], Jillian Bryce[2], Roberta Giordano[3], Federico Baronio[4], Irina Chifu[5], Martine Cools[6], Erica L.T. van den Akker[7], Henrik Falhammar[8,9], Natasha Appelman-Dijkstra[10], Luca Persani[11], Guglielmo Beccuti[3], Simona Glasberg[12], Alberto M Pereira[10], Eystein Sverre Husebye[13,14,15], Stefanie Hahner[5], Faisal Ahmed[2,10,16] & Nicole Reisch[1]

[1]Klinikum der Universität München, Medizinische Klinik und Poliklinik IV, München, Germany; [2]University of Glasgow, Office for Rare Conditions, Glasgow, United Kingdom; [3]University of Turin, Department of Clinical and Biological Sciences and Division of Endocrinology, Diabetes and Metabolism - Department of Medical Sciences, Turin, Italy; [4]IRCSS AOU S.Orsola-Malpighi University Hospital, Pediatric Unit, Department Hospital of Woman and Child, Endo-ERN Centre IT11, Bologna, Italy; [5]University Hospital of Wuerzburg, University of Wuerzburg, Division of Endocrinology and Diabetology, Department of Internal Medicine I, Wuerzburg, Germany; [6]Ghent University Hospital, University of Ghent, Department of Paediatric Endocrinology, Ghent, Belgium; [7]Erasmus MC - Sophia Children's Hospital, Erasmus University Center, Department of Pediatrics, Division of Pediatric Endocrinology, Rotterdam, Netherlands; [8]Karolinska Institutet, Department of Molecular Medicine and Surgery, Stockholm, Sweden; [9]Karolinska University Hospital, Department of Endocrinology, Stockholm, Sweden; [10]Leiden University Medical Center, Department of Medicine, Division of Endocrinology and Center for Endocrine Tumors, Leiden, Netherlands; [11]Isitituto Auxologico Italiano IRCCS and University of Milan, Milan , Italy; [12]Hadassah Medical Organisation and Faculty of Medicine, the Hebrew University, Neuroendocrine Tumor Unit, ENETS Center of Excellence, Department of Endocrinology and Metabolism, Jerusalem, Israel; [13]University of Bergen, Department of Clinical Science and KG Jebsen Center for Autoimmune Disorders, Bergen, Norway; [14]Haukeland University Hospital, Department of Medicine, Bergen, Norway; [15]Karolinska Institutet, Department of Medicine, Stockholm, Sweden; [16]University of Glasgow, Developmental Endocrinology Research Group, Glasgow, United Kingdom

Background
Only few cases of patients with adrenal disorders affected by coronavirus disease 2019 (COVID-19) have been reported so far. In this study, clinical outcome data of patients with adrenal disorders and COVID-19 infection has been collected by the ESE Rare Disease Committee and ENDO-ERN via the European Registries for Rare Endocrine Conditions (EuRRECa) project.
Methods
This questionnaire included 32 questions on collecting quantitative and qualitative data. From 06/2020 onwards, 55 cases have been reported by 12 centres of 8 different European countries. In total, 48 cases of adrenal insufficiency (AI) and 7 cases of Cushing's syndrome were reported.
Results
Of the 48 cases of AI, 3 (6 %) were suspected to have COVID-19 infection and 45 (94 %) were confirmed by testing. 40 out of these 48 cases (83 %) were affected by primary adrenal insufficiency (42,5 % Addison's disease ($n=17$), 40 % congenital adrenal hyperplasia ($n=16$), 17,5 % others ($n=7$)). Affected AI patients (21 male, 27 female) had a median age of 41 (1-77) years at the timepoint of diagnosis. Of those 17 patients with Addison's disease, 76 % suffered from additional autoimmune endocrine disorders. Most relevant comorbidities were hypertension ($n=7$; 15 %), obesity ($n=7$; 15 %) and diabetes mellitus ($n=4$; 8 %). Most frequent symptoms of COVID-19 infected patients included fever ($n=29$; 60 %), tiredness or exhaustion ($n=27$; 56 %), cough ($n=23$; 48 %), muscle pain ($n=22$; 46 %), headaches ($n=16$; 33 %) and loss of taste and smell ($n=13$; 27 %). Two thirds of patients increased their daily glucocorticoid dose from a mean of 22 mg/d (SD 13 mg/d) to 42 mg/d (SD 23 mg/d). Only two of the surveyed patients administered i.m. injection of 100 mg hydrocortisone. Hospital admission was required in 8 % of cases either due to adrenal crisis or due to the severity of infection. One of the patients with AI had to be transferred to the intensive care unit. Despite one patient, who reported persistent SARS-CoV-2 infection, all others reported complete remission.
Conclusion
This European multicentric questionnaire is the first to collect data on the outcome of COVID-19 infection in patients with adrenal insufficiency. It suggests good clinical outcome in case of duly dose adjustments and emphasizes the importance of patient education on sick day rules.

DOI: 10.1530/endoabs.81.P259

P260

Menopause and muscle mass of humans and increase in fat mass

Naween Kumar[1], Siddharth Singh[2] & A S Prakash[3]

[1]Global Healthcare & Diabetes Research Centre, Darbhanga, India; [2]IGIMS, Patna, India; [3]Prakash Diabetes Hospital, Patna, India

Background
Menopause has been related to a deficiency of bulk and an increment in fat mass. Testosterone treatment is being considered to further develop body organization in menopausal women. Notwithstanding, the portion reaction connections among testosterone and the progressions in body structure and muscle strength in women have not been set up. To decide the portion subordinate impacts of reviewed dosages of testosterone on body arrangement and muscle strength in precisely menopausal women.
Methods
76 surgically menopausal women got a normalized estrogen routine during the 12-week altercation period and were then randomized to one of 5 gatherings to get week after week IM infusions of fake treatment ($n=16$), 3 ($n=15$), 6.25 ($n=15$), 12.5 ($n=16$) or 25 mg ($n=14$) testosterone enanthate for quite some time. Aggregate and free testosterone levels were estimated by LC-MS/MS and balance dialysis, individually. Slender weight (LBM) and fat mass were estimated utilizing DXA output and muscle strength was evaluated by one-redundancy most extreme technique at pattern and week 24.
Results
76 women were randomized. A pattern, mean age was 53 yrs, BMI 30 kg/m^2, total testosterone 13.8 ng/dl and free testosterone 2.3 pg/ml. On-treatment nadir testosterone fixations were 15, 88, 107, 165 and 212 ng/dl at the 0, 3, 6.25, 12.5 and 25-mg portions, individually. Changes in LBM exceptionally corresponded with changes in testosterone focuses; the assessed between-individual contrast in LBM was 0.67 kg per 100 ng/dl change in testosterone (95% CI: 0.23, 1.11; $P=0.003$). There was a huge expansion in LBM in the 25-mg portion bunch (normal increment = 1.7 kg, $P=0.01$). No huge changes in fat mass and leg press strength were seen.
Conclusion
Testosterone organization in precisely menopausal women was related to portion and fixation subordinate additions in LBM. Long haul randomized paths are expected to decide if clinically significant enhancements in different results can be accomplished securely with testosterone dosages that don't deteriorate cardiovascular danger or incite virilization.

DOI: 10.1530/endoabs.81.P260

P261

Bilateral adrenal haemorrhage due to e.coli sepsis precipitating adrenal crisis in pregnancy: a case report

Nabeel Ahmed & Sunil Nair
Countess of Chester Hospital NHS Foundation Trust, Chester, United Kingdom

A 25-year-old primi 26 weeks pregnant was admitted with B/L flank pain & pleuritic sounding chest pain. She was septic on initial assessment by the Obstetric team and preliminary investigations revealed high inflammatory markers, raised CRP of 336 & deranged LFT's. Her USS scan suggested possible hepatitis/cholangitis and blood cultures grew E. coli & she was started on IV Ceftriaxone & metronidazole for the same. At day 3 of her admission, she started deteriorating clinically with fluid responsive hypotension, tachycardia and generally unwell with an episode of hypoglycemia. She had stopped spiking temps by then & her CRP had improved to 151. Because of the initial suspicion of PE, she underwent an urgent low dose CTPA to rule out a massive PE causing hypotension which was negative for VTE. It did however suggest B/L bulky adrenals. She subsequently went on to have an MRCP the same due to worsening LFTs which was negative for obstructive jaundice but again suggested a possibility of B/L bulky adrenals. Her scans were reviewed in the Urology MDT and a possibility of B/L Adrenal Hemorrhage was suggested. Her 9 am cortisol was 177. She was given IV Hydrocortisone 100 mg iv and was started on Oral hydrocortisone

replacement which improved her BP & settled her tachycardia. She then had a dedicated MRI Adrenal scan which confirmed T2 hyper intensities in B/L Adrenal glands suggestive of B/L Adrenal Hemorrhage. Further workup was negative for Adrenal Antibodies & Autoimmune screen including Antiphospholipid Antibodies. She completed her 10-day course of IV Antibiotics for E. coli & was discharged on maintenance Hydrocortisone replacement for her Adrenal Insufficiency with a SST planned after her pregnancy to reevaluate her Adrenal reserve. Her baby thankfully remained stable throughout her torrid clinical course. This case was interesting as Adrenal Hemorrhage is usually described in the context of Meningococcal infections & there are only few reported cases of Adrenal Hemorrhage in pregnancy causing Adrenal Crisis.

DOI: 10.1530/endoabs.81.P261

P262

Key role for vasopressin V2 receptors in hypertension development in Spontaneously Hypertensive Rats (SHRs)

Ignazio Verzicchio[1], Alice Bongrani[1], Stefano Tedeschi[1], Gallia Graiani[2], Stefania Cavazzini[3], Jessica Zappa[1], Barbara Palladini[1], Elena Cremaschi[1], Anna Calvi[1], Pietro Coghi[1], Vanni Vicini[1], Valentina Cannone[1], Riccardo Volpi[1,4], Alberico Borghetti[1] & Aderville Cabassi[1]
[1]Cardiorenal Research Unit - Clinica e Terapia Medica, Parma, Italy; [2]Histology and Histopathology Unit and Molecular Biology Laboratory, Dental School, Parma, Italy; [3]University of Parma, Laboratory of Industrial Toxicology, Department of Medicine and Surgery (DIMEC), Parma, Italy; [4]Endocrinology and Andrology Unit, Clinica e Terapia Medica, Parma, Italy

Water and electrolyte balance regulation plays a key role in essential hypertension pathogenesis. Indeed, alterations in kidney ability to excrete sodium and water in relation to intake have been proposed as a basic process of hypertension development. Vasopressin (AVP) acts through V2 receptors on the basolateral membrane of collecting duct principal cells to trigger the phosphorylation of Aquaporin 2 (AQP2) which moves from the cytoplasm to the apical membrane, making the cell water-permeable and resulting in water reabsorption. In Spontaneously Hypertensive Rats (SHRs), the alterations in water and sodium balance, as well as in osmoregulation, were evaluated from the pre-hypertensive phase to the establishment of hypertension and further to hypertension-related organ damage; early AVP V1 and V2 receptor antagonism was also evaluated on blood pressure time-course. At 4-5 weeks of age, pre-hypertensive SHRs ($n=58$) showed reduced daily urine volume ($P<0.01$), increased urine osmolality ($P<0.01$) and a trend towards lower urine sodium excretion ($P=0.079$) compared to normotensive Wystar Kyoto rats (WKYs, $n=46$). Circulating levels of AVP were not different, while the urine AQP2/creatinine ratio ($P<0.01$), as well as the expression of Na^+/K^+ ATPase and betaine-amino-n-butyric acid transporter 1 (BGT1) in thick ascending limb in outer medulla (mTAL) were higher in pre-hypertensive SHRs than in WKYs. At 28–30 weeks of age, hypertensive SHRs with moderate renal failure displayed no difference in urine osmolality and renal BGT1 expression but showed similar urine AQP2/creatinine ratios with significantly higher circulating AVP levels ($P<0.01$). Treatment of SHRs ($n=20$) with the V1-antagonist OPC 21268 from 25 to 40 days of age slightly decreased blood pressure but after its withdrawal did not prevent the hypertension onset in adult age. In contrast, administration of tolvaptan, a V2 antagonist, delayed hypertension development by 4-5 weeks. In addition, tolvaptan-treated rats showed a significantly increased urine volume ($P<0.01$), as well as a decrease in urine osmolality ($P<0.01$) and urine AQP2/creatinine ratio ($P<0.01$) compared to both untreated ($n=8$) and anti-V1-treated ($n=12$) SHRs. Thus, according to our results, increased plasma levels of AVP seem to play a key role in hypertension development in SHRs through the activation of V2 receptors in the principal cells of the collecting duct, suggesting that alterations in water balance, even before sodium balance perturbations, represent a cardinal element in the pathogenesis of high blood pressure in this experimental model of hypertension.

DOI: 10.1530/endoabs.81.P262

P263

Development of a novel treatment strategy which involves thermal ablation of adrenal adenomas using electromagnetic energy

Richard Farnan[1], Anna Bottiglieri[2], Laura Farina[2], Russell Senanayake[3], Mark Gurnell[3], Punit Prakash[4], Martin O'Halloran[2], Grazia Cappiello[2], Caoimhe Newell[2], Muireann Keating[2], George Rahmani[2] & Michael Conall Dennedy[2]
[1]NUIG, Endocrinology, Galway, Ireland; [2]NUIG, Galway, Ireland; [3]University of Cambridge, Cambridge, United Kingdom; [4]Kansas State University, Kansas, United States

Primary aldosteronism (PA) arises from one or both adrenal glands and is a common cause of secondary hypertension accounting for approximately 5-12% of all hypertension. Current therapy involves mineralocorticoid receptor antagonists for bilateral disease (60%) or adrenalectomy for unilateral disease (30%). We investigate treatment planning of percutaneous adrenal ablation as an alternative definitive therapeutic modality for unilateral and bilateral disease. The main objectives of treatment planning model the following to inform optimal therapeytic approach: (i) Localisation of the aldosterone producing adenomas. (ii) Generation of optimal power input for ablation. (iii) Probe placement for precise targeting. (iv) Heat map generation to guide thermal applicator placement. Segmentation and reconstruction was performed to produce 3D models showing the adrenal glands and the surrounding vital structures using 3DSlicer® and iSeg® respectively. 11C Metomidate PET/CT images localized functioning adrenal lesions which were then rendered in a 3D virtual environment. Microwave thermal ablation transfers electromagnetic energy, targetted to the region of interest and requires temperatures >50C to ablate adrenal tissue. The necessary power to ablate was derived by applying Maxwell's equations. These involve a system of four partial differential equations and their utility in developing the power needed to ablate biological tissue. Models of specific adrenal glands are created using dielectric and thermal properties used to determine delivery of effective thermal energy. These parameters were used to inform power settings and probe placement necessary to safely ablate adrenal nodules.

DOI: 10.1530/endoabs.81.P263

P264

Mitotane side effects in the treatment of patients with adrenocortical carcinoma - a retrospective study

Anja Barac Nekic[1], Karin Zibar Tomšić[2], Lana Sambula[3], Nino Matas[1], Martina Jambrović[4], Iva Petrak[5], Tina Dusek[2] & Darko Kastelan[2]
[1]General Hospital Dubrovnik, Department of Endocrinology, Dubrovnik, Croatia; [2]University Clinical Hospital Centre Zagreb, Department of Endocrinology and Diabetology, Zagreb, Croatia; [3]General hospital Dr. Tomislav Bardak, Koprivnica, Department of Endocrinology, Koprivnica, Croatia; [4]General Hospital Čakovec, Department of Endocrinology, Čakovec, Croatia; [5]General Hospital Nova Gradiška, Department of Endocrinology, Nova Gradiška, Croatia

Introduction
Mitotane is widely used to treat adrenocortical carcinoma (ACC) and remains the mainstay of treatment along with surgery. The aim of this study is to evaluate the adverse side effects of mitotane treatment.
Materials and Methods
This retrospective study included 36 patients with ACC, ENSAT stage I- IV, who were treated with mitotane in an adjuvant or palliative setting. Patients with ENSAT stage IV who died within 6 months after surgery were excluded ($n=6$). Patient demographic and clinical characteristics, as well as metabolic and hormonal side effects of mitotane, were collected from hospital medical records.
Results
The median age of patients was 48 (18-78) years, 72% of them were female. Twenty-seven patients (75%) received adjuvant mitotane whereas 9 patients (25%) received it in a palliative setting, as monotherapy ($n=3$) or in combination with chemotherapy ($n=6$). One patient permanently, and two temporarily, discontinued mitotane treatment due to side effects (severe liver lesion, exfoliative dermatitis and severe gastrointestinal disturbances). Of the remaining

33 patients, all achieved the target mitotane concentration (> 14 mg/L) after median time of 102 days (76-121). In 25 patients (76%), the target mitotane concentration was maintained during > 75% of the treatment period. As for the endocrine toxicity of mitotane, all patients required glucocorticoid substitution, 8 patients (24%) had mineralocorticoid insufficiency, 16 (49%) had central hypothyroidism whereas hypogonadism was observed in 89% of male patients (8/9). In addition, 29% of female patients (7/24) developed ovarian cysts and 15 (46%) patients had dyslipidaemia. Four patients had an Addison crisis during treatment. Fourteen patients (42%) experienced gastrointestinal side effects including nausea, vomiting, diarrhoea and weight loss, while 32 patients (97%) had elevated liver enzymes, predominantly GGT. Twelve patients (36%) had various neurological side effects such as dizziness, decreased ability to concentrate or speech disorders (stutter or aphasia).

Conclusion

Mitotane treatment is associated with a wide spectrum of side effects and their successful management is of paramount importance to improve patient adherence to treatment and avoid drug discontinuation.

DOI: 10.1530/endoabs.81.P264

P265

Adrenergic crisis after SARS-COV-2 infection in a patient affected by pheochromocytoma

Roberto Novizio[1], Gaetano Emanuele Rizzo[1], Rosa Maria Paragliola[1], Ettore Maggio[1], Pietro Locantore[1] & Salvatore Maria Corsello[1,2]
[1]Fondazione Policlinico Universitario Agostino Gemelli IRCCS Universitaà Cattolica del Sacro Cuore, Unit of Endocrinology and Diabetes, Rome, Italy; [2]UniCamillus, Saint Camillus International University of Health Sciences, Rome, Italy

Background

SARS-CoV-2 infection is characterized by aspecific symptoms (e.g., fever, cough) and can be complicated by viral pneumonia and many other manifestations can occur. Endocrinological complications have also been described. Pheochromocytomas are rare tumors located in the adrenal medulla, causing symptoms due to catecholamines overproduction and abrupt release. Catecholamines release can be continuous or intermittent and there can be several triggers including stress, physical exercise and some foods. SARS-CoV-2 infections have not been previously described as a precipitator of adrenergic crisis in pheochromocytoma. We report a case of adrenergic crisis caused by SARS-CoV-2 infection in a patient affected by pheochromocytoma.

Case report

A 63-year-old Caucasian male affected by right adrenal pheochromocytoma waiting for surgical removal was admitted to the emergency department (ED) for fainting episode and hypertensive crisis. Patient was known for type 2 diabetes and hypercholesterolemia treated by slow-release metformin 500 mg/day and atorvastatin 40 mg/day and was not vaccinated for SARS-CoV-2. Two months before, he was hospitalized in another center formyocardial infarction with non-obstructive coronary arteries and a chest-abdomen CT scan showed a 1.5 cm right adrenal mass. The 24-h urinary metanephrines were >5000 µg/24h and normetanephrines >2500 µg/24h. Scintigraphy with 250MBq ^{123}I-MIBG showed uptake in the right adrenal gland formation, consistent with pheochromocytoma. Patient was started on alpha-blockers (Doxazosin 2 mg twice/day). Two weeks later, patient was also started on metoprolol 50 mg twice/day. In the ED, BP was 210/108 mmHg with a HR of 105 bpm. A routine nasopharyngeal swab for SARS-COV-2 was performed. After administration of 2 mg of doxazosin and 20 mg of nifedipine, symptoms addressed to catecholamine release disappeared. As the nasopharyngeal swab resulted positive for SARS-COV-2, the patient was transferred to infectious diseases unit. Since mean BP was persistently high, doxazosin was increased to 4 mg twice/day, with beneficial effect on BP and HR. After 10 days, the patient tested negative for SARS-CoV-2 and was discharged, with normal vital parameters and indication to continue the new increased dosage of doxazosin. No other crisis was reported until surgery, that was performed without any complication.

Discussion

Since adrenergic crisis is a life-threatening condition, we suggest close BP monitoring and therapeutic adherence in patients with pheochromocytoma waiting for surgery, living in areas characterized by outbreak of Covid-19 infection. In case of infection, we suggest considering an increase in alpha-blocker dosage in order to prevent crisis.

DOI: 10.1530/endoabs.81.P265

P266

WBC count. A potential tool for suspecting Cushing's syndrome (CS)

Miguel Paja Fano[1,2], Ignacio Merlo-Pascual[1], Josune Rodríguez-Soto[1], M. Dolores Moure-Rodríguez[3], Andoni Monzón-Mendiolea[1], Nerea Egaña-Zunzunegui[4], Cristina Elías-Ortega[4], Elena Cruz-Iglesias[5] & Amelia Oleaga-Alday[1]
[1]OSI Bilbao-Basurto, Basurto University Hospital, Endocrinology, Bilbao, Spain; [2]Basque Country University (UPV-EHU), Medicine, Spain; [3]OSI Ezkerraldea-Enkarterri, Cruces University Hospital, Endocrinology, Barakaldo, Spain; [4]OSI Donostia, Donostia University Hospital, Endocrinology, Donostia, Spain; [5]OSI Bilbao-Basurto, Basurto University Hospital, Biochemistry. Hormonal Lab, Bilbao, Spain

Early diagnosis of CS could reduce the morbidity and mortality associated with endogenous hypercortisolism. Many clinical methods have been proposed to establish suspicion of CS, but they show a poor positive predictive value (PPV) and are sometimes difficult to assess. Assuming the well-known influence of hypercortisolism on white blood cell (WBC) count, we evaluated its potential usefulness as a screening test to trigger this suspicion. We analysed WBC count around the diagnosis of CS patients (cases) and compared them in a 1:2 ratio with age- and sex-matched controls who had undergone a negative Nugent's test (plasma cortisol <1.8 µg/dl after 1 mg DXM). We evaluated the predictive value of haematological parameters by applying ROC curves and tried to find a reference value to establish the suspicion of CS. We collected 72 confirmed CS cases and 144 matched controls from three centres. Mean age was similar (48.5 vs 48 years), both groups included 82% women. Controls had a higher mean BMI than cases (36 vs 29.2; $P<.001$). There was no significant difference in the incidence of diabetes (27.8% in controls and 31.9% in cases) and there was a significant higher prevalence of hypertension in cases than in controls (61.1% vs 37.5%; $P=.001$). The rate of active smoking showed no difference between the two groups. Mean WBC count, neutrophil count and percentage were significantly higher in cases, while mean lymphocyte count and percentage were significantly lower in cases than in controls. ROC curves showed an AUC greater than 0.7 for total WBC count, neutrophil count and percentage, lymphocyte count and percentage, and for the difference of total WBC count minus lymphocytes, the difference of both WBC subtypes (neutrophils minus lymphocytes) and the neutrophil/lymphocyte ratio. The two highest levels of discrimination were obtained with the ratio of neutrophil to lymphocyte count (N/L) and the percentage of lymphocytes, which both had an AUC equal to 0.865. The combination of an N/L ratio greater than 2.73 and a lymphocyte percentage less than 25% gave a sensitivity of 77.8% and a specificity of 80.5% for detecting CS, with a PPV of 66.7%. In conclusion, a simple assessment of white blood cell count could be a valuable and inexpensive clue to the suspicion of Cushing's syndrome. Its routine application in patients with metabolic syndrome could lead to increased detection of CS in endocrinology clinics and reduce the burden of late diagnosis of this disease.

DOI: 10.1530/endoabs.81.P266

P267

Screening for non-classic congenital adrenal hyperplasia revisited: proposal for a new serum 17-hydroxyprogesterone threshold for which a cosyntropin stimulation test is indicated

Afif Nakhleh[1,2], Leonard Saiegh[1,3], Lia Supino-Rosin[4], Raya Gendelman[5], Naim Shehadeh[1,2] & Moshe Zloczower[2]

[1]Maccabi Healthcare Services, Diabetes and Endocrinology Clinic, Haifa, Israel; [2]Rambam Health Care Campus, Institute of Endocrinology, Diabetes and Metabolism, Haifa, Israel; [3]Bnai Zion Medical Center, Department of Endocrinology, Haifa, Israel; [4]Maccabi Healthcare Services, Central Laboratory, Rehovot, Israel; [5]Rambam Health Care Campus, The Endocrinology Laboratory, Haifa, Israel

Introduction
The 250 μg cosyntropin stimulation test (CST) is used to diagnose non-classic congenital adrenal hyperplasia (NCCAH). The current recommendation to perform CST is when follicular morning 17-hydroxyprogesterone (17OHP) is higher than 6 nmol/L, and CST is considered positive for NCCAH diagnosis when the 60-minutes post-CST 17OHP serum level is above 30 nmol/L. These cut offs are mainly derived from radioimmunoassay (RIA) data. Recently, a validated enzyme-linked immunosorbent assay (ELISA) has widely replaced RIA in the measurement of serum 17OHP. This study aimed to determine the RIA and ELISA-based 17OHP cut offs at which CST should be performed.
Material and methods
We conducted a retrospective cohort study at Maccabi Healthcare Services, an Israeli Health Maintenance Organization (HMO). Data was retrieved from adult females (≥16 years) with suspected NCCAH, referred for CST during 2001–2020. Clinical indications that led to NCCAH testing were hirsutism, irregular menses, acne, alopecia, or infertility. NCCAH was defined as post-CST 17OHP serum level >30 nmol/L. Serum 17OHP levels were assayed by direct RIA (Wizard gamma counter, Perkin-Elmer) from January 2000 through March 2015, and by ELISA (IBL International, Tecan) from April 2015 to December 2020. We allocated the individuals into two groups according to the assay method used. For each group, a ROC curve was generated and optimal pre-CST 17OHP threshold with the highest sensitivity and specificity determined.
Results
Cosyntropin testing was performed in 2409 female subjects (1564 in the RIA and 845 in the ELISA groups). The mean (±SD) age was 24.1±7 years. NCCAH was diagnosed in 74 (4.7%) of the RIA group and 63 (7.5%) of the ELISA group. The mean (±SD) pre- and post-CST 17OHP levels were lower in the RIA group as compared to the ELISA group (4.1±6.4 vs. 5.9±9.0 and 9.9±15.3 vs. 12.3±17.3, respectively, $P<0.0001$). Using ROC analysis, the optimal pre-CST 17OHP cut off values predicting NCCAH were 6.05 nmol/L in the RIA group (sensitivity 93.2%, specificity 91.7%) and 8.16 nmol/L in the ELISA group (sensitivity 93.7%, specificity 92.3%). When the guideline-recommended pre-CST 17OHP cut off value of 6 nmol/L was used in the ELISA group, sensitivity was 95.2%, and specificity decreased to 84%.
Conclusions
Our study showed a significant number of unnecessary cosyntropin tests. The optimal RIA-based pre-CST 17OHP cut off was comparable with that recommended in the guidelines. However, the results suggest adopting a higher 17OHP cut off when using ELISA. Further studies that incorporate genetic data are needed.

DOI: 10.1530/endoabs.81.P267

P268

Almost half of patients using inhaled corticosteroids have secondary adrenal insufficiency

Vishal Batheja[1], Neeru Mittal[2] & Jubbin Jagan Jacob[3]
[1]Christian Medical College & Hospital, Department of Medicine, Ludhiana, India; [2]Christian Medical College & Hospital, Department of Respiratory Medicine, Ludhiana, India; [3]Christian Medical College and Hospital, Department of Endocrinology, Ludhiana, India

Context
Secondary adrenal insufficiency (SAI) has been identified in over 22% of adults using inhaled corticosteroids (ICS).[1] This has been co-related with the total daily dose and type of ICS along with individual genetic susceptibility among the subjects using ICS.[1,2] Our recent paper suggested that 2.8% of adults with euvolaemic hyponatremia admitted to the hospital had ICS related SAI.[3]
Objective
To determine prevalence of SAI among chronic users of ICS in India along with determining the association of SAI with the type and total daily dose of ICS and baseline clinical clues to the presence of SAI.
Methods
Adult patients using ICS for over 4 weeks were included after informed consent from among patients seen in medical and respiratory clinics of a tertiary care hospital in India. Critically unwell patients, those who received oral or intravenous steroids in the past 6 months and those already having SAI were excluded. Baseline ICS dose and type were converted to fluticasone dose equivalents as per National Asthma Education Expert panel and classified as having high (>1gm/day), moderate (0.5-1gm/day) or mild(<0.5gm/day) exposure.[4]Baseline demography and presence of symptoms suggestive of SAI was recorded. An Acton Prolongatum™ Stimulation test (APST) was done on all patients to evaluate SAI.[5] A cut-off cortisol value of <18 mg/dL after 60 min of APST was used to diagnose SAI.
Results
Seventy-five patients (F43:M32) with a mean age of 54.9±15 years were included and underwent APST testing. Among them 34 (45.3%) had SAI. There was no difference in the prevalence of SAI with type or dosing of ICS (1.0±0.4 vs. 1.1±0.4gm/day p-value=0.2). Clinically patients with asthma (52.9%) had more SAI than those with chronic obstructive airway disease (23.5%) (p-value=0.04). Among symptoms those with baseline nausea had more prevalent SAI (9.7% vs.29.4%, p-value=0.03). There was a suggestion that longer use of ICS (3.3±3.5 vs 4.7±3.7 years, p-value=0.07) was associated with more SAI.
Conclusion
Among patients who are on long-term ICS around 45% have SAI, which may require appropriate replacement during stressful periods. Clinically patients with chronic asthma, those with longer use of ICS and those who have nausea may be more likely to have SAI. The dose and type of ICS was not associated with the presence of AI.

References
1. Lancet Respir Med. 2018; 6: 442-450 2. Arch Intern Med. 1999;159(9):941-955. 3. Endocr Connect. 2021;10(12):1623-1631. 4. Eur Respir J. 2013; 42: 79–86 5. Eur J Endocrinol. 2019;181(6):639-645.

DOI: 10.1530/endoabs.81.P268

P269

Evaluation of a tertiary centre specialist adrenal MDT: The first 900 patients

Louisa Child[1], Rebecca Sagar[2], Sheila Fraser[3], Emma Collins[3], Russell Frood[3], Andrew Scarsbrook[3] & Afroze Abbas[2]
[1]University of Leeds, School of Medicine, Leeds, United Kingdom; [2]Leeds Teaching Hospitals Trust , Leeds Centre for Endocrinology and Diabetes, Leeds, United Kingdom; [3]Leeds Teaching Hospitals Trust, Leeds, United Kingdom

Background
Adrenal incidentalomas are common amongst the general population, incidence increases with age. Radiological and biochemical assessment of all lesions >1 cm is standard practice to determine appropriate future management, as per current European guidelines. We report the experiences of a recently formalised adrenal multi-disciplinary pathway in a large UK teaching hospital, where all adrenal incidentalomas are referred and systematically assessed.
Methods
902 patients presenting with an adrenal incidentaloma discussed at a multi-disciplinary team (MDT) meeting over 2.5 years were retrospectively reviewed. Data were collected on demographics, imaging, biochemistry and where relevant diagnosis, surgical outcome and histopathology. Functional testing included overnight dexamethasone suppression tests, aldosterone, plasma renin activity and plasma metanephrines. Prism v9.3.1 was used for statistical analysis.
Results
Of the 902 patients, 47% were male. Mean age was 64 years ± 14 (SD). 865 patients had some form of functional testing, of which 45% had initial results suggestive of endocrine hypersecretion. 899 had imaging available, 82.7% had unilateral lesions with 64.1% found within the left adrenal gland. Mean lesion size 2.9 cm±2.4 (range 0.6-21 cm). Mean Hounsfield Units was 4.88±15.7. 39.8% of ONDST performed had an unsuppressed cortisol (greater than 50nmol/l). 21.2% of plasma metanephrine tests performed were elevated above the normal reference range. From the entire cohort, 5.6% were diagnosed with phaeochromocytoma, 3.7% with primary aldosteronism, 9.2% had mild autonomous cortisol secretion, 2.1% had adrenal cortical carcinoma and 0.9% had paraganglioma.

Other diagnoses include metastases, lymphoma and haemorrhage. There was an overall mortality of 5.8% over the follow-up period (1-3 years).
Conclusion
Our results demonstrate a very high proportion of patients with incidental adrenal nodules have abnormal endocrine functional testing. ONDST in particular had a high positivity rate. There are significant confounders to most of these tests, with the likelihood some results will be false positives. Therefore, multidisciplinary expertise is crucial for appropriate interpretation and determination of further assessment in every case. This systematic multi-disciplinary approach to incidental adrenal nodules has led to earlier detection of a large number of phaeochromocytomas, patients with primary aldosteronism and malignancy, who may have not otherwise been referred in our centre.

DOI: 10.1530/endoabs.81.P269

P270

Proposition of the first histopathological classification of primary bilateral macronodular adrenal hyperplasia (pbmah) and its correlation with armc5 and kdm1a status

Florian Violon[1,2], Lucas Bouys[1,3], Anna Vaczlavik[1,3], Giannone Gaetan[1], Annabel Berthon[1], Bruno Ragazzon[1], Benoît Terris[2], Mathilde Sibony[1,2] & Jerome Bertherat[1,3]
[1]Institut Cochin, Equipe Génomique et Signalisation des Tumeurs Endocrines, Paris, France; [2]Hôpital Cochin, Service de Pathologie, Paris, France; [3]Hôpital Cochin, Service d'Endocrinologie, Paris, France

Introduction
Primary Bilateral Macronodular Adrenal Hyperplasia (PBMAH) is a rare cause of ACTH-independent Cushing syndrome. It is characterized by the development of supracentimetric nodules resulting in increased adrenal volume and weight. Its presentation is clinically, radiologically and biologically heterogeneous. Morphological descriptions of PBMAH are rare. Although the initial description highlights that multinodular hyperplastic adrenal glands are made of a majority of spongiocytic cells with some eosinophilic cell isles, later descriptions based on a few cases only, did not mention any morphological variation. The identification of inactivating pathogenic variants of *ARMC5* in 2013 and of *KDM1A* in 2021, argues for a genetic heterogeneity. This work aimed to describe the microscopic characteristics of a series of PBMAH and determine if morphological heterogeneity might correlate with the genetic profile.
Methods
35 PBMAH patients operated by adrenalectomy at Cochin Hospital between 1998 and 2021 whose genetic status was known. All slides were reviewed by two independent pathologists, without knowledge of the patients' genetics. Immunohistochemistry included DAB2, HSD3, Cyp17 and inhibin. DNA sequencing on multiple nodules from 25 of these patients was performed by Illumina NGS.
Results
Four morphological subtypes are identified: two subtypes with nodular architecture (with nodules within macronodules) referred as subtype 1 and 2, and two subtypes with few nodules: subtype 3 and 4. Subtype 1 consists of a majority of spongiocytic cells and eosinophilic cells (10–30%) that forms isles or bands. Subtype 2 has a higher proportion of eosinophilic cells ($>30\%$), mixed with spongiocytic cells. Subtype 3 is composed mostly of spongiocytic cells with less than 10% eosinophilic cells. Subtype 4 is composed of numerous ($>40\%$) oncocytic cells. Their immunohistochemical profile is also heterogeneous. NGS identifies somatic events in *ARMC5* and *KDM1A* mutated patients. The study of correlations between morphological data and genetic status showed that 14 out of the 17 patients classified in subtype 1 are harboring pathogenic variant in *ARMC5*gene whereas the subtype 2 is exclusively composed of 4 *KDM1A* mutated tissues. Subtypes 3 and 4 are seen in patients without known mutation. These correlations are statistically significant: $P < 0.0001$ (Fisher test).
Conclusion
The study of this series allowed us to propose four different morphological groups, in favor of a histopathological heterogeneity. Two of these subtypes correlated with the presence of specific germline mutations. The anatomopathological examination of PBMAH based on architectural analysis and cell quantification represents an advance in the classification of adult nodular adrenal hyperplasia.

DOI: 10.1530/endoabs.81.P270

P271

The accuracy of adjusted unconventional indices for the assessment of selectivity and lateralization of adrenal vein sampling in the subtype diagnosis of primary aldosteronism

Martina Bollati[1], Mirko Parasiliti-Caprino[1], Fabio Bioletto[1], Filippo Ceccato[2], Chiara Lopez[1], Maria Chiara Di Carlo[1], Giacomo Voltan[2], Denis Rossato[3], Giuseppe Giraudo[4], Carla Scaroni[2], Ezio Ghigo[1] & Mauro Maccario[1]
[1]City of Health and Science University Hospital, University of Turin, Department of Medical Sciences, Endocrinology, Diabetes and Metabolism, Turin, Italy; [2]University-Hospital of Padua, Department of Medicine DIMED, Endocrinology Unit, Padua, Italy; [3]City of Health and Science University Hospital, University of Turin, Radiology Unit, Turin, Italy; [4]City of Health and Science University Hospital, University of Turin, Surgery, Turin, Italy

Objective
This study aimed to evaluate the performance of simple and clinical/imaging-corrected unconventional indices in predicting the selectivity of adrenal vein sampling (AVS) and the lateralization of aldosterone hypersecretion in patients with primary aldosteronism (PA).
Methods
Data of all consecutive patients with a proven diagnosis of PA who underwent AVS for subtype differentiation in two Italian referral centers were analyzed retrospectively. All patients with confirmed unilateral aldosterone hypersecretion underwent adrenalectomy. For the assessment of lateralization, only bilaterally selective AVS were considered.
Results
AVS was bilaterally selective in 112/144 patients. Unilateral disease was diagnosed in 60 cases (53.6%), whereas idiopathic hyperaldosteronism was diagnosed in 52 individuals (46.4%). The aldosterone index, calculated as the ratio between aldosterone in the adrenal vein and aldosterone in the peripheral blood, showed a high accuracy in predicting selectivity using a cortisol selectivity index of 1.1 as the reference standard, and a moderate accuracy when compared to a cortisol selectivity index cut-off of 2 and 3. The simple aldosterone index also demonstrated a moderate accuracy in predicting ipsilateral and contralateral aldosterone hypersecretion. The monoadrenal index, calculated as the aldosterone-to-cortisol ratio in the adrenal vein, revealed a high accuracy in predicting ipsilateral disease and a high accuracy in predicting contralateral disease, whereas the monolateral index, calculated as the aldosterone-to-cortisol ratio in the adrenal vein vs. peripheral blood, revealed moderate accuracy in predicting ipsilateral disease and high accuracy in predicting contralateral disease. Lesion-side and hypokalemia corrected ROC curves for these unconventional indices revealed a significant improvement in the prediction of ipsi/contralateral disease. For a more straightforward clinical application, we calculated the adjusted cut-offs of covariate-corrected indices in an explicit form, for all possible combinations of lesion side at imaging and presence/absence of hypokalemia, according to the Youden's criterion and using an optimized specificity. Finally, the comparative aldosterone index, calculated as the ratio between aldosterone in the dominant vs the non-dominant vein, showed a high accuracy in the assessment of lateralization.
Conclusions
In the present study, we demonstrated a satisfactory accuracy of unconventional indices in predicting selectivity and lateralization of aldosterone hypersecretion in the setting of AVS, which became even higher after correction for hypokalemia and lesion side at imaging. After an external validation, these indices may become a useful tool in interpreting AVS results for the subtype diagnosis of PA, thereby allowing the selection of patients for adrenalectomy, when standard indices cannot be performed.

DOI: 10.1530/endoabs.81.P271

P272

Characterization of molecular pathway alterations in Cushing's Syndrome

Sharmilee Vetrivel[1], Ru Zhang[1], Ali Khan[2], Andrea Osswald[1], Martin Reincke[1], Silviu Sbieria[2] & Anna Riester[1]
[1]Medizinische Klinik und Poliklinik IV, , LMU Klinikum, Ludwig-Maximilians-University, Munich, Germany; [2]Department of Internal Medicine I, Division of Endocrinology and Diabetes, University Hospital, University of Würzburg, Würzburg, Würzburg, Germany

Context
Transcriptomic based characterization of signaling pathways in the adrenals of different subtypes of Cushing's syndrome.
Patients
For preliminary NGS analyses, a total of 27 adrenal samples were used. The cohort consisted of the following patient groups: Cortisol producing adenoma (CPA, $n=9$), primary bilateral macronodular adrenal hyperplasia (PBMAH, $n=10$). The adjacent normal adrenal tissue from pheochromocytoma patients ($n=8$) served as controls. For QPCR validation, the patient groups included: Cushing's disease (CD, $n=8$), ectopic Cushing's syndrome ($n=3$). Controls included adrenal tissues of aldosterone producing adenoma ($n=10$) and normal adrenals from patients who underwent kidney surgery ($n=10$).
Methods
Next-generation sequencing was performed in the 27 adrenal samples (Illumina HiSeq). Bioinformatic analyses was done by R to identify significantly differently expressed genes between the groups. For pathway mapping bioinformatic tools (ShinyGO and Gprofiler) were used. The significant genes related to the respective pathways were validated by real-time reverse transcription-qPCR.
Results
With reference to transcriptomic data PBMAH was found to have the most dysregulated genes compared to Controls ($n=5394$) and CPA ($n=248$). Pathway mapping using the significantly altered genes gave neuronal synaptic signalling pathways and PPARG (peroxisome proliferator-activated receptor- gamma) signalling pathway as top hits in the groups of PBMAH and CPA. Validation of the pathway genes identified PPARG (l2fc < -1.5) and its related genes - FABP4 (l2fc < -5.5), PCK1 (l2fc < -2.1), PLIN1 (l2fc < -4.1) and ADIPOQ (l2fc < -3.3) to be significantly downregulated ($P<0.005$) in CS subtypes - CPA, CD and PBMAH in comparison to the controls. The in vitro mechanistic characterization of this pathway in cortisol production using adrenal cell lines is in process.
Conclusion
This study investigated for the first time PPARG pathway, which plays a critical physiological role in lipid and glucose metabolism, in cortisol regulation and found a significant downregulation of the pathway in the adrenals of CS patients.

DOI: 10.1530/endoabs.81.P272

P273

Salivary profiles of cortisol and cortisone in patients with primary adrenal insufficiency under replacement therapy: a pilot study

Lorenzo Tucci[1,2], Valentina Vicennati[1,2], Matteo Magagnoli[2,3], Giacomo Colombin[1,2], Kimberly Coscia[1,2], Laura Rotolo[1,2], Flaminia Fanelli[2,3], Uberto Pagotto[1,2] & Guido Di Dalmazi[1,2]
[1]S. Orsola-Malpighi Polyclinic, Bologna, Italy; [2]Alma Mater Studiorum - Università di Bologna, Bologna, Italy; [3]CRBA, Bologna, Italy

Background
Evaluation of steroid replacement therapy (SRT) in adrenal insufficiency (AI) is challenging for the lack of reliable parameters. Measurement of salivary cortisol and cortisone emerged as a non-invasive tool for AI management, however poorly investigated.
Aim
To analyse the cortisol and cortisone circadian rhythm in normal controls (NC) and patients with primary AI (PAI) under different SRTs, and to identify useful biomarkers.
Methods
We evaluated 24 NC and 30 PAI under hydrocortisone (HC) ($n=8$), cortisone acetate (CA) ($n=14$), and dual-release HC (DRHC) ($n=8$), with equivalent-HC doses of 13.2 mg/m^2, 15.8 mg/m^2, and 14.6 mg/m^2, respectively. SRT was taken at 07:00 (all patients) and between 13:00-16:00 (mean 15:13, patients under HC and CA). We collected 9 saliva samples throughout a day at 7:00 (before therapy), 7:30, 10:00, 12:30, 14:00, 16:00, 19:30, 21:00, and 23:00 for cortisol and cortisone measurement by liquid-chromatography tandem-mass spectrometry (LC-MS/MS). We performed cosinor analysis, and calculated area under the curves (AUCs) and percentual variation from NC values (V%). Due to oral contamination from drug intake, we evaluated cortisol for patients under CA and cortisone for those under HC and DRHC. Patients with PAI completed the following questionnaires: quality of life (AddiQol-30), Hospital Anxiety and Depression Scale (HADS) and Pittsburgh Sleep Quality Index (PSQI).
Results
Compared to NC, AUCs between 14:00 and 23:00 were higher in CA ($P=0.001$) and HC ($P<0.001$), while similar in DRHC ($P=0.12$). In the same period, V% was lower under DRHC (-28%) than CA (+128%; $P=0.001$) and HC (+90%; $P=0.001$). Cosinor analysis showed comparable mesor, but delayed acrophase ($P=0.002$ for HC; $P=0.026$ for DRHC; $P=0.027$ for CA) and batiphase ($P=0.002$ for HC; $P=0.023$ for DRHC; $P=0.027$ for CA), compared to NC. The number of time points with salivary steroid levels within the range derived from NC was higher in DRHC than CA ($P=0.002$) and HC ($P=0.005$). Between 07:00 and 10:00, patients with PAI showed a similar percent increase in salivary steroids among different SRT groups, which was higher than NC ($P<0.001$ for all comparisons). AddiQol-30, HADS and PSQI were comparable among PAI.
Conclusion
Salivary cortisol and cortisone showed a higher excursion in the morning (all patients) and an increased glucocorticoid exposure in the afternoon/evening (patients under HC and CA), than NC. Although DRHC provides better glucocorticoid exposure than HC and CA, significant differences with NC were observed. Salivary cortisol and cortisone levels and AUC may be useful tools for SRT management in PAI.

DOI: 10.1530/endoabs.81.P273

P274

Progression of atherosclerosis after the menopause and the role of circulating Amyloid Beta 1-40

Irene Lambrinoudaki[1], Elena Armeni[1], Dimitrios Delialis[2], Georgios Georgiopoulos[2,3], Simon Tual-Chalot[4], Nikolaos Vlachogiannis[4], Raphael Patras[2], Evmorfia Aivalioti[2], Areti Augoulea[1], Nikolaos Tsoltos[1], Anastasia Soureti[1], Konstantinos Stellos[4] & Kimon Stamatelopoulos[2]
[1]National and Kapodistrian University of Athens, 2nd Department of Obstetrics and Gynecology, Aretaieio Hospital, Athens, Greece; [2]National and Kapodistrian University of Athens, School of Medicine, Department of Clinical Therapeutics, Athens, Greece; [3]School of Biomedical Engineering & Imaging Sciences, Rayne Institute, St. Thomas' Hospital, London, United Kingdom; [4]Biosciences Institute, Vascular Biology and Medicine Theme, Faculty of Medical Sciences, Newcastle University, Newcastle upon Tyne, United Kingdom

Background
A large body of evidence is supporting that the incidence of adverse cardiovascular events is increasing signfiicantly after the menopausal transition. Primary prevention practices continue to propose evolving algorithms, in an attempt to accurately estimate the actual female cardiovascular risk at midlife. Irrespectively of these attempts, considerable unrecognized cardiovascular disease (CVD) risk remains unexplained, beyond traditional risk factors (TRFs) . On the other hand, a growing body of evidence is suggesting the potential role of a proatherogenic peptide, thecirculating amyloid β 1-40 (Aβ1-40). This peptide may serve as a novel biomarker in CVD.
Aim
This study aimed to explore the role of plasma Aβ1-40 and its patterns of change over time in the progression of structural atherosclerosis in postmenopausal women.
Methods
This prospective study recruited a total of 152 postmenopausal women without history or symptoms of CVD, consecutive outpatients in the Menopause Clinic of Aretaieion Hospital, National and Kapodistrian University of Athens, Greece. Baseline assessment consisted of measuring anthropometric and demographic parameters, obtaining fasting blood samples, performing carotid high-resolution ultrasonography. Blood samples were used to measure Aβ1-40, by enzyme-linked immunosorbent assay. Follow-up assessment was performed after a median follow-up of 28.2 months, during which a repeat assessment of subclinical atherosclerosis through sonographical studies was performed
Results
At baseline, the sum of maximal wall thickness in all carotid sites (sumWT) as well as the values of carotid bulb intima-media thickness (cbIMT) associated independently with high Aβ1-40 ($P < 0.05$). Levels of Aβ1-40 levels appeared to increase over time, and were also associated with decreasing renal function. Accelerated progression of cbIMT and maximum carotid wall thickness and sumWT ($P < 0.05$ for all) was observed for women with a pattern of increasing or persistently high Aβ1-40 levels after adjustment for baseline Aβ1-40 levels, TRFs, and renal function ($P < 0.05$ for both).

Conclusion
The results of our study provide novel insights into a link between atherosclerosis progression in menopause and the time-related pattern of change in values of Aβ1-40. More specifically, the rate of progression of subclinical atherosclerosis was associated with persistently high Aβ1-40 levels or persistently high values, irrespective of the baseline levels. Further research is required to clarify the value of monitoring Aβ1-40 values, as a possible atherosclerosis biomarker in middle-aged women without clinically overt CVD.

DOI: 10.1530/endoabs.81.P274

P275

Heat shock protein 60 and Endothelial function in postmenopausal women

Elena Armeni[1], Anastasia Soureti[1], Areti Augoulea[1], Asimina Chondrou[1], Demetrios Rizos[2], George Kaparos[3], Dimitrios Delialis[4], Spyros Stefos[1], Lasthenis Angelidakis[4], Alexandros Sianis[4], Aggeliki-Maria Dimopoulou[4], Andreas Alexandrou[1], Stavroula Baka[5], Leon Aravantinos[1], Kimon Stamatelopoulos[4] & Irene Lambrinoudaki[1]
[1]National and Kapodistrian University of Athens, 2nd Department of Obstetrics and Gynecology, Aretaieio Hospital, Athens, Greece; [2]National and Kapodistrian University of Athens, Hormonal Laboratory, Aretaieion Hospital, Athens, Greece; [3]National and Kapodistrian University of Athens, Biochemical Laboratory, Aretaieion Hospital, Athens, Greece; [4]National and Kapodistrian University of Athens, Department of Clinical Therapeutics, Athens, Greece; [5]National and Kapodistrian University of Athens, Biochemical Laboratory, Athens, Greece

Background
Heat shock protein 60 (HSP60), a potentially homeostatic antigen, has been shown to be involved in physiological and non-physiological conditions. Experimental data is supporting the role of HSP60 in placental and mitochondrial steroidogenesis. Under stress conditions, HSP60 are translocated into the endothelial-cell plasma membrane and the extracellular space, promoting the atherosclerotic process.
Aim
We decided to investigate the association between HSP60 and endothelial-cell function in postmenopausal women, considering the possible atherogenic effect of androgenic hormones.
Methods
This study included a total of 160 apparently healthy postmenopausal women. Exclusion criteria were treatment for hypertension or dyslipidaemia, menopause hormone therapy during the last 6 months, previously diagnosed peripheral vascular disease or cardiovascular disease. Fasting venous blood samples were obtained for biochemical, hormonal assessment and evaluation of HSP60. Sonographical assessment of flow mediated dilation (FMD) took place immediately thereafter in one session.
Results
Univariate analysis showed log-HSP60 values differed between women with FMD lower vs higher than the median 5.12% (low vs high FMD, HSP60 values: 2.01 ± 1.16 ng/ml vs 3.22 ± 1.17 ng/ml, p-value = 0.031). Multivariable analysis showed that LogHSP60 was associated with FMD (b-coefficient = 0.244, p-value = 0.031), adjusting for traditional cardiovascular risk factors. Further adjustment for HOMA-IR and testosterone or DHEAS rendered the result non-significant. In the multivariable analysis, DHEAS was associated with FMD (b-coefficient = -0.199, p-value = 0.039), adjusting for cardiovascular risk factors.
Conclusion
The results of this study indicate an association between androgens and endothelial function, independent of HSP60 molecules, in women with low insulin resistance and androgenicity. Further prospective studies are needed to explore the significance of our findings.

DOI: 10.1530/endoabs.81.P275

P276

Adrenal lesions - the importance of a careful evaluation

Daniela Dias[1], Inês Figueiredo[2], Cristina Duarte[2], Fllipa Serra[1], Carlos Leichsenring[3], Isabel Távora[4], João Paulo Fernandes[5] & Inês Sapinho[1]
[1]Hospital CUF Descobertas, Endocrinology , Lisbon, Portugal; [2]Hospital CUF Descobertas, Internal Medicine, Lisbon, Portugal; [3]Hospital CUF Descobertas, Surgery, Lisbon, Portugal; [4]Hospital CUF Descobertas, Imagiology, Lisbon, Portugal; [5]Hospital CUF Descobertas, Hematology and Oncology, Lisbon, Portugal

Most differential diagnoses of unilateral adrenal lesions include non-functional adenoma, adrenocortical carcinoma or pheochromocytoma. Primary adrenal lymphoma(PAL) is an extremely uncommon type of primary extranodal non-Hodgkin's lymphoma(<1%). Most cases are bilateral (~75%), being unilateral PAL scarcely reported. The apparent unilateral involvement of this entity at presentation, in the CT scan/MRI may difficult the diagnosis, delaying the start of chemotherapy. We report a case of a bilateral PAL interpreted primarily as a unilateral suspicious adrenal lesion. A 68-year-old(yo) male patient presented to the emergency department with persistent fatigue for 3 months getting worse in the last 3 weeks. His past medical history included type 2 diabetes with macrovascular disease, prostate cancer at 61 yo and active smoking. Physical examination was unremarkable, except for a mild edema in the lower limbs. Laboratory investigations revealed: hemoglobin 13.1g/dL, white blood cell count 4×109/L, D-dimer 2232 ng/ml(<500), LDH 488U/L(85-227), NT-proBNP 636pg/mL(<125). A computed tomography(CT) angiogram of the chest was performed to exclude pulmonary embolism(PE)/COVID-19 infection. A lesion of 139 mm on the left adrenal gland, suggestive of a mass or hemorrhage was observed. No signs of PE were evident. The patient was hospitalized for further investigation. Hormonal evaluation revealed: ACTH 37.8 pg/mL(<46), serum cortisol 20 mg/dL, 24-hour urine cortisol levels were slightly increased with 437 mg/24h(28-213), aldosterone and total urinary metanephrines were normal, except for a slightly increased normetanephrine of 545 mg/24h(<444). An abdominal MRI confirmed a large neoformative lesion on the left adrenal gland of 140 mm. The patient underwent left adrenalectomy and nephrectomy. Histology revealed a diffuse large B-cell lymphoma, non-germinal centre B-cell. Staging 18F-FDG PET/CT scan showed intense 18F-FDG 14 mm uptake in the right adrenal gland(SUVmax 5.7). He received 6 cycles of R-CHOP(rituximab-cyclophosphamide, doxorubicin, vincristine and prednisone) chemotherapy. The follow-up 18F-FDG PET/CT scan performed at the end of the treatment revealed no evidence of tumor. Thus, this case illustrates the difficulties found in the diagnosis of PAL and draws attention to consider it as a differential diagnosis during evaluation of adrenal masses. In this case, an adrenalectomy was performed given the presence of unilateral large adrenal mass and the possibility of an adrenal carcinoma, leading to a delay in treatment initiation. Furthermore the absence of adrenal insufficiency commonly associated with bilateral adrenal lymphomas was absent. It is noteworthy that the staging 18F-FDG PET/CT scan revealed uptake in the other non-operated adrenal gland that was not evident after chemotherapy, making obvious the diagnosis of a bilateral PAL.

DOI: 10.1530/endoabs.81.P276

P277

Presenting clinical features of Cushing's syndrome and non-classic hypercortisolism

Elisa Delle Donne[1], Chiara Parazzoli[1], Vittoria Favero[1], Iacopo Chiodini[2,3], Valentina Morelli[3] & Carmen Aresta[3]
[1]University of Milan, Department of Medical Biotechnology and Translational Medicine, Italy; [2]University of Milan, Department of Medical Biotechnology and Traslational Medicine, Italy; [3]IRCCS Istituto Auxologico Italiano, Department of Endocrine and Metabolic Diseases, Italy

Background
The Endocrine Society Guidelines recommend screening for hypercortisolism especially in patients with specific features that best discriminate Cushing's Syndrome (CS): easy bruising, facial plethora, proximal myopathy and striae. Clinical experience suggests that these features, though suggestive of hypercortisolism, are not enough sensitive. Indeed, patients with hypercortisolism frequently manifest primarily less discriminatory cortisol-related features, such as arterial hypertension, diabetes mellitus, weight gain, osteoporosis, defining a hidden form of CS, also defined as "non classic hypercortisolism" (nCH). We conducted a study to retrospectively compare the biochemical and clinical data of patients with hypercortisolism, in CS and nCH forms at their first presentation.
Methods
Fifty-eight adult patients (age 47.7 ± 16.7 years, female/male 50/8) with proven biochemical hypercortisolism referred to our hospital from 2008 to 2021 were included. In all patients we evaluated the clinical features present at their first presentation to our outpatient clinic. The subjects were divided into two groups according to the presence or absence of classic and highly specific presenting symptoms, CS and nCH groups respectively. In all patients we assessed 24-hour urinary free cortisol (UFC), cortisol after 1mg-overnight-dexamethasone (F-1mgDST), the delay between estimated clinical onset and diagnosis, the therapy undertaken, the recovery and/or persistence/recurrence of the disease.

Results
In the whole sample, hypertension was the most frequent feature present at presentation (18.2% of all presenting symptoms), followed by weight gain (15.6%) and facial plethora (13%). Classic signs of CS accounted for only 25.2% among all presenting symptoms. Twenty-eight patients were classified with CS (48.3%) and 30 with nCH (51.7%). Hypertension and weight gain were the most common features (48% and 41.4%, respectively) without difference between CS and nCH. UFC and F-1mgDST levels were higher in CS patients (625.9 ± 496.3 µg/24h, 18.2 ± 13.5 µg/dl, respectively) than in nCH patients (272.1 ± 261.6 µg/24h, 9.6 ± 7.3 µg/dl respectively, $P < 0.05$ for all comparisons). Notably, hypertension was the most frequent sign in patients with nCH (56.7%) and the second most frequent in CS (39.3%), second only to weight gain (50.0%) in the latter group. Importantly, in all hypertensive patients hypertension was non controlled or resistant or with early onset. Diagnostic delay was three-fold longer for nCH than for CS (5.4 ± 5.6 vs 1.9 ± 1.7 years, $P = 0.003$).
Conclusions
Specific signs of CS are frequently absent at clinical onset of hypercortisolism, most common finding being hypertension. It is crucial for the clinician to recognize potential non-classical features of hypercortisolism which, although non-specific, may present peculiar features and allow a correct diagnosis.

DOI: 10.1530/endoabs.81.P277

P278

Success rate of adrenal venous sampling in iceland

Hrafnhildur Gunnarsdottir[1,2], Jon Gudmundsson[1], Gudjon Birgisson[1] & Helga Agusta Sigurjonsdottir[1]
[1]Landspitali University Hospital, Reykjavík, Iceland; [2]University of Iceland, Reykjavík, Iceland

Introduction
Primary aldosteronism is an important cause of hypertension. Adrenal venous sampling (AVS) is the gold-standard investigation to determine whether one or both adrenal glands are affected. AVS is a complicated procedure with success rate varying greatly from one hospital to another.
Aims
To investigate the success rate of AVS at Landspitali over a 10-year period and compare it to published results from other hospitals.
Methods
The results from all AVS procedures performed from 2007 throughout 2016 in Landspitali National University Hospital of Iceland were retrospectively reviewed. Landspitali is a tertiary referral center for the whole country. We collected data on serum concentrations of aldosterone and cortisol from both adrenal veins, inferior vena cava and a peripheral vein. All patients were started on synacthen (tetracosactrin) infusion of 93,75 µg/h at least one hour before the AVS. Selectivity index (SI) for each side was calculated by dividing the serum concentration of cortisol from the appropriate adrenal vein by the serum cortisol concentration from a peripheral vein. An AVS was considered successful if serum concentrations of cortisol were five times greater in the adrenal veins than in the peripheral vein, e.g. SI > 5 on both sides.
Results
During the 10-year period, 66 AVS procedures were performed at Landspitali. A total of 57 were successful, which gives a success rate of 86%. Six (9%) AVS procedures gave SI < 5 on the right side only and two (3%) gave SI < 5 on the left side only. One (2%) AVS gave SI < 5 bilaterally. Seven (11%) AVS procedures were repeated due to difficulties cannulating the right adrenal vein. All seven repetitions were successful.
Conclusions
Despite being a small nation, the success rate of AVS at Landspitali, Iceland, is fairly good (86%). The success rate is not far from published numbers from Gothenburg, Sweden, (92%) and Mayo Clinic, Rochester, USA, (96%). All the AVS procedures at Landspitali were performed by the same specialist throughout the study period, which is considered to be the key to this success.

DOI: 10.1530/endoabs.81.P278

P279

Effects of FSH on endothelial function

Maria Santa Rocca[1], Micaela Pannella[2], Carlo Foresta[3] & Alberto Ferlin[1]
[1]University Hospital of Padova, Department of Medicine, Unit of Andrology and Reproductive Medicine, Padova, Italy; [2]IRCCS Istituto Ortopedico Rizzoli, Regenerative Therapies in Oncology, Bologna, Italy; [3]University of Padova, Department of Medicine, Padova, Italy

Follicle-stimulating hormone (FSH) is a member of the glycoprotein hormone family that plays a pivotal role in ovarian folliculogenesis and spermatogenesis. FSH receptor (FSHR) is, indeed, highly expressed in granulosa and Sertoli cells respectively. However, recent studies have detected FSHR also in extra-gonadal tissues, such as adipose tissue, bone, endometrium, placenta, endothelium, monocytes, and malignant tissues, suggesting, that the activity of this hormone may not be limited to fertility regulation. Although the role of FSH in extra-gonadal tissues is an interesting topic, the effect of FSH in endothelial tissue has been poorly studied and the findings are sometimes discordant, mainly about angiogenic effect of FSH. However, a recent study has observed an increased vascular cell adhesion molecule-1 (VCAM-1) expression in endothelial cells after FSH treatment, suggesting a role of this hormone in the development of atherosclerosis. In this study, we aimed to evaluate the effects of FSH on human umbilical cord vein endothelial cells (HUVEC) as cell model. Wound healing and tube formation assay were performed to investigate respectively cell migration and tube length in cells treated with 5, 25, 50 mUI/ml of rhFSH for 24h and shear stress assay was performed to measure Nitric Oxide (NO) production after 24h of treatment with the same doses of rhFSH. Furthermore, we used Elisa assay to quantify eNOS (endothelial Nitric Oxide Synthase) phosphorylation and Inositol Triphosphate (IP3) production, and Fluo4-probe and immunofluorescence to assess Ca^{2+} level and VE-cadherin localization, respectively. Wound-healing and tube formation assays did not highlight any significant difference, whilst NO production and Ca^{2+} level increased after stimulation with 25 and 50mUI/ml of FSH compared to controls or cells incubated with a low FSH dose (5mUI/ml). Furthermore, eNOS phosphorylation and IP3 increased after stimulation with 50 mUI/ml FSH, suggesting that FSH could exert its biological action via Pospholipase C (PLC)/Ca^{2+}/Protein Kinase C (PKC) pathway. Although NO has a protective role in cardiovascular disease, however, over production of NO could result in a damaging effect on cellular membrane. In fact, immunofluorescence assay showed an anomalous localization of VE-cadherin, an adhesion molecule that is involved in the control of vascular permeability, after stimulation with 50 mUI/ml of FSH. This is the first study showing a putative molecular signaling triggered by FSH in endothelial cells. However, further experiments *in vivo* are necessary to clarify whether perturbation of FSH, similar to the one observed in menopause or hypergonadotropic hypogonadism, may affect endothelial function.

DOI: 10.1530/endoabs.81.P279

P280

Coagulation parameters in asymptomatic patients with adrenal incidentaloma: is mild autonomous cortisol secretion correlated with thromboembolic risk?

Marianna Minnetti, Ilaria Bonaventura, Valeria Hasenmajer, Dario De Alcubierre, Alessandra Tomaselli, Davide Ferrari, Riccardo Pofi, Alessia Cozzolino, Emilia Sbardella, Andrea Lenzi & Andrea Isidori
Sapienza, University of Rome, Department of Experimental Medicine , Italy

Background
Overt hypercortisolism is highly associated with venous thromboembolism. Patients with Cushing's syndrome (CS) typically show an alteration of the intrinsic coagulation pathway, especially an increase in factor VIII (f-VIII), and increased levels of coagulation inhibitors (i.e., antithrombin III) as a compensatory response. Mild autonomous cortisol secretion (MACS) has been variably associated with higher risk of cardiovascular events and mortality compared to patients with non-functioning adrenal adenomas (NFAA). However, dedicated studies describing coagulation status in these patients are lacking.
Aim
To describe coagulation parameters in patients with MACS compared with patients with NFAA enrolled in the ITACA study (NCT04127552)
Method
56 asymptomatic patients with adrenal incidentaloma without the classic signs or symptoms of overt hypercortisolism were prospectively enrolled. According to post-dexamethasone suppression cortisol values (post-DST), three groups were defined: NFAA (<50 nmol/L), possible MACS [MACS-1] (50 to 138 nmol/L) and MACS [MACS-2] (>138 nmol/L). Coagulation markers (fVIII, fVII, fV, fibrinogen, PT, aPTT, platelets) and coagulation inhibitors (Antitrombin III, Protein C, Protein S) were studied. Patients with an history of thrombosis were excluded.
Results
A total of 24 NFA, 22 MACS-1 and 10 MACS-2 were included in the analysis. No differences in coagulation markers and inhibitors were observed between MACS-1 and NFAA. Mean factor VIII levels were significantly increased in the MACS-2 group (167% ± 54) compared to the NFA group (129% ± 30; $P = 0.021$) and MACS-1 (122% ± 32; $P = 0.012$), respectively. Overall, a positive correlation was found between post-DST, platelets ($r = 0.214$; $P = 0.038$) and antithrombin III ($r = 0.354$: $P = 0.021$).

Conclusions
asymptomatic patients with elevated post-DST (>138 nmol/L) may show early thrombotic alterations, similar to those in patients with symptomatic CS. Coagulation parameters may help to identify patients with adrenal incidentalomas at high risk of thromboembolic events, who could benefit from anticoagulant prophylaxis prior to adrenal surgery.

DOI: 10.1530/endoabs.81.P280

P281

Management of pheochromocytoma and hyperaldosteronism coexistence

David Veríssimo, Catarina Ivo, Vitória Duarte, Ana Cláudia Martins, Joao Silva, Luis Lopes, Dolores Passos, J Jácome Castro & Mafalda Marcelino
Portuguese Armed Forces Hospital, Endocrinology Department, Lisboa, Portugal

Introduction
Primary hyperaldosteronism (PHA) and pheochromocytoma are endocrine causes of secondary arterial hypertension. The association of hyperaldosteronism and pheochromocytoma is rare and the involved mechanisms are poorly understood. Either there is coexistence of the two diseases (pheochromocytoma with PHA) or the pheochromocytoma stimulates the production of aldosterone.
Case Report
Male, 54 years old, referred to our department for type 2 diabetes and resistant hypertension (SBP>190mmHg and DBP>110mmHg), medicated with lercanidipine 10 mg, azilsartan 40 mg, chlorthalidone 12.5 mg and nebivolol 5 mg. Laboratory evaluation showed: renin <0.2 ng/ml/h (0.2-1.6); aldosterone 26.8 ng/dL (1-16); renin/aldosterone ratio 134 (<30); K+ 3.3 mmol/L (3.5-5.5); high urinary metanephrines (metanephrine 474 µg/24h (64-302); normetanephrine 1013 µg/24h (162-527); 3-Methoxytyramine 345 µg/24h (30-434)) and a negative chromogranin A. A saline infusion test was conducted, with serum aldosterone 9.5 ng/dL after 4 hours. Therapy with spironolactone was started, with a good response (blood pressure 130/80 mmHg), suggesting the diagnosis of PHA. Abdominal CT without contrast revealed bilateral adrenal gland lesions: a single nodule in the right adrenal gland with 2 cm and spontaneous density of 23 HU; 3 nodules in the left adrenal gland with 1.4 cm (12 HU), 1.3 cm and 1.0 cm (both < 10 HU). Both 123I-MIBG and PET 18F-FDOPA scintigraphy revealed a high uptake in the right adrenal gland. The patient was submitted to a right adrenalectomy, whose histological evaluation confirmed pheochromocytoma without malignancy criteria. The presence of genetic mutations was excluded. After surgery, the patient maintained difficult-to-control high blood pressure, with normal metanephrine measurement, and a captopril test was conducted which confirmed PHA (aldosterone reduction of 3%). He was medicated with eplerenone 50 mg/day, maintaining an adequate blood pressure since then.
Discussion
The simultaneous occurrence of pheochromocytoma and PHA is rare, with only 15 cases described in the literature. In the present case, due to the bilaterality of the lesions, the surgical treatment focused on the pheochromocytoma. Although the literature describes cases in which hyperaldosteronism resolves after removal of the pheochromocytoma, in this report it persisted, suggesting the presence of a contralateral aldosterone-producing adenoma.

DOI: 10.1530/endoabs.81.P281

P282

Behavior of metastatic paragangliomas and pheocromocytomas: experience from a single center

David Veríssimo[1], ines damasio[2], Ana Gomes[3], Joana Simões-Pereira[2], Sara Donato[2] & Valeriano Leite[2]
[1]Hospital das Forças Armadas, Serviço de Endocrinologia, Portugal; [2]Instituto Português de Oncologia de Lisboa Francisco Gentil, EPE, Serviço de Endocrinologia, Portugal; [3]Hospital de Santa Maria, CHULN, EPE, Serviço de Endocrinologia, Diabetes e Metabolismo, Portugal

Paragangliomas (PGL) and pheochromocytomas (PHEO) are rare neuroendocrine tumors with an estimated prevalence of 1:6500 and 1:2500, respectively. Although most PGL/PHEO are benign, approximately 10% of PHEOs and 15-35% of PGLs have metastatic disease, which it is main cause of death, with 6 years of median survival. Objective: To characterize the metastatic PHEOs and PGLs from a single center. Methods: Retrospective analysis of clinical records of patients with metastatic PHEO or PGL diagnosed from 2000 to 2022. Results: We identified 23 patients, 52.2% male, median age at diagnosis was 38 years (Δ8-77) and at metastasis diagnosis 40 years (Δ12-77). The median follow-up was 4 years (Δ0-17). A total of 8 PHEOs and 23 PGLs (30.4% multifocal) were identified. PGLs were located in the head and neck ($n=8$, 35%), abdomen ($n=8$, 35%) and mediastinum ($n=7$, 30%). The median tumor size was 50mm (Δ 20-160mm). The most frequent complaints were hypertension (39.1%), tachycardia (17.4%), hyperhidrosis and headache (13%); 13% were asymptomatic. A functional profile was detected in 56.5%. The majority of primary tumors ($n=19$, 82.6%) underwent surgery. Regarding germline mutations, 43.5% had a mutation in *SDHB* gene, 4.3% in the *SDHD*; in 52.2% mutations were not detected. Bone was the main site of secondary deposits ($n=17$, 73.9%), followed by lymph nodes ($n=16$, 69.2%), liver ($n=8$, 34.8%), lung ($n=6$, 26.1%) and kidneys ($n=1$, 4.3%). Multifocal metastases were identified in 13 patients (56.5%). Metastases were present at diagnosis in 6 cases (26.1%). Metastases-directed therapies were radiotherapy in 60.9% ($n=14$), ^{131}I-MIBG in 26.1% ($n=6$), surgery in 21.7% ($n=5$), chemotherapy in 21.7% ($n=5$), tyrosine kinase inhibitors (TKI) in 17.4% ($n=4$), peptide receptor radionuclide therapy (PRRT) in 17.4% ($n=4$) and chemoembolization in 8.7% ($n=2$). Multimodality approaches were used in 47.8% ($n=11$). Surgery obtained a remission rate of 80%. After radiotherapy 50% had disease progression, 30% stability, 5% partial response and 5% remission. PRRT achieved 50% of disease stability and 50% of progression. After chemotherapy 80% progressed and 20% showed partial response. All the patients progressed after ^{131}I-MIBG, TKI and chemoembolization. Median estimate survival from diagnosis was 14 years and from metastases diagnosis was 11 years, with 39.1% death rate.
Discussion
Metastases location is similar to what is described in the literature. Metastatic disease treatment is challenging due to the low response rate of approved treatments, with the surgical approach offering the best remission rate.

DOI: 10.1530/endoabs.81.P282

P283

A single dose of Neutrophil Elastase inhibitor Elafin does not alter CBG cleavage during post-surgical stress in humans *in vivo*

Luke D Boyle[1], Mark Nixon[1], Caroline Underhill[2], Lesley A Hill[2], John G Lewis[3], Geoffrey L Hammond[2], Oliver Wiedow[4], Peter A Henriksen[1], Roland H Stimson[1] & Brian R Walker[5]
[1]The University of Edinburgh, Centre for Cardiovascular Science, Edinburgh, United Kingdom; [2]The University of British Columbia, Department of Cellular & Physiological Sciences, Vancouver, Canada; [3]Canterbury Health Laboratories, Steroid & Immunobiochemistry Laboratory, Christchurch, New Zealand; [4]University of Kiel, Department of Dermatology, Kiel, Germany; [5]Newcastle University, Faculty of Medical Sciences, Newcastle upon Tyne, United Kingdom

Introduction
Corticosteroid Binding Globulin (CBG) binds >85% of plasma cortisol and modulates free cortisol levels. Observations *in vitro* show that CBG is cleaved by neutrophil elastase (NE), a mechanism proposed to reduce CBG binding affinity and increase free cortisol availability to inflamed tissues. However, detection of cleaved CBG *in vivo* in human plasma is controversial, and any influence of NE on CBG cleavage has not been tested *in vivo*. We hypothesised that the endogenous NE inhibitor elafin reduces CBG cleavage and thus free plasma cortisol. We tested this in humans using coronary artery bypass graft (CABG) surgery as a model of acute neutrophil-mediated inflammation.
Methods
In a randomised double-blind placebo-controlled parallel group clinical trial, 35 patients undergoing CABG surgery were randomised 1:1 to intravenous elafin 200 mg or saline placebo administered after induction of anaesthesia. Blood samples were taken at baseline (time 0, skin incision) and 2, 6 and 24 hours postoperatively. We measured elafin (LC-MS); plasma elastase activity (fluorometric assay); IL-6, TNF-alpha, NE and CBG (all ELISAs); CBG binding capacity (radioligand-saturation assay); total cortisol (LC-MS) and free cortisol (isotopic dilution and ultrafiltration). Data were analysed as area under the curve from 0-24h or by two-way ANOVA.
Results
With placebo, NE increased from baseline 91.4 ± 10.0 to peak 894.4 ± 108.4 ng/ml at 2h, accompanied by increased IL-6 and TNF-alpha. Elafin infusion resulted in >1000-fold higher plasma concentrations than those of endogenous elafin, with marked reduction in elastase activity (mean $AUC_{0\text{-}24}$; 3.83 ± 1.99 vs 8.04 ± 2.97 units/mL). Plasma CBG concentrations fell >30% between 0-2h in both treatment groups, then remained unchanged to 24h; this was mirrored by reduced binding capacity, unaffected by elafin. Total cortisol rose dramatically, a fourfold increase between 2-6h in both groups. Free cortisol fraction doubled over 0-6h from 16.4 ± 0.44 to 30.7 ± 6.1 % in placebo, while elafin tended to

increase free cortisol concentration (mean difference 24.3 nM, 95% CI -1.33 to 49.9, $P=0.062$).
Discussion
The fall in plasma CBG and increase in total and free cortisol during CABG surgery is in keeping with published studies in humans during sepsis. We also noted an increase in cytokines which downregulate hepatic CBG production. However, we did not find evidence that the fall in CBG is mediated by increased cleavage by NE. Further studies are needed to assess any effects on CBG cleavage of NE inhibition in target tissues or more potently in serum.

DOI: 10.1530/endoabs.81.P283

P284

Ang-Tie pathway in adrenocortical tumors angiogenesis

Sofia Oliveira[1], Sofia Pereira[1], Madalena M. Costa[1], Mariana P Monteiro[1] & Duarte Pignatelli[2,3,4]
[4]Abel Salazar Biomedical Sciences Institute - University of Porto, Porto, Portugal; [2]Instituto de Investigação e Inovação em Saúde (I3S) , University of Porto Portugal, Cancer , Porto, Portugal; [3]Faculdade de Medicina da Universidade do Porto - FMUP, Porto, Portugal; [4]Hospital de São João, Endocrinology, Porto, Portugal

The majority of adrenocortical tumors (ACT) are benign and hormonally non-functioning, in contrast to adrenocortical carcinomas (ACC), which are rare and usually very aggressive tumors. The differential diagnosis between these two entities is mainly based on unspecific and subjective criteria, contributing to the inaccuracy of diagnosis. Due to ACC molecular and biological heterogeneity, prognostic factors have a limited capacity to predict ACC clinical outcomes, leading to an inappropriate therapeutic strategy. Angiogenesis is a well-recognized hallmark of cancer. As a dynamic and a complex multistage mechanism, various signaling pathways regulate the growth and maintenance of blood vessels, such as the vascular endothelial growth factor (VEGF) and Ang-Tie pathways. This study aimed to evaluate the role of the VEGF and Ang-Tie pathways in ACT angiogenesis, in order to identify molecular markers that may contribute to the diagnosis and/or prognosis of ACC. The ACT studied included ACC ($n=22$), adrenocortical adenomas (ACA) with Cushing's syndrome ($n=8$) and non-functioning ACA ($n=13$). For each sample, the expression of proteins involved in angiogenesis, namely CD34, VEGF, VEGF-R2, Ang1, Ang2, Tie1 and Tie2, were analyzed by immunohistochemistry. The percentage of the stained area for each protein was quantified using a morphometric analysis tool, except for VEGF. CD34, Ang1 and Ang2 expression was found to be significantly different between benign and malignant ACT. ACC presented lower CD34 expression when compared to ACA, whereas Ang1 and Ang2 expression was higher in ACC. Despite the differences observed, none of these proteins demonstrated to be accurate biomarkers for ACT differential diagnosis. Additionally, higher Tie1 expression was observed in ACC of patients with venous invasion and shorter overall survival. As conclusion, this study demonstrated for the first time that the Ang-Tie pathway has a role in ACC angiogenesis. The higher Ang2 levels in malignant ACT could be related with higher vascular permeability, and therefore facilitating tumor dissemination. In addition, the higher Tie1 expression in ACC patients with poor prognosis may represent a possible therapeutic target for ACC.
Finding: This study was funded by the Foundation for Science and Technology (FCT) (PTDC/MEC-ONC/31384/2017).

DOI: 10.1530/endoabs.81.P284

P285

Prognostic value of endocrine biomarkers in patients admitted to intensive care unit for COVID-19

Emanuele Varaldo[1], Alessandro Maria Berton[1], Andrea Rosata[1], Giorgia Montrucchio[2], Francesca Rumbolo[3], Nunzia Prencipe[1], Ezio Ghigo[1], Luca Brazzi[2] & Silvia Grottoli[1]
[1]University of Turin, Division of Endocrinology, Diabetes and Metabolism, Department of Medical Sciences , Italy; [2]University of Turin, Division of Anesthesia and Intensive Care 1, Department of Anesthesia, Intensive Care and Emergency; [3]University of Turin, Clinical Biochemistry Laboratory, "Città della Salute e della Scienza di Torino" University Hospital Turin

Introduction
To date, there are no clear biochemical parameters to identify early COVID-19 cases at risk of complications in the Intensive Care Unit (ICU).
Aim
To evaluate the prognostic potential of endocrine biomarkers associated with acute inflammatory conditions in ICU patients for COVID-19.
Methods
Between 1/3/2020 and 31/12/2020 we recruited 126 consecutive patients at the admission to ICU 1U, Molinette University Hospital of Turin. Within 24 hours (T1), we calculated: SAPS II (Simplified Acute Physiological Score II), SOFA (Sequential Assessment of Organ Failure) and MuLBSTA (Multinodular infiltration, hypoLymphocytosis, Bacterial co-infection, Smoking history, hyperTension and Age). At T1, at 72 hours (T3) and after 7 days (T7), we measured the plasma levels of copeptin and MR-proADM. Duration of extracorporeal membrane oxygenation (ECMO) and mechanical ventilation (MV), ICU and hospital length of stay (LOS), ICU (IM) and hospital mortality (HM) were recorded. We present the results of the first 69 patients.
Results
53 males and 16 females (median age 63) were enrolled. The ICU and hospital LOS were 13 [6.7-22.2] days and 20 [13-30] days, respectively. The median time free from MV was 1 day. The need for pronation was significantly predicted by a higher MuLBSTA classification (OR 4.01, $P=0.025$). The median duration for ECMO was 17 days. The SOFA score was higher in patients requiring ECMO ($P=0.019$) and performed better when corrected for copeptin at T1 (HR 1.25, $P=0.02$). IM and HM were 62.3% and 68.1% (median survival time 18 and 24 days), respectively. MR-proADM was higher in dying patients with increasing statistical significance over time (T1 1.3 vs 0.91 nmol/L, $P=0.028$; T7 1.77 vs 0.9 nmol/L; $P=0.0001$). The MR-proADM T7/T1 ratio was significantly higher in those who died during hospitalization ($P=0.0003$) predicting HM (HR 1.35, $P=0.025$). SAPS II class at the admission also predicted HM (HR 1.39, $P=0.013$), but correcting for MRproADM (HR 1.43, $P=0.012$) or copeptin measured at T1 improved its statistical significance (HR 1.56, $P=0.003$). Likewise, SOFA score, easier to collect in ICU, significantly predicted HM (HR 1.09, $P=0.041$), but improved its performance if corrected for MR-proADM (HR 1.12, $P=0.019$) or copeptin at T1 (HR 1.11, $P=0.018$). Neither gender, estimated glomerular filtration rate, C-reactive protein, or procalcitonin affected the previous regression analyses.
Conclusions
Endocrine biomarkers evaluated at ICU admission improve the ability of prognostic scores to predict mortality and severe adverse outcomes. The increase in MR-proADM after 7 days of hospitalization in the ICU also predicts hospital mortality.

DOI: 10.1530/endoabs.81.P285

P286

A novel mutation in creb3l1 gene involved in vasopressin synthesis pathway in patients with hypertensive cardiovascular diseases

Sania Rauf[1,2], Abida Arshad[1], Roger Foo[3], Maleeha Akram[1], Shumaila Naz[2], Afzaal Ahmed Naseem[4], Mazhar Qayyum[1] & Syed Shakeel Raza Rizvi[1]
[1]Pir Mehr Ali Shah Arid Agriculture University Rawalpindi, Department of Zoology, Fisheries and Wildlife, Rawalpindi, Pakistan; [2]University of Wah, Wah Cantt, Pakistan, Department of Biosciences, Wah Cantt, Pakistan; [3]Genome Institute of Singapore (GIS), Singapore, Singapore, Singapore; [4]University of Lahore, Sihala Campus, Islamabad, Islamabad, Pakistan

Arginine vasopressin (AVP) is a neurohormone, which regulates blood and extracellular fluid volume and hence blood pressure (BP). AVP has its chief action in kidneys where it reduces flow of urine, increases permeability of convoluted tubules of kidneys to water and its reabsorption. It binds to receptors on sweat glands and decreases water loss by perspiration from the skin. Also, AVP binds to peripheral arteriolar receptors, causing vasoconstriction and increase in BP. The synthesis of vasopressin occurs in paraventricular and supra-optic nuclei of the hypothalamus. The mRNA encoding AVP is translated into preprohormone that is delivered into endoplasmic reticulum with concomitant signal peptide removal. The resulting prohormone is folded and delivered to Golgi apparatus where the precursor is cleaved and post-translationally modified into mature hormone. The newly synthesized neurohormone is packed in granules in Golgi complex, which move down the axons, through the stalk, to the posterior pituitary, where AVP is stored and released in response to appropriate stimuli. The main physiological stimulus for release of AVP is an increase in osmotic pressure in circulating blood. AVP causes retention of water by kidneys, which reduces plasma osmolality. The transcription factor cAMP responsive element-binding protein 3 like 1 (CREB3L1) is an important component for cellular homeostasis, particularly within cell types with high peptide secretory capabilities. CREB3L1 serves an important role in body fluid homeostasis through its transcriptional control of AVP gene. In this study, hypertensive cardiovascular patients were screened using whole exome sequencing (WES) to find possible pathogenic mutations in different genes of AVP pathway. Thirteen hypertensive cardiovascular patients from three families (3 patients in 1st from 21-48; 5 in 2nd from 43-72 and 5 patients in 3rd from 19-47 years of age) were

selected for WES. Genomic DNA was extracted (DNA Isolation Kit from QIAamp DNA mini Kit) at Department of Biosciences, University of Wah, Wah Cantt, Rawalpindi, Pakistan. DNA obtained was taken to Genome Institute of Singapore (GIS), Singapore, where final dilutions of 25µl DNA were outsourced to Proteomics Lab, Macrogen Asia Pacific, Singapore for WES. Subsequent bioinformatics analysis was performed at GIS, Singapore. The results identified a novel homozygous splice region variant (1524-1A>G) in *CREB3L1* gene in all patients. In addition, a novel heterozygous splice region variant (340-2_340-1insCCC) was also identified in *SEC63* gene in 10/13 patients. In conclusion, we report novel mutations in two genes involved in AVP synthesis pathway in our patients with hypertensive cardiovascular diseases.

DOI: 10.1530/endoabs.81.P286

P287

Whole exome sequencing of genes involved in dysfunctional renin-angiotensin-aldosterone system in hypertensive cardiovascular patients

Sania Rauf[1,2], Abida Arshad[1], Roger Foo[3], Maleeha Akram[1], Shumaila Naz[2], Afzaal Ahmed Naseem[4], Mazhar Qayyum[1] & Syed Shakeel Raza Rizvi[1]

[1]Pir Mehr Ali Shah Arid Agriculture University Rawalpindi, Department of Zoology, Fisheries and Wildlife, Rawalpindi, Pakistan; [2]University of Wah, Wah Cantt, Pakistan, Department of Biosciences, Wah Cantt, Pakistan; [3]Genome Institute of Singapore (GIS), Singapore, Singapore, Singapore; [4]University of Lahore, Sihala Campus, Islamabad, Islamabad, Pakistan

The renin-angiotensin-aldosterone system (RAAS) is an endocrine system within the body that is essential for regulation of blood pressure (BP) and fluid balance. The system is mainly comprised of three hormones renin, angiotensin II (Ang II) and aldosterone. The RAAS pathway is initiated in the kidney with the proteolytic conversion of liver derived angiotensinogen to angiotensin I (Ang I) by renin secreted by juxtaglomerular apparatus of the nephron. Ang I is cleaved by angiotensin converting enzyme to produce Ang II, the physiologically active component of the system. Ang II acts on the adrenal cortex through its receptors, AT-1 and AT-2, to stimulate the release of aldosterone. Aldosterone is a mineralocorticoid, a steroid hormone released from the zona glomerulosa of the adrenal cortex and plays a central role in regulation of BP mainly by acting on distal tubules and collecting ducts of the nephron, increasing reabsorption of sodium and water in the kidney and secretion of potassium. Increase in water retention causes increase in the blood volume and hence BP. In this study, whole exome sequencing (WES) was used to identify pathogenic mutations in different genes of RAAS pathway, whose dysfunction may lead to hypertension and related cardiovascular diseases. Thirteen hypertensive cardiovascular patients from three families (3 patients in 1st from 21-48, 5 in 2nd from 43-72 and 5 in 3rd from 19-47 years of age) were selected for WES. Genomic DNA was extracted (DNA Isolation Kit from QIAamp DNA mini Kit) at University of Wah (UOW), Wah Cantt, Rawalpindi, Pakistan. DNA obtained was taken to Genome Institute of Singapore (GIS), Singapore, where final dilutions of 25µl DNA were outsourced to Proteomics Lab, Macrogen Asia Pacific, Singapore for WES. Subsequent bioinformatics analysis was performed at GIS, Singapore. Our results revealed pathogenic mutations in different routes of RAAS pathway; gene mutations in *DGKB* in all 13 patients, *NCOR2* in 12 patients, *ESRRA* in 10 patients, *SEC63* in 10 patients, *RYR3* in 3 patients of 2 families and *CAMKK2* in 1 patient. Novel variants were identified in *NCOR2*, *SEC63* and *CAMKK2* genes. Missense variants were found in *RYR3* and *ESSRA* genes, splice region variants in *DGKB* and *SEC63* genes and frameshift variants were identified in *NCOR2* and *CAMKK2* genes. All the variants were found to be heterozygous except *NCOR2* gene. In conclusion, our results identified non-synonymous mutations in 6 genes involved in different steps of RAAS pathway in patients with hypertensive cardiovascular diseases.

DOI: 10.1530/endoabs.81.P287

P517

Impact of glucocorticoid-induced adrenal insufficiency on health-related quality of life

Stina Willemoes Borresen[1], Victor Brun Boesen[2], Torquil Watt[2,3], Jakob Bue Bjorner[4,5,6], Bo Baslund[7], Henning Locht[8], Toke Bjørk Thorgrimsen[8], Bente Jensen[8], Søren Schwartz Sørensen[9,10], Merete Lund Hetland[10,11], Annette Hansen[12], Jesper Nørregaard[13], Marianne Klose[1] & Ulla Feldt-Rasmussen[1,10]

[1]Copenhagen University Hospital, Rigshospitalet, Copenhagen, Denmark, Department of Medical Endocrinology and Metabolism; [2]Copenhagen University Hospital, Herlev-Gentofte, Herlev, Denmark, Department of Internal Medicine; [3]Institute of Clinical Medicine, University of Copenhagen; [4]QualityMetric, USA; [5]National Research Centre for the Working Environment, Copenhagen, Denmark; [6]University of Copenhagen, Copenhagen, Denmark, Department of Public Health; [7]Copenhagen University Hospital, Rigshospitalet Blegdamsvej, Copenhagen, Denmark, Center of Rheumatology and Joint Diseases; [8]Copenhagen University Hospital, Frederiksberg and Bispebjerg Hospital, Frederiksberg, Denmark, Center of Rheumatology and Joint Diseases; [9]Copenhagen University Hospital, Rigshospitalet, Copenhagen, Denmark, Department of Nephrology; [10]Institute of Clinical Medicine, University of Copenhagen, Denmark; [11]Copenhagen University Hospital, Rigshospitalet Glostrup, Denmark, Center of Rheumatology and Joint Diseases; [12]Copenhagen University Hospital, Herlev-Gentofte, Denmark, Center of Rheumatology and Joint Diseases; [13]Copenhagen University Hospital, Nordsjællands Hospital, Hillerød, Denmark, Center of Rheumatology and Joint Diseases

Objective

Glucocorticoid-induced adrenal insufficiency is highly prevalent, but the clinical consequences are not fully understood. Therefore, the indication of adding stress dosages of glucocorticoid during ongoing anti-inflammatory glucocorticoid treatment remains unclear. The aim of this study was to determine the impact of adrenal function on health-related quality of life (HRQoL) in patients receiving ongoing low-dose prednisolone treatment.

Methods

Cross sectional study of 181 patients treated >6 months with prednisolone for rheumatoid arthritis (RA) ($n=103$), polymyalgia rheumatica/giant cell arteritis (PMR/GCA) ($n=47$) or renal transplantation (RTx) ($n=31$). Patients received ongoing prednisolone treatment, median dose 5 mg/day (range 2.5-20 mg) and were not routinely advised to increase the dose during intercurrent illness or stress. Adrenal function was assessed by ACTH test. HRQoL was evaluated during ongoing prednisolone treatment with SF-36v2 scales *General Health* and *Vitality*, AddiQol total score (not RA patients), *Fatigue* VAS scale (PMR/GCA cohort), and self-reported hospital admissions and doctor's appointments. Analyses of the impact of stimulated P-cortisol on HRQoL controlling for underlying disease were performed in i) all patients and ii) 128 patients receiving low-dose treatment (≤5 mg/day), respectively.

Results

Adrenal insufficiency was found in 41% of patients (35% low-dose patients). Overall, *General Health*, *Vitality,* and AddiQol scores were not associated with stimulated P-cortisol. Mean total AddiQol score was 62.5 (SD 7.7). There was a trend for more medical contacts with lower stimulated P-cortisol (1.17 hospital admissions/year/-100nmol/L, CI95%:-0.05–2.23, $P=0.061$) and (1.11 doctor's appointments/year/-100nmol/L, CI95%:-0.14–2.36, $P=0.083$). In the PMR/GCA subcohort, *Fatigue* VAS score was higher with lower stimulated P-cortisol (4.8mm/-100nmol/L, CI95%:0.9–8.7, $P=0.017$) and *General Health* and *Vitality* tended to be lower (GH:-3.78 points/-100nmol/l, CI95%:-7.16–-0.40, $P=0.029$) (VT:-3.96 points/-100nmol/l, CI95% -8.38–0.45, $P=0.077$). However, low-dose patients had higher *Vitality* with lower stimulated P-cortisol (3.12/-100nmol/L, CI95%:0.17–6.07, $P=0.038$).

Conclusion

Glucocorticoid-induced adrenal insufficiency was associated with fatigue and reduced *General health* in the PMR cohort and a trend for more doctor's appointments/admissions in the whole cohort, but otherwise poorly associated with HRQoL during ongoing prednisolone treatment. Results can reflect poor HRQoL consequences of glucocorticoid-induced adrenal insufficiency during ongoing (low-dose) prednisolone treatment or insufficient sensitivity of HRQoL instruments with long recall periods rather than daily symptom monitoring during situations of stress.

DOI: 10.1530/endoabs.81.P517

P518

Laboratory evidence of hyperaldosteronism is common in patients with kidney stones – a retrospective single-center analysis

Andrej Skoberne[1] & Mojca Jensterle Sever[2]

[1]Department of Nephrology, Ljubljana, Slovenia; [2], Department of Endocrinology, Diabetes and Metabolism, Ljubljana, Slovenia

Background

Kidney stones have been linked to chronic kidney disease and a higher probability of adverse cardiovascular events. Precise mechanisms that lead to these complications have not yet been elucidated. Most cases of kidney stones are idiopathic, related to metabolic disturbances like hypercalciuria, which often have a genetic background. There have been few reports of kidney stones associated with primary hyperaldosteronism (HA); however, the prevalence of HA in patients with kidney stones has not been fully examined.

Methods
We conducted a retrospective single-center study that included 181 patients evaluated for recurring kidney stones in whom basic laboratory tests to identify HA (plasma renin activity – PRA, plasma aldosterone concentration – PAC, and aldosterone to renin ratio – ARR) had been performed. The aim of the study was to assess the prevalence of laboratory evidence of HA (LEHA) in kidney stone patients and to identify clinical and laboratory characteristics associated with LEHA in this group of patients.
Results
The prevalence of LEHA was high. High ARR was identified in 39.8% patients, while a concurrent high PAC was identified in 21.5% ($>$ 0.41 nmol/l) and 13.8% ($>$ 0.55 nmol/l) of all patients. Arterial hypertension (AH) was identified in only about a quarter of patients with LEHA and the prevalence of LEHA was similar in patients with or without AH. Patients with LEHA and AH, particularly when associated with high PAC ($>$ 0.55 nmol/l), exhibited some characteristic features of primary HA like lower serum potassium and higher serum bicarbonate. Patients with LEHA and without AH did not exhibit these features; however, they had higher serum phosphate associated with a trend towards lower urine phosphate excretion, a feature not present in patients with LEHA and AH. Patients with LEHA and AH were also older and tended to have their first stone event at a later age, while patients with LEHA and without AH had more stone-related urological procedures. An extremely low PRA value ($<$ 0.07 μg/l/h) was present in 8.3% patients and was associated with a faster rate of decline in kidney function on follow-up.
Conclusions
Our study shows that LEHA can be common in patients with recurring kidney stones. Few of these patients present with typical features of primary HA. There are some distinct features of patients with LEHA and without AH, that could represent a separate phenotype in this population. The biological relevance of these findings is yet to be determined.

DOI: 10.1530/endoabs.81.P518

P519

Brain Structure in a cohort of young adult patients with Autoimmune Addison's Disease

Annelies van't Westeinde[1], Nelly Padilla[1], Sara Ström[2,3], Olle Kämpe[4], Sophie Bensing[2,3] & Svetlana Lajic[1]
[1]Karolinska Institute, Women's and Children's Health, Sweden; [2]Karolinska Institute, Molecular Medicine and Surgery, Sweden; [3]Karolinska University Hospital, Endocrinology, Sweden; [4]Karolinska Institute, Medicine (Solna), Center for Molecular Medicine, Sweden

Background
Both cortisol and other adrenal hormones are well known to affect brain structure and function throughout development. Due to destruction of the adrenal cortex, patients with Autoimmune Addison's disease (AAD) lack production of adrenal hormones and therefore receive lifelong replacement of cortisol and aldosterone, and, for some female patients dehydroepiandrosterone (DHEA). However, replicating the natural rhythm of secretion is difficult, and patients are often exposed to either supra- or infra- physiological adrenal hormone levels. Such long-term hormonal disturbances might be expected to affect the brain on both a structural and functional level. Assessing brain structure in patients with AAD is relevant, as varying treatment-regimes may have detrimental effects on the brain and could lead to problems with cognitive function and mood. The present study therefore investigated grey and white matter structure of the brain in a cohort of young adult patients with AAD.
Methods
T1 and DWI Magnetic Resonance Imaging (MRI) of the brain was done on fifty-two patients with AAD and seventy healthy control participants (aged 19-43). A whole-brain exploratory approach was used to compare patients to controls on estimates of global and regional cortical thickness, surface area, cortical grey matter volume, subcortical volumes, hippocampal and amygdalae subfields (FreeSurfer), and white matter microstructure (FSL TBSS).
Results
Apart from reduced volume of the right superior parietal cortex in male patients, there were no differences in any of the estimates between patients with AAD and healthy controls, when correcting for total intracranial volume and multiple comparisons.
Conclusion
Brain structure of patients with AAD seems to be relatively unaffected at this young adult age. This finding is reassuring and suggests the brain is able to cope with disturbances in adrenal hormone levels. Follow-up studies are needed to determine if the brain of patients with AAD may be affected later in life, or by varying treatment regimes, such as immediate or slow-release hydrocortisone medication.

DOI: 10.1530/endoabs.81.P519

P520

Cortical-sparing adrenalectomy for bilateral pheochromocytoma - is it a game worth the candle? Systematic review with meta-analysis comparing total vs partial adrenalectomy in bilateral pheochromocytoma

Karolina Zawadzka, Piotr Tylec, Piotr Małłczak, Piotr Major, Michał Pędziwiatr & Magdalena Pisarska-Adamczyk
Jagiellonian University Medical College, 2nd Department of General Surgery, Kraków, Poland

Background
Bilateral total adrenalectomy (TA), despite causing persistent adrenal insufficiency with lifetime replacement of corticosteroids, is the method of choice in patients with bilateral pheochromocytoma. Partial adrenalectomy (PA) is an alternative approach that aims to balance tumor removal while maintaining adrenal function, although the oncological completeness of the procedure is questionable.
Objective
The aim of this systematic review and meta-analysis was to compare bilateral total adrenalectomy and partial (cortical-sparing) adrenalectomy.
Methods
A bibliographical search of databases (MEDLINE, EMBASE, Scopus, Web of Science, CENTRAL) as well as registers of clinical trials (ClinicalTrials.gov, European Trials Register, WHO International Trials Registry Platform) was conducted in order to identify eligible studies. The databases and registries were searched from inception until August 14, 2021, and no language restrictions or dates were imposed. Both randomised controlled trials and observational studies comparing TA with PA in adults with bilateral pheochromocytoma were considered for inclusion in this study. The primary outcomes were the risk of pheochromocytoma recurrence and steroid dependence. The secondary outcomes of interest were: time to recurrence after surgery, development of metastatic pheochromocytoma, incidence of adrenal crisis, morbidity, overall mortality and pheochromocytoma-specific mortality.
Results
Twenty five retrospective observational studies including 1444 patients were eligible. During follow-up, every third patient after PA required steroid supplementation: RR 0.32, 95% CI: 0.26–0.38, $P < 0.00001$, $I^2=21\%$. Patients undergoing partial adrenalectomy had lower risk of developing Addisonian-like crisis: OR 0.3, 95% CI: 0.1–0.91, $P=0.03$, $I^2=0\%$. On the contrary, PA was associated with higher risk of reccurence than TA: OR 3.72, 95% CI: 1.54-8.96, $P=0.003$, $I^2=28\%$. We found no difference between PA and TA groups in the development of metastatic pheochromocytoma: OR 1.47, 95%CI: 0.48-4.44), $P=0.5$, $I^2=0\%$, overall mortality: OR 1.04, 95% CI: 0.47-2.33, $P=0.92$, $I^2=0\%$, as well as pheochromocytoma-specific mortality: OR 0.54, 95% CI: 0.08–3.72, $P=0.53$.
Conclusions
Patients undergoing partial adrenalectomy had a three-fold lower risk of developing steroid dependence and developing an adrenal crisis, but had a higher risk of recurrence. Thus, partial adrenalectomy may be worth considering in some patients with bilateral pheochromocytoma only with careful lifelong follow-up. Our findings are based on limited certainty evidence, and further well-designed, multi-center studies are required to confirm the benefits and drawbacks of both approaches.

DOI: 10.1530/endoabs.81.P520

P521

Inflammation in Hypertensive Patients with Type 2 Diabetes on Stable Therapy with Non-dipper and Dipper Status

Lolita Matiashova & Ganna Isayeva
L T Malaya Therapy National Institute of the National Academy of Medical Sciences of Ukraine, Department of Comprehensive Risk Reduction for Chronic Non-Communicable Diseases, Kharkiv, Ukraine

Background
Hypertension has a negative effect on the cardiovascular system, but the data are limited about the connection between non-dipper hypertension and inflammation in patients with type 2 diabetes (T2D) and without.
Aim
To study the effects of dipper and non-dipper hypertension with and without type 2 diabetes on inflammatory factors.
Methods
The cross-sectional study included 97 hypertensive patients (57 men) without type 2 diabetes and 85 hypertension patients with type 2 diabetes median age 56,5 (45.00 ÷ 63.70) years old. All patients had been on stable antihypertensive and anti-hyperglycemic therapy during the last three months and had target ambulatory blood pressure at the moment of inclusion to the study. Daily blood

Table 1 The mean and standard deviation of day systolic (SBP) and diastolic (DBP) blood pressure, mm Hg in patients with type 2 diabetes (T2D) and without

	Day SBP	Day DBP	Daily SBP	Daily DPB	Night SBP	Night DBP
Dipper ($n=44$)	128.3∓15.7	76.0∓10.0	132.3∓15.4	79.14∓10.2	114.3∓16.4	65.9∓8.9
Non-Dipper ($n=53$)	128.4∓17.4	74.2∓9.4	130.0∓16.0	75.2∓8.8	123.6∓18.3	71.4∓10.6
Dipper with T2D ($n=40$)	131.8∓13.9	81.9∓8.1	134.8∓14.7	84.6∓9.2	121.1∓21.5	72.8∓11.0

pressure monitoring was done to all patients with Heaco ABPM50 monitoring. Fasting glucose (FG), blood lipids, creatinine, uric acid, high sensitive C-reactive protein (hCRP), and interleukin 1 beta (IL-1B) were measured. Physical activity was assessed using the International Physical Activity Questionnaire. Data were analyzed with SPSS IBM 19.0.

Result

According to their night blood pressure, the patients were divided into dipper ($n=84$) and non-dipper ($n=98$). The mean of day and night systolic and diastolic blood pressure according to the group presented in table 1. The mean of hCRP in dipper patients without T2D was 7.7 ∓8.4 and IL-1b 2.3 ∓ 0.5 pg/ml, non-dipper hCRP 11.4∓6.7 mg/L ($P=0.05$) and IL-1b 2.2 ∓ 0.6 pg/mL ($p>0.05$). The mean of hCRP in dipper patients with T2D was 12.2∓7.9 mg/L and IL-1b 2.3 ∓ 0.5 and non-dipper hCRP 10.2 ∓5.5 ($p>0.05$) and IL-1b 2.7 ∓ 0.7 pg/mL ($p>0.05$).

Conclusion

Non-dipper hypertension patients without type 2 diabetes could be an additional risk factor of vascular inflammation. Patients with type 2 diabetes and hypertension have a higher inflammation level, independent of dipper status; future studies are needed.

DOI: 10.1530/endoabs.81.P521

P522

Gastric monomorphic epitheliotropic intestinal T-cell lymphoma with bilateral adrenal metastases

Eirini Kaliakatsou[1], Athina Markou[1], Labrini Papanastasiou[1], Irini Giagourta[1], Athanasia Kalantzi[1], Anastasia Dimitriadi[2], Michael Lenos[2], Theodora Kounadi[1] & Athanasios Fountas[1]
[1]'G. Gennimatas' General Hospital of Athens, Department of Endocrinology and Diabetes Center, Athens, Greece; [2]'G. Gennimatas' General Hospital of Athens, Department of Pathology, Athens, Greece

Introduction

Monomorphic epitheliotropic intestinal T-cell lymphoma (MEITL), formerly known as type II enteropathy-associated T-cell lymphoma, is a rare and aggressive subtype of lymphoma of the gastrointestinal track typically noted in Asian or Hispanic populations. Adrenal involvement as part of MEITL is extremely rare. Herein we present a patient of Greek origin with MEITL and bilateral adrenal metastases.

Case Presentation

A 74-year-old man presented with a 2-week history of right upper quadrant abdominal pain, decreased appetite and fatigue, as well as weight loss (10 kgs in 8 months). Abdominal CT imaging revealed heterogenous bilateral adrenal lesions (maximum diameter 11 cm on the left and 10 cm on the right, respectively). On clinical examination, there were no signs of cortisol excess, no skin pigmentation, no palpable lymph nodes and the abdomen was soft. Hormonal investigations revealed primary hypocortisolism (basal cortisol: 61 nmol/L, ACTH: 189 pg/ml) and treatment with hydrocortisone was initiated; twenty-four-hour urine metanephrines were normal. Further investigations showed anemia and increased LDH (1365 IU/L, normal values: 134-279), β2-microglobulin (4.99 ng/L, normal values: 0.97-2.64) and inflammation markers (ESR, CRP and ferritin). Primary bilateral adrenal lymphomas were suspected and fine needle biopsy of the left adrenal lesion was performed. Staging CT scans showed no brain or lung metastases but gastric wall thickening and infiltration of the right kidney by the adrenal mass were noted on the abdominal scan. Gastroscopy revealed a mucosal lesion with a micronodular and ulcerated surface which was biopsied. Histology from both the adrenal and the gastric lesions was consistent with MEITL; Ki-67 was positive in approximately 80% of tumor cells. Bone marrow biopsy and aspiration did not show any signs of infiltration by the lymphoma. Treatment with high dose dexamethasone was initiated but the patient rapidly deteriorated. He developed sepsis with multi-organ failure and finally passed away before receiving combined chemotherapy.

Discussion

MEITL is a rare aggressive T-cell lymphoma arising from intestinal intraepithelial lymphocytes with a poor prognosis. Most often it involves the small bowel, particularly the jejunum and ileum, but it can also involve the colon or stomach, like our case. Involvement of the adrenal glands in patients with MEITL is extremely rare. To our knowledge, this is the second report of MEITL with bilateral adrenal metastases. Clinical experience, awareness and a multidisciplinary approach in such perplexing cases is required.

DOI: 10.1530/endoabs.81.P522

P523

A retrospective evaluation of the utility of overnight dexamethasone suppression tests in over 500 patients evaluated for hypercortisolism

Rebecca Sagar[1], Mohamed Elsabbagh[1], Stephen Gibbons[2] & Afroze Abbas[1]
[1]Leeds Teaching Hospitals Trust, Leeds Centre for Endocrinology and Diabetes, Leeds, United Kingdom; [2]Leeds Teaching Hospitals Trust, Leeds, United Kingdom

Background

Overnight dexamethasone suppression tests (ONDST) are conducted to investigate patients with symptoms suggestive of cortisol hypersecretion or if an adrenal incidentaloma is identified. Cortisol levels of 50 nmol/l and above following ONDST may be related to autonomous cortisol secretion (ACS) and require further investigation. Determining likely presence of ACS is essential given reported associations with type 2 diabetes mellitus (T2DM), obesity, cardiovascular disease and osteoporosis. ONDST are inherently prone to interference and false positive rates are high, often resulting in clinicians conducting multiple ONDST, with associated patient and service impacts. Our study assesses the outcomes from a large UK cohort who underwent ONDST.

Methods

560 unselected patients who underwent ONDST were retrospectively examined. Data were collected on indication, demographics including body mass index (BMI), biochemical results and co-morbidities. A positive ONDST was considered any cortisol greater than or equal to 50nmol/l, further categorised into mild ACS (MACS) between 50-138nmol/l and probable ACS >138nmol/l. Statistical analysis was conducted using Prism v9.3.1.

Results

62% of the cohort were female. Mean age was 57.3 years ±17.1 (SD). Mean BMI was 30.5kg/m^2 ± 7.2. 71.6% had an adrenal lesion as the indication for the test, with a further 16.3% undergoing ONDST for clinical suspicion. 28% had an unsuppressed cortisol on ONDST (greater than or equal to 50nmol/l), of these 6.1% were greater than 138nmol/l. 48% of patients with an unsuppressed ONDST underwent repeat testing with 90.7% of results remaining unsuppressed. 47 patients with unsuppressed ONDST had an ACTH level recorded, 25.5% had an ACTH less than 5ng/l (normal range 5-47ng/l). 89.8% had a HbA1c recorded, with 31.2% having a result greater than 48mmol/mol or known T2DM. BMI did not correlate with suppressed vs unsuppressed cortisol on ONDST. Of the 157 patients with an unsuppressed cortisol, 63.7% had a potential confounder including obesity, diabetes or depression.

Conclusion

Our data demonstrates that there are high rates of unsuppressed cortisol following ONDST. Given the large numbers of patients with adrenal incidentalomas now identified and assessed, this leads to significant increased demand on endocrinology outpatient appointments. We have also shown that repeated ONDST may be unnecessary given greater than 90% remained unchanged, and the majority of patients had a potentially irreversible confounder. Therefore, we would suggest that careful further evaluation of the likelihood of MACS following a positive ONDST, through additional biochemical and clinical investigation but without a repeat ONDST, is required prior to any clinic attendance.

DOI: 10.1530/endoabs.81.P523

P524

HIF-2α is detrimental for the functioning of the adrenal medulla

Deepika Watts[1], Nicole Bechmann[1,2], Hermine Mohr[3], Anja Krüger[1], Natalia S. Pellegata[3], Graeme Eisenhofer[1], Mirko Peitzsch[1] & Ben Wielockx[1]

[1]Institute of Clinical Chemistry and Laboratory Medicine, University Hospital Carl Gustav Carus, Medical Faculty Carl Gustav Carus, Technische Universität Dresden, , Dresden, Germany; [2]Department of Internal Medicine III, University Hospital Carl Gustav Carus, Technische Universität Dresden, Dresden, Germany; [3]Institute for Diabetes and Cancer, Helmholtz Zentrum München, Neuherberg, Germany

The adrenal gland is a crucial regulator of numerous fundamental biological processes and its hormones are essential for maintaining homeostasis in normal and stressful situations. However, the impact of hypoxia signalling on the function of the adrenal remains poorly understood. During the past years, our research group has focused on enhancing our understanding of hypoxia pathway proteins (HPPs) in the different areas of the adrenal gland. Firstly, we described a crucial role for hypoxia inducible factor-1 α (HIF-1α) during adrenal steroidogenesis (Watts *et al.*, CMLS, 2021) and secondly, we demonstrated that HIF-2α is essential for the synthesis and release of catecholamines. Briefly, HIF-2α stabilization due to loss of prolyl hydroxylase domain protein-2 (PHD2) leads to reduced phenylethanolamine N-methyltransferase (PNMT) activity and consequent epinephrine synthesis. Simultaneously, HIF-2α mediated erythropoietin (EPO) production in renal EPO producing cells (REPCs) stimulated excessive RBC formation (erythrocytosis) leading to hypoglycaemia and increased release of epinephrine from the adrenal medulla (Watts *et al.*, JMM, 2021). Recently, we generated a new set of mouse lines efficiently targeting the HPPs in chromaffin cells to further unravel the impact of HIF-2α -stabilisation during the development of medulla-related tumours. This will provide us with an excellent chance to enhance our current knowledge on potential targets for the therapeutic treatment of pheochromocytomas (PCCs) and paragangliomas (PGLs).

DOI: 10.1530/endoabs.81.P524

P525

Characterization of angiotensin II-induced dual-specificity MAPK phosphatase gene expression changes in vascular smooth muscle cells

Janka Gém[1], Kinga Kovács[1], András Balla[1,2] & László Hunyady[1,3]
[1]Semmelweis University, Department of Physiology, Budapest, Hungary; [2]MTA-SE Laboratory of Molecular Physiology, Budapest, Hungary; [3]Institute of Enzymology, Research Centre for Natural Sciences, Budapest, Hungary

Angiotensin II (AngII) is an octapeptide hormone, which participates in physiological and pathological mechanisms. AngII exerts a number of biological effects through the type 1 angiotensin II receptor (AT1R). One of the main targets of AngII are vascular smooth muscle and its stimulation activates numerous signaling pathways that cause contraction and could also result in gene expression changes in vascular smooth muscle cells (VSMCs). Next-generation sequencing (NGS) experiments were performed to analyze the effects of AngII stimulation on gene expression in VSMCs. The experiments were conducted using a rat aortic primary isolated VSMC cell line. In our experimental set-up more than 200 genes were upregulated in response to AngII stimulation in VSMCs. The transcriptome analysis revealed the upregulation of several DUSP genes, such as *DUSP 5*, *6*, *10*, *4*, and *14*. We also investigated the kinetics of the gene-expression changes and the signaling pathways involved in AngII-mediated responses. The results of the quantitative PCR measurements also confirmed the increased expression of selected genes upon AngII stimulation. Transcription of most genes was largest two hours after AngII stimulation. Based on our results, the regulation of the studied gene expression induced by AngII is much more complex than we originally thought, due to the multiple signaling pathways that mediate them. We assume that the regulation of expression changes is probably determined by the interaction of the involved signaling cascades. Based on our data, the expression changes of the studied genes can occur through classical $G_{q/11}$ activation, which triggers Ca^{2+}-mediated mechanisms leading to epidermal growth factor receptor transactivation dependent or independent responses. During the search of the signaling pathway(s) which is/are responsible for certain gene-expression changes, we found that dasatinib, an Src-family tyrosine kinase inhibitor, was able to selectively inhibit the AngII induced gene-expression changes. We have also demonstrated that the imatinib, a selective inhibitor of Bcr-Abl kinases, was not able to achieve the similar effect as the dasatinib. Our data suggest that Src-family tyrosine kinase(s) may play an important role in AngII-induced long-term cellular responses. Our data can provide new insight into the physiology of VSMCs in response to AngII stimulation, and better understanding of the mechanism of AT1-R-mediated gene expression changes in primary VSMCs, which may lead to the development of novel types of drugs for the treatment of cardiovascular and other diseases. This work was supported by the National Research, Development and Innovation Fund (NKFI K116954, K139231, VEKOP-2.3.2-16-2016-00002 and NVKP_16-1-2016-0039).

DOI: 10.1530/endoabs.81.P525

P526

Testosterone, hypogonadism, and heart failure: a systematic and critical review

Elena Di Lodovico[1], Paolo Facondo[1], Andrea Delbarba[2], Letizia Chiara Pezzaioli[1], Filippo Maffezzoni[2], Carlo Cappelli[1] & Alberto Ferlin[3]
[1]University of Brescia, Department of Clinical and Experimental Sciences, Brescia, Italy; [2]ASST Spedali Civili di Brescia, Unit of Endocrinology and Metabolism, Brescia, Italy; [3]UNIVERSITY OF Padova, Department of Medicine, Padova, Italy

Background
Male hypogonadism is defined by low circulating testosterone level associated with signs and symptoms of testosterone deficiency. Although the bidirectional link between hypogonadism and cardiovascular disease has been clarified recently, the association between testosterone and chronic heart failure (CHF) is more controversial.
Methods
We critically review published studies relating to testosterone, hypogonadism, and CHF and provide practical clinical information on the correct diagnosis and treatment of male hypogonadism in patients with CHF.
Results
In general, the published studies are extremely heterogeneous, they frequently have not adhered to hypogonadism guidelines, and they suffer from many intrinsic methodological inaccuracies; therefore, the data have low-quality evidence. Nevertheless, by selecting the very few studies that are methodologically robust, we show that the prevalence of testosterone deficiencies (30-50%) and symptomatic hypogonadism (15%) in men with CHF is significant. Low testosterone correlates with CHF severity, NYHA class, exercise functional capacity, and a worsened clinical prognosis and mortality. The interventional studies on testosterone treatment in men with CHF are inconclusive, but promising in suggesting beneficial effects on exercise capacity, NYHA class, metabolic health, and cardiac prognosis.
Discussion
We suggest that clinicians should measure the testosterone levels of men with CHF who have symptoms of a testosterone deficiency and/or conditions that predispose to hypogonadism, such as obesity and diabetes. These patients - if diagnosed as hypogonadal - could benefit from the short- and long-term effects of TRT, which include improvements to both the cardiological prognosis and systemic outcomes. Further studies with a strong collaboration between cardiologists and endocrinologists are warranted.

DOI: 10.1530/endoabs.81.P526

P527

Impact of covid-19 on arterial stiffness

Nevin Sadeep, Rakesh Sahay & Neelaveni K
Osmania General Hospital, Endocrinology, Hyderabad, India

Introduction
Recently published research works have concluded that Covid-19 infection will result in endothelial dysfunction or worsen it, especially when associated with comorbidities such as diabetes mellitus. Arterial Stiffness is a manifestation of endothelial dysfunction and it can be used as a prediction parameter as well as a target for therapies aimed at ameliorating endothelial cell dysfunction.
Aims and Objectives
To compare arterial stiffness using carotid-femoral Pulse Wave Velocity (cf-PWV) between subjects with Covid-19 and controls without history of Covid-19. Further cases and controls were further subdivided into those with or without comorbidities such as Diabetes Mellitus, Systemic Hypertension, Chronic Kidney Disease, Coronary Artery Disease & Stroke.
Methodology
This study was designed as an observational, single centre, cross sectional study to be done amongst police personnel from Telangana State Police Force, India by randomly selecting subjects who were willing to give written informed consent, after excluding subjects with chronic inflammatory diseases on chronic steroid therapy and pregnant/lactating subjects. Subjects were further divided into 4 groups. Group A did not have any history of Covid-19 or comorbidities, Group B had history of prior Covid-19 infection but no previous history of comorbidities,

Group C had history of comorbidities but no previous history of Covid -19 and Group D had history of prior Covid-19 infection as well as comorbidities. Arterial stiffness was measured indirectly by measuring carotid femoral-Pulse wave velocity (cf-PWV) with a clinically validated device known as PeriScope® [Genesis Medical Systems, India].
Results
Analysis of 170 age-matched (35years to 58 years) subjects was done using GraphPad PRISM software. The mean increase in cf-PWV was 76.2 cm/s in Group-A, 126.5 cm/s in Group-B, 210.1 cm/s in Group-C & 263.9 cm/s in Group-D. Significant p-values were obtained for the differences in the increase in cf-PWV between the 4 different groups. The Arterial stiffness values of prior Covid-19 positive subjects were found to be higher than the group of subjects without prior Covid-19. The group with comorbidities without Covid-19 had a higher increase in arterial stiffness levels compared to subjects with prior Covid-19 but without other comorbidities. Subjects with history of both Covid-19 as well as comorbidities had the highest levels of arterial stiffness.
Conclusion
Arterial Stiffness levels are elevated significantly after Covid-19 infection and is an indicator of increased cardiovascular risk. Carotid Femoral Pulse wave velocity (cf-PWV) can be considered as an easy non-invasive screening tool in post-COVID patients to identify possible high-risk candidates in day-to-day practice.

DOI: 10.1530/endoabs.81.P527

P528

The role of neuropeptide Y in the pathogenesis of vasovagal syncope

Zora Lazurova[1], Ivica Lazúrová[2], Peter Mitro[3] & Marcela Popovnakova[4]
[1]University of PJ Safarik, Medical Faculty, 4th Department of Internal Medicine, Kosice, Slovakia; [2]University of PJ Safarik, Medical Faculty, 1st Department of Internal Medicine, Kosice, Slovakia; [3]University of PJ Safarik, Medical Faculty, 1st Department of Cardiology, Kosice, Slovakia; [4]Medirex Laboratory, Department of Immunology, Kosice, Slovakia

Introduction
Vasovagal syncope (VVS) is a transient loss of conscioussness due to hypoperfusion of the brain caused by vasodepressoric and/or cardioinhibitory reflex. In the pathogenesis, a dysregulation of autonomic nervous system is playing an important role. There is a growing evidence about more complex neurohumoral background of VVS. Neuropeptide Y (NPY) is hormone involved in the regulation of blood pressure with potent vasoconstriction effect. Moreover, NPY is also a cotransmitter with noradrenaline in sympathetic nervous system and is considered to be involved in sympathetic-induced vasoconstriction. Other vasoacitve hormones such as endothelin (ET-1) and angiotensin (ANG) can be implicated in pathogenesis of VVS, too.
Aim
The aim of this study was to evaluate the serum levels of NPY before and after head up tilt test (HUTT) and to compare them between patients with tilt induced VVS and group of negative individuals. Second aim was to find a correlation between NPY and other vasoactive hormones – ET-1 and ANG.
Subjects and methods
Altogether 69 subjects were included in this preliminary study (age 39 + 3,2 years; 41 females) with the history of at least one syncope. HUTT was performed in all subjects according to Italian protocol (20 minutes of passive standing followed by 15 minutes lasting phase after provocation by sublingual nitroglycerin). According to the result of HUTT, patients were divided into HUTT-positive (HUTT+) and HUTT-negative (HUTT-) group. Blood samples were collected before and immediately after HUTT. Serum levels of NPY, ET-1 and ANG were evaluated by ELISA method.
Results
HUTT was positive in 60 patients (HUT+ group), 29 subjects were negative (HUT-) . There was no significant difference in basal levels of NPY between HUTT+ and HUTT- group (36.4 + 2.4 vs 40.1 + 1.5 ng/ml, $P = 0.1$, $T = 1.5$). The stimulated levels of NPY were significantly lower in HUT+ patients when compared to HUT- (36.7 + 2.1 vs 44.4 + 3.2 ng/ml, $P = 0.028$, $T = 2.0$). Both subgroups did not differ in ET-1 and ANG levels. Stimulated NPY levels positively correlated with stimulated ET-1 ($P = 0.001$; $R2 = 0.16$) and ANG ($P = 0.04$; $R2 = 0.06$) in all subjects. When divided into HUT+ and HUT-, NPY significantly correlated only with ANG ($P = 0.004$; $R2 = 0.4$) in HUT- group, while in HUT+ patients, there was a positive correlation with ET-1 ($P = 0.0009$; $R2 = 0.23$) found.
Conclusion
The impaired release of NPY may play a role in pathogenesis of VVS. Other vasoconstrictive hormones, such as ET-1 and ANG, can be involved in pathomechanisms, too.

DOI: 10.1530/endoabs.81.P528

P529

Characteristics of patients with life-threatening events in pheochromocytoma

Sofia-Maria Lider-Burciulescu[1], Monica Livia Gheorghiu[1,2] & Corin Badiu[1,2]
[1]C.I. Parhon National Institute of Endocrinology, Bucure|ti, Romania; [2]Carol Davila University of Medicine and Pharmacy, Bucure|ti, Romania

Introduction
Pheochromocytomas and paragangliomas (PPGLs) are rare tumors of the chromaffin tissue characterised by catecholamine excess. Cardiovascular complications, such as hypertensive crisis and catecholamine-induced cardiomyopathy, are known to be the most frequent causes of life-threatening events in PPGLs patients.
Design
We analysed records of patients diagnosed with PPGLs in one referral centre from Romania between 1976 and 2021 ($n = 106$) in order to compare demographics, symptoms, preoperative catecholamine levels, tumor diameter and outcome in patients with life-threatening events vs. patients without complications (control group).
Results
9 patients (8.4%), 8 F, 1 M presented life-threatening events before the diagnosis or during surgery for PPGL: catecholamine-induced Tako-Tsubo cardiomyopathy ($n = 3$); inverted Tako-Tsubo cardiomyopathy and pulmonary edema ($n = 1$); acute coronary syndrome and pulmonary edema ($n = 2$); pulmonary edema ($n = 1$) ; cardiac arrest and pulmonary edema ($n = 1$); pulmonary thromboembolism and feto-placental apoplexy ($n = 1$). Seven patients had the life-threatening event before the diagnosis of PPGL and two of them had the complications during surgery for PPGL. Compared to pheochromocytoma patients without life-threatening events ($n = 97$), patients with severe complications had a nonsignificantly higher mean tumor diameter (53 vs. 48 cm, $P = 0.3$), similar levels of catecholamine (median 5-6 fold ULN; $P = 0.5$), similar age at diagnosis (50 vs. 47 years; $P = 0.51$). The maximum arterial blood pressure before surgery was non-significantly higher in patients with complication (231 vs. 207 mmHg; $P = 0.1$). All patients with complications survived. Patients with Tako-Tsubo cardiomiopathy had normal cardiac function few days after the event. One patient with acute coronary syndrome and pulmonary edema but a background of other cardiac comorbidities had the ejection fraction of 40% after this event. The woman with feto-placental apoplexy had a negative outcome: her baby died in uterus and she underwent hysterectomy at 34 years old.
Conclusion
Although pheochromocytomas are rare tumors, they may induce a life-threatening complications (diagnosed in 8.4% of cases in our series). There was no specific clinical, hormonal or imaging feature that could predict a life-threatening event in patients with PPGLs.

DOI: 10.1530/endoabs.81.P529

P530

Objective markers and new indicators in adrenal insufficiency- findings from the omni-aid study comparing hydrocortisone and prednisolone replacement therapy

Sirazum Choudhury[1,2], Thilipan Thaventhiran[1,2], Katharine Lazarus[1,2], Tricia Tan[1,2] & Karim Meeran[1,2]
[1]Imperial College London, Department of Metabolism, Digestion and Reproduction, London, United Kingdom; [2]Imperial College Healthcare NHS Trust, Department of Endocrinology, London, United Kingdom

Background
Adrenal insufficiency (AI) is a life-threatening condition if left unmanaged. Despite treatment patients can expect a life expectancy that is shortened by 12 years secondary to probable inherent over-replacement associated with oral glucocorticoid regimens. Thrice-daily hydrocortisone is the most common regimen used. Very low-dose prednisolone (2-4 mg) is an alternative with lower uptake due to the absence of evidence for its use. This study fills this literature gap.
Methods
This is a cross-sectional, observational study that recruited 20 healthy volunteers (HV), 20 AI patients on prednisolone, 20 AI patients on hydrocortisone and 9 patients on anti-inflammatory doses of steroids (mainly IV methyl-prednisolone) for other medical conditions. During stereotyped study visits, subjects provided anthropometric data, blood samples, urine samples and SF-36 data. This was used to assess bone health, cardiovascular risk, diabetic risk, immune cell profiles and subjective health between groups.

Results
There was no significant difference between groups in osteocalcin, P1NP or urinary NTX. Parathyroid hormone was significantly elevated in the hydrocortisone group compared to HV at 8.2(±3.2) vs 6.1(±2.3) pmol/L ($P=0.04$). Calcium and phosphate levels were in the reference range. The waist:hip ratio was significantly lower in HV at 0.83(±0.07) compared to the cohort on hydrocortisone and prednisolone, at 0.90(±0.09) and 0.90(±0.07) respectively ($P=0.009$). High sensitivity-CRP was 1.6(2.1) mg/L compared to 0.8(1.1) mg/L ($P=0.008$) in the hydrocortisone and HV groups respectively. Potassium levels were significantly decreased in the hydrocortisone and high dose groups; 4.0(0.4) mmol/L in both compared to 4.2(0.2)mmol/L in HV ($P=0.005$). Glycaemic markers in both AI groups demonstrated significantly lower fructosamine levels compared to healthy volunteers ($P=0.0008$). The hydrocortisone group had significantly elevated insulin, c-peptide and HOMA-%β compared to HV ($P=0.039$, $P=0.025$, $P=0.025$ respectively). There was no difference in HbA1C levels between groups. Although infection rates were comparable between groups, all steroid groups had significantly elevated neutrophils compared to HV ($P<0.0001$). Monocyte count was significantly elevated in the hydrocortisone cohort at 0.6(0.2) $x10^9$/L vs 0.4(0.2) $x10^9$/L in HV. Flow cytometry showed significant HLA-DR suppression in the monocytes in the high dose group. SF36 data showed impaired energy/fatigue scores in the prednisolone group compared to the healthy volunteers (77.3±(10.2) compared to 58.2(±21.7); $P=0.021$)
Conclusion
The data suggests that hydrocortisone causes greater steroid exposure as assessed by the markers in this study, when compared to healthy volunteers. There are no overt differences between hydrocortisone or prednisolone cohorts. Both medications should be used interchangeably in the treatment of AI.

DOI: 10.1530/endoabs.81.P530

P531

Long-term efficacy and safety of pasireotide in patients with Cushing's disease: a monocentric experience

Ylenia Alessi[1], Maria Luisa Torre[2], Salvatore Giovinazzo[2], Giuseppe Giuffrida[2], Annalisa Giandalia[2], Rosalinda Casablanca[1], Filippo Flavio Angileri[3], Marta Ragonese[2], Francesco Ferraù[1,2] & Salvatore Cannavò[1,2]
[1]Endocrine Unit, "Gaetano Martino" University Hospital of Messina, Italy; [2]Department of Human Pathology of Childhood and Adulthood "Gaetano Barresi", University of Messina, Italy; [3]Department of Biomedical and Dental Sciences, and Morpho-Functional Imaging, University of Messina, Italy

Pasireotide is the first pituitary-directed approved therapy for Cushing's disease (CD), effective in reducing UFC >50% in about half of patients, and with a good tolerability profile but associated with a relatively high incidence of hyperglicemia. The aim of this study was to evaluate efficacy and safety of long-term treatment with pasireotide (PAS) in patients with CD. Methods: We retrospectively evaluated 17 consecutive patients (11 females) with CD treated with PAS (with a mean follow of 40.4±12.5 months), referred to and followed-up at the Endocrine Unit of the University Hospital of Messina (Italy), from 2013 to 2020. Data are expressed as mean±SD. Age at diagnosis was 34.7±13.0 yrs. Before PAS treatment: all patients underwent transnasosphenoidal pituitary adenomectomy, but surgery was not successful in 10 cases, while disease recurred in the other seven; five patients underwent also radiotherapy; seven patients were administered other medical therapies. Anthropometric, clinical, hormonal and metabolic (glucidic and lipidic profile) parameters were evaluated, along with cardiometabolic CD-related comorbidities, before PAS treatment and at last follow-up visit. Side-effects and adverse events related to treatment were also evaluated.
Results
Before PAS treatment, 47% of patients were obese, 59% were dyslipidemic, 47% had diabetes, and 53% were on antihypertensive treatment. Under PAS treatment, 76% of patients achieved a normalization or ≥50% reduction of UFCxULN from baseline. At last follow-up visit as compared to baseline: body weight, BMI, waist-to-hip ratio, waist circumference, systolic and diastolic blood pressure decreased but were not significantly different (p NS); lipid profile significantly improved (total and LDL cholesterol, p 0.007 and p 0.001 respectively); glycated hemoglobin significantly increased (p 0.02). In terms of safety profile, most common adverse events were related to hyperglycemia and to difficult-to-manage diabetes mellitus (41%), which led to treatment withdrawal in 4 cases. No patient experienced QTc interval prolongation.
Conclusion
Pasireotide is a safe and effective treatment in a significant figure of patients with CD, improving also lipid profile, while frequently causing glucose metabolism alterations which represent a cause of therapy discontinuation.

DOI: 10.1530/endoabs.81.P531

P532

Covid-19 in patients with hypocortisolism: clinical syndrome, disease duration and glucocorticoid replacement therapy

Chiara Simeoli[1], Serafina Schettino[1], Angelica La Rocca[1], Nicola Di Paola[1], Erminio Massimo Crescenzo[1], Francesco Ciardella[1], Alessandro Mazzarella[1], Claudia Pivonello[1], Annamaria Colao[1,2] & Rosario Pivonello[1,2]
[1]Università "Federico II" di Napoli, Dipartimento di Medicina Clinica e Chirurgia, Sezione di Endocrinologia, Napoli, Italy; [2]Unesco Chair for Health Education and Sustainable Development, Federico II University, Naples, Italy

Coronavirus disease caused by SARS-CoV-2 virus (Covid-19) is associated with a variable clinical syndrome, ranging from a mild-moderate to a severe disease, progressing towards acute respiratory distress syndrome. Hypocortisolism is associated with a depletion of innate immunity and disruption of immune response, which could contribute to an increased risk of infection and development of a severe disease. Glucocorticoid (GC) replacement therapy(GCRT), especially if administered in a non-circadian fashion, may result in immunosuppression favouring infection and disease progression. Sick day rules for GCRT during infections are still largely tailored empirically. The aim of the current study was to investigate clinical syndrome and disease duration of Covid-19, and to evaluate GCRT adjustments, in a cohort of patients with hypocortisolism who developed Covid-19. The study was performed on 20 patients [12F,8M, 16-62 years(39.2±12.5), 11 adrenal insufficiency(AI), 9 congenital adrenal hyperplasia(CAH)], adequately treated with GCs[hydrocortisone equivalent doses, HC-Eq: 10-45 mg/day(27.25±10.09)]. A purpose-built questionnaire was administered by a phone-survey, aimed at assessing Covid-19 signs and symptoms, disease duration, the occurrence of adrenal crises, the need of GCRT adjustment, and intervention for Covid-19 (antibiotics, GCs, oxygen therapy, and hospitalization), as well as persistent clinical syndrome of Covid-19 after the disease cure (Long-Covid). The most frequent symptoms and signs were ageusia(75%), anosmia(70%) and fever(70%). Additional symptoms and signs were myalgia(65%), fatigue(60%), headache(50%), cough(50%), dyspnea(30%), and diarrhea(25%). The disease duration was of 11-49days(25.55±9.71) and no adrenal crises were reported. To manage hypocortisolism, according to general sick day rules, six(30%) patients doubled oral dose of GCRT for 2-28days(11±9.28) and no patients used parenteral GCs. To manage Covid-19, nine(45%) patients received antibiotics for 5-10days(7.22±2.16)[azithromycin 600 mg/daily(55.6%), cefixime 400 mg/daily(22.2%) and amoxicillin-clavulanic acid 1750/250 mg/daily(22.2%)]; four(20%) GCs for 7-17days(10.25±4.71) [methylprednisolone 4 mg/daily(25%), deflazacort 6 mg/daily(25%), betamethasone 1 mg/daily(25%) and prednisone 25 mg/daily(25%), HC-Eq. 20-100 mg/day(41.66±39.01)], but no patients required oxygen therapy or hospitalization. No fatal events were observed over the Covid-19 period. The most frequent Long-Covid symptoms and signs were fatigue(30%), anosmia(15%) and ageusia(10%). No significant differences were observed comparing females and males, as well as AI and CAH patients. In conclusion, patients with hypocortisolism, adequately treated with GCs, display a mild-moderate Covid-19 disease course, mainly characterized by ageusia, anosmia and fever, without severe complications and adrenal crises, and requiring a double dose of oral GCRT in less than one third of cases, different GCs in a minority of cases, and not requiring oxygen therapy and hospitalization, with persistent fatigue, anosmia and ageusia as the most common Long-Covid manifestations.

DOI: 10.1530/endoabs.81.P532

P533

Renin indicates the mineralocorticoid activity of fludrocortisone: a 6-year study in primary adrenal insufficiency

Filippo Ceccato[1], Marianna Torchio[2], Irene Tizianel[2], Mattia Barbot[2], Chiara Sabbadin[2], Corrado Betterle[2] & Carla Scaroni[2]
[1]Department of Medicine, University of Padova, Padova, Italy; [2]Department of Medicine, University of Padova, Italy

Context
Fludrocortisone (FC) is the mineralocorticoid (MC) replacement treatment for patients with primary adrenal insufficiency (PAI).
Objective
To explore the dose of FC treatment and its relationship with glucocorticoid therapy, sodium, potassium, renin and clinical parameters.
Design
Longitudinal study.
Setting
Monocentric cohort.

Patients
Data of 193 patients with PAI (130 autoimmune) were collected during baseline (T0), intermediate (T1) and last follow-up visit (T2, respectively after 38 and 35 months).
Main Outcome Measure
Utility of endocrine and clinical parameters to titrate FC dose.
Results
FC dose (50-75 μg/daily) was stable in the follow-up in half patients. The MC activity of FC was dose-dependent: we observed a positive linear correlation between FC dose and sodium ($r=0.132$) and negative linear correlation between FC and potassium ($r=$-0.162) or renin ($r=$-0.131, all $P<0.01$). An overall reduction in the FC dose was observed at T2 in the group with longer follow-up (>60 months, $P<0.05$). Higher doses of FC were observed in patients with low-normal renin, especially in autoimmune PAI (86 vs 65 μg/daily, $P<0.05$). On the contrary, reduced sodium and increased potassium levels were observed in patients with high renin at T2. The number of cardiovascular events (15 in the whole cohort) was similar in patients sorted by renin levels or FC dose.
Conclusions
Renin and electrolytes are marker of MC activity: they should be routinely evaluated and used to titrate FC treatment, because FC dose can be reduced in the long-term follow-up.

DOI: 10.1530/endoabs.81.P533

P534

Reevaluation of the 1-mg overnight low-dose dexamethasone suppression test in the diagnosis of Cushing's syndrome

Cyrine Chehaider, Ibtissem Oueslati, Amani Terzi, Meriem Yazidi & Melika Chihaoui
La Rabta University Hospital, Department of Endocrinology, Tunis, Tunisia

Introduction
The 1-mg overnight low-dose dexamethasone suppression test is used as a screening tool when Cushing's syndrome is suspected. However, the biological confirmation of this syndrome is based upon the measurement of 24-hour urinary free cortisol and low-dose dexamethasone suppression test (Liddle test). The aim of this study was to assess the performance of the 1-mg overnight low-dose dexamethasone suppression test in the diagnosis of Cushing's syndrome.
Methods
This was a retrospective study including patients admitted to our department for suspicion of Cushing syndrome between 2016 and 2021. Clinical and paraclinical data and results of 1-mg overnight low-dose dexamethasone suppression test and Liddle test were collected from medical records.
Results
Fifty-one patients (39 women and 12 men) were enrolled in this study with a mean age of 54.3 ± 15.4 years. The diagnosis Cushing's syndrome was established in 28 patients and excluded in 23 patients. The median serum cortisol level after the 1-mg test was 7.65 μg/dL in patients with Cushing's syndrome and 2.1 μg/dL in those without Cushing's syndrome ($P=0.001$). It was positively correlated with serum cortisol level after the Liddle test ($r=0.852$, $P<10^{-3}$) and ACTH level ($r=0.621$, $P=0.001$). The area under the ROC curve of serum cortisol level after the 1-mg test was 0.773. A cutoff value of 1.8 μg/dL had a sensitivity of 100% and a specificity of 26%. A cutoff value of 5 μg/dL was associated with the diagnosis of Cushing syndrome (Odds Ratio = 4.11, $P=0.016$) with a sensitivity of 64% and a specificity of 70%. A cutoff value of 9.9 μg/dL confirmed the diagnosis of Cushing's syndrome in 100% of cases.
Conclusion
With a cutoff value of 1.8 μg/dL, the 1-mg overnight low-dose dexamethasone suppression test is a reliable screening tool for Cushing's syndrome. However, a higher cutoff value for serum cortisol (9.9 μg/dL) can be used alone to confirm the diagnosis. Further studies involving larger sample sizes would be useful to confirm our findings.

DOI: 10.1530/endoabs.81.P534

P535

Minimally invasive treatment of conn's adenoma: real world cases in tertiary oncology center

Claudia Costa[1], Sara Franco[2], Ana Paula Santos[1,3], Belarmino Gonçalves[4], Sara Gil-Santos[1], Joana Oliveira[1], Pedro Souteiro[1], Maria José Sousa[4] & Isabel Torres[1]
[1]IPOFG Porto, Endocrinology; [2]Hospital Garcia de Orta, Endocrinology; [3]Precancerous lesions and early cancer management group, RISE@CI-IPO (Health Research Network), Portuguese Oncology Institute of Porto (IPO Porto) / Porto Comprehensive Cancer Center (Porto.CCC); [4]Portuguese Oncology Institute of Porto (IPO Porto) / Porto Comprehensive Cancer Center (Porto.CCC) , Interventional Radiology

Introduction
Primary aldosteronism (PA) is a rare but underestimated cause of hypertension. PA has been associated with increased risk of malignancy through mechanisms involving up-regulation of the renin angiotensin system (RAS) promoting an enzymatic cascade influencing carcinogenesis. Recently, Microwave Ablation (MWA) has been established as an effective and safe minimal invasive treatment for Conn's Disease.
Aim
The authors present four clinical cases of successful treatment of PA with MWA in an oncological setting.
Patients and Methods
Retrospective review of patient's files.
Results
Four women (mean age 55y; 37-67) with pre-diagnosed cancer (1 papillary thyroid carcinoma, one with both gastric carcinoma and Chronic Lymphocytic Leukaemia; one colon carcinoma in context of hereditary syndrome and one breast carcinoma) were evaluated in the Endocrinology Department of IPOFG Porto, either for hypertension and/or hypokalemia and adrenal nodules compatible with adenoma on imaging studies. One patient (pt.) was already treated with spironolactone because of long-term previously diagnosed PA. Renin/aldosterone tests confirmed PA in one pt. In two other pts. the diagnosis was based on the normalization of PA and potassium after spironolactone treatment as diagnosis was made under active cancer treatment. All the 4 pts. were submitted to adrenal adenoma MWA performed by the same Interventional Radiology skilled specialist. Soon after the procedure that occurred without peri-procedure complications, blood pressure and potassium normalized. Re-evaluation of the renin/angiotensin tests out of cancer treatment revealed normal aldosterone and renin levels. After a mean follow-up of 34 months (15-54) there is no evidence of recurrence and/or adrenal insufficiency.
Conclusion
MWA seems to be a long-term effective and safe alternative for the treatment of Conn's adenomas, which is very important in the oncological setting. PA must be excluded in the evaluation of cancer patients with refractory hypertension and/or hypokalemia and adrenal incidentaloma. Orthodox evaluation of PA through traditional tests should be questioned in oncological pts. on active cancer treatment as it can interfere on test results and withdrawing of anti-hypertensive therapies may not be advised.

DOI: 10.1530/endoabs.81.P535

P536

Glucocorticoid resistance syndrome : Case report

Yousra Settai, Nassim Essabah Haraj, Siham El Aziz & Asma Chadli
UHC IBN ROCHD, Endocrinology and Metabolic Disorders, Casablanca, Morocco

Introduction
Glucocorticoid resistance syndrome is a rare disease, sporadic or familial, of autosomal dominant or recessive inheritance. It is a partial or complete inability of glucocorticoids to exert their effects on target tissues. Associated with compensatory increases in corticotropin and circulating cortisol with excessive secretion of adrenal androgens and mineralocorticoids.
Observation
A 67-year-old patient, having recently discovered diabetes started on insulin then on metformin 1g /d, hypertensive for 1 year on amlodipine 10 mg/d, with no personal or family endocrinopathy. Having presented a month before his admission tremors of the extremities, with muscular weakness, and walking disorders. All in a context of weight loss and asthenia. On examination, the patient did not present with clinical cushing syndrome The results showed a persistent hypokalaemia at 1.9mmol / l despite potassium supplementation, a hypernatremia at 147mmol / l. On the overnight 1mg-Dexamethasone suppression test, cortisol levels were high to 25.7 μg / dl. A high urinary free cortisol 1610 mg / 24 h (20-50), with ACTH at 408ng / l (5-60), the pituitary MRI did not reveal any abnormality. The bone densitometry was normal. The diagnosis of glucocorticoid resistance syndrome was retained and the patient was placed on dexamethasone 2 mg / day with a good clinical course, in particular a notable improvement in paresthesia and asthenia, and biological improvement with normalization of serum potassium. Furthermore, the patient presented with hypercalcemia due to

primary hyperparathyroidism having undergone resection of the parathyroid adenoma with good progress. The anatomo-pathology did not objectify signs of malignancy
Conclusion
Glucocorticoid resistance syndrome is a rare and often unrecognized condition. This should be considered in case of chronic asthenia associated with hypokalaemia in the context of excess cortisol without clinical cushing syndrome.

DOI: 10.1530/endoabs.81.P536

P537

Management of persistent subclinical hypercortisolism post left adrenalectomy in a patient with primary bilateral macronodular adrenal hyperplasia with aberrant receptors

Melpomeni Moustaki[1], Kasiani Papadimitriou[1], Vasiliki Papanikolaou[1], Eleni Cherolidi[1], Maria Rigana[1], Georgios Kyriakopoulos[2], Nikolaos Kalogeris[1] & Andromahi Vryonidou[1]
[1]Korgialeneio-Benakeio Red Cross General Hospital , Department of Endocrinology, Diabetes and Metabolism, Athens, Greece; [2]Evaggelismos General Hospital, Department of Pathology, Athens, Greece

Introduction
Endogenous subclinical hypercortisolism occurs in 5-30% of patients with adrenal incidentalomas. Adrenal adenoma is the commonest cause of autonomous cortisol secretion (ACS), while primary bilateral macronodular adrenal hyperplasia (PBMAH) is rare. In both, ACS results from activation of the cAMP/PKA pathway. This may be triggered by ligands, other than ACTH, acting upon aberrant G-protein coupled receptors (GPCRs), which may also control locally produced ACTH in paracrine/autocrine fashion. In this setting, diagnosis is challenging due to intermittent hypercortisolism and fluctuations of ACTH level.
Case presentation
We present the case of a 65-year old lady with large bilateral adrenal incidentalomas and imaging features compatible with adenomas. Initial hormonal work-up revealed ACS {cortisol post low dose dexamethasone suppression test (LDDST): 13.92 mg/dl, midnight salivary cortisol: 0,8 mg/dl, ACTH = 9.2 pg/mg}. She was not Cushingoid, but had obesity, osteoporosis, hypertension and anxiety disorder. On accounts of the size of her left adrenal adenoma (4.9 x 1.9 cm), she underwent unilateral adrenalectomy. Initial histology demonstrated adrenal adenoma (Weiss score 0/10). During hormonal follow-up, she had persistent hypercortisolism with fluctuating plasma ACTH level (11.5-44.2 pg/ml). Considering the latter, we proceeded to pituitary magnetic resonance imaging, which showed a 3mm incidentaloma. At this point, we repeated LDDST with ACTH measurement: despite adequate ACTH suppression (2.2 pg/ml) cortisol was unsuppressed (6.26 mg/dl). Thus, ACS was confirmed. Imaging-wise, the size of her right adrenal adenoma increased from 4.2 x 1.6 cm to 4,8 x 2.2 over 3 years. Pathology review of the resected left adrenal revealed absence of non-neoplastic adrenal tissue and extended nodular appearance, establishing PBMAH diagnosis. Dynamic testing for aberrant receptors post dexamethasone suppression was performed, demonstrating partial response to posture (25%) and meal (26%). In the absence of overt hypercortisolism and given that PBMAH is a benign condition, we considered medical treatment as more appropriate. To control hypercortisolism, we modified hypertension regime to propranolol and valsartan with later addition of low dose of metyrapone.
Conclusions
Patients with bilateral adrenal adenomas may represent PBMAH, in which aberrant receptor expression is present in 80% of cases. The recognition of aberrant receptor-mediated hypercortisolaemia in patients with PBMAH and unilateral adenomas is important as it may lead to targeted therapies. In this context, b-blockers, angiotensin II blockers, GnRH and somatostatin analogues have been used. Additionally, steroid enzymes inhibitors were found to restore normal circadian secretion of cortisol. Nevertheless, existing data originate from small case series and larger prospective studies are needed.

DOI: 10.1530/endoabs.81.P537

P538

Primary adrenal angiosarcoma within a hematoma

Elisabete Rodrigues[1,2], Tiago Oimenta[2,3], Jorge Pinheiro[2,4,5], Davide Carvalho[2,6] & José Manuel Lopes[2,4,5]
[1]Centro Hospitalar Universitário de S. Joao, Endocrinology, Porto, Portugal; [2]Faculty of Medicine of the University of Porto; [3]Centro Hospitalar Universitário de S. Joao, Endocrine Surgery, Porto, Portugal; [4]Centro Hospitalar Universitário de S. Joao, Pathology, Porto, Portugal; [5]IPA-TIMUP; [6]Centro Hospitalar Universitário de S. Joao, Endocrinology, Porto, Portugal

Introduction
Angiosarcomas account for < 1% of all sarcomas, and are highly agressive neoplasms whose clinical course is striking: local recurrence, metastasis, and a high mortality rate. Primary angiosarcoma of the adrenal gland was first described in 1988 by Kareti et al. and is very rare with, so far, only 51 reported cases.
Case report
A 49-year-old male, without prior malignancy, presented with a 4.9x5.9 cm right adrenal nodule and a 2.4 cm lesion at L1 both found incidentally on a chest CT. His mother died with lung cancer. Physical examination was unremarkable. Routine lab tests were within the normal range. Serum aldosterone, renin, DHEAS, cortisol post 1 mg dexametasone supression test, 24H urinary catecholamines and metanefrines were normal; 24H urinary normetanephrine slightly elevated. An abdominal MRI confimed an heterogeneous lesion 5.5x4.7x4.4 cm on the right adrenal gland with areas of possible hemorraghe. An MRI of the column revelead a 2.1x1.3x2.2 cm lesion at L1 without agressive features. No uptake was shown at MIBG scan. Right laparoscopic adrenalectomy was done. The adrenal gland (76 g and 8.2x5.8x3.4 cm) disclosed a 4.0x2.6x5.0 cm well defined mass with hemorraghic areas. On microscopic examination, the mass consisted mostly of hematoma and scattered small agregates of cytologically atypical epithelioid cells with amphophilic cytoplasm, irregular vesicular nuclei with variably prominent nucleoli and some mitoses; the cells were diffusely positive for CD31 and ERG. The features are characteristic of epihelioid angiosarcoma. After surgery, a FDG-PET scan disclosed 2 foci of uptake, one on the right thyroid lobe (SUV max 3.7) and the other at the L1 lesion (SUV max 3.2). The cervical US revealed a heterogeneous thyroid gland with characteristics of thyroiditis. Anti microssomal antibodies positive, TSH normal. A biopsy of the L1 lesion did not reveal malignancy. Because there were complete resection margins and no metastic foci were found no adjuvant chemotherapy was done. The patient has been kept under clinical and imagiological surveillance for three years with no further evidence of disease.
Discussion
Adrenal angiosarcoma is a very rare clinical entity with a propensity for local recurrence and metastasis and a median survival of 18 months. Noteworthy the prognosis is unpredictable but some times quite good as in this case.

DOI: 10.1530/endoabs.81.P538

P539

Hypertension of adrenal origin - a never-ending story

Miruna Maria Popa[1,2], Raluca Cristina Pascu[1], Mihai Lucian Pavel[1], Elisabeta Andreea Malinici[1,2], Anca Sirbu[1,2] & Fica Simona[1,2]
[1]"Elias" Emergency University Hospital, Endocrinology, Bucharest, Romania; [2]"Carol Davila" University of Medicine and Pharmacy, Endocrinology, Bucharest, Romania

Background
Pheochromocytomas and paragangliomas (PPGLs) are rare neuroendocrine tumors characterized by a high degree of variability and unpredictability. Coexistence of PPGLs and adrenocortical adenomas is an uncommon occurrence that can further complicate the clinical course.
Objective
We describe the diagnostic and management challenges of a patient with a history of surgically removed pheochromocytoma, presenting with symptoms of catecholamine excess, following a prolonged period of clinical remission.
Case Report
A 52 yo. female patient was admitted to our hospital for surgical cure of a left adrenal mass. She reports a history of right adrenal pheochromocytoma, excised 15 years before and resulting in clinical and biochemical remission. 15 months prior to presentation she started experiencing paroxysms of arterial hypertension, occurring every other day, accompanied by headache, palpitations, tremor, nausea and emesis. Abdominal CT showed a 3/2 cm left adrenal adenoma, while biochemical screening revealed elevated plasma normetanephrines (6x upper normal limit), along with normal metanephrines and chromogranin A. Renin-to-aldosterone ratio and cortisol diurnal variation were unaltered, but ACTH values were slightly decreased. Postoperatively, the patient was initially stable and exhibited normalized blood pressure under high-dose corticoid treatment, but on the 3rd day, as corticoid dosage was decreased, she developed an acute adrenal crisis. In spite of the initial suspicion of adrenal pheochromocytoma,

histopathological and immunohistochemical examinations described an adrenocortical adenoma. Unsurprisingly, normetanephrines failed to normalize postoperatively; metanephrines and chromogranin A also became marginally elevated and symptoms reoccurred. MRI examination of the head and neck was negative. Interestingly, the patient now also described lumbosacral warmth accompanying the paroxysms. Octreoscan was performed, but revealed no areas of high uptake. Conversely, a metabolically active sacral lesion was described on PET-CT. MRI confirmed the presence of an osteolytic lesion (1.8/1.4/1.1 cm) in that area and described an additional similar adjacent lesion. These were interpreted as possible metastases of a malignant PPGL. Neurosurgical intervention was performed and a histopathological diagnosis of grade I WHO paraganglioma was established. The patient exhibited clinical remission postoperatively, along with the decline of all tumoral markers. However, 6 months later, in spite of imagistic regression of the sacral lesions and lack of symptoms, both metanephrines and normetanephrines showed an upward tendency.

Conclusion

Long-term follow-up is mandatory in PPGLs, as clinical recurrence is possible even after prolonged periods of remission. Genetic testing can aid the diagnosis and management and should be ideally performed in all cases of recurrent/aggressive PPGLs.

DOI: 10.1530/endoabs.81.P539

P540

Challenges and anxiety of fluctuating normal to mild/moderate elevations of urinary catecholamines and metanephrines in clinical practice

Bonnie Grant[1], Mohammadreza Emami[1], Siraj Adam[2], Edel Casey[1], Raj Tanday[1], Anna Hawkins[1], Nemanja Stojanovic[1,2], Imran Syed[2] & Khash Nikookam[1,2]

[1]Barking, Havering and Redbridge University Hospitals NHS Trust, Greater London, United Kingdom; [2]Spire London East Hospital, Greater London, United Kingdom

We present a 70-year-old female who was initially referred to the endocrinology clinic for an assessment of her type 2 diabetes mellitus. She has a complex medical history including treated hypothyroidism, mastectomy for breast cancer and ongoing yearly surveillance for an excised benign lung lesion. On further questioning she acknowledged feeling generally unwell in the days prior to her appointment and had self-presented to the emergency department with undiagnosed hypertension (blood pressure 219/110mmHg and 190/80mmHg) but no evidence of end-organ hypertensive damage. A full clinical examination did not identify either endocrinopathies or any cardiovascular abnormalities. She was commenced on amlodipine 5 mg daily and subsequently ramipril 5 mg daily. Given her severe hypertension and a negative family history for the same, urinary catecholamines and metanephrines in addition to renin/aldosterone ratio and other relevant investigations were performed to exclude secondary causes. Table 1 shows results performed on three separate occasions, each four weeks apart. She was commenced on doxazosin 1 mg twice daily while also recommended to stop ramipril; however, she was unable to tolerate this nor a switch to phenoxybenzamine 10 mg twice daily, with debilitating side effects of palpitations and dizziness. A CT adrenal with contrast showed no adrenal nodularity bilaterally suspicious of phaeochromocytomas. Further evaluation with I-123 MIBG Scintigraphy and Ga-68 DOTATATE was also negative for any MIBG or DOTATATE avid lesions. The patient continued amlodipine 5 mg daily, achieving adequate blood pressure control with a systolic range of 125-130mmHg and diastolic range of 62-75mmHg. 24-hour urinary catecholamines were repeated six months later, shown in table 2. The patient was advised to further follow up in the endocrine clinic and regular monitoring with her General Practitioner. In conclusion, this case highlights the challenges we encounter during clinical practice with fluctuating urinary catecholamines and metanephrines when other causes of hypertension have been excluded. This can cause additional anxiety over the underlying diagnosis to both the clinician and the patient.

DOI: 10.1530/endoabs.81.P540

P541

Gender and age-matched case control study of a cohort of adrenal adenomas

Miriam Giordano Imbroll[1,2], Stefanie Agius[1,2], Sarah Craus[1,2] & Mark Gruppetta[1,2]

[1]Mater Dei Hospital, Malta; [2]University of Malta, Malta

Background

The majority of adrenal incidentalomas are benign and patients can be reassured, but a personalized and multidisciplinary approach is required when dealing with these lesions, since they might be linked with various comorbidities. The aim of our study was to carry out an in-depth analysis of the biochemical workup of adrenal incidentalomas and comparing the results with controls.

Methods

252 patients with an incidentally discovered adrenal adenoma were identified. A retrospective cross-sectional analysis of this cohort was carried out. A corresponding cohort of 252 gender and aged-matched patients (+/- 5 years) who underwent a CT scan for a similar indication and on the same day as the cases was recruited. A comparison of numerous parameters was carried out.

Results

From a total cohort of 252 patients, 55.8% were females. The mean age at diagnosis was 69 years (IQR 60-75 years). 84.1% had an overnight dexamethasone suppression test (ODST) performed, out of whom 65.1% had a cortisol post-ODST <50nmol/L. The median longest radiological diameter was 20.0mm (IQR16.0-26.0). From the patients with an adenoma, there was a statistically significant difference between those who were deceased and those alive in the following parameters: MCV ($P=0.008$), Urea ($P=0.046$), Age ($P=0.006$) and T4 ($P=0.009$). When comparing cases with controls, statistically significant different results were observed in lymphocytes ($P=0.002$), higher in cases, and total cholesterol ($P=0.036$), neutrophil-to-lymphocyte ratio (NLR) /monocyte ratio ($P=0.006$) and NLR/monocyte/platelet ratio ($P=0.001$), lower in cases. In our cohort, mortality was highest amongst the controls, compared to cases ($P=0.015$). Among all cases and controls, the following parameters were found to be significantly higher in those still alive at the end of the study: haemoglobin ($P<0.001$), lymphocytes ($P<0.001$), total cholesterol ($P=0.047$), LDL-c ($P=0.008$), Lymphocyte-monocyte ratio (LMR) ($P<0.001$) and eGFR ($P=0.003$). On the other hand, the following parameters were higher in those deceased: Neutrophils ($P=0.004$), urea ($P<0.001$), ALP ($P=0.001$), fasting blood glucose (FBG) ($P=0.008$), Age ($P<0.001$), Neutrophil-lymphocyte ratio (NLR) ($P<0.001$), Platelet-lymphocyte ratio (PLR) ($P=0.009$), Systemic immune inflammatory index (SII) ($P<0.001$), NLR/monocyte ratio ($P<0.001$), NLR/monocyte/platelet ratio ($P<0.001$) and creatinine ($P=0.002$).

Conclusion

Our cohort of adrenal adenomas did not exhibit a higher mortality rate compared to controls and some of the haematological parameters linked with increased mortality were more favourable among the adenoma cohort.

DOI: 10.1530/endoabs.81.P541

Table 1 24-hour urinary catecholamines and metanephrines. RR = Reference Range.

	Metadrenaline (RR <1.2μmols/24hr)		Normetadrenaline (RR < 3.3μmols/24hr)		3-Methoxytyramine (RR < 2.5μmols/24hr)	
First urine collection	0.25		2.81		0.82	
	Metanephrines (RR <1622 nmol/24hr)	Normetanephrines (RR <2129 nmol/24hr)	3-Methoxytyramine (RR <2300 nmol/24hr)	Adrenaline (RR < 147 nmol/24hr)	Noradrenaline (RR <573 nmol/24hr)	Dopamine (RR < 3270 nmol/24hr)
Second urine collection	346	**3990**	1769	30	**681**	-
Third urine collection	334	**3380**	1459	19	527	1950

Table 2 Repeat 24-hour urinary metanephrines

Metadrenaline (RR <1.2μmols/24hr)	Normetadrenaline (RR<3.3μmols/24hr)	3-Methoxytyramine (RR<2.5μmols/24hr)
0.38	2.66	1.41

P542

Mortality in patients with non-functional adrenal tumors: a swedish population-based national cohort study

Jekaterina Patrova[1,2], Buster Mannheimer[1,2], Jonatan D Lindh[3] & Henrik Falhammar[4,5]
[1]Karolinska Institutet, Department of Clinical Science and Education, Södersjukhuset AB, Stockholm, Sweden; [2]Södersjukhuset, Department of Internal Medicine, Stockholm, Sweden; [3]Karolinska Institutet, Division of Clinical Pharmacology, Department of Laboratory Medicine, Stockholm, Sweden; [4]Karolinska Institutet, Department of Molecular Medicine and Surgery, Stockholm, Sweden; [5]Karolinska University Hospital, Department of Endocrinology, Metabolism and Diabetes, Stockholm, Sweden

Background
It is not known if non-functional adrenal adenomas (NFAA) are associated with increased mortality.
Objective
To investigate mortality in patients with NFAA and compare with matched controls.
Design
Retrospective register-based national cohort study.
Methods
Patients diagnosed with NFAA in Sweden 2005-2019 were identified and followed until death or 2020. For each case, four age/sex/municipality-matched controls were identified. Individuals with diagnosis indicating adrenal hormonal excess or malignancy were excluded. Though, in some cases malignancy of another origin than adrenal glands was detected in conjunction with index date. Statistical analysis was made both including and excluding these cases. Main study outcomes were all-cause 1 and 5-year mortality as well as causes of death after adjustment for comorbidities and socioeconomic factors.
Results
In total, 20390 patients with NFAA and 125392 matched controls were included. Median age at diagnosis was 65 years (IQR-16) and 59.1% were women. During follow-up, 4427 (21.7%) cases and 20480 (16.3%) controls had deceased. Among all patients with NFAA both 1-year and 5-year overall mortality was higher compared to controls (OR-6.79, aOR-5.38 and OR-2.66, aOR-2.03). After eliminating controls with detected malignancy at index date, both 1-year and 5-year overall mortality was still high (OR 2.64 (2.42-2.88), aOR-1.84 (1.68-2.01) and OR 1.69 (1.61-1.77), aOR 1.18 (1.12-1.25)). While all patients with known malignancy were excluded before and at index date, mortality due to new malignancy during the follow-up period was high: 1-year mortality OR was 8.86 (7.54-10.42), aOR 8.04 (6.81-9.51) and 5-years mortality OR was 2.77 (2.55-3.01), aOR 2.43 (2.23-2.65). Moreover, 1-year mortality due to cardiovascular diseases was also increased (OR 2.02 (1.64-2.47), aOR1.33 (1.06-1.66), however 5-years mortality due to cardiovascular diseases was increased only before adjustment (OR 1.39(1.24-1.57), aOR 0.88 (0.76-1.01), the latter was adjusted for, e.g., cardiovascular disease at index date). In total 1273 (28.8%) of controls diseased due to malignancy and 1023 (23.1%) due to cardiovascular diseases.
Conclusions
Patients with NFAA have significantly higher overall mortality rate, as well as mortality due to new malignancy diagnosed during the follow-up time when compared to controls.

DOI: 10.1530/endoabs.81.P542

P543

Whole blood transcriptomic profile of Cushing's syndrome

Roberta Armignacco[1], De Murat Daniel[1], Anne Jouinot[1], Lucas Bouys[1], Karine Perlemoine[1], Franck Letourneur[1], Lucie Adoux[1], Maria-Christina Zennaro[2,3], Jerome Bertherat[1,4] & Guillaume Assié[1,4]
[1]Université de Paris, Institut Cochin, INSERM U1016, CNRS UMR8104, Paris, France; [2]Université de Paris, PARCC, INSERM, Paris, France; [3]Assistance Publique-Hôpitaux de Paris, Hôpital Européen Georges Pompidou, Service de Génétique, Paris, France; [4]Assistance Publique-Hôpitaux de Paris, Hôpital Cochin, Service d'Endocrinologie, Center for Rare Adrenal Diseases, Paris, France

Background
Cushing's syndrome, caused by an excess of circulating glucocorticoids, is associated with high morbidity and presents high inter-individual variability. The earlier the diagnosis, the better the treatment effectiveness and the prognosis. Hormone assays, routinely used, contribute to identify Cushing's syndrome. However, no biomarker is currently available to directly quantify the biological action of glucocorticoids. Blood samples represent an easily obtainable source for profiling individuals on a molecular level. In this study, we analysed the transcriptomic profile in 59 blood samples from patients with different glucocorticoid states (overt or mild Cushing's syndrome, eucortisolism, adrenal insufficiency).
Materials and methods
Total RNA was extracted from whole blood samples collected into PAXgene tubes. Transcriptome was determined by RNA sequencing performed on NovaSeq 6000 platform (Illumina). Blood cell proportions in each sample were estimated from expression profiles by using the CIBERSORT method. Unsupervised samples classification (PCA) was used to explore the transcriptomic profiles. A preliminary differential expression analysis was performed by using a linear model-based method (Limma).
Results
Unsupervised classification showed a discrimination of overt Cushing's syndrome samples (accuracy: 0.81), presenting a specific profile compared to the other glucocorticoid states. This variability also associated with blood cell proportions, particularly with a higher neutrophils percentage. The most differentially expressed genes in the group of overt Cushing's syndrome ($n=3173$ genes, with adjusted p-value <0.001) were enriched in pathways related to immunity, particularly to neutrophils activation and activity.
Conclusions
These preliminary results show that glucocorticoid excess associates with a specific whole blood transcriptome profile. Further analyses will allow to identify a set of genes representing a specific molecular signature of glucocorticoid excess, which will take into account biological factors potentially involved, such as blood cell composition.

DOI: 10.1530/endoabs.81.P543

P544

Adrenal incidentaloma follow-up

Catarina Ivo, Vitória Duarte, David Veríssimo, Ana Cláudia Martins, João Silva, Luís Lopes, Dolores Passos, João Jácome Castro & Mafalda Marcelino
Armed Forces Hospital - Lisbon, Endocrinology Department, Lisboa, Portugal

Introduction
About 5% of the adult population has adrenal incidentaloma(AI) and its incidence increases with age. AACE guidelines recommend image and hormonal evaluation during 5 years in non functioning AI. The european's guidelines advise against repeat evaluation in non-secretory AI that present with <4 cm and had benign features. According to recent studies, the risk of developing clinically relevant hormone secretion is $<0.3\%$, in patients with previous non-functioning lesions. The risk of progression to Cushing Syndrome in patients with autonomous cortisol secretion (ACS) is also low ($<1\%$). This study evaluated the risk of developing hypercortisolism or tumor growth in AI of patients followed in an endocrinology department.
Methods
retrospective study of patients with no functioning AI evaluated between 2014-2021 with a minimum follow-up of 3 years. ACS was defined based on post-dexamethasone cortisol value between 1,8-5 µg/d. Significant tumor growth was defined as $\geq$10mm. Dimensional stability was considered if $<$5mm variation between successive imaging exams.
Results
Included 84 patients, 42.8% ($n=36$) female with a median of age of 76(48-93) years-old. At first evaluation the mean AI dimension was $20{,}9 \pm 7{,}5$mm and 20 patients (23.8%) had bilateral tumors. After a mean follow-up of $5{,}6 \pm 1{,}5$ years, each patient was submitted to a mean of $3 \pm 1{,}1$ image exams. During follow-up, 2 patients (2.4%) developed ACS and none had been diagnosed with clinical Cushing syndrome. In 68 (81%) patients there was dimension stability, 7 had dimension reduction and 9 had increased size ($>$5mm). In only 2 patients there was a significant growth: 1 cyst and 1 tumor that has been transformed to an hemorrhagic lesion (pseudocyst) and submitted to surgery.
Conclusion
In this study 2,4% of patients developed ACS. A $\geq$10 mm growth was only verified in 2 cysts. Adrenal Cysts are rare and usually asymptomatic. AI could suffer hemorrhagic or cystic degeneration and become pseudocyst. Our data are similar to a recent meta-analysis that report no relevant changes in dimension or hormonal function during follow-up of AI.

DOI: 10.1530/endoabs.81.P544

P545

Abstract withdrawn

DOI: 10.1530/endoabs.81.P545

Calcium and Bone

P30

Covid-19 lockdown negatively impacted on adherence to Denosumab therapy: incidence of non-traumatic fractures and role of telemedicine

Giulia D'Angelo[1,2], Sara De Vincentis[1,2], Daniela Domenici[1,2], Anna Ansaloni[2], Gisella Boselli[1,2], Antonino Russo[1,2], Erica Taliani[2], Vincenzo Rochira[1,2], Manuela Simoni[1,2] & Bruno Madeo[2]
[1]Unit of Endocrinology, Department of Biomedical, Metabolic and Neural Sciences, University of Modena and Reggio Emilia, Modena, Modena, Italy; [2]Unit of Endocrinology, Department of Medical Specialties, Azienda Ospedaliero-Universitaria Policlinico di Modena, Modena, Italy

Background
Adherence to anti-osteoporotic therapy is fundamental to prevent harmful consequences including fragility fractures and, in the specific case of denosumab discontinuation, of rebound fractures. Coronavirus disease (Covid-19) lockdowns have impacted on management of osteoporosis, but data about adherence to denosumab and rebound fractures during the Covid-19 pandemic are still lacking. The use of telemedicine is increasingly widespread albeit supported by little evidence so far.
Aim
To assess adherence to denosumab and incidence of non-traumatic fractures (fragility and rebound) during the lockdown year compared to the pre-Covid-19 year. Thereafter, this study aims to investigate the effectiveness of telemedicine in the management of osteoporotic patients with ongoing denosumab treatment.
Methods
Retrospective, longitudinal, single-center study on patients receiving subcutaneous denosumab therapy every 6 months. Each patient was scheduled to undergo 2 visits: one during the pre-Covid-19 period (March 2019 – March 2020) and another visit during the lockdown period (March 2020 – March 2021). Adherence was defined as being punctual (with an allowable delay of up to 4 weeks) with the injection scheduled 6 months after the previous dose. Data on new fractures, risk factors for osteoporosis and the modality of visit (telemedicine or face-to-face) were collected. *Statistical analysis*: Mann-Whitney and Chi-Square tests were used to compare continuous and categorical variables, while logistic regressions were used to detect factors associated with non-adherence/new fractures.
Results
The prevalence of non-adherent patients was significantly higher in the lockdown period (35 of 269 patients, 13.0%) than the pre-Covid-19 period (9 of 276 patients, 3.3%) ($P < 0.0001$). During the lockdown the number of new non-traumatic fractures was significantly higher than the pre-Covid-19 year ($P < 0.0001$). In particular, 10 patients out of 269 (3.7%) experienced a fragility fracture and 2 patients (0.7%) a rebound fracture during the lockdown period, whereas no patient had fragility or rebound fractures during the pre-Covid-19 period. No difference was found in the prevalence of non-adherence and new non-traumatic fractures comparing patients evaluated with tele-medicine to those evaluated with face-to-face visit.
Conclusions
Non-adherent patients and new non-traumatic fractures (including rebound fractures) were more prevalent during the lockdown period in comparison to the pre-Covid-19 period, regardless of the modality of medical evaluation. Tele-medicine seems to be an alternative strategy to standard face-to-face visits, in guaranteeing the continuity of follow-up in osteoporotic patients and short-term compliance to Denosumab

DOI: 10.1530/endoabs.81.P30

P31

Application of Calcium to Phosphorus (Ca/P) ratio in the diagnosis of pseudohypoparathyroidism: Another piece in the puzzle of diagnosis of Ca-P metabolism disorders

Sara De Vincentis[1,2,3], Giulia Brigante[1,2], Giulia Del Sindaco[4,5], Antonio Moretti[1], Angela Pagnano[4,5], Lucia Zirilli[2], Vincenzo Rochira[1,2], Manuela Simoni[1,2], Giovanna Mantovani[4,5] & Bruno Madeo[2]
[1]Unit of Endocrinology, Department of Biomedical, Metabolic and Neural Sciences, University of Modena and Reggio Emilia, Modena , Modena, Italy; [2]Unit of Endocrinology, Department of Medical Specialties, Azienda Ospedaliero-Universitaria Policlinico di Modena , Modena, Italy; [3]Clinical and Experimental Medicine PhD Program, University of Modena and Reggio Emilia, , Modena, Italy; [4]Department of Clinical Sciences and Community Health, University of Milan, Milan, Milan, Italy; [5]Endocrinology Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Milan, Italy

Introduction
The serum calcium/phosphorus (Ca/P) ratio has been proposed to identify patients with primary hyperparathyroidism and chronic hypoparathyroidism (HPT) from healthy subjects. However, other disorders of the Ca-P metabolism might present similar biochemical profile of HPT, such as pseudohypoparathyroidism (PHP), for which the use of Ca/P can be useful.
Aim
To test the performance of Ca/P ratio in the diagnosis of PHP in comparison to healthy subjects and to HPT patients for differential diagnosis.
Methods
A retrospective, observational study was carried out, including 60 PHP patients and 60 HPT patients compared to 120 controls. Serum Ca, P, creatinine, parathyroid hormone (PTH) and albumin, and creatinine were collected. Serum Ca and P were expressed in mg/dL. The diagnostic performance was evaluated by receiver operating characteristic (ROC) curve, sensitivity, specificity and accuracy.
Results
The Ca/P ratio was significantly lower in PHP and HPT patients, compared to controls ($P < 0.0001$). At ROC curve analysis, the cut-off of 2.32 (1.78 if serum Ca and P measured in mmol/L) for Ca/P ratio was able to identify both PHP and HPT patients among the entire cohort (sensitivity and specificity: 76%). Selecting patients with Ca/P ratio below 2.32, no valid cut-off of Ca/P was found to discriminate PHP from HPT patients; in this case, serum PTH above 53.0 pg/mL was defined for the identification of PHP patients (sensitivity and specificity: 100%). The index (Ca/P x PTH) above 150 pg/mL identified PHP patients from controls (sensitivity 84.7%; specificity 87.4%), whereas (Ca/P x PTH) below 44 pg/mL identified HPT patients from controls (sensitivity 88.9%; specificity 90.8%).
Conclusions
This study further validates the serum Ca/P ratio below 2.32 (1.78 SI) as a highly accurate tool to identify PHP and HPT patients, but it is not reliable to differentiate these two conditions. The index (Ca/P x PTH) is excellent to specifically recognize PHP or HPT from healthy subjects. Thanks to its extraordinary simplicity and the favorable cost-effectiveness, serum Ca and P should be equally considered as first-line examinations to calculate their ratio that can be easily applied to screen/rule out disorders of Ca-P metabolism, especially in asymptomatic patients.

DOI: 10.1530/endoabs.81.P31

P32

Calcifediol 0.266 mg supplementation in adult population with 25(OH) D deficiency: 4 months results

Esteban Jódar[1,2], Pedro Guerra López[3], Noelia Vega-Gil[4], Blanca Sánchez Santiago[4], Iñaki Zorrilla Martínez[5], Mario Jiménez-Mercado[5], Aintzane García-Bea[6], Araitz Landeta Manzano[6], Cristina Campo Hoyos[6] & Jesús Frías Iniesta[3,7]
[1]Hospital Universitario Quirón Salud Madrid, Madrid, Spain; [2]Universidad Europea, Madrid, Spain; [3]Pharmacology Department, Universidad Autónoma de Madrid, Madrid, Spain; [4]Valdecilla Clinical Trials Unit, Hospital Universitario Marqués de Valdecilla, Santander, Spain; [5]Clinical Trials Unit, IIS BIOARABA, OSI Araba, Vitoria, Spain; [6]Faes Farma, Medical Affairs; [7]Clinical Pharmacology Service, Hospital Universitario La Paz, Madrid, Spain

Introduction
Prevalence of vitamin D deficiency is relatively high worldwide, it is associated with poor skeletal health and has recently been related to other extra-skeletal diseases, probably due to its immunomodulatory effects. Detection and treatment of asymptomatic hypovitaminosis D in healthy adult population is especially relevant to attempt to optimize the overall functioning of the human body.
Objectives
To assess the percentage of adult healthy population with vitamin D deficiency (25(OH)D < 20 ng/ml) who achieved plasmatic levels within optimal range (20-

60 ng/ml) after a four-month treatment with calcifediol 0.266 mg soft capsules, with monthly or biweekly treatment schedules.
Methods
Multicentre, phase I clinical trial. Volunteers (18-55 years) with vitamin D deficiency were assigned to receive calcifediol 0.266 mg for 4 months according to baseline levels: severe deficiency (25(OH)D $<$ 10 ng/ml) was supplemented biweekly, while mild-moderate deficiency (25(OH)D 10-19.99 ng/ml) was treated monthly. Subsequently, subjects within the optimal range were randomly allocated to monthly treatment (placebo or calcifediol 0.266 mg), for 5 additional months.
Results
79 subjects (65% female, mean age 31.2 years) are included in this analysis; 9% with severe vitamin D deficiency and 91% with mild-moderate vitamin D deficiency. Average baseline 25(OH)D levels (14.02 ng/ml; $n=77$, 2 subjects excluded due to protocol deviations), increased up to 20.53 ng/ml and to 27.56 ng/ml at months 1 and 4. In the biweekly treatment group, 25(OH)D levels increased by 17.05 ng/ml (month 1) and 33.05 ng/ml (month 4), whereas with monthly treatment 25(OH)D levels increased by 5.78 ng/ml and 12.18 ng/ml, respectively. 79% of subjects achieved optimal 25(OH)D levels at month 4 (100% in the biweekly group, 78% with the monthly treatment). The analysed bone metabolism parameters in all subjects (calcium, PTH, albumin, phosphate, alkaline phosphatase) showed no significant changes throughout the study. Calcium and PTH baseline levels were 9.38 $\pm$ 0.40 mg/dL and 51.36 $\pm$ 18.53 pg/ml, remaining unaltered at month 4 (9.57 $\pm$ 0.40 mg/dL and 50.40 $\pm$ 22.38 pg/ml, respectively). In terms of safety, no patient reached 25(OH)D toxic levels. No serious adverse events were reported.
Conclusions
Monthly calcifediol 0.266 mg is an effective and safe treatment for vitamin D deficiency in the overall population. Moreover, and bearing in mind the sample size limitations, biweekly calcifediol 0.266 mg showed to be a safe and effective treatment for vitamin D severe deficiency in the target population and without clinically relevant variation in bone metabolism parameters.

DOI: 10.1530/endoabs.81.P32

P33

Psychometric evaluation of the hypoparathyroidism symptom diary using data from two clinical trials

Lauren Nelson[1], Steven Ing[2], Mishaela Rubin[3], Jia Ma[1], Susan Martin[4], Rohini Sen[5] & Olulade Ayodele[5]
[1]RTI Health Solutions, Research Triangle Park, United States; [2]Ohio State University Wexner Medical Center, Columbus, United States; [3]Vagelos College of Physicians and Surgeons, Columbia University, New York, United States; [4]RTI Health Solutions, Ann Arbor, United States; [5]Takeda Pharmaceuticals USA, Inc, Lexington, United States

The Hypoparathyroidism Symptom Diary (HypoPT-SD) was developed for the daily assessment of key symptoms and impact of HypoPT as reported by patients with chronic HypoPT and includes 13-items: a 7-item Symptom subscale, 4-item Impact subscale, and single-item anxiety and depression scores. The current analysis was undertaken to confirm test-retest reliability and construct validity of HypoPT SD Symptom subscale scores using data collected during two open-label, single-arm studies of patients with chronic HypoPT treated with recombinant human parathyroid hormone (1-84) (52-week study: NCT03364738; 36-month study: NCT02910466). Test-retest reliability was determined by computing intraclass correlation coefficients (ICC) using data from two test administrations. Validity was evaluated by performing cross-sectional correlational analyses between HypoPT-SD Symptom subscale and other conceptually linked patient-reported outcome (PRO) tools. ANOVA was used to compare HypoPT-SD scores across severity groups defined by existing PRO tools to confirm the known-groups validity of the HypoPT-SD Symptom subscale. The psychometric study population included 22 patients from the 52-week study (81% women; mean $\pm$ SD age, 50$\pm$11.4 years; mean $\pm$ SD duration of HypoPT, 10.3$\pm$10.2 years) and 38 patients from the 36-month study (79% women; aged 52$\pm$12.4 years; duration of HypoPT, 18.9$\pm$12.0 years). In both studies, symptom-related item scores were generally low (eg, less severe), showed limited variability at baseline and end of treatment, most inter-item correlations exceeded 0.50, and internal consistency reliability was satisfactory ($>$0.82). ICCs were 0.67 ($n=22$) and 0.82 ($n=26$) for all patients in the 52-week and 36-month studies, respectively, and 0.92 ($n=10$) for stable patients (based on the Patient Global Impression–Severity [PGI S]) in the 52-week study and corroborated the test-retest reliability of HypoPT SD Symptom subscale. Patterns of correlations between HypoPT-SD Symptom scores and validated PRO tools (FACT-Cog [baseline], FACIT-F total score, RAND-36 physical health composite, PGI-S, and EuroQoL-visual analog scale [baseline]) were moderate to strong and supported convergent validity expectations. Mean HypoPT SD Symptom scores differed significantly across severity groups defined by PGI-S (52-week study) and RAND-36 general health perceptions (36-month study), demonstrating the known-groups validity of HypoPT SD Symptom scores. Limitations include differences in HypoPT SD recall periods (24 hours vs 7 days) in the two studies and lack of severe HypoPT symptoms in patients at baseline, which restricted the range of possible change in scores. These results provide confirmation of the reliability and validity of the disease-specific HypoPT-SD and lay the psychometric groundwork for use of HypoPT-SD in future clinical trials of adults with HypoPT.

DOI: 10.1530/endoabs.81.P33

P34

Skeletal consequences of long-term replacement therapy with human recombinant PTH(1-34) in chronic hypoparathyroidism

Rebecca Fischler[1,2], Anne-Lise Lecoq[3], Karine Briot[4], Severine Trabado[5], Florent Besson[6], Jason Bouziotis[7], Cecile Goujard[8], Sylvie Salenave[1], Sophie Leboulleux[9], Emma Carreira[1], Christine Chabrolle[1], Corvilain Bernard[2], Philippe Chanson[1,10], Agnès Linglart[11], Gilles Grimon[6] & Peter Kamenicky[1,10]
[1]Assistance Publique-Hôpitaux de Paris, Hôpital Bicêtre, Service d'Endocrinologie et des Maladies de la Reproduction, Centre de Référence des Maladies Rares du Métabolisme du Calcium et du Phosphate, Le Kremlin-Bicêtre, France; [2]Hôpital Erasme, Service d'Endocrinologie, Bruxelles, Belgium; [3]Assistance Publique-Hôpitaux de Paris, Hôpital Bicêtre, Centre de recherche clinique, Le Kremlin-Bicêtre, France; [4]Assistance Publique-Hôpitaux de Paris, Hôpital Cochin, Service de Rhumatologie, Centre de Référence des Maladies Rares du Métabolisme du Calcium et du Phosphate, Paris, France; [5]Assistance Publique-Hôpitaux de Paris, Hôpital Bicêtre, Service de Génétique Moléculaire, Hormonologie et Pharmacogénétique, Le Kremlin-Bicêtre, France; [6]Assistance Publique-Hôpitaux de Paris, Hôpital Bicêtre, Service de Médecine Nucléaire, Le Kremlin-Bicêtre, France; [7]Hôpital Erasme, Service de la Recherche Biomédicale, Bruxelles, Belgium; [8]Assistance Publique-Hôpitaux de Paris, Hôpital Bicêtre, Service de Médecine Interne, Le Kremlin-Bicêtre, France; [9]Gustave Roussy, Département de Médecine Nucléaire et de Cancérologie Endocrinienne, Villejuif, France; [10]Université Paris-Saclay, Inserm, Physiologie et Physiopathologie Endocriniennes, Le Kremlin-Bicêtre, France; [11]Assistance Publique-Hôpitaux de Paris, Hôpital Bicêtre, Service d'Endocrinologie Pédiatrique, Centre de Référence des Maladies Rares du Métabolisme du Calcium et du Phosphate, filaire OSCAR, Le Kremlin-Bicêtre, France

Context
In patients with hypoparathyroidism refractory to conventional treatment, recombinant human (rh)PTH(1-84) or rhPTH(1-34) can be used as second-line therapy and effectively control hypocalcaemia. However, whether rhPTH replacement therapy is safe in the long term is unclear. Our objective was to assess bone effects of long-term therapy of chronic hypoparathyroidism with rhPTH(1-34).
Methods
We conducted a monocenter retrospective cross-sectional study at a tertiary university hospital in France. Eligible patients were adults with chronic hypoparathyroidism receiving rhPTH(1-34) therapy uninterruptedly for more than 24 months, who underwent a two-phase whole-body technetium-99m methyldiphosphonate scintigraphy. Clinical and biochemical data were collected retrospectively, covering the period of exposure to rhPTH(1-34) from its initiation until the date of the bone scintigraphy. Images were analyzed blindly by two experts using a visual grading to calculate a total composite score of the bone scan.
Results
17 patients (13 women) were studied, with a median age of 42 [29;58] years. Median treatment duration was 55 [33;68] months and mean daily dose of rhPTH(1-34) was 37.5 [22.1;40] µg. Pathological bone uptake appearing like so-called "super bone scan" was detected in 10 (59%) patients, despite adequate calcemic control (median calcaemia over the study 2.10 [2.04;2.28] mmol/L). Patients with hypermetabolic bone scan received higher daily doses of rhPTH(1-34) compared with patients normal scan (21.0 vs 39.3 mg/day, $P=0.0380$). There was no difference in reported osteoarticular pain, in total and albumin-adjusted

calcium concentration, in phosphate concentration, in calcium-phosphate product and in 24-hour urinary calcium excretion between the two groups. Patients with pathological bone scan compared with those with normal scan had higher osteocalcin (29.2 vs 232 ng/ml, $P=0.0012$), alkaline phosphatase (81 vs 112 UI/L, $P=0.0094$) and crosslaps (0.67 vs 3.83 ng/ml, $P=0.0198$). The total composite score correlated with osteocalcin ($r_s=0.79$, $P=0.0002$), alkaline phosphatase ($r_s=0.83$, $P=0.0001$), with crosslaps ($r_s=0.51$, $P=0.045$) and tended to correlate with mean daily rhPTH(1-34) dose ($r_s=0.44$, $P=0.0769$). Osteocalcin concentration $\geq$ 87 ng/ml predicted a pathological bone uptake with 100% sensitivity and 85.7% specificity.

Discussion

Abnormally increased metabolic activity of the bone may occur under long-term PTH(1-34) therapy despite adequate calcaemic control, possibly due to the pharmacokinetics of this treatment. Bone scintigraphy can be useful in detecting iatrogenic hyperparathyroidism in patients receiving rhPTH(1–34) or rhPTH(1–84). Increased osteocalcin concentrations reliably predict bone cell over-stimulation and should be used as biochemical marker for dose adjustment or treatment interruption.

DOI: 10.1530/endoabs.81.P34

P35

Vertebral Fractures at hospitalization predict impaired respiratory function at follow-up of COVID-19 survivors

Luigi Di Filippo[1], Nicola Compagnone[2], Stefano Frara[1], Agnese Allora[1], Mauro Doga[1], Patrizia Rovere-Querini[2], George Cremona[3] & Andrea Giustina[1]

[1]San Raffaele Vita-Salute University and IRCCS San Raffaele Hospital, Institute of Endocrine and Metabolic Sciences, Milan, Italy; [2]San Raffaele Vita-Salute University and IRCCS San Raffaele Hospital, Division of Transplantation, Immunology and Infectious Diseases, Milan, Italy; [3]IRCCS San Raffaele Scientific Hospital, Unit of Respiratory Medicine, Milan, Italy

Morphometric-Vertebral Fractures (VFs), which were widely demonstrated to reduce overall-survival and respiratory function in the general population, have been recently reported to be highly prevalent in COVID-19 patients. Emerging data show negative respiratory sequelae at long-term follow-up in COVID-19 survivors. The aim of this study is to evaluate the VFs influence on respiratory function of COVID-19 survivors. We included COVID-19 patients admitted at San Raffaele-Hospital and re-evaluated at the San Raffaele-Outpatient Follow-Up Clinic. Lateral chest-X-rays on admission in emergency-department were obtained and pulmonary function tests (PFTs) were performed at six-months of follow-up. VFs were detected using a qualitative and semiquantitative assessment and PFTs were obtained by Jaeger-MasterScreen-AnalyzerUnit. Fifty patients were included in the study. Median age was 66 years, and 33 (66%) patients were males. VFs were detected in 16 (32%) patients. No differences between fractured and non-fractured groups regarding age, sex and comorbidities were observed. A Radiological-Assessment-of-Lung-Edema (RALE) score, assessing the severity of pulmonary opacities, was available for 30 patients with a median value of 5.5. Although no differences were observed in RALE score between VFs + and VFs- patients (5 vs 6, $P=0.69$), those with VFs were characterized by a significant lower SpO2/FiO2 ratio, higher CRP levels, and required hospitalization more frequently (100% vs 73%, $P=0.04$). No differences were found regarding ICU-admission. At follow-up, patients with VFs were characterized by significant lower Forced-Vital-Capacity (FVC; 2.9 vs 3.6 L, $P=0.006$; 85% vs 110% predicted, $P=0.001$), Forced-Expiratory Volume-1st-second (FEV1; 2.2 vs 2.8 L, $P=0.005$; 92% vs 110%; $P=0.001$). Moreover, a lower diffusing-capacity-for-carbon-monoxide (DLCOSB; 5.83 vs 6.98 mmol/min/kpa, $P=0.036$, 59% vs 86.3%, $P=0.043$) as well as Total Lung-Capacity (TLC; 4.9 vs 6.1 L, $P=0.027$; 84% vs 98%; $P=0.04$) were found in patients with VFs compared to those without. In linear regression analyses, the Spine-deformity-index (SDI) was significantly correlated negatively with FVC% ($P=0.02$) and positively with FEV1/FVC ($P=0.01$), and negative trends with FEV1% and DLCOSB% were observed ($P=0.12$, $P=0.12$, respectively). VFs found on hospital admission appear to be independent predictors of medium term impaired respiratory-function of COVID-19 survivors which may significantly influence their recovery. Therefore, our findings suggest that a VFs assessment at baseline may help in identifying patients needing a more intensive respiratory follow-up after discharge. Patients showing persistent respiratory symptoms and functional impairment without evidence of pulmonary disease may benefit from VFs assessment in order to preventing the vicious-circle of further fractures and respiratory deterioration.

DOI: 10.1530/endoabs.81.P35

P36

Denosumab vs. zoledronic acid treatment in post-menopausal breast cancer: a 2-year prospective observational study

Kristian Buch-Larsen, Djordje Marina & Peter Schwarz

Rigshospitalet, Endocrinology, København, Denmark

Adjuvant treatment for post-menopausal women with early breast cancer (BC) includes aromatase inhibitors (AI), known to decrease bone mineral density (BMD). In this study, we investigate whether denosumab is a valid second option for patients unable to receive standard adjuvant i.v. zoledronic acid (ZA). In total, 212 patients have been evaluated after they did not receive ZA. Of those 194 were included. After evaluation by an endocrinologist, all patients were offered ZA as their first choice and 15% accepted ($N=29$). The remaining 85% were offered denosumab ($N=165$). All patients were followed prospectively with blood tests up to 24 months. DXA scans were performed at baseline and 24 months. No difference was observed between the two treatment groups at baseline, with regard to anthropometry and standard biochemistry. Markers of bone turnover (p-PINP, p-CTX, p-bone-specific alkaline phosphatase and p-osteocalcin) all showed significant suppression compared to baseline and remained suppressed throughout the 2 years. BMD showed small and significant increases at the spine (0.024 g/cm^2) and total hip (0.019 g/cm^2) in the denosumab group but no change at the femoral neck(-0.011g/cm^2). In the ZA group, we observed no significant change at the spine (0.015 g/cm^2) and total hip (-0.001 g/cm^2) and a small significant decrease at the femoral neck (-0.037 g/cm^2). However, when we compared BMD change between the treatment groups, we found no significant difference.

Conclusions

Our data indicate that for BC patients in AI treatment who refused or were not able to receive ZA treatment, denosumab might be recommended as a second choice. Regarding markers of bone turnover and BMD denosumab is equal to ZA.

Summary

Women with early breast cancer receiving anti-estrogen treatment are at risk of developing osteoporosis. We followed 194 women receiving zoledronic acid (ZA) or denosumab for up to 2 years. We find that with regard to bone protection, denosumab is a viable alternative to ZA and might be recommended as a second choice.

DOI: 10.1530/endoabs.81.P36

P37

Relative incidence and demographics of hip fractures among subjects over the age of 50 from the Ethiopian ethnic minority in Israel: A preliminary survey from the Israel National Trauma Registry (INTR) database between 2011-2020

Karen Tordjman[1,2], Vanessa Rouach[1,2], Moran Bodas[3], Adi Givon[3], Anat Jaffe[4], Inbal Goldshtein[5,6] & Yona Greenman[1,2]

[1]Tel Aviv Sourasky Medical Center, Institute of Endocrinology, Metabolism, and Hypertension, Tel Aviv, Israel; [2]Tel Aviv University, Sackler faculty of Medicine, Medicine, Tel Aviv, Israel; [3]Gertner Institute, Sheba Medical Center, Israel National Center for Trauma and Emergency Medicine Research, Israel; [4]Hillel Yaffe Medical Center, Endocrinology and Diabetes Unit, Hadera, Israel; [5]Maccabi Healthcare Services, Maccabitech Institute for Research and Innovation, Israel; [6]Tel Aviv University, Sackler Faculty of Medicine, Public Health and Epidemiology, Israel

Background

Among the various ethnicities in the Israeli mosaic, the Ethiopian community is the most recently settled, with an immigration that started less than 40 years ago. Largely young, this 160,000-member community comprises nonetheless about 25,000 persons 50 years or older, virtually all born in Ethiopia. Despite this growing aging population, there is no knowledge regarding osteoporotic fractures in this unique East African ethnic group, not even from data originating from Ethiopia. Two isolated reports, from Ethiopia and from Israel, presented conflicting data regarding bone mineral density in this ethnic group. This study aimed to generate some preliminary data regarding the incidence of hip fractures, as a proxy for osteoporosis, in Ethiopian-born Israelis age 50 and over, between 2011-2020.

Methods
The INTR database contains reports on all injuries recorded in 21 of the 26 trauma centers in Israel. Hip fractures are the only osteoporotic fractures included in the database, as surgery within 48 hours is a nationally monitored medical quality index. Hip fracture data were retrieved from the registry, stratified by gender and age, and compared to those of the Israeli population of other ethnicity.
Results
Ethiopian-born subjects 50 yr and older comprised 0.6% of the INTR reports, while their representation in this age group in Israel was 1.24% ($P<0.0001$). The INTR included 966 reports on Ethiopian-born subjects in this age category, 3.9% of this stratum in the Ethiopian community, while it included reports on 7.4% of people of this age group of different ethnicity ($P<0.0001$). Between 2011-2020, there were 194 hip fractures among Ethiopian-born subjects age 50 or older, 20.1% of all reports for this group. While hip fractures represented 32.3% of injuries reported for other people in this age group, $P<0.0001$. Among Ethiopian-born subjects who suffered a hip fracture, 81/194 (41.8%) were men, compared to 16175/48130 (33.6%) among people of other origin ($P<0.05$). Additionally, 81/194 (41.75%) of these fractures occurred in Ehtiopian-born over the age of 85, while the corresponding figure was only 17303/48130 (35.95%) in people of different ethnicity, $P=0.02$.
Conclusions
Older Ethiopian-born Israelis, particularly women, appear to be less prone to hip fractures than the rest of the population. Additionally, hip fractures appear to occur more in the very old Ethiopian-born than in other ethnic groups, possibly suggesting less osteoporosis. Hip fracture being only a proxy for osteoporosis, a study linking all fragility fracture data with BMD is planned to further examine this question.

DOI: 10.1530/endoabs.81.P37

P38

Is the concomitant presence of osteoporosis captured by the diagnosis of sarcopenia? A cross-sectional study of 262 women with a fragility fracture of the hip

Marco Di Monaco[1], Carlotta Castiglioni[1], Francesca Bardesono[1], Margherita Freiburger[1], Edoardo Milano[1] & Giuseppe Massazza[2]
[1]Fondazione Opera San Camillo, Osteoporosis Research Center, TORINO, Italy; [2]Division of Physical and Rehabilitation Medicine, Department of Surgical Sciences, TORINO, Italy

Background
Several lines of evidence support the view that sarcopenia and osteoporosis are strictly connected. However, the capability of the updated sarcopenia definition to capture the concomitant presence of osteoporosis has been scarcely investigated.
Aim
To assess the association between sarcopenia defined according to the revised criteria from the European Working Group on Sarcopenia in Older People (EWGSOP2) and osteoporosis in women with a fragility fracture of the hip.
Methods
We focused on women who were consecutively admitted to our ward for subacute rehabilitation following a fragility fracture of the hip. A scan by dual-energy x-ray absorptiometry (DXA) was performed to assess body composition. A Jamar dynamometer was used to measure handgrip strength. Sarcopenia was diagnosed with both handgrip strength $<$ 16kg and appendicular lean mass (aLM) $<$ 15kg. Osteoporosis was identified with femoral bone mineral density lower than 2.5 standard deviations below the mean of the young reference population.
Results
We studied 262 of 290 women. Osteoporosis was found in 189 of the 262 women (72%; 95% CI from 67% to 78%) whereas sarcopenia in 147 of the 262 (56%; 95% CI from 50% to 62%). The unadjusted odds ratio to have osteoporosis for a sarcopenic woman was 2.93 (95% CI from 1.69 to 5.19, $P<0.001$). After adjustment for age, time interval between fracture and DXA scan and body fat percentage the odds ratio was 2.30 (95% CI from 1.27 to 4.14; $P=0.006$). The significant association between sarcopenia and osteoporosis persisted after substituting body mass index for body fat percentage among the potential confounders.
Conclusions
We show that the diagnosis of sarcopenia according to the EWGSOP2 criteria can successfully capture the concomitant presence of osteoporosis in women with hip fracture. The updated definition of sarcopenia can help clinicians to focus on the damages of both the components of the muscle-bone unit, thus emerging as a promising tool to investigate osteosarcopenia in older people. Our findings need confirmation by robust prospective studies.

DOI: 10.1530/endoabs.81.P38

P39

Tumor-induced osteomalacia - case report

Eva Rusu[1], Andreea Peica[1], Tudor Gliga[1], Oana Stanoiu-Pinzariu[2] & Carmen Georgescu[1,2]
[1]Clinical County Emergency Hospital Cluj-Napoca, Endocrinology Department, Cluj-Napoca, Romania; [2]"Iuliu Hatieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania

Introduction
Tumor-induced osteomalacia is a rare paraneoplastic syndrome characterized by the presence of phosphaturic hormone-secreting mesenchymal tumors - fibroblast growth factor 23 (FGF-23), which causes hypophosphatemia and osteomalacia. These tumors are small, frequently infiltrate the surrounding tissues and are located in the connective or bone tissue. Usually, these tumors are benign, but malignant tumors have also been reported.
Case report
We present the case of a 39-year-old female with persistent diffuse osteomuscular pain, progressive generalized muscle weakness and the impossibility of standing and walking for about five years. She underwent multiple medical examinations - neurologic, orthopedic and rheumatologic assessments, but did not identify any disorders to explain her symptoms. Laboratory testing showed severe hypophosphatemia (0.9 mg/dl), increased urinary phosphate excretion, increased alkaline phosphatase (320 U/l), normal renal function and elevated FGF-23 (551 kRU/l). Radiographic imaging revealed multiple, old, nontraumatic pelvic and rib fractures, evolved with vicious consolidation. SPECT CT with ^{99m}Tc-Tektrotyde demonstrated increased uptake of the radiotracer in the right supraspinatus muscle. MRI of the right shoulder confirmed a 5 cm intramuscular tumor of the supraspinatus muscle. Surgery was performed with resection of the tumor. Postoperatively, we observed progressive normalization of phosphate levels within a few days and FGF23 decreased significantly, but without normalization 48 hours or 1 month after surgery, raising the suspicion of incomplete resection. Histopathological examination and immunohistochemical profile confirmed the presence of phosphaturic mesenchymal tumor (PMT) with a predominantly hemangiomatous component, showing positive expression of CD34, CD56, CD68, SMA, vimentin and Ki-67 $<$ 5%. The resected margins showed tumor infiltration of the adipose tissue and skeletal muscle. The clinical outcome of the patient was favorable, with progressive and significant improvement of symptoms (regression of osteomuscular pain and gait abnormalities) and normalization of serum phosphate level and FGF-23 level at the upper limit of normal values. Given the histopathological result and failure of normalization of FGF-23 additional follow-up is necessary for detection of tumor recurrence.
Conclusion
Tumor-induced osteomalacia is a rare, frequently undiagnosed or misdiagnosed disease. The diagnosis is a real challenge because of the nonspecific symptoms that can delay detection of the disease. A stepwise approach, combining functional and anatomical imaging is necessary to identify the tumor. Surgery is the only curable option and should be performed whenever is possible.
Keywords
Tumor-induced osteomalacia, FGF-23, paraneoplastic syndrome, hypophosphatemia

DOI: 10.1530/endoabs.81.P39

P40

In case of acute pancreatitis; think of hyperparathyroidism! A case report

Ali Halouache[1], Benhamdane Ahlame[2], Errahali Yassine[1], Chakdoufi Sanae[1], Isouani Jad[1] & Guerboub Anas[1]

[1]Hopital Militaire d'Instruction Mohammed V, Endocrinology, and Metabolic Diseases, Rabat, Morocco; [2]Hopital Militaire d'Instruction Mohammed V, Gastro Entérology , Rabat, Morocco

Introduction
The revelation of primary hyperparathyroidism by acute pancreatitis is an exceptional situation
Case report
We report the case of a 73 years old patient, hypertensive, having the antecedent of an ischemic cardiopathy complicated by cardiac insufficiency and atrial fibrillation, admitted to the emergency for an abdominal pain evolving since 10 days, associated with vomiting, the initial biological assessment showed lipasemia at 2543IU/l, kidney failure and malignant hypercalcemia at 142mg/l. The etiological work-up showed primary hyperparathyroidism with double localizations, the patient benefited from a Para thyroidectomy with a good clinic biological evolution.
Discussion
Hypercalcemia is a rare cause of acute pancreatitis, even more so if it is secondary to primary hyperparathyroidism, its prevalence varies, according to studies, from 1.5 to 5% [1]. Authors suggest that this association is not coincidental, and several pathophysiological explanations have been proposed, but none has been experimentally proven to date. the highest prevalence of acute pancreatitis in patients with hyperparathyroidism has been observed in those with hypercalcemia [2], and the hypercalcemia-acute pancreatitis link is currently well established. For Prinz and his team [3], acute pancreatitis is the consequence of a deposit of lithiasis secondary to an accumulation of calcium in the gastric juice. The second explanation is that of intra-pancreatic trypsinogen activation, which is widely accepted as the lever leading from acinar cell injury to acute pancreatitis [4]. Recently, the role of a genetic substrate has been suggested; mutations in the SPINK1 and CFTR genes have been detected in hyper parathyroid patients who developed acute pancreatitis[5].
Conclusion
The association hyperparathyroidism - acute pancreatitis was most often explained by the link of hypercalcemia, most of the above theories have not presented scientific evidence, and the current challenge is to seek a direct link between these two pathologies, the genetic theory remains an option, but its role is not clear.
Bibliography
[1] Kusnierz-Cabana B, and al. Currents concepts on diagnosis and treatment of acute pancreatitis. Adv Clin Chem 2003;37:47–81. [2] Carnaille B, and al. Pancreatitis and primary hyperparathyroidism: forty cases. ANZ J Surg 1998; 68:117–9. [3] Prinz RA, Aranha GV. The association of primary hyperparathyroidism and pancreatitis. Am Surg 1985;51:325–9. [4] Pandol SJ, and al. Acute pancreatitis: bench to the bedside. Gastroenterology 2007;132: 1127–51. [5] Felderbauer MD, and al. Pancreatitis risk in primary hyperparathyroidism: relation to mutations in the SPINK1 trypsin inhibitor (N34S) and the cystic fibrosis gene. Am J Gastroenterol. 2008; 103:368–74.

DOI: 10.1530/endoabs.81.P40

P41

Lower than recommended doses of cinacalcet are effective and well tolerated in the control of hypercalcaemia of primary hyperparathyroidism

Nyein Nge Nge[1] & Mohamed Malik[2]
[1]Hull University Teaching Hospital NHS Trust, General Internal Medicine, Hull, United Kingdom; [2]Scunthorpe General Hospital , Endocrinology Department, Scunthorpe, United Kingdom

Background
The treatment goal in primary hyperparathyroidism (PHPT) is the achievement of biochemical control and prevention of target organ complications. Parathyroidectomy is the current recommended intervention to cure the disease. However, Cinacalcet is an alternative medical treatment for subgroup of patients in whom surgery is deemed inappropriate, those with recurrent disease, and as bridging therapy for delayed operation particularly in recent COVID pandemic. Current recommended starting dose of Cinacalcet is 60 mg/day, with up titration to a maximum dose of 360 mg/day in divided doses. It is not yet known whether a lower dose of cinacalcet can be effective in controlling hypercalcemia, with the advantage of better tolerability and reduced cost.
Objective
To assess efficacy of Cinacalcet in unselected medically managed patients with PHTH, and to explore minimal effective dose of Cinacalcet required to control hypercalcemia in ordinary clinical practice.
Methods
We conducted a retrospective study including all patients with PHPT who had initiated treatment with cinacalcet at the Endocrinology department over a period of three years. We evaluated pre-treatment baseline biochemical data and subsequent variations at 3rd, 6th and 12thmonth after cinacalcet treatment. As well we assessed effective Cinacalcet dose, treatment side effects, and rate of treatment discontinuation.
Results
Total 66 patients with PHTH (49 women and 17 men, aged 53-97 years) were included. Average baseline serum calcium was 2.95mmol/L (95%confidence interval [CI], 2.92 to 2.98), serum PTH of 17.58 ± 6.514pg/ml, and serum phosphate of 0.83mmol/L (95%CI, 0.80 to 0.86). Following three months of Cinacalcet, serum calcium reduced to average of 2.60mmol/L (95%CI, 2.54 to 2.66) and serum phosphate was up to 0.95mmol/L (95%CI, 0.90 to 1.0). Subsequent measurements at 6- and 12-months' points were consistent with trend towards eucalcaemia, normalising serum phosphate and stabilising serum PTH level. Sixty seven percent of studied population required Cincalcet dose of 60 mg/day to maintain biochemical eucalcaemia, and further 20% have achieved the desired effects at a dose of 30 mg/day. Among the 66 patients studied, only one discontinued cinacalcet due to intractable GI side effect and one missed follow-up.
Conclusion
Lower than recommended dose of Cinacalcet is effective and well tolerated to control hypercalcaemia of primary hyperparathyroidism. This observation is of clinical significance when the factors of long-term treatment compliance, and targeted elderly population with multiple comorbidities and polypharmacy, are considered. Furthermore, the observation makes Cinacalcet an attractive cost-effective treatment when compared to surgery, and the cost of managing acute and chronic complications of hypercalcaemia.

DOI: 10.1530/endoabs.81.P41

P42

Long-term complications of permanent hypoparathyroidism: prevalence and associated factors

Faten Cherchir[1], Ibtissem Oueslati[1], Meriem Yazidi[1] & Melika Chihaoui[1]
[1]La Rabta University Hospital, Department of Endocrinology, Tunis, Tunisia

Introduction
Patients with permanent hypoparathyroidism receiving conventional treatment have increased risk of subcapsular cataracts, basal ganglia calcifications, urolithiasis and renal insufficiency. The aim of this study was to assess the prevalence and the interfering factors of these complications in patients with permanent hypoparathyroidism.
Methods
We conducted a cross-sectional study including 53 patients with permanent hyperparathyroidism. Biochemical parameters, ophthalmological examination, brain computed tomography scan and renal ultrasound were performed to all patients.
Results
There were 41 (77%) women and 12 (23%) men with a mean age of 52.7 ± 16.5 years. Post-surgical HPT was the most frequent etiology of hypoparathyroidism (64%). Posterior subscapular cataract was diagnosed in 62% of cases. Age ($P < 10^{-3}$), disease duration ($P = 0.02$) and hypomagnesemia ($P = 0.014$) were positively associated with cataracts. Basal ganglia calcifications were found in 53% of cases. Brain CT-scan showed bilateral intracerebral calcifications located in the central gray nuclei (71%) or diffuse symmetric calcifications (29%). Patients with intracranial calcifications presented with headache, amnesic disorders, psychotic symptoms and seizures in 82, 71, 14 and 14% of cases, respectively. Younger age of onset of hypoparathyroidism ($P = 0.037$), disease duration ($P = 0.014$), nonsurgical etiologies ($P = 0.015$), poor adherence to treatment ($P < 10^{-3}$), hypomagnesemia ($P = 0.001$) and PTH level < 10 pg/ml ($P = 0.022$) were significantly associated with brain calcifications. Urolithiasis and renal insufficiency were found in 13 and 17% of cases, respectively. Creatinine clearance was negatively correlated with disease duration ($r = -0.338$, $P = 0.013$). Patients with urolithiasis had lower PTH level and received higher calcium salt doses ($P = 0.033$) than those who had no renal calcifications. However, sex, smoking, body mass index, calcemia, phosphatemia, phosphocalcic product, TSH and 25-OH-vitamin D did not significantly interfere with none of these complications.
Conclusion
Patients with permanent hypoparathyroidism are exceedingly exposed to neurological, visual and renal impairment because of phosphocalcic disorders and extra-skeletal calcifications. The disease duration, PTH and magnesium levels seem to be the most interfering factors.

DOI: 10.1530/endoabs.81.P42

P43

Assessment of quality of life in patients with hypoparathyroidism receiving conventional treatment: a case-control study

Faten Cherchir, Ibtissem Oueslati, Meriem Yazidi & Melika Chihaoui
La Rabta University Hospital, Department Of Endocrinology, Tunis, Tunisia

Introduction
Patients with permanent hypoparathyroidism suffer from multiple complaints and are exposed to long-term complications that compromise their well-being. The aim of our study was to assess the quality of life in patients with permanent hypoparathyroidism receiving conventional vitaminocalcic therapy.
Methods
We conducted a cross-sectional case-control study including 53 patients with permanent hypoparathyroidism and 53 age-sex-body mass index matched controls. Clinical and biochemical parameters were collected. Quality of life was assessed in all participants using the Short Form 36 Health Survey (SF-36).
Results
Among patients with hypoparathyroidism, there were 41 (77 %) women and 12 (23 %) men with a mean age of 52.7 ± 16.5 years. Neck surgery was the most common etiology of hypoparathyroidism ($n=34$, 64 %). In comparison with age-sex-body mass index matched controls, hypoparathyroid patients had significantly lower scores in all eight domains of SF-36 ($P < 10^{-3}$). Patients with postsurgical hypoparathyroidism scored worse than those with non-surgical etiologies in all domains, but significance was reached only in bodily pain score ($P=0.01$). All SF-36 scores were negatively correlated with the age. However, Sex, smoking, duration of the disease, adherence to treatment and body mass index did not significantly interfere with SF-36 scores. Hypoparathyroid patients in whom PTH level < 10 pg/ml scored worse in all SF-36 domains compared with those who had PTH level > 10 pg/ml, without reaching significance. Magnesium level was positively correlated with SF-36 scores. No significant correlations were found between SF-36 scores and biological parameters such as calcemia, phosphatemia, phosphocalcic product, TSH, 25 OH vitamin D, 24 hours calciuria, and creatinine clearance.
Conclusion
Compared with matched controls, patients with permanent hypoparathyroidism, especially post-surgical ones, suffer from a major impairment of quality of life, suggesting that conventional treatment, even if it's well conducted, fails to restore well-being.

DOI: 10.1530/endoabs.81.P43

P44

Bone mineral density, trabecular bone score and vertebral fractures in acromegalic patients

Madalina Sorohan[1,2], Ramona Dobre[3], Ionela Baciu[2,3], Simona Galoiu[1,2,2], Roxana Dusceac[1,2], Dan Niculescu[1,2], Andra Caragheorgheopol[1], Carmen Iordachescu[1] & Catalina Poiana[1,2]
[1]CI Parhon National Institute of Endocrinology, Pituitary Pathology and Neuroendocrinology, Bucharest, Romania; [2]Carol Davila University of Medicine and Pharmacy, Bucharest, Romania; [3]CI Parhon National Institute of Endocrinology, Bucharest, Romania

Background
Acromegaly is characterized by increased prevalence of fragility vertebral fractures. Nonetheless, there are no clear recommendations for prevention of acromegalic osteopathy. Both bone mineral density (BMD) and trabecular bone score (TBS) lack clear evidence as prognostic factors for vertebral fractures (VF).
Material and Methods
We performed an observational study on 31 acromegalic patients recruited prospectively. They were tested for alkaline phosphatase, 25 hydroxyvitamin D, parathormone, osteocalcin, the C-terminal telopeptide of type I collagen and total procollagen type 1 amino-terminal propeptide. Imaging techniques used were dual x-ray absorptiometry (DXA), TBS and antero-posterior and lateral x-ray scans of the dorsolumbar spine.
Results
They were characterized by normal BMD, partially degraded bone on TBS, 32.33% had VF on dorsolumbar x-ray and hypogonadism was present in 71% of subjects. Hypogonadal acromegaly subjects had significantly lower TBS (1.232 ± 0.123 vs. 1.343 ± 0.146, $P=0.040$) but higher T ($P=0.029$) and Z scores ($P=0.004$) at the femoral neck compared to eugonadal patients. Acromegalic patients with VF had significantly lower BMD at the femoral neck (0.901 ± 0.137 vs. 1.013 ± 0.131 g/cm^2, $P=0.037$) and hip (0.883 ± 0.109 vs. 1.036 ± 0.121, $P=0.002$) and T score at the lumbar spine [-2.7 (IQR: -3.4- -0.6) vs. -1.2 (IQR: -1.9-0.1), $P=0.047$] compared to those without VF but with no differences in terms of TBS values.
Conclusion
Vertebral fractures in acromegaly patients associate with low BMD but not with TBS. However, TBS is significantly lower in these patients in the presence of hypogonadism. The use of BMD might still prove to be useful in the evaluation of acromegalic osteopathy.

DOI: 10.1530/endoabs.81.P44

P45

Phosphate-mediated inhibition of calcium-sensing receptor expressed endogenously in the thyroidal TT cell-line

Khaleda Alghamdi[1,2], Hee-Chang Mun[3], Arthur Conigrave[4] & Donald Ward[5]
[1]The University of Manchester, Faculty of Biology, Medicine and Health, Manchester, United Kingdom; [2]King Abdulaziz University , Department of Pharmacology and Toxicology, Jeddah, Saudi Arabia; [3]The University of Sydney, School of Life & Environmental Sciences, Sydney, Australia; [3]The University of Sydney, School of Life & Environmental Sciences, Sydney, Australia; [5]The University of Manchester, Faculty of Biology, Medicine and Health, Manchester, United Kingdom

The calcium-sensing receptor (CaR) is the key controller of parathyroid hormone (PTH) secretion and extracellular calcium homeostasis. Hyperphosphataemia increases PTH secretion and is associated with secondary hyperparathyroidism (SHPT). We reported recently that inorganic phosphate (Pi), and sulphate, can attenuate CaR activity directly (in CaR-transfected HEK-293 cells) and Pi can increase PTH secretion rapidly from human and murine parathyroid cells. To investigate this further, here we used a thyroid parafollicular C-cell model, TT cells, which express CaR endogenously. TT cells, which exhibit CaR-induced calcitonin (CT) secretion, were assayed by epifluorescence intracellular Ca^{2+} imaging and CT assay (with a gastrin-releasing peptide (GRP)-induced CT control). When co-stimulated with the CaR-activating calcimimetic R568 (1μM) and spermine (1mM), TT cells exhibited classic CaR-induced $Ca^{2+}{}_i$ mobilisation, which the $G_{q/11}$-specific inhibitor YM-254890 largely abolished (-93 ± 8%). Similar CaR-induced responses were also inhibited by increasing the buffer Pi concentration from 0.8 mm (physiological) to a pathophysiological 2 mm (-33 ± 4%; $P<0.001$). In contrast, raising Pi concentration was without effect on carbachol-induced $Ca^{2+}{}_i$ mobilisation (acting via muscarinic receptors). Finally, 1.2 mm sulphate (high) elicited a similar CaR inhibition as for Pi (-28 ± 16%; $P<0.05$; vs physiological 0.3 mm sulphate). Similar inhibitory effects were seen when the anions were used in combination; 2mM Pi (high) & 0.3mM sulphate (normal) elicited a 15 ± 12% reduction in CaR-induced $Ca^{2+}{}_i$ mobilisation, while 2mM sulphate (high) & 0.8mM Pi (normal) produced a 19 ± 3% inhibition ($P<0.05$). Regarding CT secretion, we observed time-dependent release that was stimulated maximally 15-20 fold by increasing Ca^{2+} concentration from 0.5–3.0mM (EC_{50} ~1.5 mm). Inorganic Pi (0.8-3.0 mm) inhibited CT release in a non-competitive manner, with 3mM Pi almost abolishing CT release at all $Ca^{2+}{}_o$ concentrations tested. Even raising Pi concentration from 0.8-1.4 mm (representing the physiological range) elicited a striking 50% reduction in CT release. In contrast, 2mM Pi had no effect on 1μM GRP-stimulated CT release. Sulphate was also a non-competitive inhibitor of CT release but was less potent than Pi. These results further support the idea that the CaR is a mineral sensor, at which Pi acts directly as a non-competitive antagonist to limit CaR-induced reductions in PTH secretion. Further, Pi may also limit CaR-induced CT secretion when its serum concentration is raised. Together, our studies provide important new information regarding the physiological control of PTH and CT secretion, and, the pathophysiology of SHPT.

DOI: 10.1530/endoabs.81.P45

P46

Bleeding assessment in 195 patients with osteogenesis imperfecta

Koert Gooijer, Gabriëla Heidsieck, Arjan Harsevoort, Danielle Bout, Guus Janus & Anton Franken
Isala Zwolle, Zwolle, Netherlands

Background
Osteogenesis Imperfecta (OI) is commonly defined as 'brittle bones' disease, but there are also more characteristics like blue sclerae, hearing loss, dental problems, ligamentous laxity and a short stature. Easy bruising is also a very common feature and there are multiple case reports on haemorrhagic events in OI. Larger population studies on bleeding tendency in OI are very sparse, while other connective tissue disorders with easy bruising have much more relevant research. This paper reviews the clinical aspects of bleeding in bruising in OI based on the self-bleeding assessment tool (BAT) questionnaire among a large cohort of OI patients. The emphasis of this study will be a first translation to clinical consequences of bleeding due to surgery, tooth extraction, menstrual and obstetrical bleeding and to present therapeutic considerations relevant to bleeding in OI.
Methods
This explorative study was conducted at the national expert center for adults with OI in the Netherlands. The self-BAT was digitally distributed among 354 adults with different clinically confirmed types of OI.
Results
195/354 patients with OI types 1,3 and 4 were included. Self-BAT scores were increased in 37-44%.
Conclusion
Bleeding tendency seem to be a relevant feature in OI patients. This study should be a wakeup call for all clinicians treating OI patients for assessing bleeding tendency and taking the right interventions to reduce haemorrhagic symptoms and improve quality of life.

DOI: 10.1530/endoabs.81.P46

P47

The international x-linked hypophosphataemia (xlh) registry: overview of the dataset

Sandro Giannini[1], Jonathan Liu[2], Angela Williams[2] & Sue Wood[2]
[1]University of Padova, Department of Medicine, Padova, Italy; [2]Kyowa Kirin International Marlow Office, United Kingdom

Background
X-Linked Hypophosphataemia (XLH) is a rare, progressive, hereditary phosphate wasting disorder characterised by a pathological increase in fibroblast growth factor 23 concentration/activity. Despite XLH being increasingly recognised as a chronic progressive disease, there are few data documenting its natural history or impact of treatment. The International XLH Registry will collect data to characterise burden of disease, disease progression and long-term outcomes. It aims to describe effectiveness and safety of treatments used to manage XLH and their value in certain subpopulations.
Methods
The International XLH Registry (NCT03193476) was initiated August 2017, aims to recruit 1,200 children and adults with XLH, and will run for 10 years. This is a multicentre, non-interventional registry, capturing treatment details and clinical outcomes in patients with XLH who are followed for as long as informed consent/assent and regulatory permissions are maintained. Only data collected during standard routine examinations are recorded, no specific examinations/data entries are mandated. Parameters collected at baseline included demographics, medical history, treatment history, and clinical presentation data. The conduct of the International XLH Registry is overseen by 17 Steering Committee expert physicians representing the region.
Results
As of 31 December 2021, 1,043 subjects diagnosed with XLH were enrolled from 88 hospital sites in 19 countries. The geographic distribution of subjects is as follows: Belgium $n=29$, Bulgaria $n=7$, Czech Republic $n=8$, Denmark $n=23$, France $n=267$, Germany $n=79$, Hungary $n=11$, Ireland $n=5$, Israel $n=21$, Italy $n=88$, The Netherlands $n=26$, Norway $n=23$, Portugal $n=9$, Slovakia $n=5$, Slovenia $n=3$, Spain $n=55$, Sweden $n=43$, Switzerland $n=17$, and the UK $n=324$. A further 30 sites are still to enrol patients (including in Austria and Latvia). Overall, 400 adults (18–29y, $n=116$; 30–39y, $n=81$; 40–49y, $n=95$; 50–59y, $n=58$; $\geq$60y, $n=50$) and 620 paediatric subjects ($<$5y, $n=138$; 5–12y, $n=321$; 13–17y, $n=161$) have been enrolled (date of birth unavailable, $n=23$). The majority of the enrolled subjects are female (648 (62.1%)), with 372 male (35.7%) and 23 for whom sex was not reported (2.2%).
Conclusions
This Registry forms the largest dataset of XLH subjects worldwide to date. Patients have been recruited from a wide geographical region, and baseline demographics are consistent with a hereditary X-linked dominant disease. Information collected during the 10-year Registry duration will generate real-world evidence to help inform clinical practice throughout the EMEA region and beyond.
Acknowledgements
Authors acknowledge the contribution of all members of the International XLH Registry Steering Committee.

DOI: 10.1530/endoabs.81.P47

P48

Male osteoporosis, a still overlooked and undermanaged issue: an identikit of patients seeking bone health evaluation at a tertiary academic medical centre

Sara De Vincentis[1,2], Antonino Russo[1,2], Erica Taliani[2], Anna Ansaloni[2], Daniela Domenici[1,2], Bruno Madeo[2] & Vincenzo Rochira[1,2]
[1]Unit of Endocrinology, Department of Biomedical, Metabolic and Neural Sciences, University of Modena and Reggio Emilia, Modena, Modena, Italy; [2]Unit of Endocrinology, Department of Medical Specialties, Azienda Ospedaliero-Universitaria Policlinico of Modena, Modena, Italy

Background
Male osteoporosis is undermanaged. The characteristics of men referring to health care system for bone evaluation remain partially unknown.
Aim
To characterize from real-life data male patients seeking the first bone health evaluation at a tertiary academic medical center, referral for both andrological and bone diseases, over a 13-year observation period.
Methods
Retrospective, cross-sectional study, including adult men referring to our Center from 2007 to 2020 for bone health evaluation. Reasons for referral, risk factors for osteoporosis and comorbidities were investigated. Osteoporosis and osteopenia were defined considering DXA outcomes, according to WHO and ISCD criteria, and history of fragility fractures.
Results
A total of 455 men (age 62.5 $\pm$ 15.1years) were included: 42 aged 18–40 years, 57 aged 40–50, 79 aged 50–60, 109 aged 60–70, 122 aged 70–80, and 46 aged $>$80. Overall, 125 patients (27.4%) were already followed by endocrinologists due to endocrinological/andrological diseases known to increase fracture risk (94 men) or not (31 men); general practitioners and other specialists asked for bone evaluation for 226 (49.6%) and 101 (22.1%) men. DXA has been already performed for 354 patients. Prevalence of osteoporosis, osteopenia, and low bone mineral density for age were 25.9%, 26.4% and 13.2%, respectively. Fractures were the most frequent reasons for referral. At least one fragility fracture has already occurred in 213 patients (46.8%), with higher prevalence in non-endocrinological than endocrinological patients (56% *vs* 24%, $P<0.001$). Sites of fracture were lumbar spine (128 patients,60%), femoral neck alone or in combination with other sites (50 patients, 23.4%). A total of 344 patients (76%) was already known to be affected by one or more comorbidities associated to bone loss, with higher prevalence in fractured patients compared to non-fractured ($P=0.036$). Among fractured patients, 49 of them (23%) have never been treated with any anti-osteoporotic therapy, including calcium and vitamin D supplementation.
Conclusions
Male osteoporosis presents with a high rate of fragility fractures (about 50%) among men referring to a tertiary academic medical center. The high prevalence of comorbidities associated to bone loss suggests that secondary forms of osteoporosis prevails in men, and they should be carefully investigated to identify patients at increased fracture risk. Most of fractured patients have not been previously evaluated by a clinician with expertise in bone diseases or properly treated, suggesting that awareness for male osteoporosis needs to be reinforced in primary healthcare setting in order to prevent fractures. This disease remains still overlooked and unaddressed.

DOI: 10.1530/endoabs.81.P48

P49

Extended treatment with recombinant human parathyroid hormone (1-84) in adult patients with chronic hypoparathyroidism: a phase 4 study

Mishaela Rubin[1], Natalie Cusano[2], Shaoming Yin[3], Elena Tokareva[3], Olulade Ayodele[3] & Richard D. Finkelman[3]
[1]Columbia University Vagelos College of Physicians and Surgeons, New York, United States; [2]Lenox Hill Hospital, New York, United States; [3]Takeda Pharmaceuticals USA, Inc., Lexington, United States

In Europe, rhPTH(1-84) is an approved adjunctive treatment for adults with chronic hypoparathyroidism that cannot be adequately controlled with conventional therapy. Here we present data from the longest rhPTH(1-84)-treated study cohort of patients with hypoparathyroidism. In a single-centre, single-arm, phase 4 study (NCT02910466), long-term rhPTH(1-84) treatment (25, 50, 75, or 100 μg/day subcutaneously) was evaluated in adults with chronic hypoparathyroidism who maintained uninterrupted rhPTH(1-84) treatment from the HEXT study (NCT01199614). Doses were adjusted based on albumin-corrected serum calcium and 24-hour urinary calcium excretion to achieve target serum calcium within 2.00–2.25 mmol/l. Baseline was defined as last available value before first dose in the current study. End of treatment (EOT) was the day after last rhPTH(1-84) dose for each patient, including those who did not complete the study. Data are summarized as mean ± SD. Thirty-nine patients enrolled (age, 51.9 ± 12.22 years; 79.5% female; duration of hypoparathyroidism, 18.6 ± 12.00 years). Mean length of exposure from first rhPTH(1-84) dose was 10.8 ± 3.50 years. In the current study, 36 patients received ≥ 1 rhPTH(1-84) dose, and mean duration of participation was 30.3 ± 5.79 months. Mean albumin-corrected serum calcium was 1.94 ± 0.222 mmol/l at baseline ($n = 33$), 2.08 ± 0.304 mmol/l at month 30 ($n = 23$), and 2.07 ± 0.266 mmol/l at EOT ($n = 36$). Phosphate values were 1.25 ± 0.230 mmol/l at baseline ($n = 33$), 1.30 ± 0.241 mmol/l at month 30 ($n = 23$), and 1.31 ± 0.220 mmol/l at EOT ($n = 36$). Calcium-phosphate product levels were 2.53 ± 0.475 $mmol^2/l^2$ at baseline ($n = 33$), 2.78 ± 0.421 $mmol^2/l^2$ at month 30 ($n = 23$), and 2.82 ± 0.373 $mmol^2/l^2$ at EOT ($n = 36$). Mean 24-hour urinary calcium levels were 5.52 ± 3.243 mmol/24 hours at baseline ($n = 35$), 7.47 ± 5.170 mmol/24 hours at month 30 ($n = 18$), and 6.60 ± 3.818 mmol/24 hours at EOT ($n = 35$). Mean prescribed supplemental calcium and active vitamin D decreased from 1313.8 ± 1404.46 mg/day and 0.17 ± 0.320 μg/day, respectively, at baseline ($n = 36$) to 1180.9 ± 1065.50 mg/day and 0.12 ± 0.327 μg/day at month 30 ($n = 23$), and 1076.0 ± 832.48 mg/day and 0.11 ± 0.313 μg/day at EOT ($n = 36$). No clinically relevant changes in bone mineral density occurred between baseline and EOT. Treatment-emergent adverse events (TEAEs) were reported in 36 (92.3%) patients; the most common were anxiety (41.0%), hypocalcaemia (28.2%), and depression (20.5%). Four TEAEs were considered by study investigators to be treatment related (upper limb fracture, hypercalcaemia, renal disorder, ureterolithiasis). Study limitations are small sample size, single-arm design, and lack of pre-treatment baseline data. Among patients with chronic hypoparathyroidism previously treated with rhPTH(1-84), improvements in biochemical efficacy parameters were maintained over a mean of 30 months of additional treatment. No new or unexpected safety signals emerged.

DOI: 10.1530/endoabs.81.P49

P50

Impact of chronic hypoparathyroidism on symptom severity and interference with life as reported by patients treated with recombinant human parathyroid hormone (1-84), rhpth(1-84)

Bart L. Clarke[1], Nandini Hadker[2], Amod Athavale[2], Irana Kolev[3] & Olulade Ayodele[3]
[1]Mayo Clinic, Rochester, United States; [2]Trinity Partners LLC, Waltham, United States; [3]Takeda Pharmaceuticals USA, Inc., Lexington, United States

Chronic hypoparathyroidism is a rare mineral homeostasis disorder managed by conventional therapy (oral calcium and active vitamin D), alone or with adjunctive rhPTH(1-84). Chronic hypoparathyroidism is associated with considerable symptom burden, which can interfere with daily living. We report results from a web-based, cross-sectional survey conducted among adults with chronic hypoparathyroidism. The objectives were to quantify the impact on overall life interference of (1) time from diagnosis to rhPTH(1-84) initiation and (2) rhPTH(1-84) treatment vs conventional therapy. Overall life interference of hypoparathyroidism was patient self-reported upon considering all aspects of their condition using a 7-point rating scale (1 = none to 7 = very significant interference). Hypoparathyroidism-associated symptom severity was assessed through the disease-specific, patient-reported Hypoparathyroidism Symptom Diary. The study included 90 patients treated with rhPTH(1-84) (mean ± SD age, 54.5 ± 11.3 years; 83% female) and 57 patients treated but not adequately controlled with conventional therapy (mean ± SD age, 50.0 ± 11.7 years; 93% female). Among rhPTH(1-84)-treated patients, time from hypoparathyroidism diagnosis to rhPTH(1-84) initiation was ≤ 12 months, > 12–≤ 48 months, and > 48 months in 28%, 38%, and 34% of patients, respectively. Initiation of rhPTH(1-84) > 48 months after diagnosis was associated with higher overall life interference compared with initiation ≤ 12 months after diagnosis ($P < 0.001$ for the unadjusted and $P = 0.02$ for multivariable regression analysis adjusted for potential confounders). The life interference mean ± SE score was 2.0 ± 0.54 points higher (unadjusted) and 0.8 ± 0.34 points higher (multivariable regression) for patients who initiated rhPTH(1-84) > 48 months vs ≤ 12 months after diagnosis. Self-reported severity of hypoparathyroidism was rated as no symptoms, mild, moderate, and severe in 42%, 49%, 8%, and 1% of patients treated with rhPTH(1-84), respectively, and in 11%, 37%, 49%, and 3% of patients treated with conventional therapy. Treatment with rhPTH(1-84) was associated with lower overall hypoparathyroidism-related life interference compared with conventional therapy that did not adequately control hypoparathyroidism ($P < 0.001$ for both unadjusted and adjusted multivariable regression analyses). Mean ± SE life interference score for rhPTH(1-84)-treated patients was 1.5 ± 0.33 points lower (unadjusted) and 1.1 ± 0.29 points lower (multivariable regression) vs patients treated with conventional therapy. A strength of this study is the multivariable analysis adjusting for potential confounders; limitations include cross-sectional study design, inaccessibility of patient characteristics before treatment initiation, and recall bias. In a real-world setting, rhPTH(1-84) initiation > 48 months after hypoparathyroidism diagnosis was associated with greater overall life interference vs rhPTH(1-84) initiation ≤ 12 months after diagnosis. Compared with conventional therapy, rhPTH(1-84) treatment was associated with lower overall life interference after adjusting for confounding variables.

DOI: 10.1530/endoabs.81.P50

P51

Novel variant of the casr gene c.2192g > A in a clinical case of chronic hypocalcemic hypoparathyroidism

Blerta Papadopoulou[1], Olga Kosmopoulou[1], Taujan Georgiana[1], Felicia Baleanu[1], Mihaela Rosu[1], Iconaru Laura[1], Karmali Rafik[1], Isabelle Vandernoot[2] & Guillaume Smits[2]
[1]CHU Brugmann, Endocrinology, Brussels, Belgium; [2]Hospital Erasme, Genetics, Brussels, Belgium

A 65 year old patient who was hospitalised for a reactive arthritis of the knee due to Rickettsia infection, presented an asymptomatic persistant chronic hypocalcemia and hyperphosphoremia. In her medical history, we noted a hypertension treated with amlodipine and bisoprolol, syndrome of sleep apnoea, acquired lumbar spinal canal stenosis and sequelae of poliomyelitis acquired at 10 years of age in Congo, her place of origin. According to her blood test results, total calcium levels were low between 1,9 to 2,1 mmol/l (normal ranges 2,15–2,50), phosphorus levels high between 1,61 to 1,81 mmol/l (normal ranges 0,81–1,45), albumine levels normal between 34 to 42 g/l (normal ranges 34–48), parathormone levels abnormaly normal between 17 to 55 ng/l (normal ranges 15–65), 25OH-vitamine-D levels low to normal between 22 to 44 mg/l (normal ranges 30–60). Urinairy calcium excretion between 0,022 to 0,081 mol/mol creat (normal range <0,700). Renal function was normal with creatinine levels between 0,40 to 0,75 mg/dl (normal range 0,55–0,96). The diagnosis of hypoparathyroidism was evoked with suspicion of an activating mutation of the calcium-sensing receptor (CaSR) gene. We performed a citrate infusion test to provoke more pronounced hypocalcemia by administrating intravenously a continuous perfusion of 100 ml solution of dextrose 2.45 g, sodium citrate 2.2 g and citric citrate 0.7 g, for 30 minutes. The subsequent measures of total calcium, ionised calcium and parathormone every 10 minutes from T0 to T30 min, showed no increase of parathormone levels in response to provoked hypocalcemia. The genetic analysis didn't identify any mutation but identified a novel variant c.2192G > A (p.Cys731Tyr) of the CaSR gene. This variant has not been described in the literature before and results from the In-Silico analysis are contradictory, benign for Polyphen and pathogenic for MutationTaster and SIFT. A genetic family study could have helped us to better interpret this result, but unfortunately the patient lives alone in Belgium since 2015 and all her family

lives in Africa. Thus, the pathogenic nature of this novel variant of CaSR gene remains unknown for the time being and the variant is classified as class III.

References
1. Rate and concentration dependence of parathyroid hormone dynamics during stepwise changes in serum ionized calcium in normal humans. Grant et al. J Clin Endocrinol Metab 1990;71:370–8.
2. Citrate infusion test in the diagnosis of hypocalcemia due to a mutation in the calcium-sensing receptor gene. Poppe et al. Eur J Intern Med 2002;13(4):276–279

DOI: 10.1530/endoabs.81.P51

P52

Atherothrombotic risk in subjects with parathyroid disorders: cross-sectional study

Anda Mihaela Naciu[1], Gaia Tabacco[1], Francesco Piccirillo[2], Michele Mattia Viscusi[2], Alfonso Maria Di Tommaso[1], Giulia Sterpetti[1], Andrea Palermo[1] & Annunziata Nusca[2]
[1]Fondazione Policlinico Universitario Campus Bio-Medico, Unit of Metabolic bone and thyroid diseases, Rome, Italy; [2]Fondazione Policlinico Universitario Campus Bio-Medico, Unit of Cardiac Sciences, Rome, Italy

Background
Clinical and molecular findings have shown that parathyroid hormone (PTH) affects the heart and vasculature through downstream actions of G protein-coupled receptors in the myocardium and endothelial cells. Furthermore, the endothelium is a recognised target tissue of PTH and there is an increasing body of evidence that PTH affects functional and structural properties of arteries. Patients with chronic post-surgical hypoparathyroidism (hypoPT) have higher incidences of hypertension, arterial stiffness and increased risk of mortality.
Purpose
To assess endothelial and other atherosclerotic predictors in subjects affected by hypoPT in comparison with primary hyperparathyroidism (PHPT) and controls.
Methods
In a monocentric, cross-sectional study we enrolled hypoPT patients treated with calcium and calcitriol, PHPT subjects and age-matched controls. All patients underwent a biochemical examination including calcium-phosphorus metabolism, inflammation markers. Moreover, we evaluated brachial artery endothelial function (flow-mediated dilation-FMD), common carotid intima-media thickness (ccIMT), diastolic function and global strain measures with ultrasound.
Results
These are the preliminary results of this project that included 49 subjects (20 hypoPT, 18 PHPT and 11 controls) of 150 expected. All study groups presented similar BMI, TSH and kidney function. HypoPT patients had significantly lower PTH and calcium levels ($P<0.001$) and higher phosphorus levels ($P<0.001$) than PHPT and controls. HypoPT had higher inflammation markers (erythrocyte sedimentation rate) levels than PHPT and controls (34.5 ± 17.2 vs 27.6 ± 10.9 vs 15.0 ± 9.6 ml/h,$P=0.020$). All study groups presented no significant differences in basal brachial artery diameter, FMD and diastolic function. HypoPT showed higher global strain value than PHPT subjects (-19.6 ± 3 vs $17.6\pm2.5P=0.042$), while compared to controls presented similar values. HypoPT showed lower ccIMT than PHPT subjects and higher values than controls (10.0 ± 2.2 vs 11.2 ± 2.4 vs 7.6 ± 2.1 mm,$P=0.002$).
Conclusion
Up to now, our findings suggest that hypoPT has an increased atherothrombotic risk and needs adequate cardiovascular evaluation. We believe that further comprehensive studies are needed.

DOI: 10.1530/endoabs.81.P52

P288

Tumour induced osteomalacia: 2 years treatment with burosumab

Ludovica Aliberti, Margherita Pontrelli, Martina Verrienti, Irene Gagliardi, Maria Chiara Zatelli & Maria Rosaria Ambrosio
University of Ferrara, Section of Endocrinology and Internal Medicine, Department of Medical Sciences, University of Ferrara, Ferrara, Italy

Introduction
Tumor-induced osteomalacia (TIO) is a paraneoplastic syndrome due to an overproduction of fibroblast growth factor 23 (FGF23) by small and benign mesenchimal tumors. FGF23 increase causes hypophosphatemia, osteomalacia and muscle weakness. TIO is usually cured by tumour resection, but neoplasms may be unidentifiable/unresectable or the patient may refuse surgery. In these cases, medical treatment with high doses of oral phosphate and calcitriol is mandatory, even though it is usually insufficient to restore normal phosphate levels and is associated with low compliance. Burosumab is a human monoclonal antibody against FGF23 employed to treat X-linked hypophosphatemia(XLH), recently approved for TIO in USA. Maximum dose of Burosumab in XLH is 90 mg/2 weeks but there are no data on clinical efficacy and safety concerning the use of Burosumab in TIO
Case report
A 65 years old male presented to our attention for multiple non traumatic fractures (femoral neck, ribs, pelvic bone) and low bone mineral density. He was forced to use crutches because of pain and limb weakness, determining low personal autonomy and mobility. Biochemical evaluation showed hypophosphatemia (1.1 mg/dl), normal calcium and PTH, high ALP (514 U/l) and CTX (0.864 ng/ml), normal creatinine and low tubular phosphate reabsorption (80%), whereas c-FGF23 was elevated. After excluding drug-induced and genetic osteomalacia/-hypophosphatemia, a 68GaPET was performed, identifying a lesion at the I right rib as cause of TIO. The patient refused surgery, therefore Burosumab therapy was started (initial dose 0.3 mg/Kg, gradually increasing to 60 mg/2 weeks). After 2 years of treatment, biochemical evaluation showed phosphoremia normalization and ALP reduction (138U/l). Patient clinical symptoms improved: Brief Pain Inventory (BPI) scores decreased, indicating reduced pain severity (from 1 to 0,5pt) and pain interference (from 3 to 0,6pt) as well as reduced fatigue (Brief Fatigue Inventory from 35 to 6pt). Sit-To-Stand Test and 6-minute Walking Test also improved (from 14.83s and 372 m to 11.08s and 430 m respectively). No side effects nor tumour progression were reported during follow-up

Table 1

	Basal	2 years of treatment	Reference Range
Phosphoremia	1.1 mg/dl	2.8 mg/dl	2.5-4.5 mg/dl
Calcium	9.8 mg/dl	9.7 mg/dl	8.5-10.5 mg/dl
ALP	514 U/l	138 U/l	30-120 U/l
CTX	0.864 ng/ml	0.55 ng/ml	0,115 - 0,748 ng/ml
1,25(OH) 2vitamin D	180 pmol/l	63 pmol/l	36,5 - 216,2 pmol/l
Bone ALP	138 mg/l	72.7 mg/l	3-20,2 mg/l
TmP/GFR	0.85 mg/dL	1.53 mg/dl	2.47-4.18 mg/dl
TRP%	80%	97%	85-95%

Conclusions
Our experience supports efficacy and safety of the use of Burosumab every 2 weeks in TIO

DOI: 10.1530/endoabs.81.P288

P289

Hypercalcemia with positive calcium-sensing receptor (casr) autoantibodies

Romain Vankemmel[1], Hippolyte Dupuis[1], Pierre-Loup Herman[1], Nicole Fabien[2] & Marie-Christine Vantyghem[1,3,4]
[1]CHU Lille, Department of Endocrinology, Diabetology and Metabolism, Lille, France; [2]CHU Lyon, HCL-GH Sud, Department of Immunology, Pierre-Bénite Cedex, France; [3]Univ Lille, European Genomic Institute for Diabetes, Lille, France; [4]Inserm, Translational Research for Diabetes, UMR-1190, Lille, France

CaSR-autoantibodies may cause auto-immune hypercalcemia through either simple blocking or biased properties. The phenotype of this rare disease is most often acquired hypocalciuric hypercalcemia (AAH) (*Minanbres JCEM 2020, Makita JCI insight 2022*), but sometimes hyperparathyroidism (*Pelletier-Morel Intern Med 2008*), in elderly. Gender, auto-immune context is variable. Blood calcium may fluctuate, and acute exacerbations may be successfully treated with

prednisolone and/or calcimimetics. We present two cases of CaSR-antibodies-associated hypercalcemia with a different phenotype
Case#1
A 80-year-old women (BMI 29) had a history of cured endometrial cancer, auto-immune, thyroiditis and sclerodermic-like syndrome (Sjögren and Raynaud syndrome with severe hypertension, increased level of anti-nuclear centromeric autoantibodies ($1/512^{th}$)). In 2002, detectable CaSR-antibodies with normal calcemia (97 mg/l), hypocalciuria (78 mg/24 h), mild 25-OHvitamin D deficiency (21 pg/ml), normal PTH level (36 pg/ml) and moderate CD4 and B lymphopenia was disclosed in a systematic autoimmune screening, after an episode of oral candidosis, without identified pathogenic variant of the *AIRE* gene. In 2015, she was operated from breast carcinoma. In 2022, blood calcium level was increased (107 mg/l), with normal phosphatemia (37 mg/l), low 25-OH-vitamin D (25 ng/ml) and persistent anti-CASR and anti-nuclear autoantibodies. No parathyroid hypertrophy was identified on US examination.
Case#2
A 70-year-old lady, BMI 30, with a history of cured endometrioid uterine adenocarcinoma was referred for recurrence of hypercalcemia 12 years after a left upper parathyroidectomy with total thyroidectomy for a typical biological hyperparathyroidism profile with hypercalciuria and osteopenia, associated to multinodular goiter without thyroid antibodies. Morphological parathyroid investigations were discordant, but after surgery, blood calcium dropped from 119 to 95 mg/l and remained so until 2019, where a profile of hyperparathyroid-ism reappeared with the presence of renal lithiasis. There was no excess of 25 or 1-25-OHvitamin D. Calciuria, PTH and CaSR-antibodies levels were increased, without other positive auto-antibodies. The NGS study of the *MEN1, HRPT2, CASR, AP2S1, GNA11* and *GCM2* genes was negative. Morphological investigations remained discordant.
Conclusion
The presence of CaSR-autoantibodies in these 2 elderly female cases of hypercalcemia: without overt parathyroid adenoma, suggest an auto-immune component to this hypercalcemia. Case#1 had an asymptomatic profile of AAH in an autoimmune context with long-term preexisting CaSR-antibodies. Case#2 had a profile of hyperparathyroidism without autoimmune context except for CaSR-antibodies. Both had a neoplastic history. Measurement of CaSR-autoantibodies in atypical cases of hypercalcemia with discordant morphological investigations could help to orientate diagnosis towards an autoimmune cause and a medical treatment. The functionality of CaSR-antibodies may explain the different phenotypes.

DOI: 10.1530/endoabs.81.P289

P290

Utility of intraoperative parathyroid hormone monitoring to predict success of parathyroidectomy for primary hyperparathyroidism

Ana Rita Elvas, Andreia Fernandes, Joana Couto, Raquel G. Martins, Jacinta Santos, Teresa Martins & Fernando Rodrigues
Portuguese Oncology Institute of Coimbra, Department of Endocrinology, Coimbra, Portugal

Introduction
Parathyroidectomy is the only curative treatment for primary hyperparathyroid-ism (pHPT) and has been traditionally performed through bilateral neck exploration (BNE). However, with the use of intraoperative parathyroid hormone (IOPTH) assay along with preoperative localization exams, minimally invasive surgery can be performed with good surgical success rate.
Aim
To evaluate the usefulness of IOPTH assay in guiding adequate parathyr-oidectomy in patients with pHPT.
Materials and Methods
We retrospectively analysed the case records of patients who underwent parathyroidectomy for pHPT between 2003 and 2021 at our hospital. IOPTH monitoring was employed as an intraoperative tool to guide the surgical procedure. Blood samples were collected at pre-incision time and then 10–15 minutes after parathyroid gland excision. Successful surgery was defined as a drop of 50% or more in the IOPTH level, otherwise, BNE was performed. These results were compared to alternative strategies for IOPTH monitoring, including a 60% decline and reduction to parathormone (PTH) reference range values.
Results
A total of 99 patients were included. Post-excision PTH levels dropped $>50\%$ in 80 (80.8%) patients. 3 of 19 patients (15.8%) whose outcomes failed to reach curative criteria had confirmed multiglandular disease. Intraoperative PTH monitoring using our criteria showed a 91.7% sensitivity, 80% specificity and 89.9% accuracy. True positive among them were 77 (77.8%%), true negative 12 (12.1%), false positive 3 (3.0%) and false negative 7 (7.1%). If a normal PTH value was required as a criterion for cure, unnecessary BNE would have been performed in 32 patients (32.3%) and in 12 patients (12.1%) if a 60% decline was applied, compared with just 8 patients (8.1%) when using the previous criteria.
Conclusion
IOPTH in adjunct with other localizing studies was helpful for carrying out successful parathyroidectomy. The use of IOPTH had good sensibility in predicting cure for most of the patients with pHPT undergoing minimally invasive parathyroidectomy. The use of other criteria, such as 60% decline and normal PTH value 10–15 minutes after excision, was associated with higher rates of conversion to unnecessary BNE.

DOI: 10.1530/endoabs.81.P290

P291

Vitamin d status and bone health in adolescents and young adults with congenital adrenal hyperplasia

Ruta Navardauskaite[1,2], Kristina Semeniene[1], Neringa Umaraite[1], Emile Rudminaite[1], Aurika Vanckaviciene[3] & Rasa Verkauskiene[4]
[1], Lithuanian University of Health Sciences, Medical Academy, Department of Endocrinology, Kaunas, Lithuania; [2], Coordinating center for rare and undiagnosed diseases Lithuanian University of Health Sciences hospital Kauno Klinikos, Kaunas, Lithuania; [3], Lithuanian University of Health Sciences, Medical Academy, Department of Nursing, Kaunas, Lithuania; [4]Lithuanian University of Health Sciences, Medical Academy, Institute of Endocrinology, Kaunas, Lithuania

Background
Data on the effects of long term glucocorticoid (GC) treatment on bone mineral density (BMD) in patients with congenital adrenal hyperplasia (CAH) are controversial.
Objectives
To evaluate BMD and vitamin D status in adolescents and young adults with CAH in comparison with healthy controls.
Methods
32 patients with classical CAH (13 males; mean of age 26.0 ± 7.1 years (14.0–37.3) were compared to 32 healthy controls matched by age, gender, and Tanner stage of pubertal development. Body composition was evaluated in all subjects with DXA (Hologic Inc., Bedford, MA, USA).
Results
Mean vitamin D level was 50.1 in patients and 55.5 nmol/l in controls, $P = 0.35$. Eighteen (56.25%) patients and thirteen (40%) controls had vitamin D deficiency ($P = 0.21$). Vitamin D levels were inversely associated with age ($r = -0.29$, $P = 0.04$) and body mass index ($r = -0.282$, $P = 0.045$) in all subjects. Mean whole body and lumbar BMD Z-scores were similar in CAH and control groups (-0.57 ± 0.96 vs. -0.29 ± 0.9, $P = 0.27$, and -0.97 ± 1.0 vs. -0.6 ± 0.8, $P = 0.15$, respectively). In 12.5% ($n = 4$) of patients and 18.75% ($n = 6$) controls whole body BMD z-score was between -2 and -1 standard deviation (SD), $P = 0.5$ Whole body BMD z-score < -2 SD was found in 12.5% ($n = 4$) of patients and 0% controls, $P = 0.04$. There was no history of bone fractures in neither of study groups. In the CAH group, vitamin D levels and BMD Z-scores did not correlate with GC cumulative doses, 17-hydroxyprogesterone or testosterone (T) levels. Adjustment for T levels did not change the results.
Conclusions
Patients with CAH are at risk for the development of osteoporosis. In our study, BMD Z-score and vitamin D were not related to cumulative GC doses and markers of disease control.

DOI: 10.1530/endoabs.81.P291

P292

Parathyroidectomy decreases serum monocyte chemoattractant protein-1, and increases vitamin d metabolites in patients with primary hyperparathyroidism

Lingqiong Meng[1], chi su[2], Sue A Shapses[1], Stanley Z Trooskin[3] & Xiangbing Wang[4]

[1]Rutgers University, Nutritional Science, New Brunswick, United States; [2]Rutgers University, Graduate School of Biomedical Science, New Brunswick, United States; [3]Rutgers University-Robert Wood Johnson Medical School, General Surgery, Departments of Medicine and Surgery, New Brunswick, United States; [4]Rutgers University-Robert Wood Johnson Medical School, Division of Endocrinology, Department of Medicine

Background
Primary hyperparathyroidism (PHPT) is a common endocrine disorder accompanied by high cytokines and low total 25-hydroxyvitamin D [25(OH)D]. An inflammatory cytokine, monocyte chemoattractant protein-1 (MCP-1), is found to be higher in people with elevated parathyroid hormone (PTH), unlike other cytokines (1). Also, a rise in MCP-1 in response to high PTH is associated with bone loss (2). Parathyroidectomy (PTX) is the only cure for patients with PHPT. Whether the decline in PTH due to PTX leads to a decrease in MCP-1 and its effect on vitamin D metabolites remains unclear.
Objective
To investigate the effect of PTX on serum MCP-1 and vitamin D metabolites in patients with PHPT.
Methods
Patients with PHPT who underwent minimally invasive PTX were included. Serum samples were collected before and 3-month after surgery. Serum levels of calcium, PTH, vitamin D binding protein (DBP), total and free 25(OH)D, MCP-1, and C-reactive protein (CRP) were measured. Correlation coefficients and multiple linear regression models were used to assess relationships among PTH, vitamin D metabolites and cytokines.
Results
In 25 PHPT patients (age: 61 ± 11 years old; BMI: 31.0 ± 5.6 kg/m^2), levels of serum PTH and calcium were decreased (PTH: 118.6 ± 42.4 to 44.7 ± 25.2 pg/ml; Ca: 11.0 ± 0.6 to 9.6 ± 0.4 mg/dL; $P < 0.001$) to normal after PTX. Meanwhile, both total and free 25(OH)D were significantly increased (28.1 ± 10.2 to 37.9 ± 11.2 ng/ml; 4.9 ± 2.1 to 8.1 ± 3.8 pg/ml; $P < 0.001$), together with elevated DBP ($P < 0.001$) after surgery. The level of MCP-1 declined by 20% ($P < 0.001$), while CRP remained relatively stable after PTX. The PTH was negatively correlated with total and free 25(OH)D, and DBP ($P < 0.01$), however, positively correlated with MCP-1 ($P < 0.01$). The CRP (but not MCP-1) was found to be negatively correlated with both total and free 25(OH)D ($P < 0.01$).
Conclusion
These data show that the decline of PTH due to PTX down-regulates serum MCP-1, but not CRP. Also, PTX normalizes PTH and Ca level, and leads to an increase in DBP, total and free 25(OH)D, which appears to be independent of MCP-1. The role of MCP-1 on PTH, total and free 25(OH)D and bone in patients with PHPT remains unclear and further studies are needed.
References
1. Sukumar et al. (2011). The high serum monocyte chemoattractant protein-1 in obesity is influenced by high parathyroid hormone and not adiposity. JCEM. doi:10.1210/jc.2010-2781.
2. Siddiqui et al. (2017). Catabolic Effects of Human PTH (1-34) on Bone: Requirement of monocyte chemoattractant protein-1 in Murine Model of Hyperparathyroidism. Sci. Rep. doi:10.1038/s41598-017-15563-7.

DOI: 10.1530/endoabs.81.P292

P293

Bone mineral density (bmd) of ultra-distal radius: are we ignoring a valuable information?

Yair Schwarz[1,2], Inbal Goldshtein[3], Yehudit Eden Friedman[1,2], Naama Peltz-Sinvani[1,2], Michal Brodavka[4], David Kowal[1], Iris Vered[1,2] & Liana Tripto-Shkolnik[1,2]
[1]Sheba Medical Center, Division of Endocrinology, Diabetes and Metabolism, Ramat Gan, Israel; [2]Tel Aviv University, Sackler Faculty of Medicine, Tel Aviv-Yafo, Israel; [3]Maccabi Health Care Services, Maccabitech Institute of Research and Innovation, Israel; [4]Sheba Medical Center, Rheumatology Unit, Ramat Gan, Israel

Background
BMD measurement of a non-dominant arm is not routinely performed during dual-X-ray-absorptiometry (DXA) test. While 1/3 radius measurement is recommended under certain circumstances, ultra-distal compartment is not used for osteoporosis diagnosis or fracture risk assessment.
Aim
To evaluate the correlation of ultra-distal radius (UDR) BMD to prevalent fractures, fracture risk predicted by FRAX and diagnosis of osteoporosis by traditional sites.
Methods
Women who underwent a routine DXA (including non-dominant forearm in all patients) in a tertiary medical center were included in a retrospective cross-sectional study. Risk factors relevant to FRAX calculation were assessed via a self-administered questionnaire. Spearman correlation of UDR BMD to 10-year risks of major osteoporotic and hip fractures (assessed by FRAX) was explored. The possible added value of UDR BMD in explaining prevalent osteoporotic fractures was assessed using a multivariable regression model incorporating age and traditional osteoporosis diagnosis.
Results
The study included 1,245 women with a median age of 66 (IQR 59-73), of whom 298 (24%) had UDR T-score $\leq$ -2.5 and 154 (12%) reported prior fractures. UDR BMD was significantly negatively correlated with FRAX risk score for hip and major osteoporotic fractures ($R =$ -0.5 and $R =$ -0.41 respectively; $P < 0.001$). UDR T-score $\leq$ -2.5 was associated with higher fracture prevalence (19% vs 10%; $P < 0.001$), and remained significant after adjusting for traditional BMD and age (OR 1.49, 1.01-2.19;$P = 0.043$).
Conclusions
UDR BMD correlates both with prior fractures and with predicted fracture risks and might pose added value over traditional DXA sites.

DOI: 10.1530/endoabs.81.P293

P294

Genetic testing in patients with primary hyperparathyroidism before surgery

Magdalena Matejkova Behanova[1], Josef Vcelak[2], Jitka Moravcova[2], Kateřina Personová[1], Markéta Vaculová[3], Renata Chmelová[4], Kristýna Junková[5], Jana Ježková[6], Martina Fialová[3] & Petr Libánský[3]
[1]University Hospital Motol, Department of Nuclear Medicine and Endocrinology, Praha 5, Czech Republic; [2]Institute of Endocrinology, Department of molecular endocrinology, Praha, Czech Republic; [3]Univesity Hospital Motol, 3rd Department of Surgery, Prague, Czech Republic; [4]University Hospital Motol, Department of Pathology and Molecular Medicine, Prague, Czech Republic; [5]Institute of Endocrinology, Department of Molecular Endocrinology, Prague, Czech Republic; [6]General University Hospital in Prague, III. Internal Clinic - Endocrinology and Metabolism, Prague, Czech Republic

Introduction
Familial and hereditary forms of primary hyperparathyroidism (PHPT) represent a small minority of all patients with PHPT (5 – 10%). The surgical approach is different in such cases than in sporadic PHPT. Hereditary PHPT may be syndromic (multiple endocrine neoplasia: MEN – type 1, 2A or 4 and others) or nonsyndromic (familial isolated PHPT). The aim of the study was to identify and describe hereditary and familial forms of PHPT in patients referred to parathyroid surgery in our centre at University Hospital Motol Prague.
Patients and Methods
370 patients underwent parathyroidectomy for PHPT from January 2020 until December 2021. Familial PHPT was defined as the occurrence of PHPT at least in two first-degree relatives. Genetic testing was recommended in patients I) with familial PHPT, II) with PHPT onset $\leq$ 40 years of age, III) with recurrent disease, IV) with clinical presentation of MEN1 (PHPT and/or pituitary adenoma and/or gastroenteropancreatic neuroendocrine tumor). A total of 45 patients (33 female, 14 male) underwent genetic testing. The median age of PHPT diagnosis was 36 (range 15 - 62). 6 patients who were recommended for genetic testing did not participate. Genetic analysis was performed by next-generation sequencing of DNA obtained from peripheral blood. We sequenced the all exons and UTR regions of these genes: *AIP, AIRE, AP2S1, CaSR, CDC73, CDKN1A, CDKN1B, CDKN2B, CDKN2C, GATA3, GCM1, GCM2, GNA11, MEN1, PTH, RET, STX16.*
Results
We identified 11 different germline causal mutations in the MEN1 gene in 12 patients (2 patients were siblings): NM_130799.2:p.Pro32Arg; Asp70ProfsTer51; Ile85SerfsTer33; Asp123 MetfsTer31; Gln209Ter; Gln258Ter; Thr210Serfs-Ter13; Gln450His; Trp471Ter, c.1049+1G >C (change in mRNA restriction) and the loss of the entire MEN1 allele in one patients. Moreover we found a mutation in RET gene: NM_020975.4:p.Cys611Tyr. A variant of uncertain significance was identified in 5 patients.

Conclusion
Hereditary and familial forms of PHPT were found in 16 (4%) of all patients who underwent parathyroidectomy for PHPT in our centre. There may exist undiagnosed hereditary PHPT among those who have not been genetically tested. Germline mutations were detected in 13 patients (12 in MEN 1, 1 in RET – MEN 2A). Familial PHPT without detected germline mutation was found in 3 patients. 2 of them had variant of uncertain significance and further familial segregation study will be provided. Supported by Ministry of Health Czech Republic - DRO (Institute of Endocrinology - EÚ, 00023761)

DOI: 10.1530/endoabs.81.P294

P295

18Fluoro-choline PET/CT is a useful localization technique in patients with primary hyperparathyroidism

Laura Pierotti[1], Elisa Dinoi[1], Laura Mazoni[1], Matteo Apicella[1], Gabriele Materazzi[2], Luigi De Napoli[2], Stefano Bola[3], Alessio Faranda[1], Duccio Volterrani[3], Claudio Marcocci[1] & Filomena Cetani[1]
[1]Clinical and Experimental Medicine, University of Pisa, Endocrinology, Pisa, Italy; [2]Molecular Pathology and Critical Area, University of Pisa, Department of Surgical, Pisa, Italy; [3]Translational Research and New Tecnologies in Medicine, University of Pisa, Nuclear Medicine, Pisa, Italy

Primary hyperparathyroidism (PHPT) is a common endocrine disease mainly caused by a single parathyroid adenoma. Although the localization of the parathyroid adenoma is not a surgical criterion for parathyroidectomy (PTX), this is known to increase the cure rate and reduce the complication rate. Neck ultrasound and MIBI-scintigraphy are the first-line techniques to detect hyperfunctioning parathyroid tissue, however, they have some limitations including the operator-dependent sensitivity and limited utility in case of a deep-laying or ectopic parathyroid. Recently, it has been shown that parathyroid adenomatous cells are capable of capturing choline, making this molecule a potential tracer in parathyroid. The aim of our study was to evaluate the utility of ^{18}Fluoro-choline PET/CT in 43 patients with PHPT candidate for PTX with negative or inconclusive results on conventional imaging. All patients underwent neck ultrasound performed by an expert physician, double tracing MIBI SPECT/CT and ^{18}F-choline PET/CT. The latter both examinations were perfomed at the same site. Neck ultrasound was negative in 23/43 (53%) and inconclusive in 20/43 (47%) patients. MIBI SPECT/CT was negative in 36/43 (84%) and inconclusive in 7/43 (16%) patients. PET/CT was positive in 30/43 (70%), inconclusive in 3/43 (7%) and negative in 10/43 (23%) patients. Thirty-three patients underwent PTX, 22 mini-invasive approach, 11 open cervicotomy (1 for recurrence of parathyroid cancer, 1 for suspected parathyroid malignancy, 2 for multinodular goiter, 1 for concomitant thyroid malignancy, 4 for negative uptake and 2 for bilateral PET/CT uptake). The intraoperative PTH assay was performed in 29 cases and in all but one (96,5%) demonstrated a reduction greater than 50% of PTH levels from the highest basal value. The histology showed parathyroid adenoma in 28 (84%), parathyroid cancer in 2 (6%), papillary thyroid cancer in one and white cervicotomy in two cases. Of note, the two patients with bilateral uptake had the excision of only one pathological gland since at surgical exploration there was no evidence of other enlarged parathyroid gland. Conversely, one patient with only one abnormal uptake at PET/CT had the removal of two enlarged parathyroid glands that were both adenomas. Thus, 26 of 29 parathyroid lesions were true-positive and 3 were false-positive uptake. Overall, per-lesion sensitivity of ^{18}F-choline PET/CT was 81%, the positive predictive value was 90% and the accuracy was 75% for all parathyroid lesions. In conclusion, ^{18} F-coline PET/TC demonstrated a good diagnostic performance and it might be considered as a valid alternative in patients with negative/inconclusive conventional imaging.

DOI: 10.1530/endoabs.81.P295

P296

Risk factors for renal calcifications and determinants of hypercalciuria in patients with chronic, post-surgical hypoparathyroidism

Laura Mazoni[1], Antonio Matrone[1], Matteo Apicella[1], Paolo Piaggi[2], Federica Saponaro[1], Simona Borsari[1], Elena Pardi[1], Bianca Cosci[1], Isabella Biagioni[1], Piercarlo Rossi[3], Federica Pacciardi[3], Alessandra Scionti[3], Rossella Elisei[1], Claudio Marcocci[1] & Filomena Cetani[4]
[1]University Hospital of Pisa, Department of Clinical and Experimental Medicine, Pisa, Italy; [2]University of Pisa, Department of Information Engineering,, Pisa, Italy; [3]University Hospital of Pisa, Diagnostic and Interventional Radiology Unit, Pisa, Italy; [4]University Hospital of Pisa, Endocrine Unit 2, Pisa,

Conventional therapy with oral calcium supplements and activated vitamin D is the most diffuse and available therapy for chronic hypoparathyroidism (HypoPT). This treatment does not replace the lack of PTH and is associated with renal complications. We report the results of a case control study with a prospective design which included 178 adult patients with differentiated thyroid cancer treated with total thyroidectomy with a follow-up longer that 3 years after surgery: 89 with PoHypoPT treated with conventional therapy and 89 without PoHypoPT, matched for age and sex. Both groups were balanced for gender, age, time since thyroidectomy, supplementation with cholecalciferol, dose of levothyroxine and dietary calcium intake. Half of the patients were stable on treatment with calcitriol alone, 45% with calcitriol and calcium carbonate, and 4 with calcium carbonate alone. All patients underwent biochemical tests and renal ultrasound. Twenty-fou- hour urinary calcium, creatinine, sodium, potassium, chloride, sulfate, uric acid, phosphate, oxalate, citrate, volume and Ph were measured. The biochemical control of patients with PoHypoPT was satisfactory, but only one-third of patients was at target according to ESE guidelines. Patients with PoHypoPT, compared with those without PoHypoPT, had significantly lower alb-Ca and PTH and increased serum phosphate, calcium-phosphate product, and 24-h urinary calcium, but there was no difference in estimated GFR. Renal calcifications were detected in 26 (29.2%) patients with PoHypoPT and in 11(12.4%) without. We found a positive association between renal calcification and age ($P=0.03$) and plasma PTH ($P=0.01$), but no association with hypercalciuria or other urinary parameters. The median 24-h urinary calcium was significantly higher in patients with PoHypoPT than in those without (248 vs 162 mg, $P< 0.01$) Urinary calcium in patients with PoHypoPT was positively associated with serum calcium ($P <0.001$), urinary magnesium ($P <0.001$), and urinary volume ($P= 0.003$), and negatively associated with serum albumin ($P = 0.025$), urinary oxalate ($P <0.001$) and creatinine ($P= 0.008$). Our study confirms that conventional therapy in patients with chronic PoHypoPT is suboptimal. 24-h urinary calcium and the rate of renal calcification are higher in patients with chronic PoHypoPT compared with controls. We found no significant difference in renal function (eGFR) between patients with chronic PoHypoPT compared with controls. We found no association between renal calcification and hypercalciuria and/or other urinary stone risk factors. Further prospective studies including a large number of patients would be necessary to better define the risk factor for renal calcifications in patients with PoHypoPT

DOI: 10.1530/endoabs.81.P296

P297

Phenotype characterization of a PHEX non canonical splice-site mutation in a family affected by X linked hypophosphatemic rickets and efficacy of one-year Burosumab treatment in adult patients

Rosa Di Fraia, Lucia Digitale Selvaggio, Francesca Allosso & Daniela Pasquali
University of Campania L. Vanvitelli, Advanced Medical and Surgical Sciences, Napoli, Italy

X-linked hypophosphatemic rickets (XLH) is associated with mutations in *PHEX*, upregulation of FGF23, leading to hypophosphatemia, abnormal bone development and short stature. H-MAB to FGF23, Burosumab, is the new therapy for XLH. Among *PHEX* mutations, c.1586+6T >C, partially destroying the splice-site, is presumably associated to a mild phenotype not described so far. We describe two siblings bearing the *PHEX* c.1586+6T >C variant. **Case 1:** A 52y men, 152 cm tall (-3.4SDS), father of two pediatric patients, was referred after testing positive for same PHEX mutation found in the proband. Family history of a similar condition was negative, except for his sister. At 47y, after investigation on his affected daughters, an orthopedic consultation concluded for active rickets. He presented impaired mobility, district arthrosis, tibia vara, hypodisplasia of tooth enamel, and bilateral perceptive hearing loss. Six minutes walking test(6 MWT) showed reduced functional capacity. IQOLA-SF-36 showed poor QOL. X-ray found diffuse spondylarthrosis, coxosclerosis, dysmorphism of proximal femoral epiphyses and curvature of the diaphysis. The MOC-DEXA compatible

by gender and age. **Case 2:** A 47y woman, 143 cm tall (-3.34SDS). At 29y underwent surgery on right foot scaphoid bone and was diagnosed tibia vara. At 45y an orthopedic consultation concluded for active rickets. She showed skeletal malformations, waddling gait, diffuse polyarthrosis, hypodisplasia tooth enamel, and perceptive deep. 6 MWT showed reduced functional capacity. IQOLA-SF-36 showed poor QOL. They started conventional supplementation with active vitamin D, phosphate was added to calcitriol and suspended before Burosumab. Both patients started Burosumab (1 mg/Kg/die), after approval of the compassionate use since December 2020. Results: At start, **case 1:** showed: Ca 9.2 mg/dl, P 1.9 mg/dl, ALP 62U, PTH 31 pg/ml, vitD 44.1 ng/ml, Cau/24h 83 mg/24h, Pu/24h 512 mg/24h, after 1y of Burosumab, Ca 10,3 mg/dl, P 3,47 mg/dl PTH 63,5 pg/ml, 25OHVitD 7 ng/ml, Cau/24h 44 mg/24h, Pu/24h 86 mg/24. P increased of 46%, Pu/24h decreased of 84%. **Case 2:** showed Ca 9.2 mg/dl, P 1.9 mg/dl, ALP 62U/l, PTH 31 pg/ml, vit D 44.1 ng/ml, Cau/24h 83 mg/24h, Pu/24h 512 mg/24h, and after 12 months of Burosumab Ca 9,4 mg/dl, P 2,06 mg/dl, ALP 35U/l, PTH 33,6 pg/ml, 25OHVitD 10,6 ng/ml, Cau/24h 155 mg/24h, Pu/24h 75 mg/24h, P increased of 8%, Pu/24h decreased of 85%. After 1y of Burosumab they performed a IQOLA SF-36, and WOMAC showing a progressive and statistically significant improvement of physical, psychological condition. At 6 MWT the distance covered was significantly increased.

Conclusions

XLH due to c.1586+6T >C in PHEX is associated to a mild phenotype. Our data underline the importance of Burosumab treatment, capable to reduce a substantial disease burden also in adults.

DOI: 10.1530/endoabs.81.P297

P298

Evaluation of pth deprivation effects on spatial memory in a rat model of chronic post-surgical Hypoparathyroidism

Federica Saponaro[1], Francesca Ronca[1], Cristina Dettori[1], Sabina Frascarelli[1], Giulia Di Buono[1], Silvia Giacomelli[1], Grazia Chiellini[1], Marco Scalese[2], Filomena Cetani[3], Claudio Marcocci[3] & Riccardo Zucchi[1]
[1]Biochemistry Institute, Department of Pathology, University of Pisa, Pisa, Italy; [2]Institute of Clinical Physiology, National Council of Research, Pisa, Italy; [3]Endocrinology Unit, University Hospital of Pisa, Pisa, Italy

Introduction

Hypoparathyroidism (HypoPT) is a rare endocrine disease which is characterized by hypocalcaemia and undetectable or inappropriately low serum parathyroid hormone (PTH). Post-surgical HypoPT (PS-HypoPT) is the most common cause, caused by accidental parathyroid removal/injury during neck surgery. Conventional therapy with calcium and vitamin D analogues does not restore calcium homeostasis and patients with chronic PS-HypoPT complain with several complications. From a neuropsychological standpoint, patients with PS-HypoPT present cognitive and affective symptoms: the more plausible pathophysiological mechanism resides in a direct effect of PTH in the central nervous system (CNS), but these mechanisms are still not completely elucidated. The aim of this study was to evaluate the effects of PTH deprivation on CNS in an animal model (rat) of post-surgical hypoparathyroidism, by a cognitive/behavioural assessment approach.

Methods

A rat model (Sprague Dawley) of PS-HypoPT was obtained by the surgical removal of parathyroids at 5 weeks of age and treated with gluconate calcium 1% in drinking water to maintain normocalcemia. An experimental group of 15 PS-HypoPT rats and 15 healthy Sprague Dawley controls (WT) underwent biochemical testing (serum calcium) and behavioural testing namely Morris Water Maze – MWM-to assess spatial learning and memory at 9 weeks of age.

Results

PS-HypoPT animals treated with standard calcium therapy and controls did not statistically differ in serum calcium levels (11.5 ± 0.5 vs 11.2 ± 0.2, $P<0.001$) and body weight (320 ± 20 vs 335 ± 20 gr). At MWM, during the training test PS-HypoPT animals displayed a significantly worse performance compared to controls, as suggested by a higher escape latency parameter (1° day 23.8 ± 11.9 vs 14.6 ± 9.3 sec,$P=0.02$; 2° day 13.3 ± 11.6 vs 8.7 ± 4.7 sec,$P=0.02$; 3° day 14.5 ± 7.9 vs 11.01 ± 8.4 sec$P=0.01$). Both groups improved their results from the firs to the last day of training (escape latency PHPT 23.8 ± 11.9 vs 9.2 ± 4.5 sec $P<0.001$; WT 14.6 ± 9.3 vs 5.5 ± 0.6 sec $P<0.001$), even if PS-HypoPT group had a higher improvement compared to WT (multivariate analysis$P=0.04$) . In the last day at the probe test, PS-HypoPT group and WT did not differ for the principal parameter escape latency and for secondary parameters, namely time in platform zone, entrance in the platform zone, total distance and platform crossings.

Conclusions

Animal model of HypoPT shows an impairment in spatial learning and memory compared to WT; training could ameliorate this condition. Further studies are ongoing evaluating other cognitive functions in such a model and could help to understand the physiopathological bases of neuropsychological symptom in patients with HypoPT.

DOI: 10.1530/endoabs.81.P298

P299

Impact of body composition on skeletal health in subjects with Klinefelter's syndrome: a cross sectional study

Flaminia Carrone[1], Walter Vena[1], Andrea Delbarba[2], Letizia Chiara Pezzaioli[2], Paolo Facondo[2], Carlo Cappelli[2], Alessandro Pizzocaro[1], Gherardo Mazziotti[1,3], Andrea Gerardo Lania[1,3] & Alberto Ferlin[4]
[1]Endocrinology, Diabetology and Andrology Unit, IRCCS Humanitas Research Hospital, via Manzoni 56, 20089 Rozzano, Milan, Italy; [2]Unit of Endocrinology and Metabolism, Department of Clinical and Experimental Sciences, University Hospital of Brescia; [3]Department of Biomedical Sciences, Humanitas University, Via Rita Levi Montalcini 4, 20090 Pieve Emanuele, Milan, Italy; [4]University of Padova, Department of Medicine, Unit of Andrology and Reproductive Medicine

Background

There is growing awareness of skeletal impairment in individuals with Klinefelter syndrome (KS), involving both quantitative and qualitative alteration of the bone as well as an increased prevalence of vertebral fractures (VFs). Beyond hypogonadism, considerable evidence suggests that other factors may be responsible for the skeletal fragility observed in these patients. Abnormal body composition is a common finding in KS subjects, characterized by an unfavourable muscle/fat ratio with an increase in total and abdominal fat mass, but evidence of its relationship with bone health is scant.

Purpose

Based on the emerging evidence of a close relationship between bone and soft tissues with possible detrimental effect of body fat distribution on bone metabolism, we aimed at assessing the impact of body composition parameters on bone health in terms of bone mineral density (BMD), microarchitecture, and radiological VFs in adult subjects with KS.

Methods

Seventy-three adult males with KS were consecutively enrolled by two Endocrinology and Andrology Units (IRCCS Humanitas Research Hospital in Milan and ASST Spedali Civili in Brescia). Whole body dual-energy X-Ray Absorptiometry (DXA) was performed to assess lumbar spine, femoral neck and total hip BMD, trabecular Bone Score (TBS) and body composition. Prevalence of VFs was assessed by quantitative morphometry on lateral spine X-rays.

Results

Low BMD was observed in 16 patients (23%). No significant differences were found in body mass index (BMI) and several body composition parameters between KS subjects with normal and low BMD. Degraded TBS was found in 16 patients (26%) with a prevalence which resulted significantly higher in individuals with higher BMI ($P=0.001$), fat body mass (FBM) ($P<0.001$), visceral adipose tissue (VAT) ($P<0.001$) and/or fat mass index ($P<0.001$). VFs were detected in 14 patients (19%), without significant associations with BMD ($P=0.983$) and TBS ($P=0.371$). However, subjects with VFs had significantly higher percentage of truncal/leg fat ratio ($P=0.011$) as compared to those without VFs.

Conclusion

This study provides a first evidence that abdominal adiposity might be a determinant of VFs in KS patients, consistent with the working hypothesis that alterations in body composition could negatively affect bone health in this clinical setting. The value of TBS in predicting fractures in KS without possible interference of body composition remains to be clarified in future longitudinal studies.

DOI: 10.1530/endoabs.81.P299

P300

BCYRN/BC200: identification of a novel circulating biomarker of parathyroid carcinoma

Annamaria Morotti[1], Filomena Cetani[2], Giulia Passoni[3], Simona Borsari[4], Vito Guarnieri[5], Chiara Verdelli[6], Giulia Stefania Tavanti[7], Stefano Ferrero[8], Sabrina Corbetta[9] & Valentina Vaira[10]
[1]Department of Pathophysiology and Organ Transplantation, University of Milan, Milan, Italy; [2]Endocrine Unit, University Hospital of Pisa, Pisa, Italy; [3]Division of Pathology, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy; [4]Endocrine Unit 2, University Hospital of Pisa, Pisa, Italy; [5]Division of Medical Genetics, Fondazione IRCCS Casa Sollievo della Sofferenza, San Giovanni Rotondo (FG), Italy; [6]Laboratory of Experimental Endocrinology, IRCCS Istituto Ortopedico Galeazzi, Milan, Italy; [7] Laboratory of Experimental Endocrinology, IRCCS Istituto Ortopedico Galeazzi, Department of Biomedical, Surgical and Dental Sciences, University of Milan, Milan, Italy; [8]Division of Pathology, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Department of Biomedical, Surgical and Dental Sciences, University of Milan, Milan, Italy; [9]Endocrinology and Diabetology Service, IRCCS Istituto Ortopedico Galeazzi, Department of Biomedical, Surgical and Dental Sciences, University of Milan, Milano, Italy; [10]Division of Pathology, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Department of Pathophysiology and Organ Transplantation, University of Milan, Milan, Italy

Parathyroid carcinomas (PCas) are rare endocrine malignant neoplasia characterized by an abnormal PTH secretion and, consequently, severe and uncontrolled hypercalcemia. Clinically, the preoperative diagnosis can be misleading, because PCas share some molecular and clinical similarities with benign lesions and are often indolent. The histological diagnosis of carcinoma is achieved based on the presence of mitotic nuclear figures, capsular invasion, parenchyma infiltration, vascular invasion and, less frequently, distant metastasis. Moreover, there is no molecular biomarker that could support PCas diagnosis. LncRNAs are an important class of epigenetic regulators involved in both physiological processes and cancer development. Preliminary evidence suggested that lncRNAs could act as accurate prognostic and diagnostic biomarkers. Recently, we identified a long non-coding RNAs (lncRNAs) signature able to distinguish PCas from benign parathyroid adenomas (PAds) and normal parathyroid glands. Particularly, the lncRNA BCYRN1/BC200 emerged as an interesting candidate biomarker for the diagnosis of PCas. In gastric, colorectal and breast cancers BC200 expression is dramatically increased and positively correlates with distant metastasis, tumor size and clinical stage. We previously reported that BC200 is overexpressed in PCas tissues harboring *CDC73* gene inactivating mutations. Here, we found that BC200 is also upregulated in metastatic PCas ($n=4$) compared to the non-metastatic ($n=9$) parathyroid carcinomas. Then, we tested the hypothesis that circulating BC200 expression may provide a clinical and non-invasive biomarker to distinguish PCas from PAds. To this end, we analyzed circulating BC200 expression levels in serum samples from patients affected with PCas ($n=4$) and PAds ($n=22$) through digital PCR. All samples were collected prior parathyroidectomy. Our results show that BC200 counts are higher in the serum of patients affected with PCas compared to those detected in serum of patients harboring PAds. Moreover, serological BC200 counts positively correlate with circulating PTH and total calcium levels and age at diagnosis in PAds. Lastly, we analyzed circulating BC200 expression in the serum of 3 PCa patients before and after parathyroidectomy. BC200 counts are reduced in all 3 postoperative PCas serum samples compared to the preoperative specimens, suggesting its potential use also as a useful non-invasive biomarker in the clinical follow-up of PCa patients. These findings extend the knowledge on BC200 in parathyroid tumors, supporting its role as a novel tissue and circulating biomarker for PCas diagnosis.

DOI: 10.1530/endoabs.81.P300

P301

Assessment of the cardiovascular system in patients with primary hyperparathyroidism, including the role of aldosterone

Izabela Karwacka[1], Sonia Kaniuka-Jakubowska[1], Krzysztof Sworczak[2], Izabela Pisowodzka[2] & Marcin Fijałkowski[2]
[1]Medical University of Gdańsk, Department of Endocrinology and Internal Diseases, Gdańsk, Poland; [2]Medical University of Gdańsk, 1st Department of Cardiology, Gdańsk, Poland

Typical symptomatology of primary hyperparathyroidism (PNP) includes bone lesions and renal dysfunction in the form of recurrent nephrolithiasis but the symptoms of hypercalcemia may mimic other conditions, including cardiovascular diseases. The exact frequency of cardiac symptoms is not known. The study included 45 adult patients diagnosed with PNP, over 18 years of age, who were qualified for ptx. Laboratory tests included the determination of serum PTH, Ca, Pi and cardiac ECHO assessment of the heart, 24-hour recording of blood pressure using the Holter method and 24-hour Holter electrocardiography – the procedures were performed before the surgical treatment, and then as follow-up tests one month and six months after ptx; the follow-up ECHO assessment was performed 6 months after ptx. After ptx, the expected significant decrease in PTH concentration was achieved in all patients and the levels of Ca and Pi normalized ($P < 0.001$). The study group included 25 patients with hypertension (HT) (56%). Statistical significance was not achieved both in terms of BP change and the dipper/non-dipper parameters. The relationship between PTH and mean SBP and DBP was statistically significant. Patients were divided into two groups: patients with HT (25) and patients with normal BP (20) before ptx. After surgery, improvement in HT control was observed in 23 patients (92%); in this group it was found: BP normalization in 8 patients (35% in the improvement group), discontinuation or reduction of the amount of antihypertensive drugs in 13 patients (56% in the improvement group), achievement of the correct reduction of BP at night (non-dipper → dipper) in 14 patients (61% from the improvement group). In the analysis of ECG parameters before ptx and after surgery, a statistically significant change occurred in the QTc interval ($P < 0.001$). Among patients with SVBPs and VPBs before ptx, statistically significant improvement in SVBPs after ptx was observed. The QTc interval variable correlated with PTH and Ca before ptx. In ECHO, the IVS, LVEDD and LFEV did not differ statistically significantly between the tests before and after the procedure, whereas the parameters of RWT, LVM and LVMI differed statistically significantly – before the surgery they were significantly higher than after the surgery. The GLS value was significantly decreased in 27 (60%) patients after ptx. To conclude, the patients with PNP have a higher risk of cardiovascular diseases, observing the improvement of cardiological parameters after successful surgery.

DOI: 10.1530/endoabs.81.P301

P302

Patients' adherence and satisfaction from daily vs monthly vitamin D supplementation: results from a dedicated bone clinic

pnina rotman pikielny, Liat Barzilai-Yosef, Erez Ramaty, Sofia Braginski Shapira & osnat Tell-Lebanon
Meir Medical Center, Institute of Endocrinology, Diabetes and Metabolism, Affiliated with the Sackler Faculty of Medicine, Tel Aviv University Kfar Sava, Israel

Background
Vitamin D supplementation is an integral component of treating patients with osteoporosis/osteopenia. Data have shown that monthly vitamin D supplementation is not inferior to daily regarding target vitamin D levels. Moreover, it has been argued that monthly supplementation might increase adherence. Patients' adherence and satisfaction with daily versus monthly vitamin D supplementation have been hardly investigated. The current study evaluated osteopenic/osteoporotic patients' adherence and satisfaction from vitamin D supplementation after switching from monthly to daily (MtD) dosing and vice versa (DtM).
Methods
Ambulatory osteopenic/osteoporotic patients visiting the endocrine clinic at a tertiary medical center were asked to switch their vitamin D supplementation from MtD and vice versa. Total monthly dose remained unchanged. Patients answered questionnaires regarding socio-demographic and medical status, compliance with vitamin D dosing (Morisky Adherence Scale 8; MMAS-8), satisfaction with vitamin D regimen and physical functional status (OPAQ-15) at baseline and 6 months after switching. Each group was compared to its baseline characteristics and to the parallel group.
Results
Among 72 ambulatory patients recruited (mean age 71.5 ± 7.4, 91.7% female), 52 (72.2%) were switched from DtM treatment and 20 (27.7%) from MtD. 84.7% were taking anti-osteoporosis medications, 51.4% had a prior osteoporotic fracture and 76.5% were taking calcium supplementation. Baseline vitamin D level was 86.1 ± 17.2 nmol/l. Both groups expressed good baseline compliance (mean 98.1%) with vitamin D regimen (MMAS-8 score ≥ 8). Baseline satisfaction with vitamin D regimen was good: 74% and 77.7% from DtM and MtD dosing, respectively. Baseline physical status was good in 63.9% and moderate in 33.3%. After switching, satisfaction level, adherence to vitamin D

regimen, vitamin D level and functional capacity were not different compared to baseline. Yet, 68.8% of MtD and 52% of DtM patients wanted to remain on the current regimen. Among patients who experienced both regimens, 56.1% preferred daily and 43.9% preferred monthly.

Conclusion

Patients with osteopenia/osteoporosis had good adherence to monthly and to daily vitamin D regimens and expressed high level of satisfaction with them. All parameters remained stable after switching regimens. Most MtD patients preferred the new regimen. Additional large-scale studies are needed to evaluate the effects of various dosing regimens on patients' satisfaction and adherence.

DOI: 10.1530/endoabs.81.P302

P303

Systematic literature review of the renal and cardiovascular complications associated with chronic hypoparathyroidism

Olulade Ayodele[1], Felicia Castriota[2], Sheetal Sharma[3], Meenu Verma[3] & Elvira Gosmanova[4]

[1]Takeda Pharmaceuticals USA, Inc., Lexington, United States; [2]Takeda Pharmaceuticals USA, Inc., Cambridge, United States; [3]Parexel International, Mohali, India; [4]Albany Medical College, Albany, United States

Despite conventional treatment with oral calcium and active vitamin D, patients with chronic hypoparathyroidism (cHypoPT) can remain not adequately controlled (NAC) and have abnormal biochemistry, disease complications, or symptoms impacting quality of life. A systematic literature review (SLR) was conducted to evaluate the clinical burden for patients with cHypoPT, with an emphasis on patients with NAC disease. This abstract focuses on data related to renal and cardiovascular complications. Key biomedical databases (MEDLINE, EMBASE, MEDLINE In-Process, Cochrane Controlled Register of Trials and Cochrane Database of Systematic Reviews) were searched for pertinent studies from database inception to June 2020. Abstracts from 6 relevant congresses held from January 2017–June 2020 were searched to identify studies not published as full-text journal articles. Publication bibliographies were reviewed to identify additional sources. Eligible studies included adults with cHypoPT and were published in English, with no restrictions on study design or comparator. NAC patients were identified via ≥ 1 of the following: abnormal biochemistry, renal impairment, persistent symptoms affecting quality of life, and study-specific NAC definitions. Results were described per Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. Forty-nine studies from 91 publications were included in the SLR. Of these, 21 and 7 publications addressed renal and cardiovascular complications, respectively. Compared with the general population, patients with cHypoPT were at increased risk of renal insufficiency, renal failure, nephrocalcinosis, and nephrolithiasis. Nephrolithiasis and nephrocalcinosis were the most commonly reported renal disorders, with incidence ranging from 1.9%–48% in patients with cHypoPT. Impaired renal function and risk of renal diseases were positively related to cHypoPT duration. In one study, rates of renal disorders were significantly higher in patients with NAC vs adequately controlled (AC) cHypoPT ($P<0.01$). Patients with cHypoPT were at risk of cardiovascular outcomes including cardiomyopathy, congestive heart failure, ischaemic heart disease, and arrhythmia. Patients with cHypoPT had increased risk of both incident cardiovascular conditions and a composite cardiovascular endpoint compared with patients without cHypoPT (all $P<0.05$). Longer disease duration was associated with increased risk of cardiovascular complications, independent of disturbances in calcium-phosphate homeostasis. In one study, patients with NAC disease had significantly higher rates of cardiovascular disorders compared with patients who were AC, especially for cardiac artery calcification and QT prolongation. cHypoPT is associated with increased risk of renal and cardiovascular complications. Based on limited published data, patients with NAC disease may experience a higher clinical disease burden than patients whose cHypoPT is controlled.

DOI: 10.1530/endoabs.81.P303

P304

Weakening of short- and long-term verbal memory in patients with PHPT, evaluated by a neuropsychological approach

Federica Saponaro[1], Gaspare Alfi[2], Filomena Cetani[3], Antonio Matrone[3], Laura Mazoni[3], Matteo Apicella[3], Elisa Lai[2], Marco Laurino[2], Angelo Gemignani[2] & Claudio Marcocci[3]

[1]Biochemistry Institute, Department of Pathology, University of Pisa, Pisa, Italy; [2]Department of Pathology, University of Pisa, Pisa, Italy; [3]Endocrinology Unit, University Hospital of Pisa, Pisa, Italy

Introduction and aims

Primary Hyperparathyroidism (PHPT) is a common endocrine disease associated with hypercalcemia and elevated or inappropriately normal serum levels of PTH. Among PHPT manifestations, neuropsychological symptoms have been described, including depression, anxiety, loss of memory, impaired cognition, with a wide range (3-50%) depending on the study population. Neuropsychological/ccognitive symptoms in patients with PHPT have been evaluated as part of quality of life (QoL) assessment, mainly using validated self-administered questionnaires, such as 36-Item Short Form Health Survey (SF-36), WHO-5 Well-being Index Survey (WHO-5), which lack specificity. This study aims to evaluate cognitive functions of patients with PHPT compared to a control population, using a standardized neuropsychological approach.

Methods

Observational, monocentric study on patients with PHPT and controls, in whom a standardized neuropsychological assessment, focused on attentive functions and memory abilities was performed by a trained psychologist.

Results

Patients ($n=19$) presented a mild PHPT, and mean age 53.8 ± 11.45 years). Control population ($n=24$, mean age was 51.8 ± 10.87 years) was enrolled among patients with differentiated thyroid cancer in remission (or without residual disease), without Hypoparathyroidism and in good control under levothyroxine therapy, who were followed by Endocrine Unit (University Hospital of Pisa). Patients with PHPT had significantly worse performance at Digit Span Forward (mean score 5.41 ± 0.81 – 6.17 ± 1.64; P-value <0.05) test that provides a measure of verbal short-term memory span and Story Recall Test that provides a measure of auditory-verbal long – term memory. Regarding Story Recall Test the worse performance was confirmed both in immediate (mean score 4.54 ± 1.40 – 5.72 ± 1.46 P-value <0.05) and delayed recall (4.37 ± 1.30 – 5.44 ± 1.51; P-value <0.05).

Conclusions

Patients with PHPT might present a weakening in verbal short – and long – term memory. Further studies are ongoing to evaluate other cognitive functions and to correlate cognitive testing with biochemical parameters.

DOI: 10.1530/endoabs.81.P304

P305

Reliability of who fracture risk assessment tool (frax) and bone mineral density in predicting fractures in cancer patients under hormone deprivation therapies: a real-world clinical study

Walter Vena[1], Sara Piccini[1,2], Rebecca Pedersini[3], Flaminia Carrone[1], Deborah Cosentini[3], Paolo Zucali[2,4], Rosalba Torrisi[4], Alessandro Brunetti[1], Stella Pigni[1], Roberto Maroldi[5,6], Luca Balzarini[7], Andrea Gerardo Lania[1,2], Alfredo Berruti[3,5] & Gherardo Mazziotti[1,2]

[1]Humanitas Research Hospital, Endocrinology, Diabetology and Andrology Unit, Rozzano (MI), Italy; [2]Hunmanitas University, Department of Biomedical Sciences, Pieve Emanuele (MI), Italy; [3]ASST Spedali Civili di Brescia, Medical Oncology Unit, Brescia, Italy; [4]Humanitas Research Hospital, Cancer Center, Rozzano (MI), Italy; [5]University of Brescia, Department of Medical and Surgical Specialties, Radiological Sciences and Public Health, Italy; [6]ASST Spedali Civili di Brescia, Radiology Unit, Brescia, Italy; [7]Humanitas Research Hospital, Department of Radiology, Rozzano (MI), Italy

Background

Skeletal fragility is an important clinical issue in women with early-stage breast cancer and men with non-metastatic prostate cancer under hormonal hormone deprivation therapies (HDTs). Vertebral fractures (VFs) have been reported in a remarkable number of subjects exposed to HDT especially when the diagnosis of fractures is performed by a radiological and morphometric approach. Notably, prediction of fractures in this clinical setting is a challenge and determinants of fractures are still largely unknown. Current international guidelines rely on bone mineral density (BMD) and the WHO Fracture Risk Assessment Tool (FRAX) to identify cancer survivors at high risk of fractures to be treated in primary prevention, but their reliability in this setting of secondary osteoporosis seems to be inaccurate. In this study, reflecting the real-life clinical practice, we investigated the diagnostic performance of FRAX algorithm and BMD in identifying breast and prostate cancer survivors developing VFs during HDTs.

Methods
This cross-sectional study included 527 consecutive subjects (429 females with breast cancer, 98 males with prostate cancer; median age 61 years) at two referral centers in Italy. At study entry, all participants had been under HDTs for at least 6 months and none received bone-active drugs. Prevalence of VFs was assessed by a morphometric approach, in relationship with FRAX score, body mass index (BMI), BMD, age, duration and type of HDTs.
Results
VFs were found in 140 subjects (26.6%) with spine deformity index was significantly associated with duration of HDTs (rho 0.38; $P<0.001$). The prevalence of VFs was significantly higher in males with prostate cancer than females with breast cancer (45.9% vs. 22.1%; $P<0.001$). In females with breast cancer, VFs were significantly associated with FRAX score for major fractures [OR 1.07; $P<0.001$] after correction for age ($P=0.853$) and BMD ($P=0.097$). The best cut-off of FRAX score for major fractures for identifying subjects with VFs was 6.35%, with sensitivity and specificity of 62.0% and 61.9%, respectively. In males with prostate cancer, VFs were significantly and independently associated with BMI $\geq$ 25 Kg/m^2 (OR 11.86; $P<0.001$), BMD T-score below -1.0 SD (OR 7.89; $P=0.001$) and GnRHa plus abiraterone treatment (OR 20.28; $P=0.002$), after correction for age ($P=0.111$) and FRAX score for major fractures ($P=0.199$).
Conclusions
FRAX and BMD could be useful for predicting VFs in subjects undergoing HDTs, but the thresholds are lower than those applied in primary osteoporosis. Notably, high BMI is a determinant of VFs in males under HDT.

DOI: 10.1530/endoabs.81.P305

P306

Effects on bone mineral density and bone markers of the sequential treatment with teriparatide followed by zoledronic acid in patients with severe fractured osteoporosis: retrospective real-life data

Giorgia Dito[1], Chiara Degradi[2], Gregorio Guabello[3], Matteo Longhi[3] & Sabrina Corbetta[4]
[1]Endocrinology and Diabetology Service, IRCCS Istituto Ortopedico Galeazzi, Milan, Italy; [2]Endocrinology and Diabetology Service, IRCCS Istituto Ortopedico Galeazzi, Department of Pathophysiology and Organ Transplantation, University of Milan, Milan, Italy; [3]Rheumatology Unit, IRCCS Istituto Ortopedico Galeazzi, Milan, Italy; [4]Endocrinology and Diabetology Service, IRCCS Istituto Ortopedico Galeazzi, Department of Biomedical, Surgical and Dental Sciences, University of Milan, Milan, Italy

Osteoporosis is a chronic condition requiring long-term treatment; sequential treatment regimens with different agents represents an option aimed to increase bone mineral density (BMD) and then to maintain it. The loss of BMD occurring after withdrawal of teriparatide (TPT) can be prevented by bisphosphonates (BPs). Among BPs, data about the efficacy of zoledronic acid (ZOL) after TPT treatment are scanty. Here, we contribute to this topic providing data derived from the real-life setting of the third level centre Istituto Ortopedico Galeazzi in Milan. Twenty-two severe osteoporotic fractured patients [4 males, 18 postmenopausal females; aged 74.4 (65.8, 78.9) years, median, IQ range; BMI 26.1 $\pm$ 4.5 kg/m^2, mean $\pm$ SD] were treated with subcutaneous daily 20 microg TPT (according the Italian AIFA 79 note) for 24 months followed by two intravenous infusions of 5 mg ZOL, the first one at $<$ 6 months from TPT withdrawal, the second one 12 months from the first infusion. Eight patients were smokers; 7 patients were treated with chronic steroid therapy ($>$5 mg prednisone daily). Clinical and biochemical parameters were collected in all patients. BMD at lumbar and femur sites were measured by dual x-ray absorptiometry and recorded as T-scores. All patients experienced at least one vertebral fracture (3.0, 2.0-2.3). Mean lumbar T-score [-3.09 $\pm$ 1.18] increased after TPT treatment (-2.45 $\pm$ 1.33,$P=0.002$ by ANOVA) and the increase was consolidated by ZOL treatment (-2.17 $\pm$ 1.35,$P=0.0002$ vs basal condition by ANOVA). Mean lumbar T-score increase was 21% of the basal T-score after TPT and further 11% after TPT+ZOL. Median neck T-score [-2.70 (-3.30, -2.08)] was not affected by TPT [-2.50 (-3.00, -1.88)] as well as by TPT+ZOL treatment [-2.50 (-3.20, -1.78);$P=0.157$ by ANOVA]. Median total hip T-score [-2.40 (-2.90, -1.56)] increased after TPT+ZOL treatment [-1.75 (-2.48, -1.28);$P=0.049$ by ANOVA]. Any patient experienced incident fractures during TPT treatment, while 1 patient reported a femur fracture and one patient a non-vertebral non-femur fracture during ZOL treatment. During the sequential TPT+ZOL treatment serum calcium and phosphate levels did not show significant changes, while plasma PTH levels decreased during TPT and increased during ZOL treatment. Serum total ALP and β-CTX levels increased during TPT and decreases during ZOL treatment. Serum 25hydroxyvitamin D were constantly $>$20 ng/ml in all patients. In conclusion, our data from real-life management of severe osteoporotic patients showed that the sequential treatment TPT+ZOL is effective in increasing and maintaining lumbar and hip BMDs.

DOI: 10.1530/endoabs.81.P306

P307

Impact of underlying disease on long-term skeletal outcome after lung transplantation

Giorgia Grassi[1], Iacopo Chiodini[1], Elisa Cairoli[2], Letizia Corinna Morlacchi[3], Valeria Rossetti[3], Lorenzo Rosso[4], Ilaria Righi[5], Mario Nosotti[4], Maura Arosio[1], Francesco Blasi[4] & Cristina Eller Vainicher[6]
[1]University of Milan, Department of Clinical Sciences and Community Health, Milan, Italy; [2]Istituto Auxologico Italiano, IRCCS, Unit for Bone Metabolism Diseases and Diabetes & Lab of Endocrine and Metabolic Research, Milan, Italy; [3]Fondazione IRCCS Ca' Granda -Ospedale Maggiore Policlinico, Respiratory Unit & Cystic Fibrosis Adult Center, Milan, Italy; [4]University of Milan, Department of Pathophysiology and Transplantation, Italy; [5]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Thoracic Surgery and Lung Transplant Unit, Milan, Italy; [6]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Unit of Endocrinology, Milan, Italy

Background
fragility fractures (FX) occur frequently after lung transplantation (TX), with a higher rate (15-20%) in the first two years, which decreases subsequently. Patients affected from cystic fibrosis (CF) seem to have a lower FX risk in the first two years after TX as compared with those affected with other lung diseases (nCF). The aim of our study is to evaluate and compare the long-term skeletal outcome in CF and nCF patients after TX.
Methods
we evaluated the FX rate and the trend in bone mineral density (BMD) after the first two years post-TX in 67 patients (36 CF, 31 nCF). The mean follow-up duration was 5.4 (4-8) years and 37.3% patients (15% CF e 51.6% nCF,$P=0.023$) was taking bisphosphonates.
Results
2/67 patients (3%), both with TX rejection, had FX (1 FC 28 years old with hip FX and 1 nFC 65 years old with wrist FX). Lumbar spine (LS) BMD remained stable in both groups (-1.3 $\pm$ 1.1 vs -1.1 $\pm$ 1.1,$P=0.081$) and (-1.5 $\pm$ 1.0 vs -1.4 $\pm$ 1.1,$P=0.485$, CF and nCF respectively). Femoral neck (FN) and total hip (TH) BMD improved in CF group (-1.8 $\pm$ 1.0 vs -1.6 $\pm$ 0.9,$P=0.036$; -1.6 $\pm$ 0.9 vs -1.4 $\pm$ 0.8,$P=0.001$; respectively, FN, TH), conversely, FN worsened significantly and TH remained stable in nCF group (-1.7 $\pm$ 0.8 vs -1.9 $\pm$ 0.6,$P=0.018$; -1.3 $\pm$ 0.7 vs -1.3 $\pm$ 0.7,$P=0.666$; FN and TH respectively), in spite of a higher percentage of nCF patients taking bisphosphonates. The nCF disease was significantly associated with a worsening in both FN (OR 30.3$P=0.017$, 95%CI 1.8-500) and LS BMD (OR 11.5$P=0.027$, 95%CI 1.3-100) regardless of ongoing bisphosphonates therapy, cumulative glucocorticoids dose, age, TX rejection, spine deformity index.
Conclusions
our study confirms a low FX rate after the first two years post-TX. Also the long-term data suggest that the skeletal outcome after TX is more favourable in CF patients.

DOI: 10.1530/endoabs.81.P307

P308

The impact of age on quality of life and frailty outcomes after parathyroidectomy in patients with primary hyperparathyroidism

Theodosios S. Papavramidis[1], Panagiotis Anagnostis[2], Ioannis Pliakos[1], Georgios Tzikos[1], Angeliki Chorti[1], Kalliopi Kotsa[3] & Antonios Michalopoulos[1]
[1]1st Propedeutic Department of Surgery, AHEPA University Hospital, Aristotle University of Thessaloniki, Thessaloniki, Greece; [2]Aristotle

University of Thessaloniki, Unit of Reproductive Endocrinology, 1st Department of Obstetrics and Gynecology, Medical School, Thessaloniki, Greece; [3]Division of Endocrinology and Metabolism and Diabetes Center, First Department of Internal Medicine, Medical School, Aristotle University of Thessaloniki, Thessaloniki, Greece

Objective
Parathyroidectomy (PTx) improves quality of life (QoL) in patients with primary hyperparathyroidism (PHPT). Whether this effect is modified according to the patients' age is unknown. The aim of this study was to evaluate the impact of age on the effect of PTx on QoL and frailty in patients with PHPT, six months post-PTx.
Methods
This was a prospective cohort study, including patients with PHPT, admitted from January 2016 to December 2019, divided into two categories: younger ($\leq$65 years old) and older ($>$65 years old). QoL was assessed with the Pasieka questionnaire (PAS-Q) two days pre- and six months post-operatively. Frailty was also assessed at the same time intervals, with the Frailty Index (FI).
Results
One-hundred thirty-four patients (younger group: 96 patients, mean age 50.4$\pm$9.8 years; older group: 38 patients, mean age 72.1$\pm$4.9 years) were included. PTx resulted in a significant reduction in PAS-Q score in both groups. Notably, a greater reduction in 'mood swings', 'irritability', 'itchy skin' and 'feeling thirsty' PAS-Q domains was observed in younger group. In contrast, a greater decrease in 'bone-pain', 'tiredness', 'weakness', 'joint pain', 'getting off chair' and 'headaches' items was observed in older group. Moreover, PTx led to a decrease in FI only in this group.
Conclusions
PTx leads to an improvement in QoL both in older ($>$65 years) and younger ($\leq$65 years) patients with PHPT, attributed to a differential effect on PAS-Q items. Frailty improves only in the older group.

DOI: 10.1530/endoabs.81.P308

P309

Testosterone supplementation and bone parameters, a systematic review and meta-analysis study

Walter Vena[1], Giovanni Corona[2], Alessandro Pizzocaro[1], Vito Giagulli[3], Davide Francomano[4], Giulia Rastrelli[5], Antonio Aversa[6], Andrea Marcello Isidori[7], Rosario Pivonello[8,9], Linda Vignozzi[5], Edoardo Mannucci[10], Mario Maggi[11] & Alberto Ferlin[12]
[1]Humanitas Research Hospital,, Endocrinology, Diabetology and Andrology Unit, Rozzano (MI), Italy; [2]Azienda Usl, Maggiore-Bellaria Hospital, Medical Department, Bologna, Italy; [3]Santa Maria Hospital, GVM Care & Research, Bari, Italy; [4]Madonna delle Grazie Hospital, Unit of Internal Medicine and Endocrinology, Velletri (RM), Italy; [5]University of Florence, Andrology, Women's Endocrinology and Gender Incongruence Unit - Department of Experimental and Clinical Biomedical Sciences, Florence, Italy; [6]University Magna Graecia of Catanzaro, Catanzaro, Italy;, Department of Experimental and Clinical Medicine, Catanzaro, Italy; [7]Sapienza University of Rome, Department of Experimental Medicine, Rome, Italy; [8]Università Federico II di Napoli, Dipartimento di Medicina Clinica e Chirurgia, Sezione di Endocrinologia, Unità di Andrologia e Medicina della Riproduzione e della Sessualità Maschile e Femminile, Naples, Italy; [9]University of Naples, Chair for Health Education and Sustainable Development, Naples, Italy; [10]Azienda Ospedalireo Universitaria Careggi and University of Florence, Department of Diabetology, florence, Italy; [11]University of Florence, Endocrinology Unit "Mario Serio" Mario Serio" Department of Experimental and Clinical Biomedical Sciences, Florence, Italy; [12] University of Padova, Department of Medicine, Unit of Andrology and Reproductive Medicine, Padova, Italy

Background
Testosterone (T) is essential for bone health during all ages, helping to achieve a proper peak bone mass and, later, to maintain bone density and strength. Guidelines on management of male osteoporosis recommend testosterone replacement in young-adult hypogonadal to prevent bone loss and anti-resorbitive drugs in case of high fracture risk, but the role of T replacement therapy (TRT) alone in subjects with late onset hypogonadism is still the object of an intense debate.
Methods
All observational studies and placebo-controlled or -uncontrolled randomized trials (RCTs) comparing the effect of TRT on different bone parameters were considered. Studies using androgens other than T, as well as studies with concomitant treatment with other hormones and drugs were also excluded, unless there was a clearly defined treatment arm that received only T treatment. Similarly, studies including only patients with genetic causes of male hypogonadism were excluded.
Results
Out of 349 articles, 36 were considered, including 3103 individuals with a mean trial duration of 66.6 weeks. TRT improves significantly areal bone mineral density (aBMD) at the spine (mean +2.6%, 2-5.1%, CI 95%;P= 0,026) and femoral neck (mean +3.6%, 1-6.1%, CI95%;P=0,020) levels in observational studies, whereas placebo controlled RTCs showed a positive effect of TRT only at lumber spine (+2.2%, 0.4-4.8%, CI 95%;P= 0,097) and when trials included only hypogonadal patients at baseline (total testosterone $<$ 12 nM)(+5.2%, 0.7-9.7%, CI 95%;P=0,024). The effects on aBMD were more evident in subjects with lower T levels at baseline and increased as a function of trial duration and a higher prevalence of diabetic subjects. Either T or estradiol increase at endpoint contributed to aBMD improvement. TRT was associated with a significant reduction of bone resorption markers in observational but not in controlled studies.
Conclusion
TRT alone is able to inhibit bone resorption and increase bone mass, particularly at the lumbar spine level and when the duration is long enough to allow the anabolic effect of T and estrogens on bone metabolism to take place. However, whether or not TRT is associated with a decreased risk of bone fractures remains to be established.

DOI: 10.1530/endoabs.81.P309

P310

Impact of hypoparathyroidism on quality of life in patients with differentiated thyroid cancer

Ana Rita Elvas[1], Bernardo Marques[2], Joana Couto[1], Raquel G. Martins[1], Jacinta Santos[1], Teresa Martins[1] & Fernando Rodrigues[1]
[1]Portuguese Oncology Institute of Coimbra, Endocrinology, Coimbra, Portugal; [2]Hospital Egas Moniz, Endocrinology, Lisboa, Portugal

Introduction
Hypoparathyroidism (hypoPTH) is one of the most feared iatrogenic complications of the surgical treatment for thyroid cancer (TC). Despite supplementation with calcium salts and calcitriol, hypoPTH seems to be associated with a negative impact on quality of life (QoL), which has not been evaluated in the Portuguese patients.
Objectives
To evaluate the impact of hypoPTH on the QoL of Portuguese patients with TC and its correlation with serum analytical parameters.
Material and methods
Cross-sectional study of patients diagnosed with TC and chronic hypoPTH (persistent one year after surgery), randomly selected, compared to a control group of patients submitted to surgery for TC without hypoPTH. QoL was assessed using the SF-36v2 health questionnaire, validated for the Portuguese population (which includes eight scales: physical functioning (PF), role physical (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), role emotional (RE) and mental health (MH)). The levels of ionized and total calcium, albumin, phosphorus, magnesium, creatinine, urea, PTH, vitamin D, TSH and free T4 were measured. Hypothyroid patients were excluded. The information collected was analysed in SPSS®. Data was analysed with Independent Samples t Test and Pearson's correlation test.
Results
Of the 164 patients surveyed, 49 (29.9%) had hypoPTH and 78.7% were female. The mean age was 53.7$\pm$14.7 years. Patients with hypoPTH had statistically significant lower scores on the BP scales (55.8%$\pm$22.7 vs 63.4%$\pm$28.6;P=0.050) and SF (69.4%$\pm$25.5 vs 78. 6%$\pm$21.8;P=0.040) when compared to patients without hypoPTH. Regarding patients with hypoPTH, there was an inverse correlation between phosphorus levels and the scores of the GH (P=0.016), PF (P=0.006) and RP (P=0.020) scales; between age and scores of BP (P=0.017) and PF (P=0.019) scales. In these patients, lower PTH values were equally associated with worse results on BP scale (P=0.013).
Conclusions
This was the first study to assess the impact of hypoPTH on QoL in Portuguese patients. The results obtained suggest a relationship between phosphorus levels and QoL in patients with hypoPTH. Its monitoring seems particularly important in this population in order to identify more vulnerable patients, who may benefit from additional measures.

DOI: 10.1530/endoabs.81.P310

P546

Trabecular bone score captures low bone quality in women with normal bone mineral density or osteopenia initiating aromatase inhibitors for breast cancer

Matteo Malagrino, Paola Altieri, Uberto Pagotto & Guido Zavatta
Division of Endocrinology and Diabetes Prevention and Care, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Department of Medical and Surgical Sciences (DIMEC), Alma Mater Studiorum University of Bologna, Bologna, Italy

Introduction
Hypoparathyroidism Bone Score (TBS) has been associated with fragility fractures in post-menopausal women. Estrogen-receptor positive breast cancer is usually treated with aromatase inhibitors (AIs), with international guidelines recommending initial bone density (BMD) evaluation, since this therapy is associated with high rates of fragility fractures. Each Country has different thresholds of intervention to recommend pharmacologic treatment for fracture prevention. Patients with normal bone density or osteopenia often miss the chance of receiving any anti-osteoporotic treatment, beyond calcium and vitamin D.
Objective
To describe prevalence of low bone quality measured by TBS in women initiating aromatase inhibitors.
Design
Cross-sectional, observational.
Setting
University hospital.
Patients
From January to December 2021, 75 consecutive unselected ambulatory women with normal BMD or osteopenia referred from the Oncology Department for bone metabolism evaluation with a standardized protocol, after recent diagnosis of estrogen-receptor-positive breast cancer. The patients were naïve to any kind of osteoporotic treatment, including calcium or vitamin D3 supplements. History of clinical or morphometric fractures was an exclusion criterion.
Main outcome measures
TBS, BMD and biochemistries at first endocrine referral before the start of AIs. TBS T-score $\leq$ -2 was used to discriminate low bone quality.
Results
Twenty-five patients (33.3% of the whole cohort) aged 64.8 $\pm$ 10.7 had low TBS (1.238 $\pm$ 0.043). TBS negatively correlated with age (r=-0.41, $P<0.001$), time from menopause (r=-0.312,P=0.012) and positively associated with BMD at all sites (L1-L4, total hip and femur neck, $P<0.001$). TBS was positively associated with urinary calcium (r=0.238,P=0.047), and negatively with 25(OH)vitamin D levels (r=-0.243,P=0.033). By contrast, BMD was not associated with 25(OH) vitamin D levels. TBS showed no association with PTH, renal function or bone turnover markers. As opposed to TBS, lumbar spine BMD was negatively correlated with Beta-CTX (R=-0.231,P=0.047). Both femur neck BMD T-score (R=-0.233,P=0.044) and total hip BMD T-score (r=-0.299,P=0.009) were negatively associated with PTH levels.
Conclusions
A considerable proportion of women with normal BMD or osteopenia appears to present with low bone quality at the start of hormone adjuvant therapy for breast cancer. TBS could be used as a complementary quantitative clinical tool in the initial evaluation and management of these patients and might be adopted to recommend antifracture treatment in this gray zone. TBS might also be correlated with underlying bone metabolism indices.

DOI: 10.1530/endoabs.81.P546

P547

Effect of bisphosphonates on vertebral fractures in HIV infected males: 7-years study

Letizia Chiara Pezzaioli[1], Teresa Porcelli[2], Emanuele Storti[3], Andrea Delbarba[4], Giorgio Tiecco[3], Francesco Castelli[3], Carlo Cappelli[1], Alberto Ferlin[4] & Eugenia Quiros-Roldan[3]
[1]University of Brescia, Department of Clinical and Experimental Sciences, Unit of Endocrinology and Metabolism, Brescia, Italy; [2]Endocrinology, Montichiari Hospital, ASST Spedali Civili Brescia, Brescia, Italy; [3]University of Brescia and ASST Spedali Civili di Brescia, Department of Infectious and Tropical Diseases, Brescia, Italy; [4]University of Padova, 5Department of Medicine, Unit of Andrology and Reproductive Medicine, Padova, Italy

Objective
Osteoporosis and vertebral fractures (VFs) are frequently observed in HIV-infected men. Whereas bisphosphonates seem effective on bone mineral density (BMD) maintenance in HIV-men, data on VFs are lacking. We aimed to evaluate the long-term efficacy of bisphosphonates on VFs in HIV-infected men.
Design
Real-life longitudinal retrospective study on 118 consecutive HIV-infected males (median age at inclusion 53 years). Median time between first and second visit was 2 years, and between first and latest visit available was 7 years.
Methods
Inclusion criteria were age $>$18 years, HIV infection in stable conditions under antiretroviral therapy, no previous bisphosphonates treatment, blood samples carried out at the same laboratory, and three densitometric and morphometric assays performed with the same densitometer.
Results
At baseline, VFs were detected in 29/118 patients (24.6%), of which 18/29 (62.1%) were osteoporotic and 11/29 (37.9%) had osteopenia. Fractured patients were older (P.0.042), had longer HIV infection duration (P.0.046), antiretroviral exposure (P.0.025) and higher luteinizing hormone (LH) (P.0.044). Of the 29 patients already fractured at baseline, 11 (37.9%) developed new VFs during follow-up, of which 8 were under bisphosphonates treatment (P.0.018). Among the 89 patients without baseline VFs, 26/89 (29.2%) were osteoporotic, 50/89 (56.2%) had osteopenia and 13/89 (14.6%) had normal BMD. Of the 89 patients without baseline VFs, 11 (12.4%) developed VFs, being treated with bisphosphonates in only 2 cases (P.0.811). Overall, BMD remained stable over time and a progressive decrease of parathyroid hormone, bone alkaline phosphatase and C-terminal telopeptide was observed. Patients with worsened bone condition, both in term of BMD and VFs (n. 32), showed more frequently LH values $>$ 9.4 mIU/ml (P.0.046) and were more HCV coinfected (P.0.045). Noteworthy, 38.6% of the patients discontinued bisphosphonates, due to medical indication or personal choice, and 14.0% never started them.
Conclusions
We found that bisphosphonates were not completely effective in preventing VFs in patients already suffering from previous VFs, probably due to the multifactorial pathogenesis of fragility fractures in this population and also to poor adherence to medication.

DOI: 10.1530/endoabs.81.P547

P548

Disease characteristics, disability, and quality of life in adult HPP patients with muscular symptoms and pain without skeletal manifestations – a cross-sectional analysis from the Global HPP Registry

Kathryn M. Dahir[1], Gabriel Ángel Martos-Moreno[2], Agnès Linglart[3], Anna Petryk[4], Priya S. Kishnani[5], Cheryl Rockman-Greenberg[6], Samantha E. Martel[4], Keiichi Ozono[7], Wolfgang Högler[8] & Lothar Seefried[9]
[1]Vanderbilt University Medical Center, Nashville, United States; [2]Hospital Infantil Universitario Niño Jesús, Madrid, Spain; [3]Paris-Sud University, APHP and INSERM, Paris, France; [4]Alexion Pharmaceuticals, Inc., Boston, United States; [5]Duke University Medical Center, Durham, United States; [6]University of Manitoba, Winnipeg, Canada; [7]Osaka University, Suita, Japan; [8]Johannes Kepler University, Linz, Austria; [9]University of Würzburg, Würzburg, Germany

Background
Hypophosphatasia (HPP) is a rare, inherited metabolic disease caused by deficient activity of tissue nonspecific alkaline phosphatase (TNSALP).
Methods
Baseline/pretreatment data from the Global HPP Registry were analyzed to compare HPP disease burden between adults ($\geq$18 years of age) with skeletal manifestations (history of rickets, biopsy-proven osteomalacia, recurrent or poorly healing fractures/pseudofractures, etc; Skeletal group) and those with only non-skeletal manifestations (history of muscle weakness, fatigue, and/or pain; Non-skeletal group).
Results
Among 468 adults with HPP, 300 comprising the Skeletal group were compared with 73 comprising the Non-skeletal group (**Table**). The median number of body systems involved at baseline was higher in the Skeletal group than in the Non-skeletal group. Median 6-Minute Walk Test distance was similar between groups, although data in the Non-skeletal group were limited. Pain severity (Brief Pain Inventory-Short Form [BPI-SF]), disability (Health Assessment Questionnaire – Disability Index [HAQ-DI]), and quality of life (Medical Outcomes Study Short Form-36 Health Survey [SF-36]) were also similar between groups.

Conclusions
The impairment associated with pain, disability, and general quality of life in patients with HPP who had muscular/pain manifestations without overt bone disease was similar to that in adults who had any skeletal manifestations, regardless of HPP onset. Further analyses are required to understand the disease characteristics of these patients.

Table 1

	Skeletal ($n=300$)	Non-skeletal ($n=73$)
Age at baseline (years)		
n	300	73
Median (min, max)	50.1 (18.3, 81.2)	44.4 (19.3, 72.8)
HPP onset, n (%)		
Patients with data reported	299	72
Perinatal/infantile-onset	10 (3.3)	2 (2.8)
Juvenile-onset	126 (42.1)	16 (22.2)
Pediatric-onset, specific type unknown	29 (9.7)	6 (8.3)
Adult-onset	95 (31.8)	34 (47.2)
Unknown	39 (13.0)	14 (19.4)
Number of body systems impacted per patient		
n	282	73
Median (min, max)	3 (1, 8)	2 (1, 5)
6-Minute Walk Test, distance walked (meters)		
n	41	5
Median (min, max)	465 (180, 740)	466 (316, 580)
Pain severity (BPI-SF)[1]		
n	188	48
Median (min, max)	3.8 (0.0, 10.0)	3.6 (0.0, 9.5)
Disability (HAQ-DI)[2]		
n	191	48
Median (min, max)	0.4 (0.0, 2.7)	0.3 (0.0, 2.1)
SF-36 Physical Component Summary Score[3]		
n	191	47
Median (min, max)	40.1 (16.5, 64.7)	44.2 (17.9, 62.0)
SF-36 Mental Component Summary Score[3]		
N	191	47
Median (min, max)	42.4 (13.2, 62.3)	43.9 (20.4, 61.9)

Scales: [1]0-10, lower is less pain; [2]0-3, lower is less disability; [3]0-100, lower is more disability.

DOI: 10.1530/endoabs.81.P548

P549

Artificial intelligence based on radiomic analysis of lumbar spine computed tomography (ct) scan may improve accuracy in detecting osteoporosis

Emilia Biamonte[1], Federico Garoli[2], Riccardo Levi[3], Walter Vena[1], Flaminia Carrone[1], Simona Jafaar[1], Maurizio Fornari[4], Marco Grimaldi[2], Letterio Politi[2], Andrea Lania[1] & Gherardo Mazziotti[1]
[1]Humanitas Research Hospital, Endocrinology, Diabetology and Andrology Unit, Rozzano, Italy; [2]Humanitas Research Hospital, Radiology, Rozzano, Italy; [3]Humanitas Research Hospital, Rozzano, Italy; [4]Humanitas Research Hospital, Neurosurgery, Rozzano, Italy

Background
Osteoporosis is characterized by reduced bone mass and a compromised bone microstructure, leading to increased bone fragility and fracture risk. Currently, the gold standard for diagnosis is the bone mineral density (BMD) measurement by DXA. However, approximately half of fragility fractures occurs in the context of normal or slightly decreased BMD values.
Protocol
In this cross-sectional study, we performed an artificial intelligence (AI)-based analysis on radiomic of images of opportunistic computed tomography (CT) of lumbar spine in 240 consecutive subjects (mean age $61 \pm 14,5$, 130 males). Exclusion criteria were: 1) bone-active drugs; 2) neoplastic diseases; 3) spine surgical intervention; 4) spine trauma. Fifty-eight subjects had vertebral fractures (VFs) as assessed by a morphometric approach on CT or XR-ray spine (D4-L4) images. On CT images, the ROI was acquired as a 3D-spherical region of 9 mm in the middle of non-fractured lumbar vertebral bodies. A total of 93 RF were extracted: 19 first-order and 74 textural features. The most discriminative ones were selected by applying bootstrap recursive feature elimination procedures with random sampling for train/test split (100 iterations). The Linear Support Vector (LSV) model was adopted, and the Tree-Parzen Estimator Bayesian approach was employed. Results were evaluated on a stratified test set (25% of the total population), not included in the training phase. The final model was evaluated on the test set, using accuracy, sensitivity, specificity, and area under the ROC curve.
Results
Univariate analysis showed 20 significative RF ($P<0.05$), used to develop the LSV model. The model reached 0.83 of ROC, and the 71,7%, 78.0%, and 69,6 % of accuracy, sensitivity, and specificity respectively. Patients with VFs had significatively lower first-order features compared with those without VFs and were associated with textural features denoting a bone microarchitecture more rarefied and with higher inter-trabeculae distance. Furthermore, patients with a more compromised spine (SDI $\geq$ 2) had significatively lower first-order features compared with those without or with a mild VFs (SDI 0 and SDI 1) and, conversely, were significantly associated with textural features denoting a bone structure more rarefied and less coarse.
Conclusions
Artificial intelligence-based radiomic of lumbar CT scans identifies patients with skeletal fragility. If confirmed, these results may suggest that radiomics could be an important diagnostic tool in osteoporosis detection and in fragility fracture prediction in the next future.

DOI: 10.1530/endoabs.81.P549

P550

Biochemical parameters in metabolic bone disease of obese patients

Raquel Binda Pereira[1], Ana Carolina Santos[1,2], Joana Ferreira[1,2], Mário Rui Mascarenhas[3,4], Pilar De Quinhones Levy[1], Paula Barbosa[3,4] & Manuel Bicho[1,2]
[1]Faculty of Medicine, University of Lisbon, Genetics Laboratory, Ecogenetics and Human Health Group, Institute for Environmental Health (ISAMB), Lisbon, Portugal; [2]Scientific Research Institute Bento da Rocha Cabral, Lisbon, Portugal; [3]Faculty of Medicine, University of Lisbon, Institute for Environmental Health, Lisbon, Portugal; [4]Clinic of Endocrinology, Diabetes and Metabolism of Lisbon, Lisbon, Portugal

Introduction
Obesity is a pathological condition characterized by a low-grade systemic inflammatory state that predisposes to the onset of some diseases, such as hypertension, diabetes, and hyperlipidemia. Also, obesity can impact bone metabolism, but its effects are controversial.
Aims
This observational study aimed to evaluate and correlate the bone mass with the lipidic profile, adipocytokines, glucose metabolism, hepatic function and purine metabolism in obese patients.
Methods
372 obese patients were divided into three groups of bone mineral density (BMD) by DXA, according to the ISCD guidelines: normal (BMD-N; $n=103$), reduced (BMD-R; $n=168$), and osteoporosis (OST; $n=101$). The obesity classification was based on the fat mass index (FMI) criteria, accessed by DXA. In this classification, the body fat categories are divided into three classes, according to the sex- and race-specific reference ranges. Biochemical parameters were determined by standard methods. The Quantitative Insulin Sensitivity Check Index (QUICKI) was used to assess insulin sensitivity.
Results
The mean age was 62.4 ± 8.80 years, 72% were female, and, for obesity classification, 84,1% of patients were in class 3, 10,8% in class 2, and 5,1% in class 1. FMI was increased in BMD-N ($P<0.001$) compared to BMD-R and OST groups. The three classes of obesity and the lipid profile were similar between the three groups of BMD. The alanine aminotransferase was increased in the BMD-N group ($P=0.019$), while the other hepatic enzymes were identical between the groups. Regarding glucose metabolism, despite the similar glycemia, the insulin level was increased in the BMD-N group ($P=0.023$). By contrast, the QUICKI was decreased in the BMD-N group ($P=0.002$). Concerning the adipocytokines analyzed, adiponectin was reduced in the BMD-N group ($P=0.005$). The

uricemia was increased in the BMD-N group ($P=0.015$) and was directly correlated with insulin level ($P<0,001$, $r=0,313$).
Conclusions
In obese patients, impaired insulin sensitivity and increased purine metabolism suggested a protective role on bone, preserving its density.
DOI: 10.1530/endoabs.81.P550

P551

Relationship between serum Vitamin D and statin-associated muscle symptoms
Oksana Obertynska
National Pirogov Memorial Medical University, Vinnytsya, Department of Propedeutics of Internal Medicine, Vinnytsya, Ukraine

Muscle symptoms are the most common side effects of statin therapy and reasons for its discontinuation. Low serum vitamin D may contribute to statin-associated muscle symptoms (SAMS). The aim was to investigate the relationship between occurrence of SAMS and level of vitamin D (D), determine predictors of SAMS.
Methods
84 statin-treated patients were included in the study: 41 with SAMS (intolerant to ≥ 2 statins) and 43 patients without SAMS. We use SAMS clinical index (SAMS-CI) to determine SAMS. The vitamin D levels, parathyroid hormone (PTH), hematology and high sensitive protein (hsCRP) were performed.
Results
D was significantly lower (22.3 ± 12.20 ng/ml and 37.53 ± 10.21 ng/ml) and PTH was significantly higher (42.1 ± 14.2 and 30.4 ± 10.2 pg/l, $P<.001$) in patients with SAMS compared with those without SAMS. In 29% of patient with SAMS were observed vitamin D deficient (D < 20 ng/ml) and 43% had an insufficient D (21–29 ng/ml), while only 7% of patient without SAMS had vitamin D deficient and 11% an insufficient D. In patients with SAMS levels hsCRP was significantly higher ($P<.001$) and hemoglobin (Hb) concentrations were 0.5 g/dL lower than in patients without SAMS ($P<.05$). Regarding D, mean Hb were 1.2 g/dL lower in vitamin D deficient category than in adequate D category ($P<.001$). In multivariable modelling we have found an excellent correlation between D and SAMS-CI, Hb and hsCRP ($P<.001$; $P<.05$; $P<.05$; respectively). The correlation between vitamin D and hsCRP was highly significant ($r = -0.879$, $P<.001$) in patients with SAMS and less significant in patients without SAMS ($r = -0.402$, $P<.05$). It was shown that decreasing vitamin D levels are associated with increasing hsCRP levels (sign of inflammatory state) in non statin-treated patients. Age, D < 25 ng/ml, Hb < 12.5 g/dL and hsCRP > 3 mg/l at baseline had modest discriminative powers for predicting SAMS (0.56, $P<.01$; 0.45, $P<.01$; 0.542, $P<.001$; 0.712, $P<.001$; respectively).
Conclusion
We found an inverse association between vitamin D level and a statin-induced muscle symptoms in statin-treated patients. The prevalence of vitamin D deficiency 29% and an insufficiency D 43% in patients with SAMS. A low vitamin D concentration is accompanied by microinflammatory state and anemia risk. Age, lower level of vitamin D and Hb, higher level of hsCRP were identified as potential predictors of statin associated muscle symptoms. So, assessment of vitamin D status may be useful for the diagnosis and management of SAMS, especially in older patients with Hb < 12.5 g/dl and hsCRP > 3 mg/l.
DOI: 10.1530/endoabs.81.P551

P552

Parathyroid function index does not differentiate between Normocalcaemic primary hyperparathyroidism and Vitamin D deficiency associated secondary hyperparathyroidism
Mohsin S Siddiqui, Saradalekshmi Koramannil Radha, Sajid Iqbal, Adam Buckley & Nader Lessan
Imperial College London Diabetes Centre, Abu Dhabi, United Arab Emirates

Background
Normocalcaemic primary hyperparathyroidism (NPHPT) can be considered as an early biochemical manifestation of hypercalcaemic primary hyperparathyroidism (PHPT). Vitamin D repletion and exclusion of other conditions is recommended before diagnosing NPHPT. It is often challenging to distinguish Vitamin D deficiency associated secondary hyperparathyroidism (SHPT) from NPHPT and the two conditions may coexist. A parathyroid function (PF) index [(Parathyroid hormone (PTH) in pmol/l * Corrected Calcium in mmol/l)/ Phosphate in mmol/l] has been previously proposed as a reliable marker in distinguishing the two conditions. However, the patients in NPHPT group in that study were vitamin D deficient. We have evaluated the utility of PF index and other biochemical markers in a larger cohort of patients with or without Vitamin D replacement.
Methods
Patients were selected from electronic health records based on their consistently abnormal metabolic bone profile after exclusion of chronic kidney disease (eGFR < 60 ml/min/1.73 m^2), concomitant pregnancy, interfering drugs and conditions that could cause hypercalcemia. Patients were categorised into four groups: Classic PHPT ($n=60$), NPHPT in those with serum 25(OHD) > 50 nmol/l ($n = 329$), Vitamin D deficiency related SHPT ($n = 259$) and age matched healthy controls ($n = 118$). ROC analyses was performed to determine a reliable PF index cut-off between NPHPT and SHPT.
Results
The PF index was highest in the classic PHPT group in comparison to others [Mean(SD) was 37.95 ± 20.1 PHPT vs 21.51 ± 6.90 NPHT, 21.27 ± 6.91 SHPT, 9.36 ± 3.00 controls]. When comparing NPHPT with SHPT, AUROC was 0.51. In a separate analysis, when comparing pre-treatment PFindex between those who normalised their PTH after vitamin D repletion and those who did not, AUROC was 0.62. Thus, in patients with normocalcaemia, vitamin D deficiency and elevated PTH, PF index did not usefully predict which individuals would normalise PTH after vitamin D repletion and therefore did not distinguish patients with NPHPT from those with SHPT. Moreover, serum phosphate between the two groups was not significantly different.
Conclusion
After Vitamin D repletion, PF index did not discriminate NPHPT from those with Vitamin D deficiency related SHPT. Hence as recommended in recent guidelines, it is imperative to replace Vitamin D before diagnosing patients with NPHPT. Further studies are warranted to identify better markers for NPHPT so that they can be closely monitored for PHPT related bone and renal complications and thus referred for timely surgical intervention.
DOI: 10.1530/endoabs.81.P552

P553

Case report: an unusual presentation of hypercalcaemia in pregnancy
Scott Williams[1], Helmine Kejem[1], Sian Wynne[1], Jael Nizza[1], Rachel Tildesley[1], Susannah Shore[2] & Rebecca Lim[1]
[1]Wirral University Teaching Hospital NHS Foundation Trust (WUTH), Birkenhead, United Kingdom; [2]Liverpool University Hospitals Foundation Trust, Endocrine Surgery, Liverpool, United Kingdom

A 26-year-old Caucasian female presented at 14 weeks gestation with a 6-week history of lethargy, nausea and vomiting during her first pregnancy. Her adjusted Calcium was 4.12 mmol/l and parathyroid hormone (PTH) 26 pmol/l, consistent with possible primary hyperparathyroidism. She was previously well apart from occasional migraines. There was no known history of familial hypercalcaemia or MEN. Other biochemistry results revealed hypokalaemia of 3.2 mmol/l, low vitamin D at 16 nmol/l, raised 24-hour urine calcium at 8.11 mmol/24 hr, and a transient thyrotoxicosis, associated with hyperemesis gravidarum which later resolved. MEN screen negative. She was treated with intravenous isotonic saline and electrolytes deficiencies were replaced. She was also commenced on a maintenance dose of vitamin D with colecalciferol 400 units once daily. An ultrasound neck showed no evidence of parathyroid adenoma and a sestamibi nuclear medicine scan was contraindicated due to pregnancy. MRI neck was deemed not sufficiently sensitive to identify a small parathyroid adenoma. Her calcium level normalised prior to discharge. She was readmitted 3 weeks later with symptoms of generally unwell, nausea and vomiting, with an adjusted calcium of 3.41 mmol/l. Her calcium levels responded well to intravenous saline rehydration, and as she was now in her second trimester, she was referred to the tertiary centre hospital for exploratory neck surgery. This had demonstrated four normal parathyroid glands with no evidence of an adenoma. Working diagnosis was now towards an ectopic fifth parathyroid gland or mediastinal adenoma or possibly a placental-driven cause. Meanwhile, patient had struggled with recurrence of symptoms and persistent hypercalcaemia when not receiving aggressive intravenous rehydration. Following discussions with the patient and the multidisciplinary team across both tertiary and local hospitals, she was started on cinacalcet 30 mg twice daily. Her adjusted calcium had improved to 2.62 mmol/l. She later had spontaneous rupture of membranes and went into premature labour at

24 + 5 weeks gestation, delivering a live baby boy who needed care in the neonatal unit, in view of prematurity. Further investigations are underway, and placental histology is awaited. This case highlights the challenges of diagnosing as well as adequately treating hypercalcaemia in pregnancy. Hypercalcaemia is rare in pregnancy, and symptoms can be nonspecific and mimic those in early pregnancy. Therefore, it is important to have a low threshold in screening and early involvement of the multidisciplinary team with patient and her partner, in order to mitigate harm to both mother and fetus.

DOI: 10.1530/endoabs.81.P553

P554

Effect of glucocorticoid replacement therapy on bone mineral density in addison disease

Dhoha Ben Salah, Khouloud Boujelben, Kawthar El Arbi, Faten Haj Kacem Akid, Siddiqa Soomauroo, Mouna Mnif, Nadia Charfi, Mnif Fatma, Nabila Rekik Majdoub, Mouna Elleuch & Mohamed Abid
Hedi Chaker Hospital, Department of Endocrinology, Sfax, Tunisia

Introduction
Addison disease is associated with high risk of fractures and low bone mineral density. Causes are complex, including supraphysiologic glucocorticoid replacement therapy and concomitant autoimmune disorders. The aim of our study is to assess the influence of glucorticoid replacement therapy on bone mineral density in patients with Addison disease.
Patients and methods
Descriptive and analytical cross- sectional study including 50 patients with Addison disease. The incidence of osteoporosis and osteopenia were analyzed.
Results
The mean age of patients was 49,5 ± 13,9 years (40 females versus 10 males). Average duration of the disease was 13,9 ± 8,7 years (5-35 years). All patients were on hydrocortisone replacement, taking daily 27,4 ± 6,7 mg (15-42,1 mg) corresponding to 0,388 ± 0,128 mg/kg. Thirty-nine (78 %) patients received a mean daily dose of hydrocortisone greater than 11 mg/m^2. Mean cumulative hydrocortisone dose was 374,636 ± 283,821 mg (60 – 1184, 94 mg). The mean alkaline phosphatase level was 77,2 ± 28,5 I/l (15-190 IU/l). A total of 9 patients (18 %) had elevated alkaline phosphatase level after a mean disease duration of 14,9 ± 8,4 years and a mean cumulative hydrocortisone dose of 413;4 ± 348 mg/day. Mean mineral bone density at lumbar site and femoral neck was 0,928 ± 0,174 g/cm^2 (0,596-1,287 g/cm^2) and 0,945 ± 0,145 g/cm^2, respectively. Mean T-score at lumbar site and femoral neck was -1,61 ± 1,06 and -1,18 ± 1,33, respectively. Twenty-four (48 %) patients had reduced bone mineral density on osteodensitometry (less than 2 standard deviations [SD] of the mean value of an age-matched reference population). Twelve (24%) patients had osteoporosis.
Conclusion
Glucocorticoid replacement therapy in Addison disease may induce bone loss. Thus, glucocorticoid therapy must be adjusted to the lowest tolerable dose and regular measurement

DOI: 10.1530/endoabs.81.P554

P555

Thalassemia major: prevalence and risk factors for hypercalciuria

Ludovica Aliberti[1], maria rita gamberini[2], andrea ziggiotto[1], martina verrienti[1], Irene Gagliardi[1], Maria Chiara Zatelli[1] & Maria Rosaria Ambrosio[1]
[1]Section of Endocrinology and Internal Medicine, Department of Medical Sciences, University of Ferrara, Ferrara, Italy; [2]Day Hospital of Thalassemia, Department of Medicine, AOU Ferrara, Ferrara, Italy

Introduction
Thalassaemia syndromes are a group of inherited haemolytic disorders determining chronic anaemia, iron overload and organ damage (through the production of ROS), necessitating of iron chelation therapy. Nowadays, there is scant knowledge on hypercalciuria in thalassaemic Western patients. Therefore, aim of our study was evaluating the prevalence of hypercalciuria and identifying risk factors and clinical consequences associated with its development.
Methods
We enrolled 184 patients with β thalassaemia major (TM) aged ≥ 18 years old, regularly transfused and chelated, and followed up at the Day Hospital of Thalassemia of Ferrara. We excluded patients with severe renal failure, severe hepatopathy, primary hyperparathyroidism, hypoparathyroidism, genetic renal tubular diseases and neoplastic hypercalcemia. Females were not pregnant or breastfeeding. Hypercalciuria was defined by calciuria ≥ 4 mg/kg/day.
Results
The prevalence of hypercalciuria was 69.3% (females 52.5%, mean age 45 ± 7 years old). Hypercalciuric patients had lower ferritin as compared to normocalciuric patients (663,9 ± 766,9 vs 913,2 ± 1151,89 ng/ml, $P < 0.05$). Deferasirox was used mostly in hypercalciuric group (49.2%) rather than in normocalciuric one (28.6%) ($P < 0.05$). Plasma PTH, phosphate and uricemia were lower ($P < 0,05$) in hypercalciuric as compared to normocalciuric patients (PTH 24,1 ± 10,3 vs. 31,4 ± 16,1 pg/ml; phosphoremia 3,6 ± 0,5 vs. 3,8 ± 0,7 mg/dl; uricemia 4 ± 1,3 vs. 4,4 ± 1,4 mg/dl), whereas phosphaturia/24h was higher (0,9 ± 0,4 vs. 0,6 ± 0,3 g/day, $P < 0,05$) (iron mediated subclinical hypoparathyroidism associated with FGF-23 erythropoietin induced hyperphosphaturia?). Supplementation with oral calcium and cholecalciferol was similar in the two groups. Hypercalciuria was associated with a higher frequency of renal lithiasis, vertebral fractures and use of anti-osteoporotic therapy as compared to patients with normocalciuria. Bilateral renal lithiasis, hydronephrosis and nephrocalcinosis were found only in hypercalciuric patients.
Conclusions
Hypercalciuria is a frequent complication in TM. Deferasirox may cause hypercalciuria (through proximal renal tubulopathy) whereas supplementation with oral calcium/cholecalciferol was not associated with this complication. Our study hypothesize a role of 'FGF23 erythropoietin induced hyperphosphaturia' and 'subclinical hypoparathyroidism' in the pathogenesis of hypercalciuria. Hypercalciuric TM patients have to be monitored for the development of renal damage and osteoporosis.

DOI: 10.1530/endoabs.81.P555

P556

Fine-needle aspiration of parathyroid lesions prior to parathyroidectomy- a tertiary center experience

Pinchas Klein, Galit Avior, Ohad Cohen, Jacob Ilany, Rina Hemi, Ehud Barhod, Iris Vered & Liana Tripro-Shkolnik
Sheba Medical Center, Division of Endocrinology, Diabetes and Metabolism, Israel

Background
Parathyroid lesion aspiration as a preoperative adenoma localization tool is a matter of controversy. Concerns are being raised regarding both the immediate (hematoma, infection, alterations on a subsequent histologic preparate) and long term (seeding) safety.
Objective
To evaluate safety and efficacy of parathyroid fine-needle aspiration (FNA) with parathyroid hormone (PTH) washout as a localization of parathyroid lesions in patients with primary hyperparathyroidism.
Methods
We retrospectively reviewed all parathyroid FNA procedures performed by in a tertiary referral center between 2011 and 2021. Clinical, biochemical, and imaging information as well as cytology, surgery, and pathology reports were extracted from electronic medical records.
Results
Twenty-nine hyperparathyroid patients referred to parathyroidectomy following a positive localization with FNA -PTH washout were available for review. The indications for aspiration were re-confirmation of location (13/29), mismatch between imaging modalities (6/29), intra-thyroid lesion (4/29), previous neck operation (3/29) and unknown (3/29). PTH levels from the needle wash were 2.6-112.5 times the upper limit of serum norm. No immediate procedure complications except for mild neck discomfort were documented. Among 24 patients with an available pathology report, parathyroid adenoma was identified in 22, non-adenomatous parathyroid tissue in one and thyroid tissue in one patient.

No cases of hematoma or abscesses were reported by the surgeons, and no histologic alternations (hemorrhage, abscess, inflammation or capsule rupture) were reported by the pathologists. There was one case of necrosis and one case of parathyroid adenoma with fibrotic changes that may or may not be related to the FNA. Twenty-six (89.6%) of the 29 patients who underwent parathyroidectomy, were biochemically cured up to a follow-up of 41.6 ± 34.6 months.
Conclusions
Parathyroid FNA with PTH washout was accurate and neither immediate nor surgical or preparate-related complications were demonstrated in our series. This approach might be considered in selected cases.

DOI: 10.1530/endoabs.81.P556

P557

Hyperparathyroidism development after oncogenic osteomalacia treatment

Bohdan Patera, Federica Martina Bianchi, Ilaria Clementi, Gaia Francesca Maria Fazzino, Nicola Lanzo, Silvia Lepanto, Francesca Manzella La Barbera, Eliana Piantanida & Maria Laura Tanda
Ospedale di Circolo e Fondazione Macchi - ASST dei Sette Laghi, Department of Medicine and Surgery, Endocrine Unit, Insubria University, Varese, Italy

Tumor-induced osteomalacia (TIO) or 'oncogenic osteomalacia' is a rare paraneoplastic disorder, usually resulting from Fibroblast Growth Factor 23 (FGF23) oversecretion by a benign small 'phosphaturic mesenchymal tumor', causing hypophosphatemia and reduced 1,25-dihydroxyvitamin D synthesis. Calcium and parathyroid hormone (PTH) levels are usually normal, but secondary/tertiary hyperparathyroidism has been reported in up to 5% of the cases, mainly due to 1,25-dihydroxyvitamin D deficiency and long-term phosphate supplementation. Non-specific clinical manifestations (muscle weakness, osteomalacia, bone pain) and difficult localization of the tumor often delay diagnosis for years. Surgical removal represents the first-line treatment. We report a case of a patient with TIO, supplemented for years with phosphate salts, who developed hyperparathyroidism after tumor removal.
Case report
In 1987, after femur stress fracture, a 27-year-old man was diagnosed with 'phosphate diabetes' and then treated until 2010 with phosphate, calcium and vitamin D supplementation. The late onset of disease with no family history of hypophosphatemia nor skeletal deformities did not suggest hereditary conditions. Medical history included only beta-thalassemia trait. No further evaluation was made until 2010, when a small phosphaturic mesenchymal tumor was identified during investigations of non-healing tibial fracture. Histological specimens confirmed a FGF23-expressing neoplasia. Before surgery hypophosphatemic hyperphosphaturia with normal PTH, calcium and creatinine levels and borderline 25-hydroxyvitamin D were observed. Immediately post-surgery phosphatemia normalized. However, calcemia and PTH levels slowly increased and few months later the patient was diagnosed with primary hyperparathyroidism (PTH 110 pg/ml normal range 5-39, calcemia 11.1 mg/dl, mild hypophosphatemia, increased 1,25-dihydroxyvitamin D and reduced 25-hydroxyvitamin D levels). Neck ultrasonography and parathyroid MIBI-scintigraphy did not reveal adenomas. Exploratory cervicotomy was proposed, but the patient was lost at follow-up. In 2019 hypercalcemic hyperparathyroidism with hypophosphatemia and nephrolithiasis was observed (calcemia 10.5 mg/dl, phosphatemia 1.8 mg/dl, PTH 78 pg/ml, normal creatinine and 25-hydroxyvitamin D levels). FGF23 levels were normal. After negative imaging, exploratory cervicotomy with subtotal parathyroidectomy was performed; histology confirmed parathyroid hyperplasia. Post-surgery PTH fell to undetectable levels while phosphatemia normalized; treatment with calcium salts, calcitriol and Cholecalciferol was introduced.
Conclusions
TIO diagnosis should always be excluded when treating persistent hypophosphatemia, as tumor removal is usually curative. Long-term treatment with phosphate salts may induce secondary/tertiary hyperparathyroidism. Thus, phosphocalcic metabolism should be periodically evaluated during follow-up of surgically untreated TIO, but also after tumor removal, due to the possible hyperparathyroidism development.
References
Brandi et al. Challenges in the management of tumor-induced osteomalacia (TIO). Bone. 2021 Nov;152:116064. doi: 10.1016/j.bone.2021.116064. PMID: 34147708.

DOI: 10.1530/endoabs.81.P557

P558

Clinical and biochemical response to Burosumab treatment in two patients with X-linked hypophosfatemic rickets and tertiary hyperparathyroidism

Alberto Ghielmetti[1,2], Marta Zampogna[1,2], Serena Palmieri[2], Giorgia Grassi[2], Maria Rosa Caruso[3], Maura Arosio[1,2] & Cristina Eller Vainicher[2]
[1]University of Milan, Department of Clinical Sciences and Community Health, Italy; [2]Fondazione IRCCS Ca'Granda Ospedale Maggiore Policlinico, Unit of Endocrinology, Milan, Italy; [3]Azienda Ospedaliera Papa Giovanni XXIII, Unit of Nephrology, Bergamo, Italy

Introduction
in X-linked hypophosfatemic rickets (XLH) mutations of PHEX lead to elevated FGF-23 levels. Phosphate salts and calcitriol represented the only treatment option. Tertiary hyperparathyroidism (THPT) is a complication of XLH worsening the clinical features and constituting a contraindication to conventional treatment. Burosumab, a monoclonal antibody anti-FGF23, was recently approved in XLH. No data about Burosumab treatment in patients with XLH and THPT are available.
Patients
two patients (M 61, F 67 yrs) affected with XLH and THPT were treated with Burosumab (standard dose 1 mg/kg/28 days). Its compassionate use was approved by local Ethics Committees (Fondazione Ca'Granda Milan and Papa Giovanni XXIII Bergamo, Italy, for patients M and F, respectively).
Results
values at baseline in M and F, were, respectively, phosphoremia 1.4 and 1.4 mg/dl, Ca++ 1.53 and 1.39 mmol/l (1.13-1.32), PTH 76.4 and 91.75 ng/l (6.5-36.8), 25OHvitamin D 31.8 and 46.4 μg/l, creatinine 1.14 and 0.87 mg/dl, TmP/GFR 0.33 and 0.35 mg/dl, ALP 78 and 110U/l, CTX 846 and 902 ng/l. At 1 month: phosphoremia 2.27 and 2.2 mg/dl, Ca++ 1.57 and 1.45 mmol/l, PTH 95.2 and 70 ng/l, TmP/GFR 0.63 and 0.59 mg/dl, ALP 78 and 130 U/l, CTX 2250 and 1405 ng/l. At 6 months: phosphoremia 1.74 and 2.1 mg/dl, Ca++ 1.55 and 1.39 mmol/l, PTH 75 and 65 ng/l, TmP/GFR 0.41 and 0.52 mg/dl, ALP 78 and 130 U/l, CTX 1910 and 1605 ng/l. In both patients an improvement in myalgias, arthralgias and mood was noticed. At 6 months six-minute walk test in M improved (455 m vs 335 m at baseline, +36%). In M, after the introduction of cinacalcet at 3 months, calcium and PTH levels decreased without normalization and minimal effects on phosphoremia and TmP/GFR were observed. At 6 months in M we increased Burosumab dose to 1.2 mg/kg/28 days and the patient showed further improvement of symptoms at 9 months (pain assessed through VAS score decreased from 3 at 6 months and 5 at baseline to 2), despite persistent hypophosphatemia (phosphoremia 2.28 mg/dl, TmP/GFR 0.5 mg/dl).
Conclusions
Burosumab, in XLH complicated with THPT, ameliorates the symptoms, without normalizing phosphoremia, and in this subset of patients a higher dose may be needed. Clinical improvement despite hypophosphatemia could suggest a direct role of FGF-23 in the development of symptoms.

DOI: 10.1530/endoabs.81.P558

P559

Extreme hypercalcemia due to primary hyperparathyroidism– a look-back on over a decade in a tertiary care center

Reut Halperin, Yair Schwartz, Yehudit Eden-Friedman, Genya Hananel, Roi Shalit, Pini Klein, Ehud Barhud, Rina Hemi, Iris Vered & Liana Tripto-Shkolnik
Sheba Medical Center, Division of Endocrinology, Diabetes and Metabolism, Tel Hashomer, Israel

Background
Extreme hypercalcemia is an endocrine emergency. Given parathyroid hormone (PTH)-dependent cause, carcinoma should be suspected as a possible etiology. The prevalence of parathyroid carcinoma among patients presenting with extreme hypercalcemia is not well elucidated.
Aim
Establish proportion of patients with parathyroid carcinoma among those presenting with severe hypercalcemia and compare clinical and laboratory features between benign and malignant etiologies.
Methods
Admissions during 2009-2021 with serum calcium ≥ 14 mg/dl were identified via MD-clone platform. Cases with PTH < mid-reference range or serum creatinine

> 1.5 mg/dl were excluded. Clinical, biochemical and histological data were retrieved.
Results
Twenty-seven patients meeting an inclusion criteria were identified (44% males). Those constitutes 5.3% percent of severe hypercalcemia hospitalized during 2009-2021. Calcium level was 15.3 ± 0.3 mg\dl and PTH level 461 ± 66 pg\ml. Twenty patients (74%) were symptomatic (constipation, polyuria/polydipsia, change in mental status). Eleven (40%) had a precipitating event. Ten (37%) patients were referred due to abnormal laboratory. Twenty-one underwent parathyroidectomy, with pathology of adenoma/ hyperplasia in 19 and carcinoma in 2 cases. Long-term (up to 6 years) follow-up of 2 non-operated patients suggests benign etiology. Levels of PTH, calcium, albumin and creatinine were indistinguishable between etiologies. Age at presentation was 78 and 79 years for carcinoma compared with 57.6 years (19-82 years) in the adenoma\hyperplasia group.
Conclusions
Severe hypercalcemia is uncommon and PTH-dependent etiologies constitute a minority of those. Benign parathyroid disease was the most common etiology of severe PTH-dependent hypercalcemia. Due to the extreme rarity of parathyroid malignancy, significant clinical or laboratory predictors were not identified.

DOI: 10.1530/endoabs.81.P559

P560

Syringomyelia and neurologic symptoms as rare complications in untreated adult with X-linked hypophosphatemic rickets

Mihaela Tarna[1], Ana-Maria Stancu[2,3], Marian Andrei[1], Raluca Oprescu[1], Marina Iliescu[1], Iulia Soare[2], Anca Elena Sirbu[1,2], Luminita Nicoleta Cima[1,2] & Fica Simona[1,2]
[1]"Elias" Emergency and Universitary Hospital, Endocrinology, Bucharest, Romania; [2]"Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania; [3]National Institute of Endocrinology "C.I. Parhon", Bucharest, Romania

X-linked hypophosphatemia is a rare inherited disorder, yet the most common among the inherited causes of rickets. It is caused by different mutations in the PHEX gene leading to an impaired regulation of fibroblast growth factor 23 (FGF 23) and renal phosphate wasting. Patients with XLH show multiple musculoskeletal complications which usually can lead to early diagnosis in childhood. Nevertheless XLH is a lifelong disease, with multisystemic manifestations, including enthesopathies, dental and periodontal recurrent lesions, hearing loss, fractures and pseudofractures, muscle pain and diminished quality of life. We describe the case of a 21 years old male patient, misdiagnosed as vitamin D deficient rickets in infancy, with short stature, progressive bone deformities, leg bowing and waddling gait which required multiple orthopedic interventions. As a particular manifestation he accused episodes of moderate occipital headaches, aggravated with Valsalva maneuvers, and mildly impaired lower limb proprioception. MRI imaging showed a syringomyelic cavity at C5-T1, but with cerebellar tonsils above the foramen magnum. A few months later, episodes of bilateral upper limb paresthesia have appeared, so that repeated MRI monitoring is required and a neurosurgical approach should be considered. With this case we want to draw attention to the severe and rare neurological complications of this rare condition, and to the importance of long term follow-up with a multidisciplinary approach.

DOI: 10.1530/endoabs.81.P560

P561

Nutritional and clinical manifestations of normocalcemic hyperparathyroidism in women: interim results from a case-control cross-sectional study evaluating dietary calcium intake with three validated questionnaires

Matteo Malagrinò[1], Paola Altieri[1], Bart Clarke[2], Uberto Pagotto[1] & Guido Zavatta[1]
[1]Division of Endocrinology and Diabetes Prevention and Care, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Department of Medical and Surgical Sciences (DIMEC), Alma Mater Studiorum University of Bologna, Bologna, Italy.; [2]Division of Endocrinology, Diabetes, Metabolism, and Nutrition, Mayo Clinic, Rochester, MN 55905, USA.

Context
Normocalcemic hyperparathyroidism (NHPT) is considered as an earlier or milder phenotype compared to traditional primary hyperparathyroidism (PHPT). To make a correct diagnosis, secondary hyperparathyroidism due to low calcium intake must be excluded. Whether calcium intake might affect presentation of PHPT vs NHPT has never been addressed consistently.
Objective
To describe patients with a diagnosis of NHPT or PHPT in relation to their calcium intake, through three standard validated questionnaires.
Design
Cross-sectional study.
Setting
Outpatient, single academic medical center.
Patients
44 consecutive women recruited from March through December 2021. 22 patients with mild primary hyperparathyroidism (PHPT or NHPT) were age-matched with 22 women undergoing bone mineral evaluation for the first time due to recently diagnosed hormone-positive breast cancer. NHPT diagnosis was based on multiple determinations of both total calcium and albumin-corrected calcium within normal limits, as per current international guidelines.
Interventions
Administration of all the following: a validated local food-frequency questionnaire (LOC), International Osteoporosis Foundation Calcium Calculator (IOF) and National Osteoporosis Foundation Calcium Calculator (NOF).
Main outcome measures
Any association with biochemistries or clinical features.
Results
All three questionnaires confirmed that NHPT patients had similar calcium intake as compared with PHPT or controls. Calcium intake evaluated with all three questionnaires was not correlated with any biochemical index in NHPT nor PHPT, although it showed an association with hip T-scores in PHPT patients ($r = -0.821$, $P = 0.027$ for total hip T-scores). Maximum serum calcium reached over time (CaMax), SCa ranges and 24-Hour Urinary Calcium were significantly greater in PHPT than in NHPT. The remaining biochemistries and bone turnover markers were similar, even when compared with controls. Age positively correlated with calcium intake only in PHPT patients ($r = 0.630$, $P = 0.038$). Multivariate analysis investigating predictors of CaMax (age, BMI, albumin-corrected SCa, serum phosphate, GFR, calcium intake, PTH and 25(OH)vitamin D) showed that only albumin-corrected SCa predicted CaMax. GFR was a much milder positive predictor.
Conclusions
NHPT appears to represent a milder phenotype of PHPT. Presentation of NHPT is independent of calcium intake, when this is sufficient. The setpoint of albumin-corrected serum calcium probably determines the subtype of primary hyperparathyroidism, with greater values having greater chances of reaching calcium levels above normal, independent of other biochemistries.

DOI: 10.1530/endoabs.81.P561

P562

Serum 25-hydroxyvitamin D (25(OH)D) levels in Pregnant women with gestational diabetes mellitus

Edward Jude[1,2], Susan Mathew[1], Jennifer Heath[1], Denise Saw[1], Kate Meredith[1] & Roopa Krishnamurthy[1]
[1]Tameside and Glossop Integrated Care NHS Foundation Trust, United Kingdom; [2]The University of Manchester, Manchester, United Kingdom

Background
The importance of vitamin D supplementation in pregnancy is well known. Hypovitaminosis D is associated with adverse maternal and foetal outcomes such as pre-eclampsia, gestational diabetes mellitus, bacterial vaginosis, increased incidence of caesarean section delivery, intra-uterine growth restriction and reduced bone and muscle mass in childhood. The recommendations for vitamin D supplementation vary widely, with NICE guidelines suggesting a daily replacement dose of 400 IU/ day. The aim of this study was to determine whether the recommended replacement dose of cholecalciferol of 400 IU/day was sufficient to maintain normal vitamin D level (25(OH)D > 50 nmol/l) in pregnant patients.

Methods
Serum 25-hydroxyvitamin D (25(OH)D) levels of 129 pregnant women who attended the joint antenatal and diabetes clinic between 17/02/21 to 27/04/21 were analysed. All the patients were on standard vitamin D supplement of 400 IU/ day (pregnacare) from the time of antenatal booking. Blood was collected for 25(OH) Dat the time of oral glucose tolerance test at 26-28 weeks of gestation.
Results
The mean 25(OH)D level was noted to be suboptimal across the study population (47.92 nmol/l), with the mean in South Asians (43.99 nmol/l, $n=37$) lower than their Caucasian counterparts (49.50 nmol/l, $n=92$) ($P=0.0487$). Low 25(OH)D level (<50 nmol/l) was observed in 58.91% of the patients, more prevalent in South Asians (67.57%), compared to Caucasians(55.43%). Significantly reduced 25(OH)D (<30 nmol/l) was noted in 15.5% of the patients, also more prevalent among South Asians (21.62%) compared with Caucasians (13.04%).

Table 1 Distribution of Serum 25(OH)D levels among Caucasian and South Asian Pregnant Women.

	Caucasians ($n=92$)		South Asians ($n=37$)	
Serum 25(OH)D (nmol/l)	Number of women	Percentage (%)	Number of women	Percentage (%)
<30	12	13.04	8	21.62
30-50	39	42.39	17	45.95
>50	41	44.57	12	32.43

Conclusion
Our study suggested that vitamin D supplementation of 400 IU/day in pregnant women resulted in suboptimal 25(OH)D levels, more pronounced in South Asians compared to Caucasians. The results suggest the need to revise the guidelines for higher dose of vitamin D supplementation during pregnancy. Larger studies are required to validate the findings.

DOI: 10.1530/endoabs.81.P562

P563

Analysis of bone mass and body composition in transgender men at 1 year : a follow up study

Bruno Marcos Mazoca Orozco, Otavio Lima De Oliveira, João Victor Magliari Haddad, Livia Marcela Santos & Leonardo Alvares
University Center São Camilo, Brazil

Introduction
Sex steroid hormones play a key role in bone health, however medical therapies for gender dysphoria lead to hormonal changes.
Purpose
Understanding the change in bone mass and body composition is extremely important, because this treatment will be carried out over a long period of time
Methods
In a prospective study, we included 19 transgender men (female-to-male trans persons) before treatment and after 1 year of treatment with undecanoate (1000 mg i.m./12 weeks). Bone densitometry model Hologic-Discovery performed at baseline and after 6, 12 months of therapy. All participants signed the TCLE, project approved by CEP-CAAE: 36823220.6.0000.0062.

	Baseline	6 months	12 months	p value
Number of participants: 19				
Lumbar spine				
BMD±SD (mg/cm2)	1.075± 0.238	1.044± 0.117	1.052± 0.122	0,21
Z-Score± SD	-0.1±1.2	-0.1±1.0	-0.1±1.0	0,80
T-Score± SD	-0.3±0.9	-0.3±1.1	-0.2±1.1	0,53
Femoral neck				
BMD±SD (mg/cm2)	0.904± 0.121	0.918± 0.108	0.905± 0.107	0,98
Z-Score± SD	0.3±1.0	0.5±1.0	0.2±1.0	0,55
T-Score± SD	0.7±1.6	0.4±1.0	0.2±1.1	0,45
Total hip				
BMD±SD (mg/cm2)	1.017± 0.139	1.023± 0.134	1.032± 0.136	0,05
Z-Score± SD	0.4±1.0	0.5±1.0	0.4±1.1	0,70
T-Score± SD	0.6±1.0	0.6±1.0	0.4±1.1	0,09
Body composition				
Fat/m ^{2} (kg/m ^{2})	11.0±4.9	9.5±4.0	9.7±3.7	0.24
Total Fat (%)	38.8±6.7	34.5±7.1	34.9±9.0	0.09
Android / gynecoid fat ratio	0.93±0.16	0.94±0.17	0.94±0.18	0.13
VAT mass (g)	431.8± 262.1	401.8± 298.6	455.5± 322.7	0.17

Results
Analysis of 19 transgender men with a mean age of 24 years +/- 10 years. LS-BMD (lumbar spine) at initial time (0 m) 1,075±0,238 g/cm^2 and after 6 months (6 m) 1,044±0,117 g/cm^2 and 12 months (12 m) after 1,052±0.122 g/cm^2,$P=0.21$; FN-BMD (Femur Neck) 0 m= 0.904±0.121 g/cm^2; 6 m= 0.918±0.108 g/cm^2 and 12 m= 0.905±0.107 g/cm^2;$P=0.90$. TH-BMD (Total Hip) 0 m=1.017±0.139 g/cm^2; and 6 m= 1.023±0.134 g/cm^2; 12 m= 1.032± 0.136 g/cm^2;$P=0.05$. About body composition: the percentage of body fat: 0 m= 38.8±6.7%, 6 m=34.5±7.1%; 12 m=34.9±9.0;$P=0.09$; android/gynecoid ratio: 0.93±0.16, 6 m=0.94±0.17; 12 m=0.94±0.18$P=0.06$, VAT mass (cm3) 431.8±262.1, 6 m= 401.8±298.6, 12 m= 455.5±322.7 and Lean/Height^2 (kg/m^2) 0 m= 15.52±3.24 6 m= 16.15±2.19 kg/ m^2 ; 12 m= 15.86±2.22 kg/m^2; $P<0.01$ and Appen. Lean/Height^2 (kg/m^2) 6.92±1.74, 6 m= 7.32±1.22 and 12 m= 7.31±1.07; $P<0.01$
Conclusion
In 1 year of hormone therapy with testosterone, we did not observe significant differences in bone mass, but in body composition there was a gain in appendicular lean mass.

DOI: 10.1530/endoabs.81.P563

P564

Quantification of cerebral calcification and nephrocalcinosis in patients with hypoparathyroidism

Foteini Adamidou[1], Evagelos Chartampilas[2], Paraskevi Komzia[1], Panagiotis Prassopoulos[2], Marina Kita[1] & Theodosios S. Papavramidis[3]
[1]Ippokration General Hospital, Department of Endocrinology, Thessaloniki, Greece; [2] AHEPA University Hospital, Department of Radiology, Thessaloniki, Greece; [3]AHEPA University Hospital, A' Department of Surgery, Thesaloniki, Greece

Introduction
Various methods to quantify calcified coronary plaque have been used in common clinical practice in the past few decades to compliment cardiovascular risk assessment. The estimation of calcium load in other organs and conditions has been at best semi-quantitative. Patients with long-standing hypoparathyroidism are known to suffer with nephrocalcinosis and basal ganglia calcification. We attempted to quantify end-organ calcium burden in a series of patients with various forms of hypoparathyroidism by use of a modified Agatston score.
Patients and Methods
Five patients (4 females and one male, median age 30 years) with various forms of permanent hypoparathyroidism who had a noncontrast CT scan of the brain and/or kidneys as part of usual clinical care in the past three months were included. All CT imaging were performed on a GE Optima 660 scanner. The CT protocol included helical scanning with 0.625 mm slice thickness. The areal limit of detection was 0.1 mm^2 . Images were analyzed on a Philips workstation irrespective of whether calcium deposits were visible. The Agatston score algorithm (HeartBeat-CS, v4.1.7.22037) was modified to identify calcium-based stones using an attenuation threshold of 90 HU within the regions of interest (basal ganglia and renal medulla).

Results

Patients	Age	Condition	Duration	Treatment	Score Renal Medulla	Score Basal Ganglia
1	30	Mild Surgical hypoparathyroidism	4 years	Calcium 500 mg bid & vitamin D3 50.000IU bimonthly	0	NA
2	87	Idiopathic hypoparathyroidism	lifelong	Alfacalcidol 0.5 mcg/d	0.04	0.24
3	26	Severe Surgical hypoparathyroidism	10 years	rhPTH(1-84) 75 mcg/d	9.4	NA
4	34	Pseudohypoparathyroidism Type 1a	lifelong	vitamin D3 50.000IU bimonthly	NA	0
5	24	Severe Idiopathic hypoparathyroidism	7 years	rhPTH(1-84) 75 mcg/d	NA	260.3

NA: not performed

Conclusions

Application of an appropriately modified Agatston score may offer a practical means to accurately diagnose and follow changes in end-organ calcifications in patients with hypoparathyroidism at the point of care.

References

1) Sandfort V, Diagnostic and Interventional Imaging (2017) 98;3-10 2) Saha S et al, JCEM 105(4); April 2020: pp e1215e1224 3) Ketteler M etal, Adv Ther (2021) 38:1946–1957 4) Khan AA et al, European Journal of Endocrinology (2019)180, pp1–P23

DOI: 10.1530/endoabs.81.P564

P565

A case of severe hypercalcaemia secondary to primary hyperparathyroidism responding to steroids

Susan Mathew[1], Tracey Ellis[1] & Edward Jude[1,2]

[1]Tameside and Glossop Integrated Care NHS Foundation Trust, United Kingdom; [2]The University of Manchester, Manchester United Kingdom

Case History

A 57 year old male, who was known to have primary hyperparathyroidism was admitted to hospital due to hypercalcaemia on routine blood tests (adjusted S. calcium- 3.44 mmol/l.) He had no symptoms due to hypercalcaemia. This was his 5th admission since the diagnosis 18 months ago, each admission requiring treatment with IV fluids and IV bisphosphonates. SESTAMIBI and ultrasound scans of the thyroid and parathyroids had previously localised a likely right inferior parathyroid adenoma. Myeloma screen was negative. His past medical history included schizophrenia, vitamin D deficiency and psoriasis.

Treatment

He was initially treated with intravenous fluids, zolendronic acid and cinacalcet. Due to persistent hypercalcaemia, the dose of cinacalcet was increased to 60 mg TDS and intravenous calcitonin was added on. However, adjusted calcium remained around 3.4 mmol/l. He was hence re-referred to ENT surgeons for urgent parathyroidectomy. Unfortunately, he contracted COVID, which delayed the surgery. At this point, he was symptomatic with confusion, agitation, nausea, dehydration and abdominal cramps. He had repeat IV zolendronate 4 weeks from the previous dose and was also prescribed IV hydrocortisone 100 mg IV QDS 6 weeks into the hospital stay. The corrected calcium level reduced from 4.2 mmol/l to 2.2 mmol/l within a week. With the resolution of hypercalcaemia, his confusion resolved. He was switched to oral prednisolone 40 mg OD, which was slowly weaned down. His adjusted calcium levels started rising again shortly after the prednisolone was weaned. Three weeks later he had parathyroidectomy. Following this, his PTH level normalised from a peak pre-operative level of 660 pg/ml to 22 pg/ml post operatively. Two days following parathyroidectomy, he became hypocalcaemic with adjusted serum calcium of 1.92 mmol/l. He was discharged on 3000 mg of calcium carbonate and 1600 units of vitamin D3 daily. He was asymptomatic on follow-up.

Follow-up

The histopathology was suggestive of parathyroid carcinoma. He remains under endocrine and ENT follow-up.

Discussion

Parathyroid carcinoma should be suspected in cases with significantly raised PTH and resistant hypercalcaemia. Emergency parathyroidectomy should be considered in severe cases of hyperparathyroidism unresponsive to medical management. A trial of steroids may be useful as an adjunct in cases of severe resistant hypercalcaemia due to primary hyperparathyroidism, but remains an exception rather than the rule. The mechanism of action remains unknown. Potentiation of the action of calcitonin by upregulation of calcitonin receptors on osteoclast by steroids may be a plausible explanation.

DOI: 10.1530/endoabs.81.P565

P566

High prevalence of thoracic vertebral fractures in patients with medullary thyroid cancer

Luigi Di Filippo, Lucrezia Albanese, Laura Castellino, Mauro Doga, Anna Maria Formenti, Stefano Frara, Francesca Perticone & Andrea Giustina

Institute of Endocrine and Metabolic Sciences, Università Vita-Salute San Raffaele and IRCCS Ospedale San Raffaele, Milan, Italy

Medullary thyroid cancer (MTC) is a rare malignancy of the thyroid gland. MTCs originate from thyroid-C cells and account for 2-4% of all thyroid neoplasms. Originating from thyroid-C cells, the main secretory product of MTCs is calcitonin, used as sensitive and specific MTC-biomarker. Calcitonin is a hormone known to participate in calcium-bone metabolism suppressing bone-resorption by inhibiting the activity of osteoclasts, and inhibiting the kidney reabsorption of calcium and phosphorus. Despite these well recognized effects, little is known about skeletal health of patients affected by MTCs. Vertebral Fractures (VFs) are one of the most relevant clinical manifestations of skeletal fragility. To date, no data are reported in literature about VFs prevalence in patients affected by MTCs. The aim of our study was to investigate the VFs prevalence in patients with MTCs and in control-matched patients. VFs were detected on lateral chest X-rays using a qualitative and quantitative evaluation of vertebral shape. X-rays were performed prior the thyroid surgical treatment in MTCs patients and at hospitalization for infectious respiratory disease in control patients. MTCs and control patients were matched in a 1:1 ratio for age, sex and comorbidities, excluding those with comorbidities and therapies influencing bone metabolism. Sixty-two patients were included in the study, 31 affected by MTCs and 31 in control group. Median (IQR) age was 51 (38-66) years and 24 were male (38.7%). No statistical differences regarding age and sex were observed between the MTCs and control groups ($P=0.84$,$P=1$, respectively). VFs were detected in 9 (29%) MTCs patients and 2 (6.5%) control patients ($P=0.043$). In MTCs group, no statistical difference was observed regarding age between patients with and without VFs ($P=0.27$), and VFs were observed more frequently in male patients compared to female (50% vs 16%,$P=0.044$). No statistical associations were found between calcitonin levels and VFs occurrence. For the first-time to our knowledge, we have reported a high prevalence of VFs in patients affected by MTCs. It can be hypothesized that constantly elevated calcitonin levels directly or indirectly through changes in other parameters of bone metabolism may negatively impacts skeletal health.

DOI: 10.1530/endoabs.81.P566

P567

Remote management of osteoporosis in the first wave of the Covid-19 pandemic

Gianmaria Salvio[1], Claudio Gianfelice[2], Francesca Firmani[1], Stefano Lunetti[1], Rossella Ferroni[1], Giancarlo Balercia[1] & Gilberta Giacchetti[1]

[1]Azienda Ospedaliero-Universitaria Ancona, Clinica di Endocrinologia-Specialità Mediche e Chirurgiche, Torrette-Ancona, Italy; [1]Azienda Ospedaliero-Universitaria Ancona, Clinica di Endocrinologia-Specialità Mediche e Chirurgiche, Torrette-Ancona, Italy

We conducted a survey during the first pandemic wave of coronavirus disease 2019 (COVID-19) on a large group of osteoporotic patients to evaluate the general conditions of osteoporotic patients and the impact of the pandemic on the management of osteoporosis, finding high compliance to treatments and low COVID-19 lethality. In a telephone survey conducted from April to May 2020, patients from the Osteoporosis Center, Clinic of Endocrinology and Metabolic Diseases of Umberto I Hospital (Ancona, Italy) were interviewed.

Results

Of a total of 910 interview subjects, 892 provided consent to participate in the survey (response rate 98%), including 785 women (88%) and 107 men (12%) Among the 892 patients interviewed, 77.9% were taking osteoporosis treatment and 94.6% vitamin D supplementation as prescribed at the last visit. COVID-19-like symptoms were reported by 5.1% (44 subjects), whereas confirmed cases were 1.2% (10 patients). A total number of 33 patients had been in hospital and the hospitalization rate of those who had not discontinued vitamin D supplementation was less than 4%. There were eight deaths, two with a concomitant COVID-19 diagnosis. The COVID-19 patients (10, all female) were significantly older than non-COVID-19 subjects (79.9 ± 8.1 vs 70.8 ± 11.4 years, $P = 0.01$) but showed no significant differences in terms of comorbidities. The 2 patients who died of COVID-19 infection were both female; their family members said they were taking vitamin D, although dosing just before the lock down indicated vitamin D deficiency. The prevalence of severe osteoporosis was 50% in total COVID-19 patients and 87.5% in deceased COVID-19 patients. The overall COVID-19 mortality was 0.2%; lethality was 20%, lower than the national rate of the same age group. According to the logistic regression model considering only vitamin D supplementation, the supplement had a protective effect against the risk of hospitalization (OR 0.31, CI 0.11-0.84,$P = 0.02$).

Conclusions

Our frail patients followed up by phone felt reassured, they showed high treatment compliance, and experienced a lower COVID-19 lethality rate than patients of the same age; those who had not discontinued their vitamin D supplement also had a reduced hospitalization rate. The results of our survey, support a possible protective role of vitamin D against severity of COVID-19. The study moreover highlighted the critical value of telemedicine in the context of the pandemic as well as in the routine monitoring and care of old and frail patients and of those with chronic disease.

DOI: 10.1530/endoabs.81.P567

Diabetes, Obesity, Metabolism and Nutrition

P53

The investigation of serum and saliva phoenixin levels in patients with type 2 diabetes mellitus

Muhammed Burak Öz[1], Kader Ugur[2], Zeynep Dila Öz[3], Ramazan Fazıl Akkoç[4] & Süleyman Aydin[5]

[1]Faculty of Medicine, Firat University, Department of Internal Medicine, Elazığ, Turkey; [2]Faculty of Medicine, Firat University, Department of Internal Medicine (Endocrinology and Metabolism Diseases), Elazığ, Turkey; [3]Faculty of Medicine, Firat University, Department of Physiology, Elazığ, Turkey; [4]Faculty of Medicine, Firat University, Department of Anatomy, Elazığ, Turkey; [5]Faculty of Medicine, Firat University, Department of Medical Biochemistry and Clinical Biochemistry (Firat Hormones Research Group), Elazığ, Turkey

Purpose: Diabetes is one of the most common metabolic disease which has got many peptide hormones have in its etiology. Phoenixin (PNX), a recently discovered neuropeptide appears to have a role in energy management and metabolism through regulating insulin neogenesis and secretion, according to research. There is no research has been studied on the association between diabetes and PNX levels. The aim of the study was to see if there was a relation between PNX levels in the serum and saliva of patients with diabetes and HbA1c levels.

Materials and methods

A total of 100 participants were included in the study, with 80 patients divided into four groups based on HbA1c [Group 1: 5.7-6.4 % ($n = 20$), Group 2: 6.5-8.4 % ($n = 20$), Group 3: 8.5-9.9 % ($n = 20$), and Group 4: 10 % and above ($n = 20$)] and a control group of 20 healthy individuals. After at least 8 hours of fasting, venous serum and saliva samples were obtained from the patient and control groups., and HbA1c were measured. The levels of phoenixin in serum and saliva were determined by using the enzyme-linked immunosorbent assay (ELISA). The statistical analyses were performed with the SPSS 22 package program and also one-way Anova test and Pearson's correlation test were used. The significance value was taken as $p \leq 0.05$.

Result

When PNX serum levels were analyzed, it was shown that the prediabetic group (Group 1 (5.7-6.4 %)) had statistically higher levels than type 2 diabetes mellitus patients ($p \leq 0.05$). PNX salivary levels were found to be significantly higher than serum levels in the control and type 2 diabetes mellitus groups.

Conclusion

The PNX molecule is a neuropeptide that may be found in saliva and serum. It's thought that the prediabetic groups' higher serum PNX level is attributable to the effect of hyperinsulinemia, and that when overt diabetes occurs, it will be detected at a lower level in the serum related to relative insulin insufficiency. This leads us to believe that PNX is increased in order to control the higher glucose levels in the prediabetic group. Saliva PNX is expected to be favoured over serum PNX in future investigations on PNX metabolic pathways, as serum PNX is an invasive procedure.

Key words

Diabetes mellitus, peptide molecules, phoenixin, Hb1Ac

DOI: 10.1530/endoabs.81.P53

P54

Glucose prediction model based on continuous glucose monitoring in patients with type 1 diabetes mellitus: GlucoseML study preliminary results

Maria Christou[1], Daphne N. Katsarou[2], Eleni I. Georga[2], Christos Zisidis[1], Athanasios Siolos[1], Costas Papaloukas[3,4], Stelios Tigas[1] & Dimitrios I. Fotiadis[2,4]

[1]University Hospital of Ioannina, Department of Endocrinology, Ioannina, Greece; [2]University of Ioannina, Unit of Medical Technology and Intelligent Information Systems, Department of Materials Science and Engineering, Ioannina, Greece; [3]University of Ioannina, Department of Biological Applications and Technology, Ioannina, Greece; [4]University Campus of Ioannina, Biomedical Research Institute, FORTH, Ioannina, Greece

Introduction

Current guidelines emphasize the important role of Continuous Glucose Monitoring (CGM) for type 1 diabetes mellitus (T1DM) management. The aim of the GlucoseML study is the development of a mobile health system for T1DM self-management based on CGM data, physical activity, food intake and insulin dosage. We herein present the development and evaluation of a univariate Autoregressive Moving Average (ARMA) prediction model of interstitial glucose concentration for prediction horizons of 30-, 45- and 60-minutes.

Methods

CGM data (GlucoMen Day, Menarini®) from T1DM patients over a 4-week monitoring period under real life conditions were included in the analysis. Ambulatory Glucose Profile (AGP) report was computed for every patient. Categorical variables are expressed as number (percentage). Continuous variables with or without normal distribution are expressed as mean (standard deviation) or median (range), respectively. An ARMA (p, q) model, where p and q denote, respectively, the order of the AR and MA model of the ARMA equation, was identified upon the glucose data. The partial autocorrelation plot and the Akaike information criterion (AIC) were used to estimate the appropriate values of p and q orders in the model. The root mean square error (RMSE) and the mean absolute error (MAE), were used to evaluate the predictive performance of our models.

Results

Data were included for 29 T1DM patients (38% women) aged 38 years (12). Age at diagnosis was 15 years (2-45) and diabetes duration 20 years (11). Most patients were on insulin treatment with multiple daily injections [19 (66%)] compared to continuous subcutaneous infusion [10 (34%)]. Glycosylated haemoglobin was 7.4% (5.8-10.4). Based on AGP report, time below range (glucose $< 54, < 70$ mg/dl), time in range (70-180 mg/dl) and time above range ($> 180, > 250$ mg/dl) were 1.4% (0-10), 4% (2), 62% (21-82), 22% (6) and 8% (0.9-49), respectively. Average glucose was 150 mg/dl (130-247), glucose management indicator 6.9% (6.4-9.2) and glucose variability 39% (32-51). The RMSE for examined prediction horizons of 30-, 45- and 60-minutes was 9.04 (2.22), 11.84 (3.18) and 14.82 (3.87) mg/dl, respectively. Similarly, MAE was 6.48 (1.7), 9.04 (2.56) and 11.62 (3.38) mg/dl, respectively.

Conclusions
The predictive performance of the identified ARMA models compares favourably with that of existing models of similar or higher computational complexity. More advanced multivariate adaptive deep learning models are currently under way as part of the GlucoseML study. Further analyses are required, to test the model's predictive capacity in the critical region of hypoglycaemia.
DOI: 10.1530/endoabs.81.P54

P55

Prevalence of undiagnosed depression in patients with type 2 diabetes in central India
Bharat Saboo & Shweta Saboo
Prayas Diabetes Center, Indore, India

Introduction
Type 2 Diabetes Mellitus (T2DM) is the most common type of diabetes in adults, People with Diabetes usually have depression which is many times undiagnosed. Significant data suggest that depression in the context of diabetes is related to a variety of negative outcomes, including poor treatment adherence, decreased quality of life, deranged blood sugar values and HbA1c levels, and increased health costs.
Method
40 patients who consented to be part of the study were surveyed with **Patient Health Questionnaire (PHQ-9).** Patients with T2DM, between the age of 20 and 65 years and residing in Central India were included in the study. Exclusion criterion: Patients with type I DM, the previous history of psychiatric illness or on psychiatric treatment, a family history of depression. The responses were analyzed using MS excel.
Result
The overall depression prevalence PHQ-9 score $\geq$10 was 23%, with a higher prevalence of depression in T2DM females than males (25.5 vs. 21.5%, $P<0.0001$), We found a significant association between depression prevalence in T2DM patients and their education level more prevalent in lower education ($P<0.00001$) and employment status those not employed had higher rates of depression ($P<0.0001$).
Conclusion
This study is the first to examine depression in patients with T2DM in Central India. There is a need for the development of more awareness drives and academic programs for doctors on depression in T2DM patients. There should be a regular screening of patients with T2DM for depression which is mostly undiagnosed. Finally, new policies need to be established to focus on the mental health issues of patients with Diabetes. Which can lead to a better outcome in terms of Quality of life and disease outcome.
DOI: 10.1530/endoabs.81.P55

P56

"Correlation of biomarkers of early diagnosis of diabetic retinopathy"
Fazilyat Bakhritdinova[1], Firuza Urmanova[1] & Guzal Kengilbaeva
Tashkent Medical Academy, Tashkent, Uzbekistan

The purpose of the study is to assess the relationship of the level of growth factor level (VEGF) in blood serum with retinal microcirculation indicators according to oct-A data in patients with type 2 diabetes mellitus (DM2), with different stages of diabetic retinopathy (DR).
Material and research methods
252 people were examined ($n=504$), of which 168 patients with type 2 type and 84 practically healthy persons. The main group (I; $n=174$) with DM2, divided into subgroups, depending on the stage of DR: Easy non-proliferative DR (NDR), moderate NDR, severe NDR and PDR. As a comparison group (II; $n=162$), patients are included without clinical manifestations of others (III; $n=168$) - the control group was almost healthy faces without significant ophthalm and somatic pathology. All patients conducted a standard and specialized ophthalmological examination. Optical coherent tomography in the angio mode is made using an Optical Cherent Tomograph RevOFC with an angiography module with a 3×3 mm scan area. The level of VEGF in serum was evaluated by solid-phase immunoassay analysis using Quantikine ELISA sets.
Results
VEGF levels in blood serum in the studied groups showed a significant tendency to increase from 100.47±49.66 pg/ml (control group) to 463.18±78.69 pg/ml PDR ($P<0.001$). The increase in the VEGF indicator in the blood serum was revealed before the DR occurred clinically 137.29±84.45 pg/ml (comparison group). The average levels of VEGF at easy NDR (177.07±35.37), moderate NDR (255, 29±65.67), heavy NDR (424.34±56.67) also showed a tendency to increase. It was statistically established that the difference between all groups was significant ($P<0.05$). It was found that the VEGF level correlates with Oct-A ($P<0.05$).
Conclusions
The earliest marker of DR is to increase the average level of VEGF growth factor in the blood serum of patients 137.29±84.45 Pg/ml, which comes before the appearance of a clinical picture
DOI: 10.1530/endoabs.81.P56

P57

Diagnosis of gestational diabetes mellitus in the COVID-19 pandemic: comparative analysis of women with positive O'Sullivan test in the same trimester of 2019 and 2020
José Ignacio Martínez Montoro[1], Víctor José Simón Frapolli[1], María Molina Vega[1], Sonsoles Morcillo Espina[1,2], María Suárez Arana[3], Francisco J. Tinahones[1,2], María José & Picón César[1]
[1]Hospital Universitario Virgen de la Victoria/Instituto de Investigación Biomédica de Málaga-IBIMA, Endocrinology and Nutrition, Málaga, Spain; [2]CIBER Fisiopatología de la Obesidad y Nutrición-CIBEROBN, Spain; [3]Hospital Regional Universitario de Málaga, Gynecology and Obstetrics, Málaga, Spain

Introduction
In May 2020, during the COVID-19 pandemic, the Spanish Group of Diabetes and Pregnancy published a consensus document establishing the alternative diagnostic criteria for gestational diabetes mellitus (GDM) in case of impossibility to perform the two-step traditional approach due to the COVID-19 sanitary emergency. This study aims to compare different characteristics of pregnant women who tested positive in the O'Sullivan test in the same pregnancy trimester of 2019 and 2020 – in the latter trimester, alternative diagnostic criteria were applied due to the impracticability to perform the oral glucose tolerance test (OGTT) in our centre –.
Material and methods
Retrospective observational study comparing clinical data of pregnant women who tested positive in the O'Sullivan test in September-October-November 2019 (GDM diagnosis using 100-g OGTT) and 2020 (GDM diagnosis using basal glycaemia/HbA1c). GDM diagnosis was established if basal glycaemia was $\geq$100 mg/dl ($\geq$5.6 mmol/l) or HbA1c $\geq$5.9% in the first trimester; and basal glycaemia $\geq$95 mg/dl ($\geq$5.3 mmol/l) or HbA1c $\geq$5.7% in the second trimester
Results
Comparative characteristics of both groups are showed in table 1. Notably, in September-October-November 2019 41 women were diagnosed with GDM (16%

Table 1. Comparative characteristics of 2019 and 2020 groups

	2019 Group ($n=257$)	2020 Group ($n=268$)	p
Age (years)	33,6±6,38	33,93±5,01	0,535
Previous BMI(kg/m^2)	27,87±6,86	27,15±6,15	0,222
Primiparous	47.2%	41.9%	<0,001
Family history of GDM	24.9%	30.9%	0,139
Personal history of GDM	4.6%	11.3%	0,013
History of fetal macrosomia	2.1%	10.1%	0,001
O′Sullivan test (mg/dL)	160±16,7	159,41± 28,71	0,577
Glucose 0′ (mg/dL)	84,6±7,88	83,69±11,63	0,293
Glucose 60′ (mg/dL)	160,35± 29,81		
Glucose 120′ (mg/dL)	138,8±29,31		
Glucose 180′ (mg/dL)	109,60± 31,80		
HbA1c (%)		5,23±0,38	
OGTT gestational age(-weeks)	25,41±6,27	23,91±6,97	0,010
> 24 weeks	192(74,7%)	171(63,8%)	0,008
≤ 24 weeks	65(25,3%)	96(35,8%)	
GDM(number)	41(16%)	37(13,8%)	**0,489**
Treatment			**0,454**
Insulin	11(26,8%)	14(37,8%)	
Diet	29(70,7%)	21(56,8%)	
Metformin	1(2,4%)	2(5,4%)	

of women with positive O'Sullivan test) versus 37 in 2020 (13.8%), $P=0.489$. 10 of the women with GDM were diagnosed before week 24 in 2019 versus 17 in 2020 (15.4% vs 17.7%$P=0.699$); 31 of the women with GDM were diagnosed after week 24 in 2019 versus 19 in 2020 (16.1% vs 11.1%$P=0.165$). There were no differences between groups with regard to treatment modality during these comparison periods ($P=0.454$).
Conclusion
GDM diagnostic rate was similar using 100-g OGTT criteria (2019) and basal glycaemia/HbA1c criteria due to the COVID-19 pandemic (2020). Besides, there were no differences between periods concerning the number of patients that required pharmacological treatment.

DOI: 10.1530/endoabs.81.P57

P58

Study of change in physical activity behavior of diabetic patients after regular awareness sessions by primary care physicians

Aniket Inamdar
Samarpan Clinic, Internal Medicine, OMERGA, India

Background
Humans have been increasingly spending more time in sedentary behaviors such as prolonged sitting. Regular physical activity is associated with enhanced physical and mental health. Studies have shown that regular physical activity reduces the risk of cardiovascular diseases, diabetes mellitus, osteoporosis, depression and obesity. Patients frequently identify their family physicians as an important source of constant encouragement for physical activity.
Purpose
We wanted to assess the impact of regular awareness sessions about physical activity by Primary care physicians in diabetic patients.
Methods
73 diabetic patients between the age group 30 to 60 years were recruited in this single center study in rural India.70 participants completed this 6-month intervention study whereas 3 participants dropped out of study. Once in a month audio visual awareness session of one hour were conducted from August 2017 to January 2018 by primary care physicians to educate the diabetic patients about ill effects of sedentary lifestyle and benefits of regular physical activity. Pre and post intervention data were collected by using validated Godin leisure time exercise questionnaire from all 70 participants. Paired t test and Wilcoxon test were used to compare pre- and post-intervention data. Percentage increase in physical activity score was also calculated.
Results
In this study baseline Godin score pre intervention was 38.82 ± 12.22 (Mean $\pm$ SD) and post intervention was 65.98 ± 11.25 (Mean $\pm$ SD). Diabetic patients significantly improved Godin score post intervention which was statistically significant (**p: $<$ 0.001**). Compared to baseline pre intervention score, there was 170% increase in physical activity score post intervention.
Conclusions
Regular awareness sessions using modern technology by primary care physicians definitely showed positive change in physical activity behavior in diabetic patients. These regular sessions also helped to change the attitude and behavior about physical activity. Primary care physicians can play a significant role in counseling patients and promoting physical activity. Active involvement of primary care physician in this intervention further helped in establishing and continuing physical activity behavior. As primary care physicians have direct regular contact with their patients and their families, their role in promotion of physical activity will have more impact and long-lasting effect on diabetic patient's behavior. Similar studies are needed to assess impact of physical activity awareness sessions in diabetic patients.

DOI: 10.1530/endoabs.81.P58

P59

Impaired glucose homeostasis in a tau knock-in mouse model

Hamza Benderradji[1], Sarra Kraiem[2], Courty Emilie[3], Sabiha Eddarkaoui[2], Bourouh Cyril[3], Faivre Emilie[2], Rolland Laure[3], Caron Emilie[1], Besegher Mélanie[4], Oger Frederik[5], Boschetti Theo[4], Carvalho Kévin[1], Thiroux Bryan[1], Gauvrit Thibaut[1], Nicolas Emilie[6], Gomez-Murcia Victoria[1], Bogdanova Anna[1], Bongiovanni Antonino[7], Tailleux Anne[6], Lancel Steve[8], Bantubungi Kadiombo[6], Sergeant Nicolas[1], Annicotte Jean-Sebastien[5], Buée Luc[1], Vieau Didier[1], Blum David[1] & Buée-Scherrer Valérie[1]
[1]Univ. Lille, Inserm, CHU Lille, U1172 LilNCog - Lille Neuroscience & Cognition, Lille, France.; [2]Univ. Lille, Inserm, CHU Lille, U1172 LilNCog - Lille Neuroscience & Cognition, Lille, France; [3]Univ. Lille, INSERM, CNRS, CHU Lille, Institut Pasteur de Lille, Inserm U1283-UMR8199 - EGID,, Lille, France; [4]Univ. Lille, CNRS, Inserm, CHU Lille, Institut Pasteur de Lille, US 41 - UMS 2014 - PLBS, Animal Facility, F-59000 Lille, France.; [5]Univ. Lille, INSERM, CNRS, CHU Lille, Institut Pasteur de Lille, Inserm U1283-UMR8199 - EGID, F-59000 Lille, France.; [6]Univ. Lille, Inserm, CHU Lille, Institut Pasteur de Lille, U1011-EGID, Lille, France., Lille, France; [7]Univ. Lille, CNRS, Inserm, CHU Lille, Institut Pasteur de Lille, US 41 - UMS 2014 - PLBS, BioImaging Center Lille, F-59000 Lille, France, Lille, France; [8]Univ. Lille, Inserm, CHU Lille, Institut Pasteur de Lille, U1167 - RID-AGE - Facteurs de risque et déterminants moléculaires des maladies liées au vieillissement, F-59000 Lille, France., Lille, France

Introduction
Alzheimer disease (AD) is the leading cause of dementia. While impaired glucose homeostasis has been shown to increase AD risk and pathological loss of tau function, the latter has been suggested to contribute to the emergence of the glucose homeostasis alterations observed in AD patients. However, the links between tau impairments and glucose homeostasis, remains unclear.
Objective
In order to better understand the links between tau and glucose homeostasis, the present study aimed at investigating the metabolic phenotype of a new knock-in (KI) mice model.
Method
Males and females Tau KI mice model expressing a human tau protein bearing the P301L mutation under the control of the endogenous mouse *Mapt* promoter and their non-transgenic littermates (referred as WT) were used. A complete metabolic phenotyping was explored under high fat diet (HFD) versus CHOW diet in both sexes. Also, glucose-stimulated insulin secretion (GSIS) was studied using isolated islets from tau KI and tau knock-out mice and mouse β pancreatic cell line (MIN6).
Results
While under chow diet tau KI mice do not exhibit significant metabolic impairments, we could observe that under HFD male, but not female tau KI animals exhibited glucose homeostasis alterations as compared to control littermates. Interestingly, using immunofluorescence, tau protein was found colocalized with insulin in the β cells of pancreatic islets. Additional experiments performed on isolated islets from tau KI and tau knock-out mice revealed that both exhibit impaired insulin secretion, an effect recapitulated in the mouse β pancreatic cell line (MIN6) following tau knock-down.
Conclusion
Altogether, our data suggest that loss of tau function in pancreatic β cell might favor the development of glucose homeostasis impairment and could contribute to metabolic changes observed in AD.

DOI: 10.1530/endoabs.81.P59

P60

Performance of EKFC, FAS and 2021 CKD-EPI equations for estimating glomerular filtration rate in people with type 2 diabetes

Bruna Martins Rocha[1], Gustavo Monteiro Escott[1], Luíza Carolina Fagundes Silva[1], Indianara Franciele Porgere[1], Luis Afonso Tochetto[2], Letícia de Almeida Brondani[2] & Sandra Pinho Silveiro[1,2]
[1]Federal University of Rio Grande do Sul, Brazil; [2]Hospital de Clínicas de Porto Alegre, Brazil

Background
Diabetes mellitus (DM) is the leading cause of chronic kidney disease (CKD) worldwide. In clinical practice, kidney function is routinely assessed through glomerular filtration rate (GFR) estimated by equations. However, the accuracy of current equations has been questioned for people with diabetes mellitus (DM).
Aim
To evaluate the performance of the European Kidney Function Consortium (EKFC), the Full Age Spectrum (FAS) and the 2021 Chronic Kidney Disease Epidemiology Collaboration (2021 CKD-EPI) equations based on serum creatinine to estimate GFR in healthy and type 2 DM participants.
Methods
This cross-sectional study evaluated three creatinine-based equations in two different populations: healthy adults (eligibility criteria: BMI ≤ 30 kg/m^2) and people with type 2 DM (eligibility criteria: mGFR $>$ 60 ml/min/1.73 m^2). GFR calculated by the equations was compared with measured GFR (mGFR) by the plasma clearance of ^{51} Cr-EDTA as the reference method. The performance of the

equations was assessed using Bland-Altman plots, bias and P30 accuracy (defined as the percentage of GFR estimations falling within 30% of mGFR values).
Results
We included 100 healthy adults (aged 39±15 years, 67% women), with mean mGFR, 2021 CKD-EPI, FAS and EKFC of 112±20 109±14, 102±18 and 104±19 ml/min/1.73 m^2, respectively ($P=0.109$ between mGFR and 2021 CKD-EPI; $P<0.001$ for the other equations). Overall, the smallest bias was found for 2021 CKD-EPI (5 ml/min/1.73 m^2). All equations presented an acceptable P30 accuracy (92% [CI 95% 86-96] for 2021 CKD-EPI, 89% [82-94] FAS and 87% [79-93] EKFC;$P=0.348$) in the healthy participants. We also included 122 people with type 2 DM (aged 61±10 years, 55% women) in our study. Comparing with mean mGFR (100±28 ml/min/1.73 m^2), 2021 CKD-EPI, FAS and EKFC equations underestimated GFR (mean 86±20, 79±24, and 77±19 ml/min/1.73 m^2, respectively; $P<0.001$ for all equations). No equation achieved optimal P30 accuracy in participants with DM, but 2021 CKD-EPI tended to perform more accurately (74% [CI 95% 65-81] vs. FAS 66% [58-74],$P=0.082$; vs. EKFC 64% [56-72],$P=0.01$). The Bland Altman plots showed positive bias for all equations, with larger biases found in participants with type 2 DM, demonstrating that the underestimation was more pronounced in the presence of diabetes.
Conclusion
In healthy adults, 2021 CKD-EPI, FAS and EKFC are suitable to estimate GFR. However, none of the three equations reached an optimal performance for estimating GFR in participants with type 2 DM. There is still a necessity of improving GFR estimation in people with diabetes.

DOI: 10.1530/endoabs.81.P60

P61

Single nucleotide polymorphism in the ADIPOQ gene modifies adiponectin levels and glycemic control in type two diabetes mellitus patients

Samir Al Bashir[1], Mahmoud A. Alfaqih[2] & Mohammed Alorjani[1]
[1]Jordan University of Science and Technology, Pathology and Microbiology, Irbid, Jordan; [2]Jordan University of Science and Technology, Physiology and Biochemistry, Irbid, Jordan

Diabetes Mellitus (DM) is the ninth leading cause of death worldwide. Mortality from DM is largely attributed to disease complications. Glycemic control of DM patients reduces mortality. Studies indicated that the lack of glycemic control in DM patients could be influenced by the genetic background of the patients. Evidence suggests that adiponectin levels are dysregulated in DM patients with poor glycemic control. Serum adiponectin level is a heritable trait influenced by single nucleotide polymorphisms (SNPs) in the ADIPOQ gene. It is hypothesized that SNPs in ADIPOQ could modify glycemic control in DM patients. To test this hypothesis, 375 type-II DM (T2DM) patients were recruited. Patients were classified into good vs. poor glycemic control according to Hemoglobin A1c levels. Study subjects were genotyped for variations in rs17300539, rs266729, rs2241766 and rs1501299; SNPs in ADIPOQ. Adiponectin levels were measured from the serum. Our analysis showed that reduced serum adiponectin, a longer duration of treatment, and increased insulin resistance were all significant predictors of poor glycemic control. Moreover, the T allele and the TT genotype of rs2241766 were significantly more frequent in patients with poor glycemic control ($P<0.05$). Individuals with the TT genotype of rs2241766 had significantly lower levels of serum adiponectin ($P<0.05$). It was concluded that lower levels of serum adiponectin and the T allele of rs2241766 SNP in ADIPOQ were associated with poor glycemic control in T2DM patients.

DOI: 10.1530/endoabs.81.P61

P62

The link between type of antidiabetic agents and COVID 19 severity in patients with pre-existing type 2 diabetes

Ivona Risovic[1], Danijel Djekic[2] & Anja Stanic[3]
[1]University Clinical Center of the Republic of Srpska, Faculty of Medicine, University of Banja Luka, Endocrinology, Banja Luka, Bosnia and Herzegovina; [2]University Clinical Center Republic of Srpska, Endocrinology, Banja Luka, Bosnia and Herzegovina; [3]University Clinical Center of the Republic of Srpska, Endocrinology, Banja Luka, Bosnia and Herzegovina

Introduction
Type 2 diabetes is one of the main risk factors for severe COVID 19 infection. Inadequate glycemic control is related to high inflammation, hypercoagulability, and mortality in COVID-19 patients . Glucose lowering medications commonly used to treat diabetes mellitus (DM) might have effects on COVID 19 pathogenesis. Overall, evidence is conflicting as to which glucose-lowering drugs are associated with the most favourable outcomes in patients with COVID-19. The aim of our study was to evaluate association of COVID-19 severity with different types of DM therapy.
Patients and Methods
CThe retrospective study included 95 patients with type 2 DM and COVID 19: 25 (26.9%) received metformin, 16 (16.8%) metformin and sulfonureas, 12 (12.7%) metformin and dipeptidyl peptidase type 4 inhibitors (DPP-4), 8 (8.5%) metformin and glucagon-like peptide receptor agonists (GLP-1 RA), 13 (13.8%) metformin and basal insulin, 10 (9.5%) premix insulin and 11 (11.8%) basal and bolus insulin. Clinical presentation, ICU admission and death rate has been compared in patients with different types of DM therapy.
Results
Clinical presentation was mild in patients with metformin, metformin and DPP-4, metformin and GLP-1 RA and more pronounced in patients with premix insulin and basal bolus insulin. The three most common symptoms were: fever, cough and fatigue. Glycemic at admission were highest in patients with premix insulin (13.6±4.58 mmol/l), and the lowest in patients with metformin and DPP-4 (7.5±4.23 mmol/l). Our studies showed that inflammatory response and ICU admission rate were the highest in patients with premix insulin therapy and the lowest in metformin group (12.3 vs 7.1%). A total of 16 patients died (16.8 %) during hospitalization. The highest rate was in patient who received premix insulin 6 (50%) and the lowest in patients who received metformin 2 (2.1%).
Conclusion
Our results had showed that therapy with premix and basal bolus insulin had link with severe clinical presentation, ICU admission and death.
Key words
COVID 19, type 2 diabetes mellitus, metformin, insulin

DOI: 10.1530/endoabs.81.P62

P63

Exceptional genetic transmission of a ABCC8 mutation in two cases of diffuse hyperinsulinism in a dichorionic diamniotic (DCDA) twin pregnancy

Daniela Telehuz[1], Plesa Oana[1], Bouilloud Florence[1], Voican Adela[1], Banu Isabela[1], Arnoux Jean-Baptiste[2], Wucher Helene[1] & Dupuy Olivier[1]
[1]Hospital Paris Saint-Joseph, Endocrinology, Paris, France; [2]Necker Hospital, Paris, France

We present the case of a 36-year-old female with a focal neonatal hyperinsulinism diagnosed at birth in a context of hypoglycemia that was resistant to Diazoxide treatment. A subtotal pancreatectomy was performed and histology showed a focal hyperinsulinism. The mutation of ABCC8 was not searched at this point. The patient developed an insulin dependent diabetes at the age of 9 and required an insulin pump. In 2017 the patient was planning a pregnancy so she consulted a geneticist doctor for his opinion. Considering the patient's history, a genetic test was performed that evidenced a local pancreatic recessive heterozygotic mutation for the ABCC8 gene (exon 39 c.4716C>A, p.Ser1572Arg). This phenotype is related to a uniparental disomy of a paternal origin situated at the pancreatic level. The geneticist concluded that the risk of transmission is very small (1/600) and was favorable for the pregnancy. As there was no consanguinity in the family, testing the father was not deemed necessary. A pregnancy starts in 2020 and at a gestational age of 21 weeks the mother goes into premature labor (premature rupture of membranes) and an emergency C-section is performed in April 2021 which concluded with the birth of bichorial bi amniotic male twins. Right after birth both babies experience severe hypoglycemia which requires a prolonged hospitalization with diazoxide treatment followed by an introduction of a somatostatin analogue treatment by pump and continuous enteral nutrition. The genetic tests evidenced the same two genetic mutations for both babies: exon 28 c63550del=p.Val1184 and exon 39 c.4716C>A=p.Ser1572Arg, which is responsible for a form of diffuse hyperinsulinism. As the already known mutation of ABCC8 was transmitted maternally, the greater risk lied in the transmission of a paternal heterozygotic mutation that was asymptomatic. This situation is very rare outside a consanguinity and was the consequence of the birth of two children that suffer from a severe diffuse hyperinsulinism which requires a somatostatin analogue pump treatment, as their insulin requiring diabetic mother is treated by an insulin pump.

DOI: 10.1530/endoabs.81.P63

P64

The bidirectional relationship between testosterone and metabolic disorders: testosterone deficiency as an early marker of cardiovascular risk in young men

Davide Menafra[1], Cristina De Angelis[1], Francesco Garifalos[2], Michele Castoro[2], Nunzia Verde[2], Mariangela Piscopo[2], Giacomo Galdiero[2], Claudia Pivonello[2], Renata Simona Auriemma[2], Paolo Chiodini[3], Annamaria Colao[2,4] & Rosario Pivonello[2,4]
[1]Università Federico II di Napoli, Dipartimento di Medicina Clinica e Chirurgia, Sezione di Endocrinologia, Unità di Andrologia e Medicina della Riproduzione e della Sessualità Maschile e Femminile (FERTISEX-CARES), Naples, Italy; [1]Università Federico II di Napoli, Dipartimento di Medicina Clinica e Chirurgia, Sezione di Endocrinologia, Unità di Andrologia e Medicina della Riproduzione e della Sessualità Maschile e Femminile (FERTISEXCARES), Naples, Italy; [3]University of Campania "Luigi Vanvitelli", Medical Statistics Unit, Naples, Italy; [4]Federico II University of Naples, Unesco Chair for Health Education and Sustainable Development, Naples, Italy

In the last years an increasing incidence of cardiovascular diseases (CVD) has been reported in young adults (18-45 yrs), probably accounted by the significant increase in CV risk (CVR) factors. Observational and interventional studies, mainly focused on middle-aged and elderly men, demonstrated that metabolic CVR (mCVR) factors and CVD manifestations are common in hypogonadal men and, conversely, testosterone deficiency is highly prevalent in metabolic disorders; the lack of corresponding robust evidence in younger adults requires more focused investigation. The current single centre, observational, cross-sectional study aimed at better defining the mutual relationship between androgenic status and the prevalence of mCVR factors in a large cohort of 720 young (18-35 yrs) adult men, subjected to physical examination and fasting morning venous blood sampling for the assessment of anthropometric, metabolic and hormonal parameters. Body weight, BMI and waist circumference (WC) significantly decreased across total testosterone (TT) ($P<0.0001$), SHBG ($P<0.01$; $P<0.01$; $P<0.0001$) and calculated free testosterone (cFT) ($P<0.05$) tertiles, whereas systolic blood pressure (SBP) and triglycerides (TG) significantly decreased across TT ($P<0.05$; $P<0.01$) and SHBG ($P<0.05$; $P<0.0001$) tertiles, and diastolic blood pressure (DBP) across SHBG ($P<0.05$) tertiles. Spearman correlation analysis revealed a negative association of TT, SHBG and cFT with BMI ($r=$-0.204; $P<0.001$)($r=$-0.165; $P<0.05$)($r=$-0.132; $P<0.05$), and of TT and SHBG with WC ($r=$-0.234; $P<0.001$)($r=$-0.225; $P<0.01$), SBP ($r=$-0.112; $P<0.05$)($r=$-0.142; $P<0.05$) and TG ($r=$-0.017; $P<0.01$)($r=$-0.204; $P<0.001$), whereas a positive association of TT and SHBG with HDL-cholesterol ($r=0.167$; $P<0.01$)($r=0.251$; $P<0.001$) was demonstrated. In multiple linear regression analysis in models adjusted for age, BMI and WC, TT and SHBG were strong independent predictors of serum HDL-cholesterol ($\beta=0.151$; $P<0.01$) ($\beta=0.186$; $P<0.01$), and SHBG was an independent predictor of SBP and DBP ($\beta=$-0.177; $P<0.05$) ($P=$0,008; $\beta=$-0,204). Lastly, in the subgroup of men with hypotestosteronemia (TT $\leq$ 12.1 nM), the prevalence of normal weight was significantly lower and that of obesity, visceral obesity (WC > 102 cm), hypertension and metabolic syndrome was significantly higher, compared to normal-testosterone subgroup. Consistently, in the subgroup of overweight/obese men, the prevalence of hypotestosteronemia was significantly higher, compared to normal weight subgroup. In conclusion, the current study demonstrated that in young adult men a bidirectional relationship between testosterone deficiency and metabolic disorders exists, and that a worse androgenic status is associated to a worse cardiometabolic profile and might represent a strong early predictor of mCVR factors, potentially associated to the onset of future CVD.

DOI: 10.1530/endoabs.81.P64

P65

Hypoglycaemia associated with variable rate intravenous insulin infusion and concurrent administration of balanced electrolyte solution: A single hospital experience

Vinit Shah, Sara Jasionowska, Sarah Kelly, Reshma Joseph & Maisarah Amran
London North West University Healthcare NHS Trust, United Kingdom

Background
Variable rate intravenous insulin infusion (VRIII) or 'sliding scale' is required for certain patients with diabetes to keep their blood glucose within the recommended target range during an acute illness or a period of starvation. When used in the right context this has shown to improve outcomes but can also lead to morbidity especially hypoglycaemia.

Aim
Evaluate risk of hypoglycaemia in patients on VRIII with concurrent use of balanced electrolyte solution
Methods
This was an observational study and we included patients who were admitted to medical or surgical wards over a six-week period and who were on a VRIII. Relevant data was collected from patients' paper notes, observation nursing charts and drug charts. The data was collected for the entire duration patients were on the VRIII. Our hospital has guidelines for the management of patients on VRIII including recommendations on frequency of glucose monitoring and choice of concurrent IV fluids. The recommended balanced solution with carbohydrate substrate used in our hospital is combined 0.18% sodium chloride with 4% glucose (0.18% NaCl + 4% glucose). Hypoglycaemia is defined as when the capillary blood glucose falls below 4 mmol/mol.
Results
We included a total of 16 patients in our study with a mean age of 59 years with the majority of patients having type 2 diabetes (87.5%). 0.18% NaCl + 4% glucose was used concurrently with the VRIII in 75% of patients. For all the patients that were included in the study a total of 434 hours were spent on a VRIII for which there were 324 capillary blood glucose readings with 3 recorded hypoglycaemia events (< 1%) with 2 out of 3 occurring in those who were not on a balanced electrolyte solution.
Discussion
Use of concurrent IV fluids (Normal saline or 5% dextrose) is not a new concept, but often this has been prescribed separately and the infusion switched between the two depending on the threshold levels of capillary glucose levels that has been set by the prescriber. This is prone to human error and consequent adverse events. This study demonstrates that with the concurrent use of balanced electrolyte solution such as 0.18% NaCl + 4% glucose, there is a minimal incidence of hypoglycaemia and its concurrent use is recommended to prevent harm to patients on VRIII. This would be of particular importance in general ward or less intensively monitored settings.

DOI: 10.1530/endoabs.81.P65

P66

The role of empagliflozin in palmitate-induced ER stress and apoptosis in H9C2 cells

Jae Yeop Jeong[1], Sung-E Choi[2], Min Woo Song[1], Suck Ho Park[2], Yup Kang[2], Tae Ho Kim[3], So-Yeon Ahn[4], Hae Jin Kim[1], Seung jin Han[1], Ja Young Jeon[1], Nami Lee[1], Dae Jung Kim[1] & Kwan-Woo Lee[1]
[1]Ajou University School of Medicine, Department of Endocrinology and Metabolism, Suwon, Rep. of South Korea; [2]Ajou University School of Medicine, Department of Physiology, Suwon, Rep. of South Korea; [3]Seoul Medical Center, Division of Endocrinology and Metabolism, Department of Internal Medicine, Seoul, Rep. of South Korea; [4]Busan Bumin Hospital, Division of Endocrinology and Metabolism, Department of Internal Medicine, Busan, Rep. of South Korea

Aim/hypotheses
Ectopic lipid accumulation in the heart contributes to the abnormal function of the heart and to the death of cardiomyocytes.Saturated FFA is one of the most important causes of death in cardiomyocytes. Although empagliflozin has been reported to be beneficial for people with diabetic complications and/or CVD, it has not been confirmed as to how it affects cardiomyocytes death by FFA. This study was designed to evaluate the protective effects of SGLT2 inhibitor on palmitate-induced ER-stress and apoptosis in cardiomyocytes.
Methods
We used differentiated H9C2 cells as cardiomyocytes and palmitate as a saturated fatty acid. To clarify the effects of empagliflozin on apoptosis, free fatty acid was treated with or without empagliflozin in cardiomyocytes and several stress signaling pathways were measured, such as inflammation, endoplasmic reticulum (ER)-stress, and insulin signaling using immunoblotting. Inflammation and cardiac metabolism were analyzed in several related genes. Cardiomyocyte apoptosis was detected using DNA fragmentations assay and immunoblotting using cleaved caspase 3 antibody. DAPI staining was also performed.
Results
Palmitate stimulated increment of ROS (reactive oxygen species) and ER-stress markers such as phospho-eIF2a, CHOP, and phospho-JNK. In addition, cleaved caspase3 and DNA fragmentation was induced by treatment of palmitate. Interestingly, empagliflozin significantly decreased expression levels of ER-stress markers (including phospho-eIF2α, CHOP, and phospho-JNK [Jun N-terminal kinases]) in PA-treated cells. Empagliflozin significantly decreased the activity of cleaved caspase-3 (a well-known apoptotic induced molecule) and DNA fragmentation. To investigate the protective molecular mechanism of empagliflozin, we measured AMPK activation and upstream signal pathways.

Empagliflozin significantly stimulated phospho-CAMKK2 and phospho-AMPK. In addition, phosphorylation of acetyl-CoA carboxylase, target protein of AMPK, was also activated by treatment of empagliflozin. But, LKB did not change. Beneficial effects of empagliflozin was abolished by compound C.
Conclusions/interpretation
This data suggests SGLT2 inhibitors protect palmitate induced cardiomyocytes, ER-stress, and apoptosis. Therefore, attempts to use treatment of SGLT2 inhibitor might be a useful strategy for preventing diabetes associated ventricular remodeling and diabetic cardiac complication.

DOI: 10.1530/endoabs.81.P66

P67

Leptin increases VLDL triglyceride secretion and reduces hepatic lipid content in lean male subjects

Matthaeus Metz[1], Marianna Beghini[1], Lorenz Pfleger[1], Peter Wolf[2], Magdalena Bastian[2], Jürgen Harreiter[3], Sabina Baumgartner-Parzer[2], Rodrig Marculescu[4], Michael Krebs[2], Martina Hackl[1], Michael Trauner[5], Martin Krssak[3], Herbert Stangl[6], Alexandra Kautzky-Willer[7], Clemens Fürnsinn[3] & Thomas Scherer[1]
[1]Medical University of Vienna, Division of Endocrinology and Metabolism, Vienna, Austria; [1]Medical University of Vienna, Division of Endocrinology and Metabolism, Vienna, Austria; [1]Medical University of Vienna, Division of Endocrinology and Metabolism, Vienna, Austria; [4]Medical University of Vienna, Department of Laboratory Medicine, Vienna,; [5]Medical University of Vienna, Division of Gastroenterology and Hepatology, Vienna, Austria; [6]Medical University of Vienna, Institute of Medical Chemistry, Vienna, Austria; [7]Medical University of Vienna, Department of Medicine III, Division of Endocrinology & Metabolism, Vienna, Austria

Background
Leptin reduces hepatic lipid content in lipodystrophic and overweight, relatively hypoleptinemic NAFLD patients. However, the underlying mechanism is unknown. In rodents, the anti-steatotic action of leptin is mediated by an increase in VLDL secretion and depends on an intact vagal innervation of the liver.
Methods
In this randomized, placebo-controlled, crossover trial, we study the effects of a single metreleptin injection (0.1 mg/kg body weight) on VLDL1 secretion and hepatic energy/lipid metabolism in 13 male, overnight-fasted volunteers. VLDL1 secretion rate was determined with an intralipid infusion test 4 hours after injection. Hepatic lipid content and phosphorous metabolites were measured with ^{1} H/^{31} P-MRS at baseline and 3h after metreleptin injection. In an additional cohort of 10 overnight-fasted, male subjects, we assessed hepatic VLDL1 secretion after modified sham feeding, an established method to stimulate the vagus nerve, where subjects smell, taste and chew, but do not swallow a standardized test meal. Water was served in the control condition.
Results
VLDL1 triglyceride secretion rate was higher after metreleptin than placebo (360 ± 36 vs. 464 ± 45 mg/h; $P = 0.049$) without differences in circulating insulin. As a consequence of the prolonged fasting period, we observed a similar increase in plasma NEFA, ketone bodies and acylcarnitines in both conditions. However, the almost uniform, fasting-associated increase in liver fat in the placebo condition (+ 19% relative to baseline, $P = 0.01$) was prevented by the metreleptin injection. VLDL1 triglyceride secretion correlated with changes in hepatic lipid content ($r = 0.5$, $P = 0.02$). Hepatic ATP/Pi ratio and ATP synthesis rate changed similarly after placebo and metreleptin. In the second cohort, plasma pancreatic polypeptide increased after modified sham feeding ($+296 \pm 109$% vs. -4 ± 35% in the placebo condition) indicating that our test meal stimulated the vagus nerve. Similar to metreleptin, vagus nerve stimulation was associated with an increased hepatic VLDL1 triglyceride secretion (244 ± 39 vs. 348 ± 32 mg/h; $P = 0.02$).
Conclusion
Our study supports the hypothesis that, in humans, leptin's anti-steatotic action is mediated by an increase in hepatic triglyceride export independent of food intake via a brain-vagus-liver axis.

DOI: 10.1530/endoabs.81.P67

P68

Development and validation of a new gestational diabetes mellitus (gdm) risk algorithm

Leire Mendizabal[1], Maddi Arregui[1], Johanna Valerio[2], Ana María Ramos[2], Ana Barabash[2], Nuria Garcia de la Torre[2], mirella zulueta[3], Eunate Arana[4], Eva Saez[1], Igotz Aránbarri[1], Juan Martinez-Lage[1], Alicia Cortazar[4], Sonia Gaztambide[4], Luis Castaño[4], Laureano Simon[1] & Alfonso Luis Calle-Pascual[2]
[1]Patia Europe, San Sebastian, Spain; [2]Hospital Clínico San Carlos, Madrid, Spain; [3]Patia, Boston, United States; [4]Hospital de Bilbao Biocruces, Bilbao, Spain

Background and Objective
Gestational Diabetes Mellitus (GDM) is associated with life-long adverse outcomes for the mother and the baby. To date there is no rigorous clinical test for the assessment of GDM risk, since estimation of GDM risk is currently primarily based on clinical risk factors. Additional markers are needed to identify women at high risk. Our aim was to develop and validate a risk assessment model to identify women at high risk of GDM through an algorithm that integrates genetic and clinical variables.
Methodology
We analyzed a retrospective cohort of 711 women with 425 control pregnancies and 286 GDM cases. The entire cohort was randomly divided into a training/development dataset (70% of the cohort) for algorithm development and a test dataset (30% of the cohort) for validation. A total of 112 SNPs (Single Nucleotide Polymorphisms) were selected for this analysis after exhaustive exploration of the databases published to date of SNPs associated with GDM. The SNPs were selected based on their predictive power and population frequency, with the following criteria: $OR > 1.2$, $RAF > 0.20$, $P < 1 \times 10^{-5}$. SNPs were grouped into glycemic traits categories. Genotyping was performed using iPlex Gold-MassARRAY from Agena Bioscience. In the clinical and genotype data set of the development/training group, significant attribute selection was performed using Sequence Feature Selection (SFS) techniques. Logistic regression analysis was then applied to obtain prediction coefficients for the selected attributes in the training group data set. Discrimination and calibration of risk scores were evaluated using the receiver operating characteristic (ROC) curve in the training and the validation dataset.
Results
An algorithm was developed on the training dataset that provides a risk score for GDM. The algorithm includes 10 SNPs, maternal age, pregestational body mass index, and number of previous pregnancies. In the training dataset the AUC was 0.7420. The AUC of the 10 SNPS alone (0.6981) and the clinical variables alone (0.6133) were significantly lower than their combination. AUC in the validation set was 0.7139.
Conclusions
a new tool for GDM risk assessment is presented, which suggests that the utilization of genetic markers in combination with clinical characteristics may improve accuracy of GDM risk evaluation and reinforce the adoption of preventive intervention as early as possible. Further clinical validation studies in different patient cohorts are ongoing.

DOI: 10.1530/endoabs.81.P68

P69

Evaluating a novel virtual simulation tool for clinical training to improve clinician confidence managing cases in diabetes and endocrinology

Wentin Chen[1], Gobeka Ponniah[1], Meghnaa Hebbar[1], Jameela Sheikh[1], Dengyi Zhou[1], Kashish Malhotra[2], Nia Evans[3], Emily Warmington[1], Anisah Ali[1], Fatema Rezai[1], Isabel Allison[4], Carina Synn Cuen Pan[1], Rachel Nirmal[1], Pavithra Sakthivel[1], Vina Soran[1], Zakee Abdi[5,6], Harjeet Kaur[1], Dwi Delson[7], Simran Piya[8], Eka Melson[9,10], Meri Davitadze[11], Punith Kempegowda[10,12] & Simba Simulation[10]
[1]University of Birmingham Medical School, Birmingham, United Kingdom; [2]Dayanand Medical College, Ludhiana, India; [3]Royal Glamorgan Hospital, Ynysmaerdy, United Kingdom; [4]West Middlesex University Hospital, London, United Kingdom; [5]Medical University - Plovdiv, Plovdiv, Bulgaria; [6]Barts and The London School of Medicine and Dentistry, United Kingdom; [7]School of Medicine - University of Dundee, Dundee, United Kingdom; [8]University of Edinburgh Medical School, Edinburgh, United Kingdom; [9]Ninewells Hospital, Dundee, United Kingdom; [10]Institute of Metabolism and Systems Research - University of Birmingham, Birmingham, United Kingdom; [11]Medical House, Tbilisi, Georgia; [12]Queen Elizabeth Hospital Birmingham, Birmingham, United Kingdom

Introduction
The delivery of medical education has transformed from in-person to remote teaching, accelerated by the ongoing COVID-19 pandemic. Simulation is a useful teaching modality increasingly used to develop healthcare professionals' knowledge and skills while protecting patients from unnecessary risks. Although simulation has traditionally occurred face-to-face, many of its principles can be

adapted for remote teaching. Simulation via Instant Messaging – Birmingham Advance (SIMBA) is a virtual simulation-based learning tool, run by medical students and junior doctors with support from experts, aimed to increase clinician confidence in managing clinical scenarios. We evaluated the effectiveness of SIMBA to improve participants' confidence and competencies in diabetes and endocrinology.
Methods
Eight sessions were conducted between May 2020 and October 2021 on various endocrine subspecialities (adrenal, thyroid, pituitary, diabetes, metabolic bone, and reproductive). Moderators used standardised transcripts to simulate anonymised, real-life clinical cases via WhatsApp. Following the simulation, specialists chaired interactive Zoom sessions to discuss simulated cases and participant queries. Participants' self-reported confidence levels in approaching clinical scenarios were measured using a Likert scale, and responses were categorised as confident, unsure, and not confident. Changes in these categories pre- and post-SIMBA were compared using Wilcoxon signed-rank test. Improvements in clinical core competencies were also analysed.
Results
326 international participants completed the pre- and post-SIMBA surveys and were included in the analysis. Significant improvements were observed in clinician confidence following SIMBA (pre- vs post-survey, confident: +40.6%, unsure: -34.3%, not confident: -6.3%; $P<0.0001$). In addition, 92.6% ($n=302/326$) participants strongly agreed/agreed that sessions were engaging, while 88.7% ($n=289/326$) strongly agreed/agreed that SIMBA accommodated their learning style and 80.5% ($n=236/293$) preferred SIMBA to traditional pedagogy. The overall quality of the sessions was rated as excellent/good by 96.2% ($n=282/293$) participants. 93.9% ($n=306/326$) participants strongly agreed/agreed that the simulated topics were applicable to their clinical practice, while 93.9% ($n=306/326$) and 92.6% ($n=302/326$) strongly agreed/agreed the content was impactful at personal and professional levels, respectfully. Clinicians reported improvements in core clinical competencies: patient care [56.7% ($n=185/326$)], patient management [83.4% ($n=272/326$)], systems-based practice [43.3% ($n=141/326$)], and practice-based learning [66.9% ($n=218/326$)].
Conclsion
SIMBA proved to be an effective postgraduate training tool in endocrinology which improved clinician confidence managing various endocrine conditions and was highly accepted among learners. In addition, the ubiquity of online platforms enabled international participation, which transcends geographical and financial barriers and could help standardise endocrine training globally. Further studies are underway to explore the long-term translation of SIMBA to clinical practice.

DOI: 10.1530/endoabs.81.P69

P70

Cause of Death for Patients with Diabetes Mellitus in Korea: Multicenter study

Hyeyeon Moon, Mi Kyoung Park & Sunghwan Suh
Dong-A University Hospital, Endocrinology, Busan, Rep. of South Korea

Background
In Republic of Korea, prevalence of type 2 diabetes mellitus (T2DM) has increased substantially in recent decades, but there are no reliable estimates of the excess mortality currently associated with diabetes.
Methods
We analyzed all subjects were T2DM patients over the age of 30 whose death certificates were issued at three hospitals in the Busan metropolitan area from 2010 to 2014. The causes of death were retrospectively determined based on the information from attending physicians or death certificates.
Results
The study comprised 777 patients of which 60.1% were male. The average age of death was 71 years. The most common cause of death in these patients was infectious disease (28.1%), followed by cardiovascular disease (25.5%), malignant neoplasm (24.5%), and kidney disease (8.1%). This trend was consistent when we sub-analyzed them according to glycemic control status. However, cancer was the most common cause of death in male patients which may be driven by higher rate of smoking and alcohol drinking compared to female patients.
Conclsion
Preventive strategies to promote primary prevention and early detection of infectious disease is urgently needed to reduce this excess mortality in patients with T2DM. In addition, gender difference in cause of death should be taken into consideration.

Table 1 The proportion of cause of death in patients with diabetes mellitus

Cause of death	Total ($n=777$)	Men ($n=467$)	Women ($n=310$)
	Numbers (%)	Numbers (%)	Numbers (%)
Infectious disease	218 (28.1)	120 (25.7)	98 (31.6)
Malignant neoplasm	190 (24.5)	134 (28.7)	56 (18.1)
Cardiovascular disease	198 (25.5)	116 (24.8)	82 (26.4)
Cerebrovascular disease	75 (9.7)	50 (10.7)	25 (8.1)
Ischemic heart disease	67 (8.6)	35 (7.5)	32 (10.3)
Heart failure	56 (7.2)	31 (6.6)	25 (8.1)
Kidney disease	63 (8.1)	38 (8.1)	25 (8.1)
Liver disease	40 (5.1)	25 (5.4)	15 (4.8)
Diabetes mellitus	14 (1.8)	7 (1.5)	7 (2.3)
All other cause*	54 (6.9)	27 (5.8)	27 (8.7)

*All other causes included gastrointestinal bleeding, pulmonary thromboembolism, epilepsy, acute pancreatitis and panperitonitis.

DOI: 10.1530/endoabs.81.P70

P71

The neural mechanism of selective activation of kisspeptin neurons in the ARC of the hypothalamus regulate bown adipose thermogenesis in female mice

Qinyu Liu[1], Qian Li[2], Xiaofeng Lin[1], Xieyu Xu[1], Gang Chen[1] & Junping Wen[1,3]
[1]Shengli Clinical Medical College of Fujian Medical University, Fujian, China; [2]Department of Endocrine and Metabolic Diseases, Shanghai Institute of Endocrine and Metabolic Diseases, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China; [3]Department of Endocrinology, Key Laboratory of Endocrinology, Fujian Provincial Hospital, Fujian, China

Objectives
Overweight and obesity currently burden our public health, and especially with the aging process in the world, the incidence of obesity is significantly higher in women than that in men partly. Recent studies reported that hypothalamic kisspeptin neurons, with obvious changes of number and structure in female during life, play a crucial role in the regulation of central energy homeostasis. But the precise mechanism remains an enigma.
Methods
High-fat fed Kiss1-CreGFP female mice were used in this study. Selectively activated kisspeption neurons by using Designer-receptors-exclusively-activated-by-designer-drugs(DREADDs) technology and denervation of the sympathetic nerve in iBAT were used to demonstrate the mechanism by which ARC Kisspeptin neurons activate brown fat thermogenesis in female mice.
Results
The Kiss1-CreGFP female mice were injected with AAV-DIO-hM3D(Gq)-mCherry virus in ARC through Stereotactic injection. Three weeks later, AAV was successfully transfected and expressed the corresponding receptor, which were greatly activated by CNO, then the expression of neuronal activation marker c-fos was significantly enhanced. Selective activation of Kisspeptin neurons resulted in decreased body weight, improved glucose metabolism, increased energy expenditure, increased iBAT(brown adipose tissue), decreased sWAT, gWAT, rWAT (white adipose tissue) in female mice($P<0.05$). The norepinephrine(NE) concentration, sympathetic specific indicator tyrosine hydroxylase (TH), the number of brown adipose cells and the expression of thermogenic related genes were significantly increased in activated group ($P<0.05$). The metabolic improvement effect disappeared in activating kisspeptin^{ARC} neurons after sympathetic nerve denervation of iBAT, and female mice gained weight, impaired glucose metabolism, failed activation of brown fat, and significantly decreased thermogenesis ($P>0.05$). But the control group of beneficial effects by chemogenetics activation on weight reduction, glucose metabolism improvement and brown fat thermogenesis activation still existed ($P<0.05$).
Conclusion
Chemogenetics can relatively specifically activate Kisspeptin neurons in the ARC of the hypothalamus in female mice, and the activated Kisspeptin has an effect on energy metabolism, mainly reduced weight, improved glucose metabolism,

increased thermogenic and dissipative, increased brown adipose tissue, strengthened sympathetic activity innervating iBAT, and significantly improved high fat induced obesity. iBAT sympathetic denervation experiments confirmed that Kisspeptin^{ARC} neurons in female mice modulate iBAT activation through sympathetic nerve to improve systemic energy metabolism.

Keywords
Kisspeptin, Female, Sympathetic Nerve, BAT, Thermogenesis
DOI: 10.1530/endoabs.81.P71

P72

Clinical and nutritional risk factors for insulin requirement during gestational diabetes mellitus

Rahma Khalaf, Yosra Htira, Zohra Hadj Ali, Chaima Jemai, Imen Hedfi & Faika Ben Mami
National Institute of Nutrition, Department C, Tunisia

Background and aim
Gestational Diabetes Mellitus (GDM) is the commonest medical pregnancy complication. Nutritional interventions come to the fore as one of the few levers for managing GDM, as many medications are either harmful to the growing fetus, or their toxicity is uncertain. The aim of this study was to assess the potential clinical features and nutritional risk factors of insulin treatment during GDM.
Methods
This was a prospective study including 150 patients with GDM. Patients who failed to achieve glycemic targets, defined according to the American Diabetes Association guidelines 2021, were treated with insulin. Clinical caracteristics and dietary intake were compared between the two groups. Dietary intake data were collected by trained nutritionists using a 24-hour recall method.
Results
Among the 150 patients with GDM, insulin use, along with lifestyle interventions, was necessary in 20.3% of patients. Univariate analysis showed that insulin use was significantly associated with a family history of type 2 diabetes in a first degree relative ($P=0.016$), history of GDM ($P=0.02$), pregestational Body Mass Index superior to 25 kg/m^2 ($P=0.005$) and presence of four risk factors of GDM ($P=0.005$). Insulin therapy group had higher protein intake than nutritional therapy group (100.86 $\pm$38.8 g/d vs 80.28 $\pm$36.97 g/d,$P=0.025$) and lower vitamin B12 levels (3.93 $\pm$2.84 µg/d vs 2.59$\pm$1.78 µg/d,$P=0.01$). Energy consumption, carbohydrate intake, fat intake and fiber intake did not statistically differ between the two groups ($P=0.7$,$P=0.09$,$P=0.89$, p=0.6 respectively). The calcium, iron, zinc, magnesium, vitamin B1,B2,B3,B5,B6 and folic acid intakes did not statistically differ between the two groups. Multivariate analysis showed that vitamin B12 level was an independant factor for insulin requirement during GDM (OR 5.52, 95% CI 1.33-22.83, $P=0.018$). The cut-off value of vitamin B12 level, determined by ROC curves analysis, was 2.28 µg/d (sensitivity of 80% and specificity of 52%,$P=0.01$).
Conclsion
The association between vitamin B12 levels during pregnancy and the risk of GDM remains unclear with conflicting data. To our knowledge, this is the first study to elucidate the association between vitamin B12 levels and insulin requirement during GDM. More studies are needed to further strengthen this finding and to clarify possible pathogenetic mechanisms.

DOI: 10.1530/endoabs.81.P72

P73

Different treatment outcomes (acute dietary restriction vs conventional treatment) in women with new-onset type 2 diabetes (T2DM), with previous gestational diabetes (GDM)

Natalia Asatiani[1,2], Ramaz Kurashvili[3], Ekaterine Inashvili[3], Elena Shelestova[3] & Mzia Dundua[3]
[1]National Center for Diabetes Research, Diabetes in Pregnancy, Tbilisi, Georgia; [2]Petre Shotadze Tbilisi Medical Academy, Tbilisi, Georgia; [3]National Center for Diabetes Research, Tbilisi, Georgia, Tbilisi, Georgia

Some literary data demonstrate that the twin defect of beta-cell failure and insulin resistance that underline T2DM can be reversed by acute negative energy balance alone. The aim of the present work was to assess treatment outcomes in women with new onset T2DM, who were previously diagnosed with GDM treated with acute dietary restriction or conventionally at 32 weeks postpartum (PP).
Methods
In total 174 women with T2DM at 32 weeks PP, were enrolled in the study. Patients were tested at 32, 40 and 48 weeks PP. Patients were divided into two groups (Gr.): Gr.1 - Acute Dietary Energy Restriction - 61 women - 600kcal/day for 8 weeks, during next 8 weeks- 1 200 – 1 400kcal/day. Gr.2 - Conventional Therapy - 113 women - 1 400 – 1800 kcal/day and Metformin.
Results
At entry levels of HbA1c, fasting plasma glucose (FPG), insulin, triglycerides and BMI statistically did not differ in Gr.1 and Gr.2. At week 33 PP (one-week post treatment) FPG decreased: Gr.1 – 170.5 $\pm$18.6 vs. 96.4$\pm$9.1;$P=0.000$ and Gr.2– 169.9$\pm$ 18.8 vs. 145.7$\pm$ 14.9;$P=0.32$, and at week 48 PP- FPG levels decreased in both groups, but in Gr.1 decrease was statistically more evident, than in Gr.2 ($P=0.004$). At week 40 PP HbA1c levels decreased in both groups (Gr.1 – by 1.42 $\pm$0.12 and Gr.2 – 0.68$\pm$ 0.08;$P=0.000$), and at week 48 PP HbA1c levels were statistically lower in Gr.1 ($P=0.000$). At week 40 PP fasting plasma insulin fell from 16.1 $\pm$3.6 to 5.2$\pm$ 1.7 (Gr.1 – $P=0.000$), and 15.9 $\pm$3.1 to 12.1 $\pm$2.3 (Gr.2 -$P=0.3$); and at week 48 PP these indices were statistically lower in Gr.1 when compared to Gr.2 ($P=0.000$). After 16 weeks of treatment BMI also reduced in both groups (Gr.1 – by 7.8$\pm$0.08kg/m$_2$ and Gr.2 – by 2.61 $\pm$0.1%) while at week 48 PP statistically lower BMI was observed in Gr.1 ($P=0.055$). Triglyceride levels have dropped in Gr.1 and 2 (by 0.60 $\pm$0.05 and 0.68 $\pm$0.06 mg/dl, respectively) though this decrease was not statistically evident.
Conclusion
In women with T2DM, who were previously diagnosed with GDM acute dietary restriction at 32 weeks PP significantly reduced plasma fasting glucose, insulin levels, HbA1c, and BMI when compared to traditional dietary management and Metformin. Our data are in complete accordance, that abnormalities underlying T2DM are reversible by reduced dietary energy intake, that is of an utmost importance for young women after pregnancy and breastfeeding.

DOI: 10.1530/endoabs.81.P73

P74

Prevalence and predictive factors of factitious hypoglycemia in non-diabetic patients

Amani Terzi, Ibtissem Oueslati, Meriem Yazidi, Elyes Kamoun & Melika Chihaoui
La Rabta University Hospital, Department of Endocrinology, Tunis, Tunisia

Introduction
Spontaneous hypoglycemia in non-diabetic patients is a rare metabolic emergency caused by multiple etiologies. Factitious hypoglycemia, a form of the Munchausen syndrome, is defined as the surreptitious use of insulin or oral hypoglycemic agents to deliberately induce self-harm. It is one of the most challenging diagnoses associated with significant morbidity and mortality. The aim of this study was to assess the prevalence and the associated factors of factitious hypoglycemia in non-diabetic patients.
Methods
This was a single-center, retrospective study including 70 non-diabetic patients who were admitted to our department between 2004 and 2020 for the exploration of a spontaneous hypoglycemia. All enrolled patients fulfilled the Whipple triad. Exclusion criteria were: pregnancy, severe renal failure, hepatic failure, cirrhosis, heart failure, and a history of malignant tumors. Age, gender, epidemiological parameters, medical history, clinical and paraclinical data, and the etiology of hypoglycemia were collected from medical records.
Results
The diagnosis of factitious hypoglycemia was confirmed in 11 patients (9 women and 2 men) corresponding to a prevalence of 16%. It was secondary to an intentional insulin use in 6 patients and to the ingestion of Glibenclamide in 5 patients. Their mean age was 30.27 $\pm$13.02 years with extremes of 14 and 54 years. Two patients with factitious hypoglycemia had a personal history of psychiatric disorders. Age $\leq$ 35 years (Odds Ratio= 5.6,$P=0.017$), family history of diabetes mellitus (Odds Ratio=1.29,$P=0.015$), attention disorders (Odds Ratio=12.5,$P=0.017$), and fasting glucose level<0.7 g/l (Odds Ratio= 5.75, $P=0.017$) were positively associated with factitious hypoglycemia.
Conclusion
Factitious hypoglycemia is more frequent in middle-aged women with psychosocial issues and a family history of diabetes mellitus explaining the ease to access to insulin and anti-diabetic agents. A psychiatric referral and a supportive follow up are warranted to provide the appropriate guidance for patients and perform an essential role in the long-term management of factitious hypoglycemia.

DOI: 10.1530/endoabs.81.P74

P75

Type 1 diabetes technology and quality of life: glucose control and beyond

Silvia Irina Briganti[1], Daria Maggi[2], Rocky Strollo[2], Shadi Kyanvash[2], Oreste Lanza[2], Paolo Pozzilli[3] & Silvia Manfrini[2]
[1]Campus Bio-Medico, Metabolic Diseases, Rome, Italy; [2]Campus Bio-Medico, Metabolic diseases, Rome, Italy; [3]Campus Bio-Medico, Rome, Italy

Background
Technological advances in continuous glucose monitoring (CGM) and continuous subcutaneous insulin infusion (CSII) should aim to improve glucose control and quality of life in patients diagnosed type 1 diabetes (T1D).
Aim
The aim of our study was to compare different CGM and CSII devices on these targets.
Methods
Sixty-nine T1D patients (mean age 39 ± 12; 31 males) were recruited. 36 were on multiple daily insulin injections (MDI), 33 on CSII devices including Medtronic Minimed 640G and 670G, Theras Omnipod, Roche Insight and Movy Tandem. Glucose monitoring was performed with Dexcom-G6, Guardian sensor and Flash Freestyle Libre. The Diabetes Treatment Satisfaction Questionnaire (DTSQ), the Diabetes Specific Quality Of Life Scale (DSQOLS) and The Short Form (36) Health Survey (SF-36) were administered to test quality of life. HbA1c, time in range (TIR), time above the range (TAR) and time below the range (TBR) were investigated as glucose control parameters.
Results
Patients in the CSII group had higher treatment-related satisfaction (84.8% vs 52.8%, $P = 0.005$), and better disease acceptance (84.8% vs 52.8%, $P = 0.012$) compared with patients on MDI, despite similar age (MDI mean age 38 ± 12.5, CSII 41 ± 11.6). No differences were observed among devices ($P =$ ns). TIR resulted higher in the CSII group than in the MDI group ($P = 0.001$). The Dexcom G6 group had higher TIR values than the Freestyle ($P = 0.03$) group, but similar to the Medtronic ($P = 0.12$) group.
Conclusions
Technological devices may improve quality of life over MDI treatment. Type of glucose monitoring system may also impact glucose control.

DOI: 10.1530/endoabs.81.P75

P76

Glucagon-like peptide-1 analogues: a new way to quit smoking? SKIP – a randomised controlled study

Sophia Lengsfeld[1], Thilo Burkard[2,3], Andrea Meienberg[3], Nica Jeanloz[1,4], Tanja Vukajlovic[1], Katja Bologna[1], Michelle Steinmetz[1], Clara Sailer[1], David Coynel[5], Deborah R Vogt[1,6], Lars G. Hemkens[7,8,9], Benjamin Speich[7], Jill Kühne[1], Fabienne Baur[1], Linda Lutz[1], Cemile Bathelt[1], Davide Zanchi[10,11], Mirjam Christ-Crain[1] & Bettina Winzeler[1]
[1]University Hospital Basel, Endocrinology, Diabetology and Metabolism; Department of Internal Medicine, Basel, Switzerland; [2]University Hospital Basel, Department of Cardiology, Basel, Switzerland; [3]University Hospital Basel, Medical Outpatient Department, Basel, Switzerland; [4]Kantonsspital Baselland Standort Liestal, Endocrinology, Diabetology and Metabolism; Medical University Clinic, Liestal, Switzerland; [5]University of Basel, Division of Cognitive Neuroscience, Faculty of Psychology and Transfaculty Research Platform,, Basel, Switzerland; [6]University Hospital Basel, University of Basel, Clinical Trial Unit, Department of Clinical Research, Basel, Switzerland; [7]University Hospital Basel, University of Basel, Basel Institute for Clinical Epidemiology and Biostatistics, Department of Clinical Research, Basel, Switzerland; [8]Stanford University, Meta-Research Innovation Center at Stanford (METRICS), Stanford, California, United States; [9]Berlin Institute of Health, Meta-Research Innovation Center Berlin (METRIC-B), Berlin, Germany; [10]F. Hoffmann- La Roche, Roche Innovation Centre Basel, Basel, Switzerland; [11]Stanford University Graduate School of Business, Stanford, California, United States

Background
Cigarette smoking is the leading preventable cause of premature death. Smoking cessation is one of the central goals in medicine, but despite dedicated programs, quit rates remain low due to barriers such as nicotine withdrawal syndrome or post-cessation weight gain. Glucagon-like peptide-1 (GLP-1) analogues reduce energy intake and body weight and seem to modulate addictive behavior. These GLP-1 properties are of major interest in the context of smoking cessation. The aim of this study was to evaluate the GLP-1 analogue dulaglutide as a new add-on therapy for smoking cessation.
Methods
This was a placebo-controlled, double-blind, parallel group, superiority, single-center randomized study including 255 patients. The intervention consisted of a 12-week treatment phase with dulaglutide 1.5 mg or placebo injected subcutaneously at a weekly study visit, in addition to standard of care (behavioral counselling and pharmacotherapy with varenicline). Point-prevalence abstinence rate at week 12 as primary outcome was assessed by self-reported smoking status and biochemical confirmation (end-expiratory exhaled carbon monoxide measurement). We further investigated changes in weight and glucose homeostasis at week 12. In a substudy ($n = 71$), we compared behavioral (i.e., nicotine craving measured by a Visual Analogue Scale) and brain activity changes in response to smoking cue videos using functional magnetic resonance imaging at baseline and week 12.
Results
The point-prevalence abstinence rate after 12 weeks of treatment was 80/127 (63%) in the dulaglutide group and 82/128 (65%) in the placebo group (difference in proportions [95%CI] -1.9% [-10.7, 14.4],$P = 0.859$). We observed an increase in weight in the placebo (+1.8kg [SD 2.4]) and a decrease in the dulaglutide group (-0.7kg [SD 3.3]) between baseline and week 12; baseline-adjusted difference in weight change [95%CI] -2.5kg [-3.3, -1.7], $P < 0.001$. Craving in response to smoking cue videos decreased from baseline to week 12 (estimated mean difference [95%CI] -3.0 [-3.7, -2.3], $P < 0.001$), with no difference between dulaglutide and placebo (estimated mean difference [95%CI] 0.4 [-1.2, 2.0], $P = 0.6$). Similarly, no difference in whole brain functional activity was seen between the two treatments, at both time points and between baseline and follow up.
Conclusion
In this study, an exceptional high point prevalence abstinence rate in both groups was observed, most probably due to the very close (weekly) supervision of the patients. Our data provides no evidence that dulaglutide modulates nicotine craving or smoking cessation rates. Nevertheless, GLP-1 analogues such as dulaglutide may be a promising treatment during smoking cessation as it may avoid post-cessation weight gain.

DOI: 10.1530/endoabs.81.P76

P77

Comparison of hyperphagia and problem behaviors in participants with prader-willi syndrome (PWS) receiving diazoxide choline extended-release (DCCR) with matched participants in PATH for PWS (PfPWS)

Evelien Gevers[1], Theresa Strong[2,3], Jennifer Miller[4], Eric Felner[5], Tony Goldstone[6], Nicola Bridges[7], Jack Yanovski[8], Lynne Bird[9], Merlin Butler[10], Kathryn Obrynba[11], Melissa Lah[12], Ashley Shoemaker[13], Jorge Mejia-Corletto[14,15], David Stevenson[16], John Wilding[17], Virginia Kimonis[18], Jennifer Abuzzahab[19], Laura Konczal[20], Verghese Mathew[21], Neil Cowen[22], Michael Woloschak[22] & Anish Bhatnagar[22]
[1]Queen Mary University of London, Barts Health NHS Trust, London, United Kingdom; [2]Foundation for Prader-Willi Research, Walnut, United States; [3]PATH for PWS Investigators; [4]University of Florida, Gainesville, United States; [5]Emory Children's Center, Druid Hills, United States; [6]Hammersmith Hospital, London, United Kingdom; [7]Chelsea and Westminster Hospital, London, United Kingdom; [8]National Institutes of Health, Bethesda, United States; [9]Rady Children's Hospital - San Diego, San Diego, United States; [10]Kansas University Medical Center, Kansas City, KS, United States; [11]The Research Institute at Nationwide Children's Hospital, Columbus, United States; [12]Indiana University School of Medicine, Indianapolis, United States; [13]Vanderbilt University, Nashville, United States; [14]NYU Winthrop Hospital, Mineola, United States; [15]NYU Langone Hospital-Long Island, Pediatrics, Division of Pediatric Endocrinology, Mineola,; [16]Stanford University, Palo Alto, United States; [17]University of Liverpool, Liverpool, United Kingdom; [18]University of California Irvine, Irvine, United States; [19]Children's Minnesota, Saint Paul, United States; [20] UH Cleveland Medical Center, Cleveland, United States; [21] Hull and East Yorkshire Hospitals NHS Trust, Hull, United Kingdom; [22] Soleno Therapeutics, Inc., Redwood City, United States

Background
PWS is a rare neurodevelopmental genetic disorder characterized by hyperphagia, obesity, hormonal deficiencies, and problem behaviors for which there are no approved treatment. DCCR administration (100-525 mg/day) up to 52 weeks in participants with PWS improved hyperphagia, behavior, body composition and metabolic markers.
Objective
The objective of this study was to compare changes in hyperphagia (using Hyperphagia Questionnaire for Clinical Trials [HQ-CT]) and PWS-related behaviors (via PWS Profile Questionnaire [PWS-P]) between 114 participants enrolled in DCCR placebo-controlled, double-blind (C601, NCT03440814) and

open-label extension (C602, NCT03714373) studies (sponsored by Soleno Therapeutics) and a matched sub-cohort from PfPWS sponsored by Foundation for Prader Willi Research, NCT03718416) ($n=229$) who did not receive experimental treatment.
Methods
C601/C602 and PfPWS studies were conducted concurrently. The creation of the PfPWS sub-cohort was conducted prospectively by an independent group prior to receiving the results from either study. Participants from both groups had genetically confirmed PWS and their caregivers completed the HQ-CT and PWS-P questionnaires prior to enrollment. Availability of participant-level data in PfPWS allowed for the creation of a propensity matched control cohort ($n=195$) similar to the C601/C602 study population by applying the defined inclusion criteria (age, gender, baseline HQ-CT score, baseline weight, and data collection time points).
Results
Statistically significant reductions in HQ-CT score for C601/C602 compared to PfPWS sub-cohort at Week 26 were observed for propensity-adjusted [Difference (C601/C602 – PfPWS), Adjusted Least-Square means, SE (standard error), 2-sided 95% CI=-5.7 (-7.43, -3.95)] and non-propensity-adjusted analyses [Difference=-5.9 (-7.53, -4.34)] (all $P<0.001$), which were sustained at Week 52 [Difference (C601/C602 - PfPWS)=-5.5 (-7.39, -3.64) for propensity-adjusted;=-5.9 (-7.65, -4.23) for non-propensity-adjusted; (all $P<0.001$)]. The difference in HQ-CT score between the two cohorts was consistent across age, sex, baseline HQ-CT, PWS genotype, geographical subgroups and growth hormone use. Reduction of PWS-P scores for C601/C602 were statistically significant across all domains (aggression, anxiety, rigidity/irritability, compulsivity, depression, disordered thinking) in comparison to PfPWS sub-cohort ($P<$ 0.001 for all) at Week 26 and were maintained at Week 52 ($P<0.001$ to 0.03).
Conclusions
These data demonstrate that improvements in hyperphagia and other PWS-related behaviors achieved by 26 weeks and maintained through 52 weeks in subjects receiving DCCR were significantly greater than in matched controls from an untreated observational cohort, in line with previous results of C601/C602 studies. This further suggests that DCCR may be an effective treatment option for individuals with PWS.

DOI: 10.1530/endoabs.81.P77

P78

Habit-intervention induces an amelioration of prediabetics cardiometabolic traits by lowering the miR-21/ROS/HNE damaging axis

Lucia La Sala[1,2], Elena Tagliabue[2], Simona Mrakic-Sposta[3], Pamela Senesi[1,4], Ileana Terruzzi[1,4], Livio Luzi[2,4] & Emilio Trabucchi[1]
[1]Multimedica, Milano, Italy; [2]IRCCS, Lab of Cardiovascular and Dysmetabolic Diseases, Italy; [3]National Research Council Research Area Milan, Milano, Italy; [4]University of Milan, Milano, Italy

The prevalence of prediabetes is increasing in the global population and its metabolic derangements may expose to a higher risk to develop type 2 diabetes (T2D) and its cardiovascular burden. Lifestyle modifications might have considerable benefits on ameliorating metabolic status. In light of this scenario, preventive programmes are focusing on the modification of lifestyle that notoriously decreases the incidence of T2D, to reduce the risk and delay T2D and its burden: Diabetes Prevention Program (DPP) recommended healthy habits (diet and physical activity), avoiding smoking, alcohol, and stress as hints to reduce the risk to develop T2D. Intensive lifestyle intervention was able to reduce the incidence of T2D by 58% over 3 years Alternative biomarkers, such as circulating miR-21, has been recently discovered associated with dysglycemia. Here we evaluated, in a longitudinal cohort of dysglycemic population the relation between the circulating miR-21/ROS/HNE levels and the habit-intervention (HI) after 1 year of follow-up.
Methods
1506 subjects from DIAPASON study were screened based on the Findrisc score. 531 subjects with Findrisc ≥ 9 were selected for dysglycemia (ADA criteria) and tested for circulating miR-21, ROS and HNE levels, as damaging-axis. 207 dysglycemic subjects were re-evaluated after a habit intervention (HI), 1-year later. Repeated measures tests were used to evaluate changes from baseline to 1-year of follow-up. Furthermore, linear regression and logistic regression models were implemented to evaluate the association between glycemic parameters and miR-21/ROS/HNE.
Results
We observed, after HI, a significant reduction of miR-21/ROS/HNE axis in dysglycemic subjects, concomitantly with ameliorating of metabolic parameters, including insulin resistance, BMI, microalbuminuria, reactive hyperemia index and skin fluorescence. Significant positive interaction was observed between miR-21 axis with glycaemic parameters after HI. Lower miR-21 levels after HI, strongly associated with a reduction of glycemic damaging-axis, in particular, within-subjects with values of 2hPG <200 mg/dL.
Conclusions
Our findings demonstrated that HI influenced the epigenetic changes related to miR-21 axis, and sustain the concept of reversibility from dysglycemia. These data support the usefulness of novel biological approaches for monitoring glycemia as well as provide a screening tool for preventive programmes.

DOI: 10.1530/endoabs.81.P78

P79

Non-invasive quantification of pancreatic islet beta-cell function in people with type 1 diabetes mellitus

Shruti Joshi[1], Trisha Singh[1], Lucy Kershaw[1], Fraser Gibb[1,2], Marc R Dweck[1], Michelle Williams[1], Scott Semple[1,3], Shareen Forbes[1], Rebecca Reynolds[1] & David Newby[1]
[1]University of Edinburgh, Department of Cardiovascular Science, Edinburgh, United Kingdom; [2]NHS Lothian, Edinburgh Centre for Endocrinology, Edinburgh, United Kingdom; [3]University of Edinburgh, Edinburgh Imaging, Edinburgh, United Kingdom

Background and Aims
Type 1 diabetes mellitus (T1DM) is characterised by autoimmune destruction of pancreatic beta-cells resulting in insulin deficiency. Evaluation of novel therapies for T1DM requires reliable methods to measure beta-cell function, which is unattainable using traditional non-invasive imaging techniques. A new approach is manganese-enhanced magnetic resonance imaging (MEMRI). As a calcium analogue, manganese is taken up into pancreatic beta-cells during insulin secretion, serving as intracellular contrast. We conducted a proof-of-concept study to investigate whether MEMRI can be used as a measure of beta-cell function in people with T1DM.
Methods
In a prospective case-control study, 20 people with T1DM (age 52 [44-61] years, 6 female; 10 with very low [<50 pmol/l], and 10 with reduced [>50pmol/l] C-peptide concentrations) and 15 healthy volunteers (age 32 [23-36] years, 6 female) underwent MEMRI of the pancreas following a standardised oral glucose load (Fortisip Compact, 125 mL). MEMRI was performed using intravenous manganese dipyridoxyl diphosphate administered over 10 minutes. Pancreatic T1 mapping was performed prior to and every 2.5 min for 30 min after manganese infusion. Quantitative manganese uptake analysis was performed by measuring T1 relaxation times in regions of interest drawn within the pancreas and compared with the left ventricular blood pool. The rate of pancreatic manganese uptake was determined by Patlak modelling [1]. Scan-rescan reproducibility was performed in 10 participants at least 8 weeks apart.
Results
People with T1DM had impaired pancreatic manganese uptake (Ki) in those with reduced (median Ki 24 [interquartile range 21-25] ml/100 g of tissue/min) or very low (15 [8-16] ml/100 g of tissue/min) C-peptide concentrations compared to healthy volunteers (30 [27-34] ml/100 g of tissue/min; $p\leq 0.002$ for both). Compared to healthy volunteers, participants with T1DM had visibly lower pancreatic enhancement 30 min after manganese infusion, especially in those with very low C-peptide concentrations. Ki correlated with C-peptide levels in people with T1DM ($r=0.73$,$P=0.0002$) but not in healthy volunteers ($r=$-0.054, $P=0.88$). There were no correlations between Ki and age, body-mass index or glycated haemoglobin. We found strong intra-observer (0.98[0.96-0.99]) and inter-observer (0.84[0.51-0.95]) repeatability and scan-rescan reproducibility (0.73[0.23-0.92]) for Ki.
Conclsions
MEMRI can provide a non-invasive imaging technique to assess beta-cell function in people with T1DM. This has important implications for investigation of the pathophysiology of T1DM, monitoring disease progression and assessment of novel immunomodulatory interventions.
References
1 Spath NB *et al.* Manganese-enhanced MRI of the myocardium. *Heart*. doi:10.1136/heartjnl-2019-315227

DOI: 10.1530/endoabs.81.P79

P80

The COVID-19 in patients with diabetes mellitus in tashkent: a retrospective cohort study

Anna Alieva[1], Abdulaziz Djalilov[2], Feruza Khaydarova[1], Anvar Alimov[3], Dilovar Khalilova[1], Nasiba Alimova[1], Iroda Tajieva[1] & Vasila Talenova[1]

[1]Republican Specialized Scientific-and-Practical Medical Centre of Endocrinology, Tashkent, Uzbekistan; [2]Westminster International University in Tashkent, Uzbekistan; [3]Tashkent City Health Department, Uzbekistan

Background
Since the very first outbreak, scientists have been trying to determine the most critical pathogenetic mechanisms for the development of COVID-19 and related complications, analyze individual subpopulations of patients with chronic diseases and develop optimal tactics to combat not only the infection itself but also its acute and chronic complications.
Aim
to identify and analyze factors influencing the severity of the COVID-19 course among patients with Type 1 and Type 2 DM, including the glucose-lowering therapy effects.
Materials and Methods
A retrospective cohort study of 5023 Tashkent inhabitants, who had COVID-19 from April to December 2020, was performed. The data were obtained from the single electronic database of registered cases of COVID-19. All data were analyzed by univariate and multivariate logistic regression models using STATA 17.0 software. Further, the matched case-control study was performed for patients with type 2 DM and no DM based on age, gender, and BMI.
Results
Of the 5023 analyzed subjects, 72.63% had no diabetes mellitus (DM), 4.24% had type 1 DM, 15.19% had type 2 DM, and 7.94% was diagnosed with DM during the COVID-19 infection. DM, overweight, and obesity were associated with severe COVID-19; the most significant risk of a severe course was found in persons with type 2 DM. The risk of a lethal outcome and the need for prescription of glucocorticoids did not show a significant association with diabetes in Tashkent. The clinical features of COVID-19 were more common in patients with type 2 DM, especially for shortness of breath, chest pain, and arrhythmia. The persons receiving SU have complained of dyspnea significantly more often than matched patients without DM. Metformin and DPP4i were the groups of drugs that were not associated with significantly increased risk of hospitalization of patients because of COVID-19. The matched case-control study did not reveal statistically significant differences in the disease course severity, need for hospitalization and glucocorticoids, and death depending on the glucose-lowering therapy preceding the onset of COVID-19.
Conclusion
Diabetes, age and overweight/obesity were associated with severe course of COVID-19 in Tashkent. There was no statistical difference in COVID-19 severity depending on initial glucose-lowering therapy.
Keywords
diabetes mellitus, COVID19, metformin, insulin, complications, mortality
DOI: 10.1530/endoabs.81.P80

P81

Adipocytokines profile in patients with Graves' orbitopathy and the effect of high-dose corticosteroids

Jan Schovanek[1], Michal Krupka[2], Lubica Cibickova[1] & David Karasek[1]
[1]Faculty of Medicine and Dentistry, Palacky University Olomouc and University Hospital Olomouc, Department of Internal Medicine III – Nephrology, Rheumatology and Endocrinology, Olomouc, Czech Republic; [2]Faculty of Medicine and Dentistry, Palacky University Olomouc and University Hospital Olomouc, Department of Immunology, Olomouc, Czech Republic

Graves' orbitopathy (GO) is a serious, progressive eye condition seen in patients with autoimmune thyroid disease. GO is characterized by inflammation and swelling of soft orbital tissues. Adipose tissue produces cytokine mediators called adipokines. The present study focuses on the relationship between serum levels of selected adipokines in patients with GO, comparing them with the control group, and uniquely describes the effect of high-dose systemic corticosteroids (HDSC) on their levels. For the purposes of this study, we collected blood samples before and after the treatment with HDSC from 60 GO patients and 34 control subjects and measured serum levels of adiponectin, AIF-1, A-FABP and FGF-21. Levels of adiponectin significantly differed among the three study groups (ANOVA $P = 0.03$). AIF-1 levels were also highly significantly different among the study groups (ANOVA $p < 0.0001$) with the highest value in GO patients after HDSC treatment, which was, however, not statistically different to the value in patients before HDSC treatment ($P = 0.82$). We did not observe any statistically significant difference in the levels of A-FABP or FGF-21 between controls and our patients, nor did HDSC treatment have an effect (ANOVA $P = 0.19$; $P = 0.11$). AIF-1 was in a multivariate analysis significantly associated with the presence/absence of GO after adjusting for clinical factors (age, sex, smoking and BMI) and level of TSH (Odds ratio 1.003, $p < 0.01$). No other adipokine showed this association. This finding could enforce targeting macrophages in treatment strategies for GO since AIF-1 is considered as a marker of their activation. This work was supported by the Ministry of Health of the Czech Republic – Conceptual development of research organization (FNOL, 00098892) and grant no. NU21J-01-00017.
DOI: 10.1530/endoabs.81.P81

P82

Irisin in pediatric patients with Prader Willi Syndrome: the role of body composition and glucose metabolism

Stefania Mai[1], Danilo Fintini[2], Chiara Mele[3], Alessio Convertino[2], Sarah Bocchini[2], Graziano Grugni[4], Gianluca Aimaretti[3], Roberta Vietti[1], Massimo Scacchi[1,5], Antonino Crinò[2] & Paolo Marzullo[1,3]
[1]Istituto Auxologico Italiano IRCCS, Laboratory of Metabolic Research, San Giuseppe Hospital, Verbania, Italy; [2]Bambino Gesù Children's Hospital, Reference Center for Prader Willi Syndrome, Rome, Italy; [3]University of Piemonte Orientale, Division of Endocrinology, Department of Translational Medicine, Novara, Italy; [4]Istituto Auxologico Italiano IRCCS, Division of Auxology, San Giuseppe Hospital, Verbania, Italy; [5]University of Milan, Department of Clinical Sciences and Community Health, Milan, Italy

Irisin is a myokine involved in the browning of white adipose tissue and in the regulation of energy expenditure, glucose tolerance and insulin sensitivity. It was previously demonstrated that obese adults with Prader-Willi syndrome (PWS) harbor lower irisin levels than individuals with common obesity. Significant associations seem to relate irisin to muscle mass, REE, insulin resistance and triglycerides and also the strongest independent predictors of irisin levels were PWS status, %FM and triglycerides (Mai S et al., 2020). The divergent models of obesity herein studied suggest a potential link between circulating irisin and muscle mass and metabolic dysfunction relating to adiposity. Scanty and debated information exists on the role played by irisin in obese children. In this context, the obese phenotype of children with PWS markedly differs from that of BMI-matched subjects with common obesity. Based on these considerations, the present study aimed at exploring circulating irisin in relation to body composition and metabolic profile in obese children with and without PWS. For this purpose, 25 PWS children and adolescents (15 DEL15/10 UPD15, 16 M/9 F; age 6.6-17.8y; BMI SDs 2.5 ± 0.3) and 25 age, and BMI-matched control subjects (11 M/14 F; age 6.8-18.0y; BMI SDs, 2.8 ± 0.1) underwent analysis of irisin levels, body composition and metabolic profile, in particular glucose homeostasis assessed by OGTT. Expected differences in body composition and metabolic profile existed between study groups. PWS displayed lower FFM ($P < 0.05$), as well as lower fasting insulin level ($P < 0.0001$), 2h post-OGTT insulin ($P < 0.05$) and C-peptide levels ($P < 0.0001$), together with better insulin resistance, expressed as HOMA-IR ($P < 0.0001$). Irisin levels were significantly lower in PWS group than in controls with common obesity ($P < 0.05$): more specifically, irisin levels of PWS patients with DEL15 were reduced compared to controls with common obesity ($P < 0.05$). Exploring the relation between irisin and glucose metabolism in obesity, univariate correlation analysis in our obese population as a whole showed positive associations between irisin, insulin $OGTT_0$ ($P < 0.05$), insulin $OGTT_{120}$ ($P < 0.005$), HOMA-IR ($P < 0.05$) and C-peptide ($P < 0.05$). In stepwise multivariable regression analysis on merged data, irisin levels were independently predicted by insulin $OGTT_{120}$. Overall, current results show that irisin levels are lower in obese PWS compared to matched children, possibly due to differences in body composition and insulin resistance. A strong association links irisin to measures of insulin resistance, particularly post-OGTT insulin levels, suggesting a link between this myokine and insulin sensitivity in our two divergent models of obesity.
DOI: 10.1530/endoabs.81.P82

P83

Menstrual cycle abnormalities as distinctive sign of type 1 diabetes mellitus: results from a meta-analysis

Rossella Corleto[1,2], Carla Greco[1,2], Marta Cacciani[1,2], Giorgia Spaggiari[2], Manuela Simoni[1,2] & Daniele Santi[1,2]
[1]Department of Biomedical, Metabolic and Neural Sciences, University of Modena and Reggio Emilia, Modena, Italy., Modena, Italy; [2]Unit of Endocrinology, Department of Medical Specialties, Azienda Ospedaliero-Universitaria di Modena, Ospedale Civile di Baggiovara, Modena, Italy., Modena, Italy

Background
Type 1 diabetes mellitus (T1DM) management profoundly changed across years, with increasing emphasis on stringent glycaemic control. While it is well demonstrated that the progressive improvement of glycaemic control allows a tighter command of diabetes-related complications, the positive implications thereof on reproductive functions are still unclear. Indeed, it is well known that oligomenorrhea and amenorrhea are more frequently detected in young women with T1DM compared to healthy age-matched controls. However, whether the menstrual abnormalities incidence changed across years is still matter of debate.
Aim of the study
To evaluate the menstrual cycle abnormalities rate in T1DM young women, compared to healthy subjects, and to search for potential T1DM-related factors influencing female reproductive system. Secondary aim was the evaluation of the possible effects of the change in T1DM management, occurred in the late 90's, on menstrual cycle dysfunction.
Methods
A meta-analysis was performed considering all clinical trials in which menstrual cycle abnormalities in T1DM young women were reported, compared to healthy age-matched subjects. Primary endpoint was the rate of oligomenorrhea/amenorrhea and secondary objective was age at menarche. Sensitivity analysis was conducted dividing studies into two groups, i.e. before and after 2000, according to the change in T1DM management. Three meta-regression analyses were performed, considering the influence of diabetes duration, body mass index (BMI) and glycated haemoglobin (HbA1c) serum levels on menstrual irregularities.
Results
From 623 papers initially identified, 12 studies were finally included. Menstrual cycle dysfunction rate was significantly higher in T1DM women compared to controls, also considering only studies published after 2000 (OR:2.08; 95%CI: 1.43,3.03, $P<0.001$). Age at menarche was significantly higher in T1DM women compared to controls ($P<0.001$) also when studies published after 2000 were evaluated separately (mean difference:0.53; 95%CI: 0.32,0.74 years, $P<0.001$). In meta-regression analyses, the menstrual abnormalities rate in T1DM women were inversely related to diabetes duration ($R^2=0.396$,$P=0.023$), but not to BMI ($R^2=0.134$,$P=0.373$) and HbA1c serum levels ($R^2=0.083$,$P=0.409$).
Conclusion
The meta-analytic approach confirmed the high incidence of menstrual cycle dysfunction in T1DM young women. The improvement in T1DM management, introduced after 2000, seems not able to influence this rate, leaving menstrual cycle abnormalities one of the distinctive signs of this chronic condition. Indeed, T1DM-related menstrual dysfunction is associated neither to anthropometrical variables, nor glycemic control. Although actual pathogenetic mechanisms are not fully understood, here we demonstrate a potential association with T1DM duration, suggesting that the process of disease acceptance could underlie these irregularities.

DOI: 10.1530/endoabs.81.P83

P84

Vitamin D supplementation lowers the serum levels of branched chain amino acids in a cohort of patients with type two diabetes mellitus

Mahmoud A. Alfaqih[1], Samir Al Bashir[2] & Nebras Melhem[1]
[1]Jordan University of Science and Technology, Physiology and Biochemistry, Irbid, Jordan; [2]Jordan University of Science and Technology, Pathology and Microbiology, Irbid, Jordan

Background
Type two Diabetes Mellitus (T2DM) is a rapidly growing crisis. Data from several T2DM cohorts demonstrate that elevated levels of serum branched chain amino acids (BCAAs) increase the risk of the disease. BCAAs levels correlate with parameters that reflect glycemic control. Elevated levels of BCAAs in T2DM is associated with a higher risk of complications. Vitamin D plays an important role in regulating insulin action on target tissues. Normalization of serum vitamin D levels in T2DM patients with vitamin D deficiency was shown to improve their glycemic control.
Aim
To determine whether the positive effect of vitamin D on insulin sensitivity in T2DM could be partially mediated through the ability of vitamin D to reduce BCAAs.
Methods
A case-control design was used followed by a therapeutic intervention cohort for 3 months. In the case control part, 231 subjects were recruited, 137 subjects had a confirmed diagnosis with T2DM and 93 subjects were disease free. Patients were frequency matched with the controls by age and body mass index. The serum levels of 25(OH) vitamin D, glucose, total cholesterol, triglycerides, and BCAAs were measured from the serum samples of all subjects while HbA1c levels were measured from whole blood samples. Of the 137 subjects with T2DM, 26 subjects had 25(OH) vitamin D deficiency. These patients were recruited to a therapeutic intervention where they received 50,000 IU of vitamin D_3 tablets weekly for 3 months while maintaining standard treatment of care. Following the intervention; 25(OH) vitamin D, glucose, HbA1c, total cholesterol, triglycerides and BCAAs were measured.
Results
T2DM subjects had significantly higher levels of glucose, HbA1c, triglycerides and BCAAs ($P<0.05$) but significantly lower levels of 25(OH) vitamin D. Serum levels of BCAAs negatively correlated with serum 25(OH) vitamin D ($P=0.043$, $r=-0.173$). In the intervention cohort, vitamin D supplementation significantly lowered the serum levels of glucose, triglycerides, BCAAs ($P<0.05$) and the whole blood levels of HbA1c ($P<0.05$) compared to baseline levels measured a day prior to the intervention.
Conclusion
Normalization of 25(OH) vitamin D using clinically approved supplementation protocols significantly reduces circulating levels of BCAAs in T2DM patients; an effect that may reduce T2DM patient risk of future complications.

DOI: 10.1530/endoabs.81.P84

P85

Ramadan fasting without the doctor's consent: which patient, and what impact? Results of a prospective study

Ali Halouache[1], Errahali Yassine[1], Chakdoufi Sanae[1,1], Isouani Jad[1] & Guerboub Anas[1]
[1]Hopital Militaire d'Instruction Mohammed V, Endocrinology and Metabolic Diseases, Rabat, Morocco

Background and aims
The objective of our study is to evaluate the respect of Muslim diabetics for the contraindication of fasting and the control metabolic impact of fasting during the month of Ramadan.
Materials and methods
This analytical cross-sectional study was conducted during the period from Mars to June of the year 2021, within the department of endocrinology and metabolic diseases of the Military Hospital of Instruction Mohamed V of Rabat.
Results
Among the 89 patients included in our study, 54 (60%) fasted against their physician's advice, among whom 77.77% had a low level of education (versus 71.4%) ($P=0.498$), the age of diabetes ($P=0,004$), the presence of degenerative complications($P<0,001$), and the degree of glycemic control($P=0,018$) were the main predictors of fasting against medical advice. The mean HbA1C level in the patients who decided to fast was 7.77+/-1.6% before Ramadan and 7.79+/-1.56% after Ramadan, while that in the non-fasting group was 8.84+/-2.34% before Ramadan and 8.58+/- 1.89% after Ramadan. Hypoglycemia concerned 37% of the patients who fasted(versus 0%) ($P<0.001$).
Discussion
Of the 89 patients who were not allowed to fast, more than half(60%) fasted during the month of Ramadan. This result is similar to that of the study by Meriem Bencharif and al, in which 58.5% of patients with type 2 diabetes fasted during the holy month, The EPIDIAR study, found that among type 2 diabetics, 78.7% fasted for more than 15 days of the holy month. In our study, patients with long-standing diabetes tend to comply with their doctor's instructions; this can be explained by the improvement of the knowledge of diabetics regarding their disease with time as proved by the study of C. Bel Hadj Sliman and al . The presence of degenerative complications, and the glycated hemoglobin level, also influence, the attitude of diabetic patients during the month of Ramadan ($P<0.001$). The EPIDIAR study showed a significant increase in hypoglycemic events during Ramadan in diabetic patients, the same finding was noted in our study, Nevertheless, no change in the incidence of hypoglycemia was found in diabetic who fasted and were well controlled at baseline in several studies
Conclusion
Our study proves that a large Muslim diabetic population does not respect the doctor's instructions when it comes to fasting during Ramadan

DOI: 10.1530/endoabs.81.P85

P86

Effect of an extract of the Andean plant Lampaya on insulin signaling and proinflammatory markers in human adipocytes treated with palmitic acid

Paulina Ormazabal[1,2], Gabriela Yuri[1,2], Isidora Villagran[1], Alexis Cerda[2], Mariana Cifuentes[2], Adrian Paredes[3] & Glauco Morales[3]
[1]Institute of Health Sciences, Universidad de O'Higgins, Rancagua, Chile; [2]Laboratory of Obesity and Metabolism in Geriatrics and Adults (OMEGA), Institute of Nutrition and Food Technology (INTA), Universidad de Chile, Santiago, Chile; [3]Laboratorio de Química Biológica, Instituto Antofagasta (IA) and Departamento de Química, Facultad de Ciencias Básicas, Universidad de Antofagasta, Antofagasta, Chile

Background
Obesity is strongly associated with a state of chronic low grade systemic inflammation and insulin resistance (IR). IR at the molecular level may be defined as a diminished activation of the metabolic phosphatidylinositol-3-kinase (PI3K) /Akt pathway of insulin. On the other hand, inflammatory response may be activated by NF-κB. Subject with obesity have elevated plasma levels of saturated fatty acids, such as palmitic acid (PA), which triggers insulin and inflammatory signaling disruption *in vivo* and *in vitro*. Additionally, protein phosphorylation is an important regulatory mechanism to activate intracellular signaling. The protein tyrosine phosphatase 1B (PTP1B) is well known to regulate PI3K/Akt route and NF-κB inflammatory signaling. Infusions of *Lampaya medicinalis* Phil. (*Verbenaceae*) are used in folk medicine of Northern Chile to counteract inflammatory diseases. Hydroethanolic extracts of lampaya (HEL) contain considerable amounts of flavonoids that may explain the biological activity of the plant. The aim of this study was to assess whether HEL exposure protects against PA- induced inflammation and disruption of PI3K/Akt signaling in human adipose cells.
Methods
Cytotoxicity of a range of HEL concentrations (0.01– 10 μg/ml) was evaluated by MTS assay in *in vitro* differentiated adipocytes from the adipose cell line SW872. Adipocytes were incubated or not with PA for 24 h in the presence or not of HEL (2-h preincubation), and thereafter stimulated with insulin or vehicle. Thereby, experimental conditions were: control (untreated cells), 0.4 mM PA, 0.01 μg/ml of HEL, 0.01 μg/ml of HEL (2 h before) + 0.4 mM PA for 24 h, in insulin-stimulated (100 nM, 10 min) or basal conditions. Phosphorylation of Tyr-IRS-1, Ser-Akt, Ser-NF-κB and protein expression of PTP1B were evaluated by Western blot.
Results
In SW872 adipocytes, HEL was not cytotoxic at any concentration assessed. Insulin-stimulated phosphorylation of IRS-1 and Akt as well as phosphorylation of NF-κB and PTP1B protein content were not affected by treatment with 0.01 μg/ml HEL compared with vehicle-treated cells. PA-treated adipocytes showed a reduction in insulin-stimulated phosphorylation of IRS-1 and Akt compared to control ($P<0.05$), while the phosphorylation of NF-κB and PTP1B protein expression were elevated compared to untreated cells ($P<0.05$). Interestingly, these effects were prevented by HEL treatment.
Conclusion
These findings give new insights about the effect of HEL ameliorating PA-impaired insulin signaling and inflammatory markers in adipocytes. More studies should focus on lampaya, since might represent a preventive approach in individuals whose circulating PA levels contribute to inflammation and IR.

DOI: 10.1530/endoabs.81.P86

P87

COVID-19 and Steroids- How well are we monitoring blood glucose levels?

Aye Me-Me-Ko, Ashutosh Kapoor, Fatima Riaz, Stuart Wightman & Prasanna Rao-Balakrishna
Manchester University NHS FT, Manchester, United Kingdom

Background
The Covid-19 pandemic has led to various unprecedented challenges and obstacles, especially in the field of Diabetes and Metabolism, many of which are as novel as the pandemic itself. Discovering efficacious therapeutic options resulting in positive outcomes has been a challenge. Dexamethasone has been shown to reduce mortality in patients with Covid-19 pneumonitis who require oxygen therapy and/or ventilation. Exogenous steroid therapy is renowned to cause adverse metabolic side effects, including Hyperglycemia. In addition to this, concurrent Covid-19 infection further exacerbates the issue at hand.
Aims
The main aim of the Quality Improvement Project (QIP) was to improve adherence and compliance of capillary blood glucose (CBG) monitoring in patients with Covid-19 pneumonitis treated with steroid therapy by implementation of educational tools. Our results were compared with the standard of care guidance as set out by the Joint British Diabetes Societies (JBDS) Specific emphasis was placed upon early recognition of Hyperglycaemia, leading to improved Glycaemic control and patient outcomes.
Methods
Phase one of the project involved data collection on a retrospective basis of patients admitted to both the medical and COVID wards. This involved obtaining relevant information from the patient's medical, nursing, and electronic notes. Changes were implemented in the form of teaching and educational sessions for the nursing staff. Posters focusing on the important of Blood Glucose monitoring were circulated on the medical wards including the COVID wards. This was followed by discussions emphasising the importance of Blood Glucose monitoring on the board rounds.
Results
Data collection prior to changes showed that out of the cohort of 23 patients, only 5 patients (21.74 %) met the desired standard of care as per the guidance set out by the JBDS**.** Following implementation of changes, data collection revealed an improvement of compliance from 21.74 % to 56.52 %. Out of 23 patients, the desired level of care was now met in 10 of the patients. The project was carried out over a period of 3 months, commencing in October 2020, and concluded in January 2021
Conclsions
Hyperglycaemia was associated with worse outcomes. Our QIP improved rates of blood glucose monitoring, followed by early recognition of hyperglycaemic states. This was also reflected in the fact that early recognition led to early therapeutic measures and prevention of diabetic emergencies. Despite significant changes, we aim to instigate further improvement by reinforcing learning among the frontline staff to achieve 100% compliance with the guidelines.

DOI: 10.1530/endoabs.81.P87

P88

Sodium glucose cotransporter 2 inhibitors treatment in acromegalic patients with diabetes

Adnan Zaina[1], Yuval Grober[2], Ali Abid[3], Eldad Arad[4], Elena Golden[4] & Samih Badarny[5]
[1]Bar-Ilan University, Azrieli Faculty of Medicine, Division of Endocrinology and Metabolism, Zvulon Medical Center, Clalit Medical Health Care Services, Safed, Israel; [2]Bar-Ilan University, Azrieli Faculty of Medicine, Division of Neurosurgery, Galilee Medical Center, Nahariya, Safed, Israel; [3]Clalit Health Services, Division of Endocrinology and Metabolism, Zvulon Medical Center, Clalit Medical Health Care Services, Israel; [4]Clalit Health Services, Division of Endocrinology and Metabolism, Zvulon Medical Center, Israel; [5]Bar-Ilan University, Azrieli Faculty of Medicine, Department of Neurology, Galilee Medical Center., Safed, Israel

Introduction
Acromegaly is a chronic disease generally caused by a GH-secreting pituitary adenoma. GH excess causes insulin resistance and impair β cell function, predisposing patients with acromegaly to develop DM. Treatment of diabetes has been revolutionized since the introduction of sodium-glucose cotransporter inhibitors (SGLT2i). This novel class is widely used in type 2 diabetes mellitus (T2DM) and recently was approved for patients with heart failure with reduced ejection fraction and patients with chronic kidney disease (CKD) without diabetes. Taking into consideration the cardiorenal protection aspects, SGLT2i seems to be also attractive for diabetes management in acromegalic patients with already known increased cardiovascular risk. However, despite the known favorable aspects, SGLT2i is less recommended for acromegalic patients with diabetes due to the increased risk of diabetic ketoacidosis (DKA).
This study aims
To report data regarding the use of SGLT2i in patients with acromegaly and diabetes.
Methods
In the present case series, data was collected using an electronic computerized registry at Clalit Medical Health (CMH) Services from Western Galilee and Haifa district between the years 2000-2020. Charts of patients with acromegaly and diabetes were reviewed thoroughly for current and previous anti-diabetic and acromegaly medications. Notably, electronic computerized files enable health care practitioners to follow the monthly treatment dispensing and report drug side effects. Laboratory results for fasting plasm glucose (FPG), hemoglobin A1c, IGF-1, and GH were reported before SGLT2i administration. In addition, actual hemoglobin A1c, body mass index (BMI), duration of diabetes, tumor size was reported for patients with and without SGLT2i treatment.
Results
34 acromegalic patients with diabetes were identified. Treatment with SGLT-2i was documented in nine patients, out of them 5 females and 4 males with a mean

age (SD) of 61 ± 12 yr. The mean (SD) duration of treatment with SGLT2i was 27.5 ± 7.3 months. Mean HbA1c before and after SGLT-2i initiation was 8.1 ± 1.1% and 7.0 ± 0.9% respectively. Mean IGF-1 level (SD) before SGLT-2i initiation was 177 ± 68 ng/ml and the mean GH level (SD) was 0.7 ± 0.5 µg/l. All nine patients are still under treatment with SGLT2i and none of them had reported any adverse reaction related to SGLT2i.

Conclsions

This study provides us for the first time with new data regarding the use of SGLT2i among acromegalic patients with diabetes. The use of SGLT2i among patients with already treated acromegaly and diabetes seems to be attractive.

DOI: 10.1530/endoabs.81.P88

P89

Predictors of persistant abnormal glucose tolerance in post partum in women with gestational diabetes mellitus

Rahma Khalaf, Yosra Htira, Zohra Hadj Ali, Chaima Jemai, Imen Hedfi & Faika Ben Mami

National Institute of Nutrition, Department C, Tunisia

Background and aim

To determine clinical and metabolic predictors of persistant abnormal glucose tolerance in post partum after gestational diabetes mellitus (GDM).

Methods

This was a prospective study including 150 patients with GDM who underwent 75 g oral glucose tolerance test (OGTT) at 4-12 weeks after delivery.

Resulats

The prevalence of abnormal glucose tolerance in post partum after GDM was 32,8 %, inclusive of 3.3% type 2 diabetes and 29.5% pre-diabetes. After univariate analysis, persistent carbohydrate tolerance disorders in post partum were statistically associated with age (34,77 ± 4,02 vs 32,07 ± 6,29 years ;p = 0.015) and AB blood group (10.3% vs 0% ;p = 0.012). Family history of type 2 diabetes in a first degree relative, personal history of GDM, fetal macrosomia, pre-gestational Body Mass Index and parity did not statiscally differ between the two groups. Thirty minutes of moderate physical activity five times per week was a protective factor ($P = 0.004$) while sedentary lifestyle was associated with impaired carbohydrate tolerance in post partum ($P = 0.004$). Fasting blood glucose, glycemia at 2 hour in 75 g oral glucose tolerance test (OGTT) > 1.6 g/l and insulin use according to a full basal bolus regimen were significantly associated with the persistence of carbohydrate tolerance disorders (respectively $P = 0.005$, $P = 0.02$, $P = 0.03$). After multivariate analysis, the independent factor associated with abnormal glucose tolerance in post partum was glycemia at 2 hour (OGTT) (OR 5.18, 95% CI 1.27- 21.16, $P = 0.02$).

Conclsion

Antenatal caracteristics may predict abnormal glucose tolerance in post partum after GDM. High prevalence of persistent carbohydrate tolerance disorders highlights the importance of ongoing screening for all women with previous GDM in order to delay the onset of type 2 diabetes in this high risk population.

DOI: 10.1530/endoabs.81.P89

P90

Evening chronotype is associated with hormonal and metabolic disorders in Polycystic Ovary Syndrome

Ludovica Verde[1], Luigi Barrea[2], Claudia Vetrani[1], Annamaria Docimo[1], Giulia De Alteriis[1], Silvia Savastano[1], Annamaria Colao[1] & Giovanna Muscogiuri[1]

[1]Federico II University, Department of Clinical Medicine and Surgery, Endocrinology Unit, Naples, Italy; [2]Pegaso Telematic University, Department of Humanities, Naples, Italy

Objective

Polycystic ovary syndrome (PCOS) is the most common female endocrine disorder. Recently in the context of obesity, which often coexists with PCOS, it has been highlighted the role of chronotype as risk factor for obesity-related cardiometabolic complications. Given the importance of chronotype categories in the context of metabolic diseases and being PCOS characterized by metabolic derangements, we aimed to investigate the prevalence of chronotype categories in women with PCOS compared to healthy controls and their role in determining hormonal and metabolic aspects of PCOS.

Design and methods

In this case-control study, we investigated the chronotype categories in 112 women with PCOS and in 112 age and Body Mass Index (BMI) matched healthy women. Anthropometric (weight, height, BMI, and waist circumference), clinical [Ferriman-Gallwey (FG) score], biochemical [fasting plasma glucose (FPG), insulin levels and Homeostasis Model Assessment (HoMA-IR)], inflammatory [C-reactive Protein (CRP)] and hormonal (testosterone levels) parameters were assessed.

Results

Women with PCOS had a lower chronotype score ($P < 0.001$) and thus a higher prevalence of evening chronotype category ($P = 0.037$) than controls. Women with PCOS and evening chronotype had significantly higher levels of FPG, insulin levels and therefore HoMA-IR, CRP, testosterone levels and FG score than women with PCOS with neither and morning chronotype. After adjusting for BMI, chronotype score showed significant negative correlations with CPR, testosterone levels and FG score. Linear regression analysis showed that high testosterone levels were among the factors most associated with a lower chronotype score ($P < 0.001$), followed by BMI ($P < 0.001$) and HoMA-IR ($P < 0.05$).

Conclsions

In summary, the current study reports the first evidence that women with PCOS had a higher prevalence of evening chronotype than women without PCOS. In women with PCOS evening chronotype has been associated with a worse hormonal and metabolic profile. Thus, given the importance of chronotype in women with PCOS emerging in our study, the assessment of chronotype should be included in the clinic evaluation of women with PCOS Moreover, a chronotype-driven lifestyle approach could potentially improve the treatment of women with PCOS thus increasing the number of women with PCOS achieving their therapeutical goals.

DOI: 10.1530/endoabs.81.P90

P91

PCSK-9 inhibitors and the reduction of serum lipoprotein (a) levels: experience of the reference center

Dunja Leskovar, Drazen Perica, Nediljko Sucur, Ana Godan Hauptman & Ivan Pečin

University Hospital Centre Zagreb, Divison for Metabolic Diseases, Zagreb, Croatia

Introduction

PCSK-9 (proprotein convertase subtilisin/kexin type 9) inhibitors are monoclonal antibodies that affect metabolism of low-density lipoprotein (LDL) by binding to the LDL receptor and promoting lysosomal degradation. There are two pcsk-9 inhibitors currently available: alirocumab (Praulent) and evolocumab (Repatha) which are administered subcutaneously every 14 days. Two large randomized studies (FOURIER, ODYSSEY) have shown that pcsk-9 inhibitors reduce LDL-cholesterol levels by 50-60% and additionally lipoprotein (a) levels by 25-30%. Such results broadened the indications for the usage of pcsk-9 inhibitors. Since serum levels of lp (a) is exclusively genetically determined, the possibility of its reduction is very important as high serum lp(a) levels increase cardiovascular risk by up to three-fold. Lowering of lp(a) levels is especially important for younger patients with cardiovascular incident in history Although the mechanism how pcsk-9 inhibitors reduce lp (a) levels is unclear, some studies show that at lower LDL-cholesterol levels, lp (a) levels decrease more with the assumption of better competence for LDL-receptor site.

Methods and results

Polyclinic of Reference Center for Rare and Metabolic Diseases has a total of 51 patients on PCSK-9 inhibitor therapy which was indicated due to elevated lp (a) concentration (> 75 nmol/l, > 0.5 g/l). The average age of patients is 52.74 years with almost equal distribution of male and female gender (53%, 47%). The overall percentage in reduction of lp(a) levels during 3 months of PCSK-9 inhibitor therapy was 30.78%, with a maximum reduction of 72% and a minimum of 5%. T-test of paired samples for the effect of pcsk-9 inhibitors on the reduction of lp(a) concentration revealed a statistically significant difference ($t = 5{,}2015$; $P = 0.00000156$, < 0.0001) at serum lp(a) concentrations before (M = 127.05, SD = 133.93) and after pcsk-9 inhibitor therapy (M = 82.29, SD = 81.06). The strength of the test is 0.982. The maximum observed reduction of 72% was observed in a patient who was previously on the statin therapy at the maximum dosage.

Conclusion

The experience of our Center confirms previous research on the effect of pcsk-9 inhibitors on the reduction of lp (a) concentration by 30%. Comparing targeted concomitant therapy, we have observed a trend of greater reduction in lp (a) levels with pcsk-9 inhibitor therapy in patients who are previously on the maximum

statin dose, suggesting possible metabolism of the particle itself via the LDL receptor by the mechanism of competition.
Keywords lipoprotein (a), PCSK-9 inhibitors, statins

DOI: 10.1530/endoabs.81.P91

P92

Transforming growth factor beta 1: a new factor reducing hepatic sex hormone binding globulin production during liver fibrosis development

Laura Briansó Llort[1], Lidia Fuertes Rioja[1], Lorena Ramos Perez[1], Maria Teresa Salcedo Allende[2], Cristina Hernandez[1], Rafael Simo Canonge[1] & David Martinez[1]
[1]VHIR - Vall d'Hebron Institut de Recerca, Diabetes and Metabolism, Barcelona, Spain; [2]Hospital Universitari Vall d'Hebron, Pathology, Barcelona, Spain

Low plasma sex hormone-binding globulin (SHBG) levels are present in fatty liver disease, which represent a spectrum of diseases ranging from hepatocellular steatosis through steatohepatitis to fibrosis and irreversible cirrhosis. We have previously determined that fat accumulation reduces SHBG production in different non-alcoholic fatty liver disease (NAFLD) mouse models and that SHBG plays an active role in the development of this disease. In the present work, we are interested in elucidating the molecular mechanisms reducing SHBG plasma levels in liver fibrosis development. To do so, *in vivo* studies were performed using the human *SHBG*transgenic mice developing liver fibrosis induced by carbon tetrachloride (CCl_4). Our results showed that CCl_4 induced liver fibrosis and decreased SHBG production by reducing hepatocyte nuclear factor 4 alpha (HNF-4α). The SHBG reduction could be influenced by the increase in TGF-β1 levels, which were elevated in mice developing liver fibrosis. Results obtained in human *SHBG* transgenic mice showed that TGF-β1 reduced significantly SHBG mRNA and protein levels through TGF-β1 receptor I via STAT3 signaling pathway, resulting in a transcriptional repression of the *SHBG* gene. Overall, TGF-β1 is a new factor downregulating hepatic SHBG production in liver fibrosis development.

DOI: 10.1530/endoabs.81.P92

P93

Determination of serum and cord blood vitamin D status in women in twin pregnancies using liquid chromatography-tandem mass spectrometry – a preliminary results

Magdalena Zgliczynska[1], Iwona Szymusik[2], Konrad Kowalski[3], Magdalena Ostrowska[4] & Katarzyna Kosinska-Kaczynska[1]
[1]The Center of Postgraduate Medical Education, Second Department of Obstetrics and Gynecology, Warsaw, Poland; [2]Medical University of Warsaw, First Department of Obstetrics and Gynecology, Warsaw, Poland; [3]Masdiag Sp. z o.o. Company, Warsaw, Poland; [4]The Center of Postgraduate Medical Education, Department of Endocrinology, Warsaw, Poland

Objective
Vitamin D has a pleiotropic effect on the human body. Besides its classical function as a regulator of calcium and phosphorus metabolism, it influences the secretion of other hormones, modulates the immune response and regulates cell proliferation and differentiation. Because women in twin pregnancies have higher metabolic needs, it can be expected that they might have higher risk of vitamin D deficiency.
Aim of the study and method
The aim is to analyze the serum and cord blood concentrations of vitamin D metabolites in women in twin pregnancies with the use of liquid chromatography-tandem mass spectrometry (LC-MS). Until the submission of this abstract (January 2022) 15 maternal and 30 cord blood samples were tested. We have collected data on supplementation and dietary intake questionnaires.
Results
The mean maternal age was 34.1 years (±3.5). The delivery took place at an average 34.8 week of pregnancy (±3.3). All patients supplemented vitamin D in doses ranging from 200-4000 international units per day. The median concentration of total 25-hydroxyvitamin D (25(OH)D) in maternal serum was 43.9 ng/ml (interquartile range [IQR] 42.0-54.1). Its deficiency was found in one patient. Elevated vitamin D levels were found in 36.4% of the mothers (maximum 73.6 ng/ml). The median concentration of 25(OH)D in cord blood was 25.2 ng/ml (IQR 20.1-28.8). Maternal and cord blood levels were highly correlated ($r=0.58$). However, in each case, 25(OH)D level in the cord blood was lower than in the serum of corresponding mother (difference ranging from 7.1-48.2 ng/ml). In each pair of twins cord blood 25(OH)D concentrations were similar (differences: minimum 0.2, maximum 5.8, mean 2.2 ng/ml). In the described group, 25(OH)D levels in mothers were also determined by the commonly used in clinical practice chemiluminescent immunoassay (CLIA). The 25(OH)D levels obtained using the LC-MS method were significantly higher (median 43.9 ng/ml, IQR 42.0-54.1), than in case of CLIA (median 31.3 ng/ml, IQR 23.4-40.2;$P=0.003$). The differences in individual patients ranged from 5.4 ng/ml up to 36.7 ng/ml. These finding seem particularly important in terms of clinical decision making.
Conclusions
In the studied group of women in twin gestation that supplemented vitamin D, low prevalence of its deficiency determined by LC-MS was found. Maternal and cord blood levels of 25(OH)D were highly correlated. There are large discrepancies in the 25(OH)D concentrations obtained with LC-MS compared to CLIA in maternal samples.

DOI: 10.1530/endoabs.81.P93

P94

The prevalence of non alcoholic fatty liver disease among diabetic patients attending the diabetic clinic in a tertiary care institute in colombo

Ishara Ranathunga, J P Naveenkumar, T G Athukorala, Manilka Sumanatilleke & Noel Somasundaram
NHSL, Colombo, Sri Lanka

Background and Objectives
Non-alcoholic fatty liver disease (NAFLD) is the presence of hepatic steatosis in the absence of other causes for secondary hepatic fat accumulation. The incidence and the prevalence of the NAFLD has risen exponentially in the recent past especially in the patients with diabetes. We have studied the prevalence of NAFLD in patients with diabetes attending the diabetes clinic based on the biochemical and ultrasonic criteria, the risk factors for disease development and associated comorbidities.
Methods
A descriptive cross sectional study was conducted from August 2020 to March 2021 at the Diabetes Unit of the National Hospital of Sri Lanka. Systematic sampling was done recruiting participants who are attending the diabetic clinic for annual end organ screening. After obtaining informed written consent, the data was collected using an interviewer administered questionnaire. The diagnosis of NAFLD is made according to the NHANES III criteria and the USS criteria. Categorical and numerical variables were analyzed using Chi-square and independent sample t-tests respectively. Multiple linear regression was used to determine the predictors of NAFLD diagnosis.
Results
The study enrolled hundred and one patients. The mean age was 58.3 years (range 23-80) and 69.3% were females. The mean weight was 65.7 (SD=12.5) kg and BMI was 26.8 (SD=4.7) kg/m^{-2} . The prevalence of NAFLD according to the biochemical and/or USS criteria was 72.3% ($n=73$). Out of that 34.7% met both biochemical and USS criteria. Furthermore, 7.9% ($n=8$) met only the biochemical criteria while 29.7% ($n=30$) met only the USS criteria. More females were diagnosed with NAFLD compared to males ($P=0.009$). Pioglitazone use was protective against the development of NAFLD ($P=0.000$). The younger age ($P=0.021$), higher HbA1c ($P=0.033$), higher Body mass index (BMI) ($P=0.014$) are other statistically significant factors contributing to the development of NAFLD. Multiple linear regression model identified BMI ($P=0.002$), pioglitazone use ($P=0.002$), gender ($P=0.000$) as predictors of diagnosis of NAFLD.
Conclsions
The prevalence of NAFLD is higher in the diabetes patients when compared to the general population. The use of biochemical criteria only identifies a proportion of patients with NAFLD. Early diagnosis with suitable tests will allow early intervention and prevention of long term deleterious complications. Optimization of modifiable factors such as high HbA1c, BMI is paramount in the prevention of the disease development. Further large scale studies including community studies are needed to recognize the current prevalence of NAFLD in the general as well as diabetic populations.

DOI: 10.1530/endoabs.81.P94

P95

Perceived stigma in type 2 diabetes patients

Mehrez Achwak[1], Najoua Lassoued[2], Selma Mohsen[2], Khalil Chedly[3], Marwa Majdoub[4], Fedya Boubaker[4], Baha Zantour[4], Wafa Alaya[5] & Habib Sfar[6]
[1]Taher Sfar University Hospital, Endocrinology Department, Moknine, Tunisia; [2]Taher Sfar University Hospital, Endocrinology Department, Mahdia, Tunisia; [3]Taher Sfar University Hospital, Endocrinology Department, Mahdia, Tunisia; [4]Taher Sfar University Hospital, Endocrinology Department; [5]Taher Sfar University Hospital, Endocrinology Department, Moknine, Tunisia; [4]Taher Sfar University Hospital, Endocrinology Department, Tunisia

Introduction

Diabetes stigma (DS) refers to the experience of negative feelings such as exclusion, blame, rejection, or judgment due to having a chronic disease. The objective of this work was to measure the DS and its clinical determinants in type 2 diabetic patients.

Patients and methods

Cross-sectional study conducted on 84 type 2 diabetic patients who consulted on an outpatient basis between September and December 2021. DS was assessed using the arabic version of the type 2 Diabetes Stigma Assessment Scale (DSAS-2).

Results

Women represented 42% of the patients. The duration of diabetes was meanly 9.4 ± 6.4 years. The mean glycated hemoglobin was 9.9 % ± 2.4. The mean BMI was 27.7 Kg/m^2 ± 4.7. The mean Total Diabetes Stigma score was 46.9 ± 10.2 (range 19– 90). Subscale scores were as follows: Treated differently: 15.4 ± 4.2 (range 6– 30), Blame and Judgment: 17.5 ± 4.3 (range 7– 35), and Self stigma: 13.9 ± 2.3 (range 6– 30). A total of 26 (30%) respondents scored more than the mean total diabetes stigma score, suggestive of potentially problematic perceived diabetes stigma. Higher Total Diabetes Stigma Scores were associated with level of therapeutic education (P = 0,045), social coverage (P = 0,043), diabetes treatment (P = 0,044), HbA1c level (P = NS).

Discussion and conclusion

The results of this work highlights the importance of identifying DS in type 2 diabetics. High levels of DS have been associated with poor glycemic control, poor diabetes self-management and poor quality of life. These data support the need to focus on increasing awareness efforts to educate the public about type 2 diabetes and its management.

DOI: 10.1530/endoabs.81.P95

P96

Increased haematocrit mediates lowering of blood glucose in mice exposed to hypoxia or treated with erythropoetin

Thomas Scherer[1], Matthaeus Metz[1], Marianna Beghini[1], Sabine Dürr[1], Andreea Corina Luca[1], Mairam Kaplanian[1], Sameer Abu Eid[1], Alexandra Kautzky-Willer[2] & Clemens Fürnsinn[1]
[1]Division of Endocrinology & Metabolism, Department of Medicine III, Medical University of Vienna, Vienna, Austria; [2]Medical University of Vienna, Department of Medicine III, Division of Endocrinology & Metabolism, Vienna, Austria

Introduction

Mountain dwellers show a lower prevalence of diabetes, which among countless other factors could be due to lower partial oxygen pressure at high altitude. The present study was to investigate in an experimental setting, if and how reduced oxygen availability affects blood glucose.

Methods

Male obese mice on high fat diet were continuously maintained under a normobaric hypoxic atmosphere (10% oxygen) for three months. To exclude indirect effects via blunted appetite and reduced weight gain, control groups kept on normal air were fed restrictedly, so to match the weight curves of their hypoxia-exposed counterparts. To track down involved mechanisms, wild type mice as well as mice, which expressed the erythropoetin receptor in the haematopoetic lineage only, were treated with erythropoetin (300 U/kg i.p., three injections per week for two months). The immediate response to infusion of donor erythrocytes was also examined. Treatment-induced effects on blood glucose and insulin sensitivity were studied.

Results

Life under hypoxia increased the haematocrit (44 ± 1 *vs.* 55 ± 1 %, P < 0.001) and lowered blood glucose of obese mice (166 ± 5 *vs.* 132 ± 3 mg/dl, P < 0.001), which went along with improved insulin sensitivity (HOMA: 1.4 ± 0.2 *vs.* 0.60. ± 0.1, P < 0.001; euglycaemic-hyperinsulinaemic clamp experiments, mg glucose/kg/min: rate of disappearance, 42 ± 2 *vs.* 50 ± 2,P = 0.03; rate of appearance, 9 ± 4 *vs.* -5 ± 1,P = 0.008). Parameters of lipid metabolism were unaffected by hypoxia. Similar effects were observed in wild type mice under regular injections of erythropoetin (haematocrit: 44 ± 2 *vs.* 69 ± 3 %, P < 0.001; blood glucose: 173 ± 7 *vs.* 108 ± 9 mg/dl, P < 0.001; HOMA: 1.8 ± 0.4 *vs.* 0.3 ± 0.1,P = 0.008). Absence of the erythropoetin receptor in all tissues except bone marrow and spleen did not impair the glucose lowering action of erythropoetin injections (haematocrit: 46 ± 2 *vs.* 63 ± 1 %, P < 0.001; blood glucose: 160 ± 4 *vs.* 97 ± 10 mg/dl, P < 0.001; HOMA: 2.6 ± 0.7 *vs.* 0.8 ± 0.3,P = 0.048). This excluded direct action of erythropoetin on non-haematopoetic organs as the cause of decreased blood glucose. In line with such evidence for haematopoesis-mediated lowering of blood glucose, an acute increase in the haematocrit from 46 ± 1 % to 60 ± 1 % (P < 0.001) by infusion of donor erythrocytes induced a significant reduction in blood glucose (169 ± 6 *vs.* 135 ± 4 mg/dl, P < 0.001).

Conclusion

Reduced blood glucose in mice living in a hypoxic environment is associated with improved insulin sensitivity and is obviously the direct consequence of an erythropoetin-mediated increase in the haematocrit. Elevated haematocrit thus likely explains lower blood glucose found in people living at high altitude as well as in patients under treatment with erythropoetin.

DOI: 10.1530/endoabs.81.P96

P97

Chronotype: a tool to screen eating habits in Polycystic Ovary Syndrome?

Ludovica Verde[1], Luigi Barrea[2], Claudia Vetrani[1], Silvia Savastano[1], Annamaria Colao[1] & Giovanna Muscogiuri[1]
[1]Federico II University, Department of Clinical Medicine and Surgery, Endocrinology Unit, Naples, Italy; [2]Pegaso Telematic University, Department of Humanities, Italy

Background

Polycystic Ovary syndrome (PCOS) is the most common endocrine disorders in women of reproductive age whose lifestyle approach is an essential part of the treatment. Recently chronotype, i.e. a trait that determines individual's circadian preference in behavioral and biological rhythms, has been reported to play a role in determining nutrition preferences and the risk of developing chronic diseases. Thus, the aim of the study was to investigate if chronotype categories (morning, evening and neither) could be used as tool to screen eating habits in PCOS in order to drive the most appropriate nutritional approach.

Methods

In this observational cross-sectional study, we assessed anthropometric parameters, lifestyle habits, chronotype categories, adherence to MD, dietary pattern, and metabolic parameters in 112 women with PCOS.

Results

Chronotype was classified as morning in 27.7%, evening in 42.9% and neither in 29.5% of subjects. Women with PCOS with evening chronotype showed significantly higher percentages of grade I (P = 0.003) and grade II obesity (P = 0.001), did less regular exercise (P < 0.001) and most of them were smokers (P < 0.001) compared to those with neither and morning chronotype. In women with PCOS with evening chronotype there was a significantly higher prevalence of subjects with HoMA-IR cut off > 2.5 than neither and morning chronotype (P < 0.001). Women with PCOS with evening chronotype had the lowest PREDIMED score, consumed more calories (P < 0.001), total (P < 0.001) and simple carbohydrates (P < 0.001), total fat (P < 0.001) and SFA (P < 0.001), PUFA (P < 0.001) and n-6 PUFA (P < 0.001) and less fiber (P < 0.001) than women with PCOS with other chronotype categories. In addition, women with PCOS with evening chronotype consumed less EVOO (P = 0.001), legumes (P = 0.038), fish/seafood (P < 0.001) and tree nuts (P = 0.041) than women with PCOS with other two chronotype categories and less red wine (P < 0.001) and more red/processed meat (P < 0.001) than women with PCOS with morning chronotype.

Conclsion
In women with PCOS evening chronotype has been associated with a most severe IR and unhealthiest eating habits. Thus, chronotype assessment could be effective tool to screen the eating habits, and more generally the lifestyle, of women with PCOS.

DOI: 10.1530/endoabs.81.P97

P98

VLCKD: a real time safety study in obesity

Ludovica Verde[1], Luigi Barrea[1,2], Claudia Vetrani[1], Francesca Marino[1], Sara Aprano[1], Silvia Savastano[1], Annamaria Colao[1] & Giovanna Muscogiuri[1]
[1]Federico II University, Department of Clinical Medicine and Surgery, Endocrinology Unit, Naples, Italy; [2]Pegaso Telematic University, Department of Humanities, Naples, Italy

Very Low-Calorie Ketogenic Diet (VLCKD) is currently a promising approach for the treatment of obesity. However, little is known about the side effects since most of the studies reporting them were carried out in normal weight subjects following ketogenic diet for other purposes than obesity. Thus, the aims of the study were: 1) to investigate the safety of VLCKD in subjects with obesity; 2) if VLCKD-related side effects could have an impact on its efficacy. In this prospective study we consecutively enrolled 106 subjects with obesity (12 males and 94 females, BMI 34,98 $\pm$ 5,43 kg/m^2) that underwent to VLCKD. In all subjects we recorded side effects at the end of ketogenic phase and assessed anthropometric parameters at the baseline and at the end of ketogenic phase. In a subgroup of 25 subjects, we also assessed biochemical parameters. Ninety-nine (93,4%) of the subjects enrolled experienced at least one mild side effect but none of the most severe ones. From the most to the less frequent, the percentages of occurrence of the mild side effects were as follows: 49 (46,2%) lethargy, 49 (46,2%) halitosis, 48 (45,3%) headache, 41 (43,5%) dry mouth, 30 (28%) constipation, 19 (17,9%) hypotension, 17 (16%) dizziness, 16 (15,1%) vomiting/nausea, 16 (15,1%) hair loss, 13 (12,3%) diarrhoea, 11 (10,4%) hyperuricemia, 5 (4,7%) visual disturbances, 1 (0,9%) low blood sugar. No one experienced urolithiasis and gallbladder disease. In addition, 9 (8.5%) subjects stopped VLCKD before the end of the protocol for the following reasons: 2 (1.9%) due to palatability and 7 (6,1%) due to excessive costs. Finally, there were no differences in terms of weight loss percentage (13,5 $\pm$ 10,9 % vs 18,2 $\pm$ 8,9 %; P = 0.318) in subjects that developed side effects and subjects that did not developed side effects. Our study 2 demonstrated that VLCKD is a safe and effective nutritional tool in the management of subject with obesity.

DOI: 10.1530/endoabs.81.P98

P99

A novel successful therapeutic option after a journey of treatment failures in a patient with heterozygous melanocortin-4 receptor deficiency

Mila Welling[1,2], Mostafa Mohseni[1,2] & Elisabeth van Rossum[1,2]
[1]Erasmus MC, University Medical Center, Obesity Center CGG, Rotterdam, Netherlands; [2]Erasmus MC, University Medical Center, Dept. of Internal Medicine, division of Endocrinology, Rotterdam, Netherlands

Introduction
Obesity is a complex and multifactorial disease with a chronic and relapsing nature, and is associated with over 200 co-morbidities. In a minority of patients, the obesity is caused by gene defects in the leptin-melanocortin pathway. As lifestyle interventions often fail in these patients, additional anti-obesity pharmacotherapy is needed. In this case report, we describe the therapeutic journey of a patient with early-onset obesity and hyperphagia due to heterozygous *melanocortin-4 receptor* deficiency.
Case presentation
A 33-year-old woman presented herself at our outpatient clinic with severe obesity, hyperphagia, and mild intellectual deficit. She developed obesity at the age of 6 years, resulting from hyperphagia. After regular lifestyle treatment without sufficient effect, a gastric bypass was performed at the age of 26 years leading to -40 kg weight loss, but eventually in greater weight regain. At the age of 27 years, genetic testing revealed a heterozygous pathogenic variant in the *melanocortin-4 receptor*gene, explaining her early-onset severe obesity and hyperphagia. Glucagon-like peptide-1 receptor agonist (GLP-1 RA) treatment, i.e. liraglutide 3 mg, was started which resulted in -7.3 kg of body weight (-3.8%, weight at start 193.5 kg), sustained hyperphagia (after a temporary, short term decrease), and increased fasting insulin after 5 months of treatment. GLP-1 RA treatment was therefore terminated and treatment with metformin was started at a dosage of 1500 per day, without any effects on weight or hyperphagia. Additionally, naltrexone-bupropion treatment was initiated after a 2.5 months wash-out period of liraglutide. In 6 months of naltrexone-bupropion treatment, she lost -29.5 kg of weight (-15.8%, weight at start 186.4 kg), of which -27.9 kg (-7.3%) was fat mass. Most importantly, her subjectively reported hyperphagia, satiety, and subsequently quality of life improved.
Discussion
To our knowledge, this case report is the first to describe that naltrexone-bupropion can effectively reduce weight and improve subjectively reported hyperphagia and quality of life in a patient with genetic obesity. This extensive journey learns us that in patients with genetic obesity various anti-obesity agents can be initiated and when ineffective terminated and substituted to another anti-obesity agent to find the most efficient treatment with regard to weight loss, hyperphagia, and quality of life. It also demonstrates that genetic screening should be considered in patients with early-onset obesity, hyperphagia, or other specific symptoms of monogenic obesity, prior to bariatric surgery as they are at higher risk for weight regain.

DOI: 10.1530/endoabs.81.P99

P100

The trigliserid-glucose index shows a stronger correlation with serum adiponectin levels than HOMA-IR

Suleyman Nahit Sendur[1], Kubra Isgin Atici[2], Busra Turan Demirci[2], Incilay Lay[3], Zehra Buyuktuncer[2] & Tomris Erbas[1]
[1]Hacettepe University, Endocrinology and Metabolism, Ankara, Turkey; [2]Hacettepe University, Nutrition and Dietetics, Ankara, Turkey; [3]Hacettepe University, Medical Biochemistry, Ankara, Turkey

Objective
Different methods are used to identify individuals with insulin resistance. The gold standard is the euglycemic-hyperinsulinemic clamp. However, in clinical practice, clamp is not preferred because it is cumbersome, the HOMA-IR index is used more often. The Trigliserid-glucose (TyG) index is a new and practical way to identify individuals with insulin resistance (IR). When compared to HOMA-IR, this index has been shown to be more reliable in determining insulin resistance and more effective to predict common diseases related to IR. In this study, the relationship between TyG index/ HOMA-IR and adiponectin were investigated.
Method
A total of 400 individuals, aged 24-50, were included in the study. Two hundred of participants had normal (Group 1) body mass index (BMI) values (18.5-25 kg/m2), while 200 were either overweight or obese (Group 2) (BMI > 25 kg/m2). Demographic characteristics of all participants have been recorded. Height, weight and waist circumference were measured; BMI values were calculated. Body fat content was determined by the electrical impedance method. Glucose, insulin, triglyceride, total cholesterol, LDL, HDL and adiponectin were measured.
Results
There was no difference between groups in terms of gender distribution. Group 1 were younger (33.3 $\pm$ 6.8 years vs. 36.4 $\pm$ 7.0 years, P < 0.001). BMI, waist circumference, fat weight, fat ratio, plasma glucose levels, insulin, triglyceride, total cholesterol, LDL, HOMA-IR and TyG index values were higher in group 2 (TyG index; Group 1: 8.25 $\pm$ 0.51 vs Group 2: 8.58 $\pm$ 0.57). HDL cholesterol and adiponectin concentrations were found to be lower in Group 2. There was a stronger correlation between the TyG index and the adiponectin levels in Group 1, Group 2 and whole cohort compared to the HOMA-IR (Group 1, adiponectin-HOMA-IR, r = -0.19,P = 0.006, adiponectin-TyG index, r = -0.37, P < 0.001; Group 2, adiponectin-HOMA-IR, r = -0.26, P < 0.001, adiponectin-TyG index, r = -0.38, P < 0.001; Whole cohort adiponectin-HOMA-IR r = -0.27, P < 0.001, adiponectin-TyG index, r = -0.41, P < 0.001).
Conclusion
The TyG index is correlated with adiponectin levels better than HOMA-IR. This index could be an easy, practical and powerful method to predict unfavorable adipokine profile.

DOI: 10.1530/endoabs.81.P100

P101

Hypothyroidism and obesity in a population of Italian women with lipedema and correlation with the clinical stage

Laura Patton[1] & Lorenzo Ricolfi[2]
[1]Rehabilitation Department, Valdobbiadene, Italy; [2]Lymphological Clinic, Bordighera, Italy

Aim
Lipedema is a painful fat disorder that affects ~11% of the female population, characterized by bilateral, disproportionate accumulation of subcutaneous adipose tissue predominantly in the lower body. The initial manifestations of lipedema arise in phases of hormonal change (puberty, pregnancy, menopause). The pathophysiology of lipedema is unclear. The putative causes proposed include altered adipogenesis, microangiopathy, and disturbed lymphatic microcirculation The diseases is diagnosed on the basis of its main manifestations: pain, a feeling of tension, and increased tendency to form hematomas in the affected areas. Treatment is symptomatically oriented and based on complex decongestive therapy and nutritional regimen, low carb or ketogenic. There are four stages of lipedema that refer primarily to changes in the skin, based on the progression of fat accumulation and changes to the skin. The fourth stage is a condition characterized by lymphological complications secondary to the failure of lymphatic system. A higher incidence of endocrinopathies, such as obesity and thyroid diseases, has been described in woman with lipedema, but no studies have been done in Italy. The aim of the study was to evaluate the prevalence of these endocrine diseases in an Italian population of women with lipedema
Materials and methods
Sixty-five women suffering from lipedema, who arrived consecutively at the lymphological clinic, underwent an endocrinological examination, with particular reference to the presence of obesity and thyroid diseases.
Results
The median age was 41.1 $\pm$ 13.5 years. Twenty-two women had stage 1 lipedema, twenty-five stage 2 lipedema, fifteen stage 3 lipedema and three stage 4 lipedema. Thirteen women (20%) were normal weght (BMI $<$25 kg/m2), twenty-two women (33.8 %) were overweight (BMI $\geq$ 25 $<$30), thirty women (46.2%) were obese (BMI $\geq$30.0). The prevalence of obesity increases with the lipedema stage ($P<0.001$): 9.1% in stage 1, 48 % in stage 2, 86.7 % in stage 3, 100 % in stage 4. Hypothyroidism was present in twenty-seven patients (41.5%). The prevalence of hypothyroidism (autoimmune and non-autoimmune hypothyroidism) increases with the lipedema stage ($P<0.001$): 18.2 % in stage 1, 40 % in stage 2, 66.7 % in stage 3, 100 % in stage 4.
Conclsion
The study confirms a high prevalence of obesity and hypothyroidism in patients with lipedema in Italian population and suggests a correlation between these diseases with the lipedema stage. Obesity and thyroid dysfunction should be evaluated in patients with lipedema, especially because for the possible worsening effect on the evolution of lipedema.

DOI: 10.1530/endoabs.81.P101

P102

Design of a phase 2, double-Blind, placebo-controlled trial of setmelanotide in patients with genetic variants in the melanocortin-4 receptor pathway

Sadaf Farooqi[1], Martin Wabitsch[2], Wendy Chung[3], Olga Ohayon[4], Cecilia Scimia[4], Guojun Yuan[4] & Bhavik P. Shah[4]
[1]University of Cambridge, Wellcome-MRC Institute of Metabolic Science and NIHR Cambridge Biomedical Research Centre, Cambridge, United Kingdom; [2]Ulm University, Division of Pediatric Endocrinology and Diabetes, Department of Pediatrics and Adolescent Medicine, Ulm, Germany; [3]Columbia University, Division of Molecular Clinical Genetics, Department of Pediatrics, New York, United States; [4]Rhythm Pharmaceuticals, Boston, United States

Introduction
Rare genetic causes of obesity result from disruption of the melanocortin-4 receptor (MC4R) pathway, a regulator of energy balance. Patients with obesity due to variants in multiple genes, including *POMC, LEPR*, *SRC1*, and *SH2B1*, have shown weight and hunger reductions after treatment with setmelanotide, an MC4R agonist. DAYBREAK is a Phase 2 trial of setmelanotide in patients with additional gene variants with suggested relevance to the MC4R pathway (ClinicalTrials.gov identifier: NCT04963231).
Methods
This Phase 2, double-blind, placebo-controlled, 2-stage study will enroll ~500 patients in Stage 1 to achieve ~130 qualified patients in Stage 2. Patients (aged 6 to 65 years) with pathogenic, likely pathogenic, or uncertain significance genetic variants based on American College of Medical Genetics criteria in a preselected set ($n=31$) of MC4R pathway genes, including *LEP*, *SIM1*, *MRAP2*, and *KSR2*, and body mass index (BMI) $\geq$40 kg/m^2(aged $\geq$18 years) or BMI $\geq$97th percentile (aged $<$18 years) according to age and sex are eligible. Exclusion criteria include recent diet or exercise resulting in $>$3% weight loss, bariatric surgery within 6 months of enrollment, significant features or diagnosis of syndromic obesity, glycated hemoglobin $>$10.0%, and glomerular filtration rate $<$60 ml/min. Setmelanotide will be self-administered subcutaneously. Daily dosage will be age dependent: 2 mg will be administered for 14 days, then 3 mg thereafter in patients $\geq$12 years old or 1 mg will be administered for 7 days, 2 mg for 7 days, and 3 mg thereafter in patients 6–12 years old. Patients will be eligible to enter Stage 2 (randomized withdrawal period) if they have achieved $\geq$5% weight loss from baseline ($\geq$18 years old) or $\geq$0.1-point reduction from baseline in BMI Z score ($<$18 years old) at the end of Stage 1 (16-week open-label run-in). Eligible patients will be randomized 2:1 to daily setmelanotide or matching placebo for 24 weeks. Primary endpoints include proportion of patients achieving $\geq$10% weight loss (aged $\geq$18 years) or $\geq$0.3-point reduction from baseline in BMI Z score (aged $<$18 years) from baseline at Week 40. Secondary endpoints are initial response to open-label setmelanotide and changes in body weight, waist circumference, hunger, and quality of life. Safety will be assessed by severity and frequency of adverse events.
Results
Patient dosing has been initiated as of January 2022.
Conclusions
The Phase 2 DAYBREAK trial will evaluate setmelanotide for weight loss and hunger reduction in individuals with variants associated with the MC4R pathway.

DOI: 10.1530/endoabs.81.P102

P103

The crosstalk between adiposity and bone: a potential role for SIRT1 and sclerostin

Rossella Tozzi[1], Davide Masi[2], Fiammetta Cipriani[2], Maria Elena Spoltore[2], Savina Contini[2], Mikiko Watanabe[2], Sabrina Basciani[2], Carla Lubrano[2], Lucio Gnessi[2] & Stefania Mariani[2]
[1]Sapienza University of Rome, Molecular Medicine, Roma, Italy; [2]Sapienza University of Rome, Department of Experimental Medicine, Section of Medical Physiopathology, Food Science and Endocrinology, Roma, Italy

Background and aim
Sirtuin1 (SIRT1) and sclerostin play important roles in adipose tissue and bone metabolism. SIRT1 pharmacological induction improves bone quality both in murine and human models and- as adiposity increases – its expression decreases both in peripheral tissues and blood. Sclerostin reduces osteoblasts' differentiation and mineralization and is associated with DMT2, obesity and cardiovascular risk. We evaluated the circulating SIRT1 and sclerostin relationship with mass and quality of bone considering the degree of adiposity.
Materials and methods
66 premenopausal women (16 underweight, 25 normal weight and 25 with obesity), aged $<$50 years, were enrolled. Plasma SIRT1, sclerostin, and DXA body composition [total-fat mass (FM), abdominal visceral adipose tissue, lean mass, trabecular bone score (TBS), lumbar spine and femoral neck-bone mineral density (BMD)] were assessed.
Results
The patients with obesity showed the lowest SIRT1 and TBS values and the highest sclerostin concentrations; BMD increased with FM and BMI and had an inverse association with SIRT1. Sclerostin was negatively correlated with SIRT1 ($P=$-0.37, $P=0.002$). When spine-BMD, femoral neck -BMD and TBS were standardized for BMI, a positive correlation with SIRT1 and a negative correlation with sclerostin were seen ($P<0.005$). In a regression analysis, sclerostin was the best independent, negative predictor for BMD and TBS, while SIRT1 directly predicted TBS ($P<0.05$).
Conclusion
Blood measurement of SIRT1 and sclerostin could represent a snapshot of the bone status that, taking into account the degree of adiposity, may reduce the interference of confounding factors in the interpretation of the bone health parameters.

DOI: 10.1530/endoabs.81.P103

P104

Impact of basal bolus insulin therapy on glucose control and mortality in patients with type 2 diabetes hospitalized with COVID -19: a retrospective study

Elena Chertok Shacham[1], Nimra Maman[2] & Avraham Ishay[1]
[1]Endocrinology, Afula, Israel; [2]Statistics, Afula, Israel

Introduction
Previous studies have reported that SARS-CoV-2 infection is associated with a more severe disease and worse outcome in patients with diabetes mellitus. Insulin is the mainstay of diabetes therapy in the inpatient setting. However, the treatment of diabetes in patients with COVID-19 remains unclear. In this study we investigate the influence of different insulin regimens and other antidiabetic medications on glucose control and mortality in COVID-19 patients with type 2 diabetes.
Methods
We conducted a retrospective electronic medical record analysis of 359 type 2 diabetes patients hospitalized with COVID-19 between 01/04/2020 and 31/03/2021 in the Emek Medical Center. The following baseline characteristics included in the study are: gender, age, BMI, GFR, CRP, preadmission diabetes treatment regimens, and comorbidities. We divided the patients into two groups based on their diabetes treatment during hospitalization. The first group included patients treated only with insulin, and the second group of patients were treated with insulin and other classes of antidiabetic drugs. We recorded data of patients' 28-day mortality rates, preadmission diabetes treatment, average blood glucose, diabetes treatment regimens at discharge, and HbA1C levels 6 months before and after hospitalization in both groups.
Results
Of 359 patients, 82 were mechanically ventilated and 110 patients suffered a severe course of COVID-19. The mortality rate on day 28 after admission was similar in patients treated with insulin only and those treated with a combination of insulin and other treatment modalities ($P=0.29$) and remains non-significant after exclusion of mechanically ventilated patients from the statistical analysis. Patients who survived their hospital stay had lower CRP levels at admission (11.5 ± 8.2 vs 16.1 ± 9.7;$P=0.000$). During hospitalization, most of the patients in the combination therapy group received metformin on top of insulin (131 out of 162, 80%), 28 patients (17%) received SGLT-2 inhibitors, 12 (7%) were treated with DPP-IV or GLP-1 agonists, and seven patients (4%) with sulfonylureas. Regarding diabetes control, HbA1C levels improved after hospitalization in both groups of treatment, and overall: A1C levels before admission were 7.9 ± 1.9 mg% and after 7.5 ± 1.7 mg% ($P=0.002$).
Conclusion
Basal bolus insulin regimens, as well as a combination of insulin and other classes of antidiabetic medications, were not associated with dissimilar mortality rates in patients affected with *SARS-CoV-2*. Our study shows that new antidiabetic medications, such as incretin-based therapy and SGLT-2i, as well as metformin in combination with insulin may safe, and effectively control glucose levels in hospitalized COVID-19 patients.

DOI: 10.1530/endoabs.81.P104

P105

Relationship between change in glycemic parameters and body weight with IDegLira in type 2 diabetes

Ivona Risovic[1], Mirjana Sumarac-Dumanovic[2], Mirjana Bojic[3] & Danijel Djekic[4]
[1]University Clinical Center of the Republic of Srpska, Faculty of Medicine, University of Banja Luka, Endocrinology, Banja Luka, Bosnia and Herzegovina; [2]School of Medicine, University of Belgrade, Clinic for Endocrinology, Diabetes and Diseases of Metabolism, Endocrinology, Belgrade, Serbia; [3]University Clinical Center of the Republic of Srpska, Endocrinology, Banja Luka, Bosnia and Herzegovina; [3]University Clinical Center of the Republic of Srpska, Endocrinology, Banja Luka, Bosnia and Herzegovina

Introduction
IDegLira is the first fixed ratio combination of a basal insulin degludec and a glucagon-like peptide-receptor analogue liraglutide. These combination producer-eduction in glycated hemoglobin A1c (HbA1c) and help to mitigate the weight gain. The aim of this study was to evaluate relationship between change in glycemic parameters and body weight in patients who began therapy with IDegLira.
Patients and Methods
Retrospective study included 86 patients with type 2 diabetes who began therapy with IDeg Lira, previously uncontrolled on basal insulin and metformin, and follow up for 6 months. Patients were devide in two groups according HbA1c: group I with HbA1c <9 ($n=50$) and group II with HbA1c ≥ 9 ($n=46$). We examined glycemic parameters (HbA1c, fasting plasma glucose, FPG) and antropomethric parameters (body weight and BMI).
Results
The analysis showed that patients in group II with higher HbA1c from baseline had higher reduction in HbA1c and FPG (0.9% vs. 0.6%, $P<0.05$ for HbA1c, 1.0 mmol/l vs. 0.6 mmol/l, $P<0.05$ for FPG). Patients in all groups had decreased body weight at the end of study. The higher decreased in HbA1c in group II didn't followed with significance higher weight loss (1.9 kg vs 1.8 kg, $P>0.05$) and higher reduced BMI (0.8 vs 0.7 kg/m^2, $P>0.05$). We founded in both groups a significant direct correlation between reduction HbA1c and BMI ($r=0.35$, $P<0.05$ vs. $r=0.42$, $P<0.05$), but with no significant difference between groups. At the end of study, no difference had showed in dosage of IDegLira between groups. Patients with poorer glycemic control from baseline were older and obese according BMI, but with no difference in duration of diabetes.
Conclusion
Our results showed that reduced glycemic parameters and weight loss depends on baseline value with IDegLira. The higher reduction glycemic parameters had no relationship with significantly higher weight loss.

Key words
insulin degludec, liraglutide, weight loss, type 2 diabetes.
DOI: 10.1530/endoabs.81.P105

P106

Features of the level of amylinemia in patients with latent autoimmune diabetes in adults

Iryna Tsaryk[1] & Nataliia Pashkovska[2]
[1]Bukovinian State Medical University, Department of Clinical Immunology, Allergology and Endocrinology, Chernivtsi, Ukraine; [2]Bukovinian State Medical University, Clinical Immunology, Allergology and Endocrinology, Chernivtsi, Ukraine

Background
Among the heterogeneous types of diabetes mellitus (DM), latent autoimmune diabetes in adults (LADA) is the most common and attracts the attention of scientists, the pathogenesis of which combines the main mechanisms of classical type 1 (T1DM) and type 2 diabetes mellitus (T2DM). The role of hyperamylinemia in the development and progression of LADA remains out of the researchers' attention.
The objective
of the study was to determine the features of the level of amylinemia in patients with LADA compared to classical types of DM.
Methods
89 patients with diabetes and chronic kidney disease (CKD) were examined, as well as 15 representatives of the control group. The patients were divided into three groups by the types of DM (25 patients with classical T1DM, 36 patients with LADA, 28 patients with T2DM). The LADA group included patients with LADA1 phenotype (antiGAD ≥ 180 U/ml) and LADA2 phenotype. Serum amylin levels were measured using the ELISA method.
Results
In patients with classical T1DM, the level of amylinemia did not change, whereas in T2DM group it was 10.8 times significantly higher compared to the control and 8.3 times higher than in the group of patients with classical T1DM. In the group of patients with LADA, the amylin content was 9.0 times higher than in control and 6.8 times higher compared to classical T1DM. In the distribution of patients with LADA into phenotypes, in patients with LADA1, the serum level of amylin was 5.9 times higher relative to the control ($P<0.01$), 4.1 times higher relative to classical T1DM ($P<0.01$), but almost half as low as in T2DM ($P<0.01$). In LADA2 group, the above indicator exceeded that in the control group by 13.5 times ($P<0.01$), in the group of classical T1DM – by 9.3 times ($P<0.01$) and in patients with LADA1 – by 2.3 times ($P<0.05$). In patients with LADA, an interdependence was found between the content of amylin and insulin ($r=0.64$;$P=0.000$), C-peptide ($r=0.74$;$P=0.000$), the HOMA-IR index ($r=0.54$;$P=0.001$).
Conclusions
Serum amylin level significantly increase in patients with latent autoimmune diabetes in adults, especially in LADA2 phenotype compared to classical types of diabetes, which indicates the role of hyperamylinemia in the development and progression of this subtype of diabetes.

DOI: 10.1530/endoabs.81.P106

P107

The relation between insulin resistance and both growth hormone and insulin-like growth factor (IGF-1) levels in a sample of Iraqi patients with type 2 diabetes

Hasanain Mohammed Alrubyae[1], Araz Al-Saffar[2] & Khalid Allehibi[3]
[1]The National Center for Diabetes / Al-Mustansirya University, Diabetes, Baghdad, Iraq; [2]Daisy Hill Hospital, Diabetes and Endocrinology, Newry, United Kingdom; [3]Specialised Center of Endocrinology and Diabetes SCED, Baghdad, Iraq

Introduction Background
Over the last decade, scientific attention has been drawn to the potential role of Growth hormone (GH) and Insulin Like Growth Factor-1 (IGF-1) in the pathogenesis and progression of T2DM. Both hormones are interrelated but exert variable effect on glucose homeostasis. While GH increases blood glucose level, IGF-1 maintain insulin secretion and enhance insulin sensitivity.
Methods
A cross sectional study conducted in the National Diabetes Centre, Baghdad, Iraq, from May 2020 to May 2021. Sixty patients with types 2 diabetes were investigated for fasting plasma glucose (FPG), GH, lGF-1 HbA1c, HOMA-IR, HOMA-B and anthropometric measures. Patients with Type 1 diabetes mellitus, thyroid disease, pituitary disease, chronic kidney disease, hepatic disease and Pregnancy were excluded from the study.
Results
There was no significant difference between gender and other variables of studied sample. There was association between HOMA-IR with HbA1c, IGF-1, fasting insulin, HOMA-B, and with QUICKI. A significant association between IGF-1 and body mass index (BMI), glycated haemoglobin (HbA1c), the duration of type 2 diabetes, quantitative insulin sensitivity index (QUICKI), and the age of patients was found. IGF-1 showed a significant negative correlation with BMI and a significant positive correlation with HbA1c and QUICKI. fasting GH correlated negatively with waist hip ratio (WHR), fasting insulin, HOMA-IR and positively with age and QUICKI. HbA1c was significant positive correlations with duration of T2DM, WHR, FPG, fasting TG, IGF-1, HOMA-IR and negatively correlated with QUICKI. There was a significant negative correlation between QUICKI index and BMI, WHR, FPG, HbA1c, fasting TG, fasting GH, Fasting insulin, and HOMA-IR. While HOMA-IR was significantly positive correlated with BMI, Fasting Plasma Glucose, HbA1c, Fasting TG and fasting insulin.
Discussion
GH and IGF-1 play a complex role in type 2 Diabetes Mellitus. In this study, IGF-1 in obese patient was low while in uncontrolled diabetes was high. GH decreased upon increased insulin resistance. Targeting IGF-1 in type 2 diabetes can be utilized as a potential therapy in the near feature. However, this needs further well designed randomized controlled trials. Conduct larger scale study to specify the cut off value of HOMA-IR for Iraq.
Conclusion
GH and IGF-1 play a complex role in type 2 Diabetes Mellitus. In this study, IGF-1 in obese patient was low, while in uncontrolled diabetes was high. GH decreased upon increased insulin resistance.
Keywords
Growth Hormone, IGF-1, Type two diabetes, insulin resistance, HOMA, QUICKE.

DOI: 10.1530/endoabs.81.P107

P108

Prevalence of autosomal dominant mutations of Familial hypercholesterolemia in Finnish patients with premature coronary artery disease and elevated LDL-C levels

Antti Jokiniitty[1,2], Markku Eskola[2,3], Tanja Saarela[2,4] & Saara Metso[1,2]
[1]Tampere University Hospital, Department of Internal Medicine, Tampere, Finland; [2]Tampere University, Faculty of Medicine and Health Technology, Tampere, Finland; [3]Tampere University Hospital, Heart Hospital, Tampere, Finland; [4]Kuopio University, Department of Clinical Genetics, Finland

Background and aims
To assess the prevalence and variability of pathogenic or likely pathogenic autosomal dominant mutations (ADM) of Familial Hypercholesterolemia (FH) in a Finnish cohort of patients with premature coronary artery disease (CAD) and elevated LDL-C levels.
Methods
Study population was enrolled from 162 patients diagnosed with premature CAD (men $<$ 55 years and women $<$ 60 years) and history of high LDL-C ($\geq$ 5 mmol/l) levels, without apparent secondary reason for hypercholesterolemia, treated in the Heart Hospital at Tampere University Hospital between 2007 and 2017. A total of 80 patients were available for genetic testing for FH, 21 patients were studied during standard treatment and 59 patients were recruited for genetic testing retrospectively. Clinical probability of FH was assessed using the Dutch Lipid Clinic Network (DLCN) – Criteria: possible (DLCNC = 5), probable (DLCNC 6-8), definite (DLCNC $\geq$ 9). All patients were studied for Finnish *LDLR* gene founder mutations (FH-Helsinki (9,5 kb deletion including exons 1–18), FH-North-Karelia (c.925_931delCCCATCA, p.(Pro309Lysfs*59)), FH-Pori (c.1202T$>$A, p.(Leu401His)), FH-Turku (c.2531G$>$A, p.(Gly844Asp)). Further testing of the genes *LDLR* (Sanger sequencing and MLPA), *PCSK9* (Sanger sequencing) and *APOB* (Sanger sequencing for mutations affecting codon 3527 in exon 26) was conducted to 62 (78%) patients if a founder mutation was not discovered.
Results
Out of 80 patients four (5%) had definite FH, 54 (68%) had probable FH and 22 (27%) had possible FH based on DLCN - criteria. Pathogenic ADM of FH was found in five patients (6%). Four founder mutations and one additional *LDLR*-mutation were discovered. Based on clinical criteria three patients had definite FH and two patients had probable FH. ADM's of FH weren't discovered in 91% (53/58) of patients with probable/definite FH and in none of the patients with possible FH.
Conclusions
Despite possible selection bias, proportion of patients with ADM's of FH was lower than expected in a population with elevated LDL-C levels, premature CAD and clinical phenotype of FH. Only a minority of patients with clinically defined FH, studied for genetic mutations, had monogenic FH. Further studies in our area are required to identify the population where genetic testing of FH is likely to offer the greatest clinical advantages.

DOI: 10.1530/endoabs.81.P108

P109

Maternal triglyceride levels, and not fructosamine, in early pregnancy are associated with birth weight

Isabel Clinck[1,2], Faro Verelst[1,2], Marcel Twickler[2,3] & Tanja Vrijkotte[4]
[1]University of Antwerp, Internal medicine, Antwerp, Belgium; [2]AZ Monica, Antwerp, Department of Endocrinology, Diabetology and Metabolism, Deurne, Belgium; [3]University of Antwerp, Faculty of Medicine and Health Sciences, Antwerp, Belgium; [4]Amsterdam University Medical Centers, University of Amsterdam, Department of Public and Occupational Health, Amsterdam Public Health Research Institute, Amsterdam, Netherlands

Objectives
Maternal metabolism has a major impact on foetal growth, and the risk of developing obesity, cardiovascular disease and diabetes in later life. Identification of maternal metabolic parameters in early pregnancy that predict birth weight (BW), is pivotal in the prevention of these diseases. We evaluated whether maternal triglyceride (TG) or fructosamine levels in early pregnancy, as possible reflectors of maternal insulin resistance (IR), could predominantly contribute to BW and whether this is sex dependent.
Study design
The data were obtained from the Amsterdam Born Children and their Development cohort study. Non-fasting TG and fructosamine levels were determined in early gestation (median 13 weeks). Associations between maternal TG and fructosamine levels, and BW - small for gestational age (SGA) - large for gestational age (LGA), were analysed for each sex separately.
Results
In total 3514 pregnant women were included. With every increase of 1 mmol/l TG, the BW increased significantly by 81.7 g. This increase was larger with boys (107.3 g, 95% CI 66.0-148) compared to girls (60.5 g, 95% CI 23.6-97.4). However, no association was found with fructosamine. The results were adjusted for gestational age at blood sampling, total duration of pregnancy, maternal height, age, parity, ethnicity, educational level, smoking, alcohol and pre-pregnancy BMI. These covariates were also used in a different statistical test (R-squared), and explained 29.2% of the variance in BW. Adding fructosamine to this model, had no added value in predicting BW (R^2 stayed 0.292). Contrary, TG levels raised the R^2 from 0.292 to 0.299 ($P<0.001$). In total 8.3% children in our population were LGA. The odds of a new-born LGA with higher maternal TG levels were increased (OR 1.6, 95% CI 1.3-2.0). No increased odds were found for fructosamine levels (OR 1.0, 95% CI 1.0-1.0).
Conclusions
This study shows that fructosamine levels, measured in the first trimester of a physiological pregnancy, are not significantly associated with BW, in contrast to maternal TG levels. This association is more prominent with boys. Our data suggest that the lipid profile in early pregnancy is more predictive for pregnancy outcomes, like LGA, than glycaemic metabolic parameters, such as fructosamine. This may give a different focus on metabolic variables (TG vs fructosamine) involved in early patterns of maternal IR during a physiologic pregnancy. Additional studies could show whether maternal TG levels should be included in the screening or follow-up of pregnancies with a pronounced IR (e.g. in gestational diabetes).

DOI: 10.1530/endoabs.81.P109

P110

Evaluation of a new transition organization for young adults with endocrine or metabolic diseases

Enora Le Roux[1] & Philippe Touraine[2]
[1]INSERM, Université de Paris, ECEVE UMR 1123, Paris, France; [2]AP-HP. Sorbonne Université, Hôpital Universitaire Pitié Salpêtrière, Service d'Endocrinologie et Médecine de la Reproduction HCP-ENDO European Reference Network, Paris, France

Objective
To evaluate the effect of a new care organisation on multiple outcomes of transition success and its cost-effectiveness in patients with any endocrine or metabolic disease diagnosed during childhood and transferred to adult care.
Design
Non-randomized controlled trial in a French University Hospital.
Methods
Patients transferred to adult care during the control period (04/2014-08/2016) and the intervention period (09/2016-06/2018) were included. The intervention is based on case management involving liaising with pediatric services, personalising care pathways, and liaising with structures outside hospital (general practitioner, educational and social sector). The primary endpoint was the percentage of patients lost to follow-up at 24 months post transfer. Other outcomes were collected from medical files, consultation software, and questionnaires. A cost analysis was performed.
Results
202 patients were included (101 per period), the most represented pathologies were congenital and non-congenital hypopituitarism (respectively $n=34$ (17%) and $n=45$ (22%)) and thyroid diseases ($n=21$, 10%). Patients were aged 22.5 in median at 24 months post transfer where 12 were lost to follow up in the control group vs 9 with the intervention ($P=0.49$). The percentage of honoured consultation among those planned during 24 months was higher with intervention ($P=0.0065$). Patient satisfaction, physician trust, transfer delay did not differ between the groups. The incremental cost-effectiveness ratio was €179 per patient not lost to follow-up.
Conclusions
At 24 months post transfer the rate of lost to follow-up does not differ significantly, but indicators of a steadier follow-up are increased and the intervention appears to be cost-effective.

DOI: 10.1530/endoabs.81.P110

P111

Analysis of the nutritional status of women in twin pregnancies in terms of key vitamins and microelements – preliminary results

Magdalena Zgliczynska[1], Iwona Szymusik[2], Magdalena Ostrowska[3] & Katarzyna Kosinska-Kaczynska[1]
[1]The Center of Postgraduate Medical Education, Second Department of Obstetrics and Gynecology, Warsaw, Poland; [2]Medical University of Warsaw, First Department of Obstetrics and Gynecology, Warsaw, Poland; [3]The Center of Postgraduate Medical Education, Department of Endocrinology, Warsaw, Poland

Objective
Diet and nutritional status during pregnancy are critical for the health of both mothers and the neonates. Women in twin pregnancies have higher metabolic needs compared to women in single pregnancies and it can be expected that they have higher risk of key vitamins and micronutrients deficiencies. However, very scarce data are currently available on this topic.
Aim of the study and method
The main aim is to analyze the nutritional status of women in twin pregnancies in terms of selected vitamins and microelements: iodine, vitamin D, calcium, magnesium, iron, folic acid and vitamin B12. It will be achieved through analysis of the nutritional status of the mentioned nutrients in 100 women with twin pregnancies after 22 weeks of pregnancy. A comparison with a control group of women in single pregnancies is also planned.
Results
Until the submission of this abstract (January 2022) 69 women in twin pregnancies were recruited. The median age in this group was 34 years (interquartile range [IQR] 31-36), whereas median gestational age was 30.4 weeks (IQR 25-33.3). 52.2% women were in dichorionic diamniotic, 43.5% in monochorionic diamniotic and 4.3% in monochorionic monoamniotic pregnancies. Deficiency of at least one of the tested micronutrients or vitamins occurred in 72.5% of the respondents. Iron deficiency was the most common and affected 55.1% of the examined patients. The second most common was vitamin D deficiency, which concerned 44.4% of the group. Vitamin B12 deficiency turned out to be the third most common and it was found in 8.7% of women. Almost 1 in 4 patients had excess level of folic acid. Moreover, in 5.8% of patients the concentration of 25-hydroxyvitamin D was increased. In terms of the remaining tested vitamins and microelements, no laboratory features of significant excess or shortage were found.
Conclusions
Basing on the preliminary results, it can be concluded that women in twin pregnancies may constitute a high-risk group for the deficiencies of iron, vitamin D and vitamin B12 deficiency.

DOI: 10.1530/endoabs.81.P111

P112

Expression of beta2 adrenergic receptors in pancreatic islets of metabolic syndrome induced C57BL/6J Mice

Vijayalakshmi Gangadhara & Asha Abraham
St Aloysius College, Department of Post Graduate Studies and Research in Biotechnology, Mangaluru, India

Background
The global prevalence of metabolic syndrome (MetS) characterized by type 2 Diabetes (T2D), obesity, and cardiovascular diseases, has reached alarming proportions worldwide. The prevalence is rapidly increasing among all the age groups due to calorie dense food intake and sedentary lifestyle. Beta adrenergic receptors (β ADRs), are known for its role in thermogenesis, lipolysis and glucose metabolism. Ceasrine *et al*., 2018, reported that pancreas-specific deletion of Adrb2 resulted in glucose intolerance and impaired insulin secretion in mice.
Objective
To develop an animal model by feeding high fat simple carbohydrate diet (HFSC) and to study the expression pattern of β2 ADRs in the pancreatic islets.
Methodology
The MetS was induced in male C57BL/6J mice ($n=10$) by feeding HFSC. The control animals were fed with standard diet. The MetS was confirmed by anthropometrical analysis, fasting blood glucose, total cholesterol, triglycerides, HDL and LDL. At the end of 5thmonth of feeding, the experimental animals were sacrificed, the pancreas was isolated. The morphology of the pancreas was studied by histology and SEM. The pancreatic islets were isolated by collagenase digestion. The quality of islet was accessed by Dithiozone staining. The total islet protein was extracted by RIPA lysis method and quantified by BCA assay. The protein was separated by SDS PAGE, immune blotted and probed with β2 ADR polyclonal antibody followed by Goat anti rabbit IgH(H+L) cross adsorbed DyLight488. The blots were quantified using Biorad Geldoc XR+ with *Imagelab* software.
Results
The metabolic syndrome was developed in male C57BL/6J mice by feeding HFSC diet up to 5thmonth. Blood glucose ($P>0.01$), triglyceride level ($P>0.001$), total cholesterol ($P>0.01$), LDL ($P>0.01$) of HFSC fed mice was significantly increased compared to control. The number of pancreatic islets was reduced in the HFSC fed mice compared to control. In comparison to control mice, HFSC-fed mice's islets were depleted and had higher lymphatic infiltrates. The expression of β2 ADRs were found to be altered in the HFSC fed mice.
Conclusion
Serving as a model, HFSC fed mice more closely resembled human obesity with altered blood glucose and lipid profile. The presence of lymphatic infiltration around the islets of HFSC-fed mice indicates that the inflammatory process may also contribute to islet destruction, which could lead to T2D. Additional changes associated with the β2 ADRs and its downstream signaling will be discussed during the congress.

DOI: 10.1530/endoabs.81.P112

P113

Impact of hyperuricemia at metabolic syndrome and diabetic nephropathy, among patients with diabetes mellitus

Ergita Nelaj[1], Sonila Gozhita[2], Irida Kecaj[1], Ilir Gjermeni[1] & Mihal Tase[1]
[1]UHC 'Mother Teresa', Internal Medicine, Tirana, Albania; [2]Hygeia Hospital, Tirana, Albania

Hyperuricemia is a high risk factor for atherosclerotic diseases such as CVD and carotid atherosclerosis, hypertension, type 2 diabetes mellitus (T2DM), metabolic syndrome (MS). There are complex interrelationships between hyperuricemia,

T2DM, chronic kidney disease (CKD) and MS. The purpose of our study was to investigate the relationship between hyperuricemia, CKD, MS, and its components.
Materials and methods
179 patients with T2DM were included. The baseline presence of components of metabolic syndrome as defined by the World Health Organization was determined. CKD was defined according to the guidelines by reduction of GFR below 60 ml/min/1.73 m2, with a minimum duration of 3 months or renal impairment lasting more than 3 months. Hyperuricemia was determined as serum uric acid level above 7 mg/dl in men and 6 mg/dl in women.
Results
Following the analysis of the studied group, out of the 179 cases, 131 were identified with hyperuricemia and 48 with normo-uricemia. The prevalence of hyperuricemia was 73%. The average age of the patients was 73 years. In patients with hyperuricemia, the mean values of SBP and DBP were statistically significant higher than in patients with normo-uricemia ($P<0.003$). Triglycerides had statistically significant higher values in the hyperuricemia group ($P<0.005$). The mean HDL-cholesterol value being statistically significant lower in the hyperuricemia group ($P<0.01$). Renal function evidenced by creatinine, blood urea nitrogen and GFR, was statistically significant lower in patients with hyperuricemia ($P<0.001$). There was statistically significant relation between hyperuricemia and albuminuria ($P=0.008$), as predictor of diabetic nephropathy.
Conclsions
Among diabetic patients with hyperuricemia, the prevalence of CKD, obesity, hypertension, MS and its components are statistically significantly higher than in patients with normo-uricemia.

DOI: 10.1530/endoabs.81.P113

P114

Management of patients with Diabetes Mellitus and concurrent Covid-19 infection at a centre in Manchester with tertiary diabetes services: A retrospective single-centre audit

Amr Mohammed, Ashutosh Kapoor, Asfand Yar Malik Ganjera & Prasanna Rao-Balakrishna
Manchester University NHS FT, Manchester, United Kingdom

Background
The prevalence rate of Diabetes within Manchester is higher than the national average of England. Association of British Clinical Diabetologists (ABCD) guidance highlights an increased risk of typical and atypical presentations of diabetic emergencies in patients with Diabetes and COVID-19. In the absence of early recognition and treatment, this could lead to adverse outcomes and poor prognosis, thus leading to increased mortality rates.
Aims
The aims involved evaluation of outcomes in patients with diabetes and concurrent Covid-19 infection followed by identification of compliance with the ABCD front door guidance for immediate management of these cohort of patients, in order to improve clinical care.
Methods
We collected clinical data on a retrospective basis from electronic records of patients admitted to our centre with a diagnosis of Covid-19 and Diabetes Mellitus between January and July 2020. Patients were identified using coding within Discharge Notification Forms (DNFs).
Results
Thirty-four (34) patients were selected to create our sample population. Thirty-one (91.2%) patients had a recorded blood glucose on admission. Two (5.9%) patients had blood ketone levels recorded on admission. The median and mean blood glucose on admission was Ten point one (10.1 mmol/l) and Twelve point four (12.4 mmol/l), respectively. Metformin was withheld in five (5) out of Sixteen (equating to 31.9%) patients taking on admission, pending review of the biochemical and hypoxic status. Sodium-Glucose Transport Protein 2 (SGLT-2) inhibitors were appropriately withheld in all Thirty-four (equating to 100%) patients on admission. Out of the entire cohort of patients, eleven (equating to 32.3%) did not survive admission.
Conclusions
Severe Covid-19 is associated with significant morbidity and mortality. Data from this single centre audit suggests that a large proportion of patients with diabetes and diagnosis of Covid-19 are at risk of hyperglycaemia with ketosis at time of admission, yet only a small number have a recorded ketone level. Steps should be taken to improve awareness and education of admitting clinicians to identify and reduce the risk of possible diabetic emergencies within this high-risk cohort of patients. In addition to this, it is also recommended that in this group of patients, health care professionals must consider additional safety measures, namely review of medications such as SGLT-2 inhibitors and Metformin on admission, which in turn is likely to improve outcomes and prognosis of these patients. Following the acute phase, Metformin needs to be reviewed on the basis of the biochemical and Respiratory status of the patient.

DOI: 10.1530/endoabs.81.P114

P115

Immunotherapy-induced Diabetes Mellitus is not uncommon

Janessa Bell[1,2], Mahamud Bashir[1], Hassan Rehmani[1] & Gideon Mlawa[3]
[1]Queen's Hospital, Acute Medicine, United Kingdom; [2]American University of the Caribbean School of Medicine, Sint Maarten (Dutch Part); [3]Queen's Hospital, Diabetes and Endocrinology/Acute Medicine, London, United Kingdom

Background
Lung cancers are one of the leading causes of death worldwide which has resulted in an increase in immunotherapy, particularly immune checkpoint inhibitors (ICIs). Recent studies have shown induced endocrinopathies secondary to ICIs as a result of pancreatic beta cells, thyroid, and pituitary dysfunction.
Aim
We aim to present an interesting case of Type 1 Diabetes mellitus secondary to immunotherapy. Pembrolizumab is used to treat melanoma, non-small cell lung cancer, head and neck cancer, Hodgkin lymphoma, stomach cancer, and cervical cancer. Pembrolizumab is a human monoclonal IgG4 antibody that selectively binds to programmed cell death ligand-1 (PD1) receptor on the cell surface, thus blocking PD-1 (Programmed cell Death 1) which prevents T-cells from recognising and attacking cancer cells.
Case
In this case, a 62-year-old lady presented to hospital with polyuria, polydipsia, and weight loss after 8 months of immunotherapy. She was found to be hyperglycaemic and new of type 1 diabetes. Her background includes poorly differentiated adenocarcinoma of right lung diagnosed in March 2017, dermatomyositis, and an ex-smoker. She had received 4 cycles of chemotherapy (Cisplatin/Pemetrexed) between April 2017- June 2017 and then radical radiotherapy which completed August 2017 with good response and then she commenced Pembrolizumab in July 2020. Initial investigations were not consistent with DKA; pH 7.431, serum glucose 29.7 mmol/l, HCO3 26.2 mmol/l and urinary ketones 4+. She was commenced on NovoRapid 4 units 3 times a day and Levemir 10 units in the morning and 4 units in the evening. TSH was 0.90 mU/l and cortisol of 263 nmol/l excluded adrenal insufficiency. She was negative for Islets-cell antibodies, anti-GAD antibodies, and ZNT8.
Discussion
ICIs are commonly associated with endocrinopathies which are categorized as immune-related adverse events (Ruggeri 2019). New type 1 diabetes mellitus is a frequent toxicity of immunotherapy and can potentially be life-threatening if not diagnosed promptly. Therefore, during immunotherapy treatment, serum glucose should be regularly monitored. The UK National Institute of Health and Care Excellence (NICE) recommends developing an early plan of care, blood glucose management (periodic HbA1c and serum fasting glucose level tests), and managing long-term complications for adults diagnosed with Type 1 Diabetes mellitus. It is also recommended that patients started on ICIs have other endocrine toxicities testing. Current treatment is targeted to replace the specific hormone deficiency, e.g insulin in the case of new T1DM, as well as immunosuppression depending on the severity of the endocrinopathy (Ruggeri 2019).

DOI: 10.1530/endoabs.81.P115

P116

Association of uric acid levels with diabetic retinopathy in filipino patients with type 2 diabetes mellitus at a tertiary government hospital: a cross-sectional analytic study

Irene Kei Bariuad-Garcia[1], Cecilia Jimeno[1] & Paul Siopongco[2]
[1]East Avenue Medical Center, Internal Medicine, Section of Endocrinology, Quezon City, Philippines; [2]East Avenue Medical Center, Ophthalmology, Quezon City, Philippines

Objectives
Diabetic retinopathy, is the most frequent cause of new cases of blindness among adults aged 20–74 years in developed countries. In 15 of the 23 studies in developing countries and in ethnic minority groups within developed countries, the prevalence of diabetic retinopathy was over 35%. In developed countries, only 2 of 16 studies reported a prevalence of 35% or over. Variation in neither population demographics nor method of retinopathy assessment appeared to account for these differences in prevalence. Serum uric acid is one of the major

sources of oxidative stress thru generation of free radicals and exhibits pro-inflammatory actions. This study aims to investigate the association of serum uric acid levels and diabetic retinopathy.
Methodology
Consecutive patients at the Diabetes Clinic at East Avenue Medical Center, diagnosed with Type 2 Diabetes Mellitus by the ADA criteria for diabetes from August 2019 to May 2020 were recruited. We excluded patients with pre-diabetes, Type 1 DM, diabetes induced by steroid use and other endocrine diseases, gestational diabetes, significant co-morbidities (cancer, COPD, decompensated heart/liver failure, ESRD on HD), kidney transplanted patients, renal artery stenosis, autoimmune kidney diseases and patients who undergone cataract or any retinal surgeries. Demographic, medical and laboratory data were obtained. Blood examinations were performed in the same diagnostic center by the same device. All recruited patients were examined by one retina fellow to prevent inter-observer variability.
Results
117 (67 with DR and 50 no DR) patients were analyzed. The mean age of patients with diabetic retinopathy was younger (55.73 + 8.18) than those patients without diabetic retinopathy (56.34 + 11.31) however the difference between the two groups was not statistically significant (P= 0.736). The mean serum uric acid level was 6.44 + 1.54 mg/dl in patients with DR whereas it was 6.10 + 1.59 mg/dl in those without DR. The levels however were not statistically significant (P=0.249). Using the binary logistic regression, duration of DM, presence of anemia as well proteinuria and low estimated glomerular filtration rate (eGFR) were independently associated with DR (P=0.006, 0.008, 0.012 and 0.037, respectively).
Conclusion
Serum uric acid levels were not associated with diabetic retinopathy, but it was shown in this study that there was a higher concentration of uric acid levels in patients with more severe retinopathy. Duration of diabetes, anemia, lower eGFR and presence of proteinuria reflecting chronic kidney disease were independently associated with the presence of diabetic retinopathy.

DOI: 10.1530/endoabs.81.P116

P117

Sound mind at the expense of diabetes: olanzapine induced hyper-osmolar hyperglycaemic state (HHS) in acute setting

Patricia Kessy[1], Gideon Mlawa[2], Kirtanya Ramachandran[3], Barney Low[1,3], Belayet Hossain[3], Hassan Rehmani[3], Muhammad Saleem[1] & Janessa Bell[1]
[1]Queen's Hospital, Acute Medicine, London, United Kingdom; [2]Queen's Hospital, Diabetes and Endocrinology/Acute Medicine, London, United Kingdom; [3]Queen's Hospital, London, United Kingdom

Background
Second generation antipsychotics (SGAs) are increasingly playing a bigger role in the treatment of schizophrenia and other psychiatric conditions due to their lower extra pyramidal side effect profile However, SGAs are known to cause clinically relevant metabolic derangements including hyperglycaemia
Case
A 70-year-old gentleman was admitted with generalised weakness and increased urinary frequency (polyuria) and polydipsia. His blood glucose was noted to be significantly elevated (72.6 mmol/l) and was diagnosed with hyperosmolar hyperglycaemic (HHS) and other blood test revealed acute kidney injury. He was not acidotic on venous blood gas analysis; blood ketones were negative with normal bicarbonate. His background includes pre-diabetes (diet controlled type 2 diabetes), which was diagnosed in May 2021 after about 2 years of olanzapine exposure, Paranoid schizophrenia, Bronchiectesis, Chronic kidney disease and abdominal aortic aneurysm. He was on olanzapine started in 2018. HHS was probably triggered by being on Olanzapine. He was started on IV fluid replacement followed by insulin infusion. His medications include aspirin 75 mg od, furosemide 20 mg od, atorvastatin 40 mg od, omeprazole 20 mg od, olanzapine 7.5 mg od He made improvement clinically and his renal function was better following which his oral metformin as well as Gliclazide. Olanzapine was continued.
Discussion
The prevalence of diabetes in bipolar/schizophrenic patients is 10-15%. This is 2-3 folds that of general population (3.5-5%-Holt *et al* 2005. Diabetes and other metabolic risk factors contribute to increase rate of CVD. Life expectancy is reduced by 10-15 years in people with schizophrenia (Brown *et al* 200). Postulated mechanism of olanzapine induced hyperglycaemia include: increased appetite(dopaminergic), induction of weight gain, possible direct beta cell toxicity and pancreatitis, increased insulin resistance and decreased insulin sensitivity, 2-3-fold increased risk of diabetes in mental health patients as well as the role of prolactin in dysregulation of glucose. Ethnicity, family or personal history of diabetes poverty, urbanisation, poor diet, physical inactivity also contribute to hyperglycaemia. The time taken for clinical manifestations of hyperglycaemia varies from a few days to a few years.
Conclsion
Managing diabetes in patients with mental health problems can be challenging. It has to be integrated, MDT team (psychiatry and diabetology teams), use of cognitive behavioural therapy (CBT), use of motivational interview. NICE recommends screening for diabetes at baseline, 3-4 months after initiation of anti-psychotic and then annually.

DOI: 10.1530/endoabs.81.P117

P118

Association between hyperuricemia and degenerative complications of type 2 diabetes

Meriam Dalhoum, Zohra Hadj Ali, Bani Ines, Htira Yosra & Ben Mami Faika
National Institute of Nutrition, Department C, Tunis, Tunisia

Introduction
Hyperuricemia is associated with increased cardiovascular mortality and morbidity hence the interest in screening for hyperuricemia in the type 2 diabetic population.
Objective
To investigate the association between hyperuricemia and degenerative complications in type 2 diabetics.
Patients and Methods
This is a retrospective study including 130 patients followed in the C department of the National Institute of Nutrition in Tunis.
Results
The mean age of our patients was 61 ± 11 years, with a sex ratio M/F = 0.63. The average duration of diabetes was 14 ± 8 years. Obesity was present in 63.2% of patients. The incidence of hyperuricemia was 47.1% with a higher incidence in women: 54.4% of these patients were women vs 45.6% of men. In this population, microangiopathic and macroangiopathic degenerative complications were noted in 80.8% and 45% of cases respectively. For macroangiopathic complications, coronary artery disease topped the list with a frequency of 43.1%, followed by obliterative arteriopathy of the lower limbs with a frequency of 25.5% and finally stroke with a frequency of 3.9%. For microangiopathic complications, diabetic retinopathy was noted in 56.9% of cases. The frequency of diabetic nephropathy was 50%, of which 26.3% were at the stage of renal failure. The frequency of diabetic neuropathy was 38.5%. This analysis showed that hyperuricemia was significantly associated with macroangiopathic complications (P=0.06) and microangiopathic complications (P=0.049).
Conclusion
Our study showed a significant association between hyperuricemia and degenerative complications of type 2 diabetes.

DOI: 10.1530/endoabs.81.P118

P119

Spondylodiscitis after diagnostic lumbar puncture in a post COVID -19, diabetic patient

Marjeta Kermaj[1], Tea Shehu[1], Jona Troshani[1], Violeta Hoxha[1], Klodiana Poshi[1], Dorina Ylli[1], Jonida Kito[2], Ermira Muco[3] & Agron Ylli[1]
[1]UHC 'Mother Tereza', Endocrinology, Tirana, Albania; [2]UHC 'Mother Tereza', Emergency Unit, Tirana, Albania; [3]UHC 'Mother Tereza', Infectious Disease Department, Tirana, Albania

Background
During the COVID-19 outbreak, there are rising concerns about long-term complications of COVID-19. On the other hand, discitis is a rare neurologic diagnosis, often delayed or missed due to the rarity of the disease. Patients usually present at an average age of 69 years with a history of diabetes or with a systemic infection. The lumbar spine is the most frequent site of infection (54%), and the cervical is the least at 10%. This is a case of post-COVID-19, diabetic patient complicated by discitis after a lumbar puncture.
Case presentation
A 77 years old patient presented in our emergency unit with intermittent temperature, headache and nuchal rigidity. Medical history: Patient was diagnosed with Diabetes Mellitus and hypertension 5 years ago. He was being treated with Metformin and antihypertension drugs. He was diagnosed with COVID-19, two months ago, since then he has had temperature between 38-39°C. Laboratory analysis: hyperglycemia and hypoalbuminemia, in haemogram:

microcytic hypochromic anemia and neutrophilic leukocytosis. CRP(C Reactive Protein) and D-dimer were very high (22 mg/dl and 4 times normal range respectively). Kidney, liver and thyroid gland function resulted normal. In cranio-thoracal CT: Large multinodular thyroid gland with calcified nodules that slightly compressed trachea. Head and thorax normal. A diagnostic lumbar punction was obtained but the result excluded meningitis. Because of disequilibrated diabetes and need for thyroid exploration, the patient was hospitalized in Endocrinology Department where insulin, antibiotics (ceftriaxone and moxifloxacine), antic-oagulation therapy and human albumin were started. After being hospitalized he complained a severe lumbar pain. CRP firstly, started to fall but then started to raise (10 days later even on antibiotic therapy, CRP was 18 mg/dl again), and immediately CT and then MRI with contrast were performed and confirmed presence of L2-L3 spondylodiscitis. ASLO, C3, C4, RF, and tumoral markers were normal. Infectionist changed antibiotic therapy to Imipenem and Ciprofloxacine,10 days later, CPR level decreased to 6.6 mg/dl, but lumbar pain persisted even under painkiller. Sub febrile temperature kept persisting also. Our patient also achieved better glycemic control under basal-bolus insulin regimen but inflammatory parameters (PCR, D-dimer and Fibrinogen) remained high and actually he is transferred to local hospital for further treatment with intra venous antibiotics.

Conclusion

Post-covid-19 diabetic patients who are imunocompromised, are in higher risk of developing serious infections (like spondylodiscitis) even after diagnostic procedures like lumbar spine diagnostic puncture. Physicians must be careful to prevent.

DOI: 10.1530/endoabs.81.P119

P311

Oxidative stress decreased after six months testosterone treatment compared to placebo in ageing men – a randomized, double-blind trial

Louise Lehmann Christensen[1], Marianne Andersen[1], Henrik Enghusen Poulsen[2] & Dorte Glintborg[1]
[1]Odense University Hospital, Endocrinology, Odense, Denmark; [2]Rig-shospitalet, Pharmacology, Copenhagen, Denmark

Background

High oxidative stress is associated with increased morbidity. The effect of testosterone treatment (TT) on oxidative stress in ageing men with reduced bioavailable testosterone is undetermined.

Aim

To determine the effect of TT compared to placebo on oxidative stress biomarkers.

Methods

Double-blinded, placebo-controlled study in 38 men, aged 60–78 years, with bioavailable testosterone <7.3 nmol/l and waist circumference $\geq$ 94 cm, randomized to six-month testosterone gel therapy ($n=20$) or placebo ($n=18$). Whole body oxidative stress was assessed at baseline and after 6 months therapy by measuring 24-h urine oxidized derivatives of nucleic acids: 8-oxoguanosine (8-oxoGuo) and 8-oxo-2'-deoxyguanosine (8-oxodG) by ultra-performance liquid chromatography tandem mass-spectrometry. Fat and lean mass were measured by whole body dual x-ray absorptiometry. Changes between TT and placebo groups were compared using Mann-Whitney test. Δ-values for clinical and biochemical markers were calculated as 6 months minus pretreatment level. Bivariate associations of Δ-values of clinical and biochemical data were investigated by Spearman's Rho correlational analyses. Linear regression analysis was used to adjust for changes in body composition. P-value of < 0.05 was considered significant.

Results

At baseline, median (interquartile range) age was 67 (64-72) years, BMI 29.8 (26.6-33.3 kg/m2, total testosterone 12.6 (8.9-16.1) and bio-available testosterone 4.7 (3.7-5.9) nmol/l. Levels of 8-oxodG/24h decreased during TT compared to placebo ($P=0.038$). Δ8-oxoGuo/24h was inversely associated with Δ-total testosterone ($\rho=$-0.35, $P=0.04$) and Δ-bio-available testosterone ($\rho=$-0.37, $P=0.03$). Δ-8-oxoGuo/24h and Δ-8-oxodG/24h were associated with Δ-fat mass ($\rho=0.47$, $P=0.006$ and $\rho=0.40$, $P=0.02$, respectively). Δ-8-oxodG/24h was inversely associated with Δ-lean mass ($\rho=$-0.38, $P=0.03$). In linear regression analyses. The inverse association between Δ-oxidative stress biomarkers and Δ-total testosterone remained significant after adjustment for Δ-fat mass and Δ-lean mass.

Conclusion

Oxidative stress biomarkers decreased during six-month TT compared to placebo in ageing men.

DOI: 10.1530/endoabs.81.P311

P312

Gastric dysmotility in diabetes

Irodakhon Inoyatkhodjaeva
Center of Endocrinology, Tashkent, Uzbekistan

The prevalence of diabetes is growing every year. One of the important complications of diabetes is the effect of diabetes on the gastrointestinal tract. Purpose of the study: to identify the frequency of delayed gastric emptying in patients with diabetes.

Materials and methods

122 patients with type 2 diabetes were examined for complaints from the upper gastrointestinal tract. For this, the GCSI questionnaire was used. After a thorough clinical, laboratory and instrumental examination, 34 patients were excluded. The remaining 88 patients underwent gastric scintigraphy to determine the motor-evacuation function of the stomach.

Results

A comprehensive examination was carried out of 88 patients with type 2 diabetes mellitus All patients were divided into three groups depending on the age of diabetes: the first group (up to 5 years) - 23 people (27.27%), the second (6-10 years) - 26 (29.5%), the third (more than 11 years) –39 people (43.2%). The average age was 52.8 $\pm$ 6.51 years. Clinical and metabolic compensation of diabetes (HbA1c $<7\%$) was observed in 12 people (13.6%), decompensation of carbohydrate metabolism - in 76 people (86.4%). A labile course of diabetes mellitus was observed in 19 people (11.36%). Dynamic scintigraphy revealed the following data. Accelerated intake of the first portions of Tc into the intestines was observed more often in 37 people (42.3%), in 27 people (30.76%) - there was a delayed intake, in 4 patients (3.84%) - normal. Gastroesophageal reflux was observed in 27 people (30.7%), and duodenogastric reflux in 4 patients (3.84%). The time of maximum accumulation of Tc in the stomach, was slow in most patients in all three groups. In 15.9% of patients there were no complaints from the organs of the gastroduodenal zone, while 80% of them had a delayed motor-evacuation function of the stomach (T1 / 2av = 81.2 min), in 20% - within normal limits. Mathematical modeling with the construction of 3D graphs made it possible to identify the relationship between the motor-evacuation function of the stomach, the duration of diabetes and the presence of hypoglycemia, namely, with an increase in T1 / 2 (stagnation of food in the stomach), the frequency of hypoglycemia increases, and with an increase in the duration of diabetes, evacuation is even more delayed test breakfast from the stomach.

Conclusion

A comprehensive and targeted examination of 88 patients with type 2 diabetes mellitus showed a high prevalence of pathology of the gastrointestinal tract.

DOI: 10.1530/endoabs.81.P312

P313

Obesity and obesity-related diseases as a new clinical features in 3q27.3 microdeletion syndrome involving adipoq gene: a case study

Davide De Brasi[1], Vincenzo Novizio[1], Livia Barba[1], Elisabetta Scarano[1], Domenico Serino[1], Roberto Novizio[1], Matteo Della Monica[2], Roberta Petillo[2] & Francesco Scavuzzo[1]
[1]Azienda Ospedaliera di Rilievo Nazionale 'Antonio Cardarelli', Unit of Endocrinology and Diabetes, Naples, Italy; [2]Azienda Ospedaliera di Rilievo Nazionale 'Antonio Cardarelli', Genetics, Naples, Italy

Introduction

Adipose tissue is recognized as an important endocrine organ, secreting many endocrine factors. Adiponectin is the most abundant peptide released into circulation, encoded by ADIPOQ gene localized in chromosome 3q27.3. Adiponectin decreases intracellular ceramide, implicated in insulin resistance, inflammation and atherosclerosis. It stimulates fatty acid oxidation in skeletal muscle and inhibits glucose production in the liver. Hypo-adiponectinemia plays a central role in obesity and obesity-related disease. Since the advent of Comparative Genomic Hybridization Array (CGH-Array), numerous new microdeletional syndromes have been described. Few cases of autosomal dominant 3q27.3 microdeletion syndrome have been described, mostly characterized by intrauterine growth retardation, marfanoid habitus, cranio-facial

dysmorphism, intellectual disability, psychosis and mood disorder. We describe a family affected by 3q27.3 microdeletion involving ADIPOQ gene, adding obesity and obesity-related disease to constellation of major clinical findings reported in 3q27.3 microdeletion syndrome.
Case Study
A 21-year-old Caucasian male underwent genetic investigation by CGH-Array during a diagnostic study for familiar schizoid-type personality disorder, cognitive delay, macrocephaly and thickening of skull cap. Array analysis revealed a 1.43-Mb deletion in the long arm of chromosome 3 (3q27.3), including ADIPOQ gene and other two OMIM disease genes (KNG1 and BCL6). The analysis was then extended to parental couple, demonstrating the paternal origin of the rearrangement. Afterwards, same microdeletion was demonstrated in his 26-year-old sister. Deletions were confirmed by fluorescent *in situ* hybridization. All family members shared a complex syndromic clinical spectrum consisting of severe neuropsychiatric impairment, schizoid-type personality disorder, cognitive delay and thickening of skull cap, signs compatible with other clinical findings reported in literature for 3q27.3 microdeletion. No marfanoid habitus was reported, even though all had history of ligament laxity-related disorders. All three members of the family shared moderate-severe hyperphagia, early central obesity, marked hyperinsulinemia, obstructive sleep apnea syndrome, arterial hypertension, dyslipidemia and hepatosplenomegaly with hepatic steatosis, composing a new syndromic frame in the context of 3q27.3 microdeletion syndrome.
Discussion
This new clinical spectrum associated with 3q27.3 microdeletion involving ADIPOQ gene reinforce a suggested role of adiponectin haploinsufficiency in central obesity, atherogenic metabolic status, fat accumulation in the liver and dyslipidemia. A possible role of adiponectin on food intake at hypothalamic level is also suggested. The involvement of adjacent loci and genes, such as OMIM genes, may contribute to these novel features in 3q27.3 microdeletion syndrome. The fewer number of bases involved, 1.43-Mb vs >5-Mb described in literature, could explain the absence of some syndromic features.

DOI: 10.1530/endoabs.81.P313

P314

Diabetes and cervical pathologies: The phenotype and genotype connection

Prakhar Gupta[1,2], Shivani Bhadauria[3] & Bushra Khanam[4]
[4]L.N. Medical College, Internal Medicine, Bhopal, India; [2]William Harvey Research Institute, Endocrinology, United Kingdom; [3]Government Medical College, Ratlam, India; [4]Index Medical College, Hospital & Research Center, Indore, India

Cervical cancer is the fourth most common cancer among women globally and second most common in India. As per WHO, almost 90% of new cases and deaths worldwide, occurred in low to middle income countries in 2020. More than 95% of cervical cancers are associated with chronic Human papilloma virus infection (HPV), particularly of the types 16 and 18. High income countries have vaccination and screening programs that are in place for young girls but low-and middle-income countries usually do not have access to such facilities. Another disease that is increasing in incidence and prevalence in such populations is diabetes mellitus. Diabetes is known to be associated with increased incidence of various cancers like endometrial, cervical, breast, stomach and pancreas. It is also observed that cancer patients with diabetes have an overall reduced survival as compared to non-diabetics. We undertook this study to observe frequency and pattern of cervical pathologies (using routine pap smear) among diabetic females from reproductive age group and compared them with non-diabetic females. The idea was to observe if diabetic females have higher prevalence of cervical pathologies which might progress to cervical cancer in future. We found that diabetes was associated with higher occurrence of cervical pathologies like cervicitis (Odd's Ratio 10.9), vaginitis (OR 1.23), HPV infection (OR 1.4) and malignant changes (OR 1.52). We then attempted to find genetic association between diabetes and cervical pathologies to determine if there are overlapping predisposing genes that can explain higher preponderance of diabetics towards cervical pathologies. This was done by applying gaussian mixture modelling on available genetic data for diabetes mellitus (types 1 and 2), chronic HPV infection, cervical intra-epithelial neoplasia (CIN) and cervical cancer. Some MHC loci like HLA-DQA1, HLA DQB1 were found to be overlapping, which was expected. Apart from MHC genes, certain genes showed positive association with both spectrums (diabetes and cervical pathologies) like INS-IGF2, TTC7B, SILC1. The genetic association may help in understanding the connection between the two diseases in a better way and may also help in predicting higher chances of cervical pathologies in populations with higher preponderance towards upregulation of such genes.

DOI: 10.1530/endoabs.81.P314

P315

Participation in Diabefly® digital therapeutics program leads to significant improvement in glycemic control and reduction in weight and BMI among people with T2D

Ritika Verma[1], Mohammed Khader[2], Tejal Lathia[3], Snehal Tanna[4], Amit Saraf[4], Piya Ballani Thakkar[5], Vivek Raskar[6], Chitra Selvan[7], Saimala Guntur[8] & Arbinder Singal[9]
[1]Fitterfly Healthtech Pvt Ltd, Scientific writing and Research, Navi Mumbai, India; [2]Fitterfly Healthtech Pvt Ltd, Department of Scientific Writing and Research, Navi Mumbai, India; [3]Apollo Hospital, Department of Endocrinology and Diabetology, Navi Mumbai, India; [4]Jupiter Hospital, Department of Endocrinology and Diabetology, Mumbai, India; [5]Bombay Hospital, Department of Endocrinology and Diabetology, Mumbai, India; [6]Dr Raskar's Diabetes Clinic, Department of Endocrinology and Diabetology, Mumbai, India; [7]MS Ramaiah Memorial Hospital, Department of Endocrinology and Diabetology, Bangalore, India; [8]Fitterfly Healthtech Pvt Ltd, Department of Operations, Navi Mumbai, India; [9]Fitterfly Healthtech Pvt Ltd, Chief Executive Officer, Navi Mumbai, India

Background
People with chronic metabolic conditions such as type 2 diabetes (T2D) encounter challenges with self-management regimens to improve their glycemic control, weight and as well as to reduce complications associated with diabetes. Optimal management of T2D requires regular monitoring by physician, access to multidisciplinary care and achieving target HbA1c without hypoglycemia. Digital therapeutics (DTx) provide highly accessible, cost-effective, evidence-based solutions for better management of T2D using high-quality software. This study explores the real-world effectiveness of the Diabefly® DTx program in improving glycemic control among people with T2D.
Methodology
The 90 days Diabefly® program offers mobile application enabled real-time digital logging of daily meals, physical activity, and provides access to remote lifestyle coaching from health coaches and experts (psychologist, physiotherapist, and nutritionist). The aim of the study was to evaluate the changes in HbA1c, weight, body mass index (BMI) and waist circumference at the beginning and at the end of the program. All the outcomes were evaluated using paired t-test with $P < 0.05$ considered as significant.
Results
De-identified data of 205 participants (Mean age: 47.14 $\pm$ 12.67 years, Gender: 55.60% female) was analyzed. After the completion of the Diabefly® program, a significant mean reduction in HbA1c by 1.55 $\pm$ 1.88% ($P < 0.001$) from the baseline of 8.59 $\pm$ 2.01 % was observed. HbA1c levels were reduced in 87.80 % (180/205) participants while reduction of >1% in HbA1c levels was observed in 56.11 % (101/180) participants. A significant mean reduction in body weight and BMI by 2.39 $\pm$ 3.25 kg and 0.82 $\pm$ 1.14 kg/m^{2}from the baseline of 75.33 $\pm$ 15.43 kg and 27.41 $\pm$ 4.68 kg/m^{2}was observed respectively ($P < 0.001$ for both). Reduction in body weight was observed in 68.29 % (140/205) participants and a reduction of >5 kg body weight was observed among 20.71 % (29/140) participants. Furthermore, complete data on waist circumference was available for 109 participants which showed a significant mean reduction by 3.49 $\pm$ 8.24 cm from the baseline of 98.80 $\pm$ 14.08 cm ($P < 0.001$).
Conclusion
At the end of the program, a significant improvement in glycemic control and reduction in weight and BMI was observed. Thus, the study showed that usage of the Diabefly®program along with standard medical care by a physician can be effective in better management of T2D by providing multidisciplinary care and continuous support to people with diabetes.

DOI: 10.1530/endoabs.81.P315

P316

Simultaneous pancreas-kidney transplantation: long-term survival and metabolic profile analysis among functioning pancreatic graft patients – A 20 year experience from a center in Portugal

Ariana Maia[1], Miguel Saraiva[1], Inês Sala[2], Daniela Soares[1], Diana Borges Soares[1], Sílvia Monteiro[1], Joana Vilaverde[1], Lia Ferreira[1], La Salete Martins[2] & Jorge Dores[1]
[1]Centro Hospitalar Universitário do Porto, Serviço de Endocrinologia, Diabetes e Metabolismo, Porto, Portugal; [2]Centro Hospitalar Universitário do Porto, Serviço de Nefrologia, Porto, Portugal

Introduction
Simultaneous pancreas-kidney transplantation (SPKT) is the treatment of choice for type 1 diabetic patients with advanced kidney chronic disease (CKD), restoring normoglycemia, insulin independence and improving survival. The

present study aims to analyse survival of patients undergoing SPKT and the post-SPKT metabolic profile of patients with a functioning pancreatic graft.
Methods
Retrospective observational study. T1DM patients with CKD stages 4-5 KDIGO undergoing SPKT at Centro Hospitalar Universitário do Porto from May 2000 to November 2020 were included. Pre-SPKT baseline data collection. Survival analyses were performed using Kaplan-Meier method. Metabolic profile of patients with a functioning pancreatic graft was secondarily investigated in the latest post-SPKT medical visit.
Results
242 patients were included with a mean age at SPKT of 35.4 ± 6.1 years, mean duration of DM and dialysis of 24.1±5.9 years and 25.8±19.5 months, respectively. Patients had mean values of HbA1c, total daily insulin dose (TDID) and BMI of 8.5±1.6 %, 38.8 ± 12.5 U/day and 22.4 ± 2.8 kg/m2 pre-SPKT. Cumulative patient survival was 96.3%, 94.4%, 90.1%, 83.4%, and 80.6% at 1, 5, 10, 15, and 20 years post-SPKT. Pancreatic graft survival of 85.5%, 79.4%, 74.5%, 65.0% and 61.8% at 1, 5, 10, 15 and 20 years. Renal graft survival of 93.8%, 88.6%, 80.1% and 73.5% at 1, 5, 10 and 20 years. The main causes of failure were graft rejection and thrombosis. The metabolic profile of the individuals analysed at the most recent post-SPKT consultation included 178 patients with functioning pancreatic graft, with a mean follow-up of 9.3±5.2 years post-SPKT, and of these, 94.4% with functioning renal graft. Mean BMI, creatinine clearance, C-peptide, HbA1c, LDL-cholesterol and non-HDL-cholesterol were 23.7±4.0 Kg/m2, 63.8±21.2 ml/min/1,73 m^2, 3.1±2.0 ng/ml, 5.6±0.7%, 89.0±35.3 mg/dl and 111.3±40.0 mg/dl. Intermediate hyperglycaemia was present in 29.8% of patients and 5.1% had HbA1c ≥ 6.5%.
Conclusion
Results of our center reinforce SPKT as a valid option in the treatment of T1DM, aiming to improve quality of life, with sustained maintenance of euglycemia, without the need for exogenous insulin, in the medium/long term within a selected group of patients with advanced diabetic kidney disease.
Keywords
Type 1 diabetes mellitus, simultaneous pancreas and kidney transplantation, transplant, transplantation, chronic complications of diabetes, metabolic profile.
DOI: 10.1530/endoabs.81.P316

P317

Changing trends in the aetiology of diabetes-related ketoacidosis(DKA)-a blueprint to identify preventable causes

Dineshwaran Rajendran[1], Catherine Cooper[2], Wai Nga Alice Yip[3], Gobeka Ponniah[3], Anjitha Anilkumar[3], Dengyi Zhou[3], Shamanth Soghal[4], Parijat De[5] & Haaziq Sheikh[6]
[1]Good Hope Hospital, Acute Medicine, The Royal Town of Sutton Coldfield, United Kingdom; [2]Walsall Manor Hospital, Walsall, United Kingdom; [3]University of Birmingham Medical School, United Kingdom; [4]Queen Elizabeth Hospital Birmingham, United Kingdom; [5]Sandwell General Hospital, United Kingdom; [6]Haberdashers' Adams' Grammar School, United Kingdom

Introduction
Diabetes-related Ketoacidosis (DKA) is a commonly-encountered acute endocrine emergency requiring prompt recognition and treatment. DKA is triggered by risk factors that are often preventable. There are limited studies evaluating the precipitating causes of DKA and depicting their trends over the years. The latter is important in the prevention of DKA by ensuring appropriate education and interventions.
Aim
To study the trends of aetiologies that precipitate DKA over the years.
Methods
We conducted a retrospective analysis of all DKA related admissions across six regional hospitals in the United Kingdom between April 2014 to November 2021. DKA was diagnosed as serum glucose ≥11 mmol/l, ketones ≥ 3 mmol/l and pH ≤7.3 or bicarbonate ≤ 15 mmol/l. Precipitating factors were classified as Alcohol-related, COVID-19, Drug-induced, Intercurrent illness, New Diagnosis of type-1 diabetes, SGLT-2 inhibitor-associated, Sepsis, Suboptimal compliance to treatment and Trauma respectively. Statistical analysis was done using SPSS version 27. Results are expressed in percentage and proportion.
Results
A total of 1463 DKA episodes were included in the analysis. Intercurrent illness (34.8%, $n=509$) and Suboptimal compliance to treatment (28.2%, $n=413$) were the most common factors identified. Other notable causes of DKA were: New diagnosis of type 1 diabetes (8.9%$n=130$), Sepsis (4.2%, $n=62$), Alcohol-related (3.9%, $n=57$). The proportion of these aetiologies has remained consistent over the years. Newer varieties of precipitating causes such as SGLT2 inhibitor-associated (1.3%, $n=19$) and other Drug-induced (1.1%, $n=16$) had an increasing trend since 2019. COVID-19 accounted for 5% of the total episodes ($n=41$). Precipitating aetiology was unclear in 8%($n=187$) of the DKA admissions. However, the proportion of unclear causes as precipitating aetiology for DKA has been steadily down trending since 2016 (24.0% in 2016, 19.2% in 2017, 14.5% in 2018, 16.2% in 2019, 12.6% in 2020 and 8.0% in 2021)
Conclusion
Infections and Suboptimal compliance to treatment accounted for a majority of 63% of the DKA cases, suggesting more work needs to be done to minimize these preventable causes. A rise in medication-induced DKA prompts the need to educate patients and clinicians to be aware of the role of these contributory medications. Down trending seen in Unclear Causes of DKA is a welcome result as this can help us prevent recurrences in patients by educating them regarding the known or established precipitating factors so that they could be vigilant in regards to these in future.
DOI: 10.1530/endoabs.81.P317

P318

Effect of treatment of gestational diabetes mellitus with insulin on pregnancy outcomes

Olfa Lajili, Aroua Temessek, Rim Rachdi, Yosra Htira & Feika Ben Mami
National Institute of nutrition of Tunis, The Research Unit of GDM (Department C), Tunis, Tunisia

Introduction
Gestational diabetes mellitus (GDM) complicates approximately 3% to 9% of pregnancies. Diagnosis and treatment of GDM remain essential to limit maternal and neonatal outcomes. The aim of the study was to evaluate the difference in pregnancy outcomes between insulin- and diet-treated tunisian women with gestational diabetes.
Methods
It was a prospective longitudinal study including 220 patients followed for GDM at the research unit of the C department of the national institute of nutrition in Tunis. The patients were followed during pregnancy and until post partum. Patients were divided into two groups: group 1 (G1): Insulin treated and insulin therapy and group 2 (G2): Patients treated by diet alone.
Results
At the end of our study, 68 patients were treated with insulin, 11 patients developed gestational hypertension or pre-eclampsia. Two thirds of the patients (68%) delivered by cesarean section. Neonatal outcomes were dominated by macrosomia (13.5%) and transient respiratory distress (11.4%). insulin-treated patients had a higher incidence of gestational hypertension (G1: 11.9% vs G2: 2.1%;$P=0.03$). insulin treatement did not reduces the rate of caesarean section (G1: 64.7% vs G2: 63.2%;$P=0.785$). Insulin therapy did not reduce fetal outcomes, including intrauterine growth retardation (G1: 0% vs G2: 1.3%;$P=0.326$), fetal death in utero (G1: 0% vs G2: 1.3%;$P=0.306$), neonatal hypoglycemia (G1: 0% vs G2: 1.3%;$P=0.333$), macrosomia (G1: 17.6% vs G2: 11.2%;$P=0.203$), hydramnios (G1: 13.2% vs G2: 6.6%;$P=0.111$), transient respiratory distress (G1: 11.8% vs G2: 10.5%;$P=0.781$), neonatal jaundice (G1: 5.9% vs G2: 3.3%;$P=0.787$) and prematurity (G1: 7.4% vs G2: 4.6%;$P=0.452$).
Conclsion
Our study showed that patients treated with insulin had a higher incidence of pregnancy induced-hypertension. However, treatment of gestational diabetes with insulin did not reduces the rate of caesarean section and noenatal morbidity.
DOI: 10.1530/endoabs.81.P318

P319

Feeding and DKA resolution

Elaine Louise Fernandez & Maria Jocelyn Isidro
Makati Medical Center, Medicine, Makati, Philippines

Background
Diabetic ketoacidosis (DKA) is a complication of Diabetes Mellitus and is a life-threatening medical emergency usually requiring admission to an intensive care unit. There is no established guideline regarding timing of initiation of oral/enteral feeding in DKA patients.
Purpose
To determine if there is a difference in clinical outcomes for DKA patients whose oral/enteral feeding was started early vs patients whose feeding was started beyond 24 hours.
Methods
A 10-year retrospective observational cohort was conducted in a single medical center. Subjects consisted of DKA patients admitted in the Intensive Care Unit.

Clinical outcomes were compared among DKA patients who were fed within 24 hours of admission (early feeding) vs those fed beyond 24 hours (late feeding). Primary outcome was DKA resolution. Secondary outcomes were Anion gap closure, Length of hospital stay, Length of ICU stay, and inpatient Mortality.
Results
A total of 68 patients were included in the study – 39 in the early feeding group and 29 in the late feeding group. Baseline characteristics, classification of Diabetes, DKA severity, and complications were comparable among the two groups. The odds of early DKA resolution or resolution of DKA within 24H was 4.8x higher in early feeding group compared to the late feeding group (95% C.I.: 1.2 – 19.6). Time to DKA resolution, time to anion gap closure, and length of hospital stay were also significantly shorter for the early feeding group. There was no significant difference in the ICU length of stay and inpatient mortality between the two groups. The power of the study is 87.34%.
Conclusion
DKA patients benefit from early feeding because it significantly shortens time to DKA resolution and anion gap closure, also length of hospital stay, without significant increase in the rate of DKA complications. Early feeding is also associated with DKA resolution within 24 hours.

DOI: 10.1530/endoabs.81.P319

P320

Differences in diabetic neuropathy in type 1 and type 2 diabetes mellitus

Laura Šiauliene[1,2], Ieva Sereike[3], Juozas Rimantas Lazutka[1] & Zydrune Visockiene[2,4]
[1]Life Sciences Center, Institute of Biosciences, Vilnius University, Vilnius, Lithuania; [2]Vilnius University Hospital Santaros Klinikos, Center of Endocrinology, Vilnius, Lithuania; [3]Vilnius University Hospital Santaros Klinikos, Center of Neurology, Vilnius,; [4]Institute of Clinical Medicine, Clinic of Internal Diseases, Family Medicine and Oncology, Vilnius University Faculty of Medicine, Vilnius, Lithuania

Background
Diabetic neuropathy (DN) is the most common chronic diabetes complication in type 1 (T1DM) and type 2 (T2DM) diabetes mellitus. Due to diagnostic issues, it is the least studied complication with limited and controversial data about the differences of various types of DN between T1DM and T2DM patients.
Aim
To evaluate the differences of diabetic polyneuropathy (DPN) and cardiac autonomic neuropathy (CAN) - between T1DM and T2DM patients.
Materials and Methods
Three methods were used to evaluate DPN: clinical examination was done using neuropathy symptom score (NSS) and neuropathy disability score (NDS); neurometry (NM) – using Neurometer NervScan™ LLC device; electroneurography (ENG) – using Nihon Kohden Neuropack M-1 Electromyogram Machine. CAN was assesed by performing cardiovascular autonomic reflex tests (CARTS) using Cardiosys Extra MDE diagnostic device.
Results
There were 53 T1DM and 63 T2DM patients enroled in to the study. T1DM patients were significantly ($P<0,05$ for all) younger (41,6 $\pm$ 15,9 vs 60,0 $\pm$ 11,7 years), had lower BMI (23,5$\pm$3,5 vs 36,0$\pm$6,32 kg/m2), systolic and diastolic blood pressure (124,5$\pm$16,3 vs 138,7$\pm$13,7 and 74,2$\pm$8,9 vs 80,5$\pm$8,3 mmHg respectively), incidence of arterial hypertension (35,8% vs 90,5%), heart failure (3,8% vs 20,6%) and coronary artery disease (5,7% vs 20,6%). T2DM patients had significantly higher scores of symptomatic neuropathy compared to T1DM (NSS 4,3 $\pm$ 3,3 vs 3,1$\pm$3,4; $P<0,049$), but the severity of pain, evaluted by self reported numerical rating scale did not differ (1,8 $\pm$ 2,5 vs 1,4 $\pm$2,5, $P=0,17$). The prevalenceof DPN did not differ between the groups, however the proportion of DPN depended on method used, being the highest diagnosed with NM (67,3% vs 61,3%, $P>0,05$), followed by ENG (40,9% vs 44,1%, $P>0,05$) and clinical examination (30,2% vs 35,5, $P>0,05$). Tuning fork vibration perception was the only test of clinical evaluation that showed significantly worse vibration perception in T2DM patients compared with T1DM (impaired in 78,3% vs 57,1%, $P=0,023$), CARTs showed significantly higher incidence of CAN in T2DM compared to T1DM patients (67,3% vs 32,7%, $P=0,011$).
Conclusions
There was no difference in the prevalence of DPN between T1DM and T2DM, however significant difference in diagnostic accuracy of different methods was observed. T2DM patients were more likely to have symptomatic polyneuropathy, large fiber damage and CAN.

DOI: 10.1530/endoabs.81.P320

P321

Effect of a novel-app based strategy for carbohydrate counting on glucose control in type 1 diabetes

Silvia Irina Briganti[1], Rocky Strollo[2], Daria Maggi[2], Shadi Kyanvash[2], Oreste Lanza[2], Silvia Manfrini[2] & Paolo Pozzilli[2]
[1]Campus Bio-Medico of Rome, Metabolic Diseases, Rome, Italy; [2]Campus Bio-Medico of Rome, Metabolic Diseases, Rome, Italy

Background
carbohydrate counting is often performed inaccurately by patients with type 1 diabetes (T1D). We hypothesized that mobile App 'Dietrometro', that estimates CHO content of food figures, would ameliorate glucose control.
Aim
To study the effect of 'Dietometro' on glucose control.
Methods
54 T1D subjects (aged 18-60 years, 26 males), on multiple daily injections ($n=23$) or continuous subcutaneous insulin infusion ($n=31$), were randomly assigned to three groups: no counting (group 1; $n=19$), 'self-managed' counting (group 2; $n=19$) and App-assisted counting (group 3; $n=16$). Outcomes were one- and three months follow-up TIR (time in range), TAR (time above the range) and TBR (time below the range), estimated by flash or continuous glucose monitoring, and HbA1c.
Results
At the baseline TIR were similar between groups, while HbA1c was lower in group 3 compared to group 1 (6.9$\pm$1.06 vs. 7.8$\pm$0.85%; $P<0.05$). At one-month follow-up, TIR was higher in group 2 and 3 compared to group 1 (63.58 $\pm$ 11.55 vs. 52.32 $\pm$ 13.22%; $P=0.014$, and 71.25 $\pm$ 9.75 vs. 52.32 $\pm$ 13. 22%, respectively; $P<0.001$). TAR at one-month follow-up was significantly lower in group 3 (31.25 $\pm$ 19.18 vs. 22.31 $\pm$ 10.89%; $P<0.001$), while no differences were observed in TBR. At three-months follow-up, groups 2 and 3 had a lower HbA1c than group 1 (7.16 $\pm$ 0.647 vs. 6.56 $\pm$ 1.91 vs. 7.96 $\pm$ 1.0%; $P<0.05$).
Conclusions
App-assisted CHO counting might improve glucose control. Larger sample size and longer follow-up are needed to define the long-term effect of this system.

DOI: 10.1530/endoabs.81.P321

P322

Higher levels of psychological stress are associated with lower levels of the insulin sensitizer FGF-21 in patients with obesity

Susanne Kuckuck[1,2], Robin Lengton[1,3], Eline S van der Valk[1,2], Anand M Iyer[1,2], Mostafa M Mohseni[1,2], Sjoerd A A van den Berg[2,3] & Elisabeth van Rossum[1,2]
[1]Erasmus Medical Center Rotterdam, Department of Internal Medicine, Division of Endocrinology, Rotterdam, Netherlands; [2]Erasmus Medical Center Rotterdam, Obesity Center CGG, Rotterdam, Netherlands; [3]Erasmus Medical Center Rotterdam, Department of Clinical Chemistry, Rotterdam, Netherlands

Background
Altered signaling of hormones regulating appetite and metabolism is often observed in individuals with obesity (BMI $\geq$ 30 kg/m^2) and related diseases, potentially resulting in increased hunger signaling and metabolic dysfunctions. Previous research indicates that such disturbances may be induced by weight gain itself, but also by other factors such as glucocorticoid excess (e.g. due to stress). However, knowledge regarding the associations between hormonal appetite signals and biological or psychological measures of stress is still limited, particularly in patients with obesity.
Methods
Data were collected from 68 patients with obesity (47 women). We assessed psychological stress perceived over the last month (via the Perceived Stress Scale (PSS)-14, ranging from 0 to 56) and biological stress (using the average of 24h urine cortisol levels of two consecutive days). In addition, we measured overnight-fasted serum levels of the hormonal appetite regulators leptin, insulin, adiponectin, FGF-21, PP, GIP, PYY, CCK and AgRP (pg/ml). To investigate cross-sectional associations between psychological/biological stress and hormonal appetite regulators, we used linear regression analysis with PSS-14 scores or urine cortisol levels as predictors, adjusted for pre-defined potential confounders (age and sex).

Results
There was a negative association between PSS-14 scores and log10-transformed FGF-21 levels (β = -0.015 (-0.028; -0.003 95% CI), $P < .05$) which persisted after adjustment for the potential confounders (β = -0.015 (-0.029; -0.001 95% CI), $P < .05$). We did not see any other associations of hormonal appetite regulators with PSS-14 scores, nor with 24h urine cortisol levels.
Conclusion
A 1-point increase on the PSS-14 score was associated with a 3.4% decrease in serum levels of the insulin sensitizer FGF-21. In patients with obesity, FGF-21 levels are often increased compared to normal weight controls, probably to compensate for metabolic challenges associated with the disease. We hypothesize that chronic stress may interfere with FGF-21 actions in these patients by decreasing FGF-21 levels; resulting in a failure to compensate for metabolic challenges. Future studies should further investigate the directionality of this association and its potential implications for eating behaviour and the development of metabolic disorders such as type 2 diabetes.

DOI: 10.1530/endoabs.81.P322

P323

Sleep quality in patients with type 1 diabetes: a large cross-sectional study

Claudio Bongiorno[1], Simona Moscatiello[2], Gilberto Laffi[2], Danilo Ribichini[2], Valentina Lo Preiato[2], Michele Grimaldi[2], Uberto Pagotto[1] & Guido Di Dalmazi[1]
[1]Alma Mater Studiorum - Università di Bologna, Bologna, Italy; [2]S. Orsola-Malpighi Polyclinic, Bologna, Italy

Background
Altered sleep quality and duration have been reported in 26-67% of patients with type 1 diabetes (T1D). However, differences in study designs, populations, and methods of sleep quality assessment have led to heterogeneous results in terms of association with clinical data and blood glucose parameters.
Aims
To investigate the sleep quality of a large cohort of adult patients with autoimmune diabetes under insulin treatment, and to analyze the relationship with clinical and biochemical data.
Methods
We administered the Pittsburgh Sleep Quality Index (PSQI) questionnaire to 553 adult subjects (>18 years) with T1D or latent autoimmune diabetes of the adult (LADA). We excluded 44 patients without clinical data. Patients were also administered additional questionnaires: Diabetes Distress Scale (DDS), Diabetes-Related Quality Of Life (DRQOL), Diabetes Treatment Satisfaction Questionnaire (DTSQ), and Hypoglycemia Attitudes and Behavior Scale (HABS). We retrieved biochemical and clinical data at the time of the PSQI administration (+/- 4 months). Glucose metrics up to 3 months before PSQI administration were analyzed in 183/329 patients under continuous glucose monitoring (CGM).
Results
PSQI questionnaires had complete data in 465 patients. Altered sleep quality (PSQI score >5) was detected in 150/465 subjects (32.3%). Short sleep duration (< 7 hours) was detected in 181/465 patients (38.9%). PSQI score was higher in females *vs* males (5.3 ± 4.3 *vs* 4.7 ± 2.9; $P=0.031$), with higher values of sleep latency ($P=0.010$), sleep disturbances ($P=0.001$), and daytime dysfunction ($P<0.001$). No difference in PSQI score were detected between patients under multiple daily injections ($n=390$) and insulin pump ($n=75$; $P=0.412$), and among subjects under self-monitoring of blood glucose ($n=159$), intermittently-scanned CGM ($n=221$) and real-time CGM ($n=85$; $P=0.403$), even when analyzed separately by sex. When compared to those with normal values, patients with altered sleep quality had higher glycated hemoglobin (56.4 ± 12.1 *vs* 60.4 ± 11.5; $P=0.001$), higher distress (DDS scores 1.9 ± 0.9 *vs* 2.4 ± 1.1; $P<0.001$), lower treatment satisfaction (DTSQ scores 29.3 ± 5.4 vs 27.1 ± 5.7; $P<0.001$) and lower quality of life (DRQOL scores 1.7 ± 0.3 vs 2.0 ± 0.4; $P<0.001$), whereas duration of diabetes was not different ($P=0.751$). No correlation was found between glucose metrics derived from CGM and parameters of sleep quality.
Conclsion
Altered sleep quality was detected in one third of the patients with autoimmune diabetes and was associated with higher glycated hemoglobin levels, rather than altered parameters of glycemic variability, irrespective of the specific treatment for diabetes. Higher distress and lower quality of life were detected in patients with altered sleep quality.

DOI: 10.1530/endoabs.81.P323

P324

Characterization of the somatostatin and ghrelin hormonal systems revealed their potential therapeutic role in chronic liver disease

Natalia Hermán Sánchez[1], Juan Luis López-Cánovas[1], Antonio Garcia-Estrada[1], Prudencio Sáez-Martínez[1], Victor Amado[2], Manuel de la Mata[2], Jose Cordoba-Chacon[3], Andrá Sarmento-Cabral[1], Manuel Rodriguez-Peralvarez[2], Raul M. Luque[1] & Manuel D. Gahete[1]
[1]University of Cordoba, Cell Biology, Physiology and Immunology, Spain; [2]Reina Sofia Hospital, Spain; [3]University of Illinois at Chicago, United States

Hormonal signalling plays a key role in the progression of metabolic (dysfunction)-associated fatty liver disease (MAFLD) to hepatocellular carcinoma (HCC). However, the role of somatostatin (SST), cortistatin (CORT), neuronostatin (NST) and ghrelin systems in MAFLD-HCC progression has not yet been elucidated. We characterized the role of SST/CORT/NST and ghrelin systems in chronic liver disease and evaluated their clinical potential. The expression of the components of the SST/CORT/NST/ghrelin systems (ligands, receptors and accessory proteins) was analysed in different mouse models of MAFLD/non-alcoholic steatohepatitis (NASH)/cirrhosis, in two retrospective human cohorts [cohort 1: HCC vs. adjacent ($n=93$); cohort 2: HCC vs. adjacent ($n=58$), cirrhosis ($n=39$), and healthy livers ($n=5$)], in different in silico MAFLD and HCC human cohorts (mRNA/protein), and in three liver-derived cell lines (HepG2, Hep3B and SNU-387). Proliferation after treatment with natural (SST/CORT/NST) and synthetic (Lanreotide, Ocreotide, Pasireotide) peptides was evaluated in cell lines and human liver primary cultures. Our results revealed that MAFLD mouse models showed a damage-dependent differential expression pattern of SST/CORT/NST components. Indeed, early MAFLD stages were characterized by a decreased expression of Cort, Sstr1, Sstr2, Sstr3 and the truncated Sstr5 md3 receptor, while there was a marked increase in the expression of Sstr3, Sstr4, Sstr5 and Sstr5 md3 in advanced stages. Some of these observations were validated in a human in silico cohort of MAFLD (i.e. SSTR5 overexpression and CORT downregulation), confirming CORT dysregulation as an early event in MAFLD. In tumoral stages, retrospective cohorts revealed a decreased expression of CORT, SSTR1, SSTR2 and ghrelin receptor and the overexpression of SSTR5 and the NST receptor (GPR107) in tumoral tissues. These alterations were validated in in silico cohorts of HCC. Besides, the decreased expression of CORT was associated with the dedifferenciation of the tissue while GPR107 overexpression was associated with key aggresiveness parameters (survival, recurrence, tumoral diameter, etc.) in the retrospective and in silico cohorts. In vitro assays revealed a decreased proliferation after treatment with SST, CORT, NST and the synthetic analogues, which was dependent on the expression of the receptors. Specifically, NST reduced proliferation of the most aggresive cell lines, Hep3B and SNU-387. Altogether, this study demonstrates an profound alteration in the expression levels of the SST/CORT/NST and ghrelin systems in human, animal, and cellular models of chronic liver disease, and suggests a potential prognostic and therapeutic role of certain components of these hormonal systems in chronic liver disease.
Fundings
ISCIII (PI20/01301), JdA (PEMP-0036-2020, BIO-0139), FSEEN and CIBERobn.

DOI: 10.1530/endoabs.81.P324

P325

Association between the coefficient of glycemic variation and time in range, below and above range in continuous monitoring glucose systems in type 1 diabetes

Cristiana Gomes da Costa[1], Tânia Matos[1] & Sónia Vale[1,2]
[1]Hospital Santa Maria, Endocrinology, Lisbon, Portugal; [2]Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal

Introduction
Glycemic variability (GV) is a major consideration when evaluating quality of glycemic control. Coefficient of glycemic variation (%CV) is the metric of choice to define GV. International consensus on continuous glucose monitoring (CGM) recommends a %CV <36. Additional studies suggest that low %CV minimize hypoglycemia events <54 mg/dl.
Aims
The aim of this analysis is to examine the expected relationship between the coefficient of glycemic variation and time in range (%TIR), time below range (%TBR) and time above range (%TAR) in continuous glucose monitoring systems.

Methods
We analysed a subset of 71 patients with type 1 diabetes followed at our endocrinology outpatient clinic using a continuous glucose monitor system that uploads data to a database accessible for clinicians. 16 out of 71 patients were excluded, 11 patients because they had less than 70% of data captured by the sensor in the previous 2 weeks and 5 patients because they had a diagnosis within the previous year. A bivariate analysis was performed to evaluate the relation between the %CV and %TIR, %TBR and %TAR in 55 patients. Time in range is defined as between 70 and 180 mg/dl. Furthermore, a bivariate analysis was performed to evaluate the relation between %CV and the subgroup time below 54 mg/dl (%TB 54).
Results
Patients were between 22 and 66 years old (mean 43, SD 12) and 42% were male. The %CV showed a strong positive correlation and statistically significant with %TBR ($r=0.708$, $P < 0.0001$) and a weak negative correlation, but statistically significant with %TIR ($r=-0.398$, $P=0.003$). There was no correlation between %CV and %TAR. Both correlations are independent of age and sex. Moreover, the %CV showed a strong positive correlation and statistically significant with %TB 54 ($r=0.664$, $P < 0.0001$).
Conclsions
The coefficient of glycemic variation is an important metric to evaluate the risk of hypoglycemia, in our analysis it is closely correlated with time below 70 mg/dl and also with time below 54 mg/dl. These results are consistent with results from other studies. Although weak it is important to note the negative correlation between coefficient of glycemic variation and time in range, as the latest is an indicator for evaluating the efficacy of glycemic control and predicting diabetic complications. Our analysis highlights the importance of %CV in the management of type 1 diabetic patients.

DOI: 10.1530/endoabs.81.P325

P326

Personalized glycemic response based Diabefly-Pro® digital therapeutics improves dietary patterns, glycemic control and reduces postprandial hyperglycemia in real-world settings

Shilpa Joshi[1], Ritika Verma[2], Mohammed Khader[2], Sneha Nikte[3], Suresh Ade[4], Saifuddin Bandukwala[5], Mitali Joshi[6], Vinod Methil[7], Mangesh Tiwaskar[8] & Arbinder Singal[9]
[1]Fitterfly HealthTech Pvt Ltd, Department of Metabolic Nutrition, Navi Mumbai, India; [2]Fitterfly HealthTech Pvt Ltd, Department of Scientific Writing and Research, Navi Mumbai, India; [3]Dr Nikte Clinic, Department of Endocrinology and Diabetology, Mumbai, India; [4]Ayush Diabetes and Neurology clinic, Department of Diabetology and Neurology, Mumbai, India; [5]Advance Diabetes Care Clinic, Department of Internal Medicine, Mumbai, India; [6]The Clinic, Department of Diabetology, Mumbai, India; [7]Sweet Clinics, Department of Diabetology, Mumbai, India; [8]Shilpa Medical Research Center, Department of Diabetology, Mumbai, India; [9]Fitterfly HealthTech Pvt Ltd, Cheif Executive Officer, Navi Mumbai, India

Background
CGM based monitoring can help in development of personalized digital therapeutics programs based on the understanding of the effect of diet, physical activity and medications on everyday blood glucose excursions. The variation in intra-individual glycemic response to the same food has been reported in many studies. Thus, understanding of personalized glycemic response (PGR) of each individual becomes important for effective diabetes management.
Methods
De-identified data of 108 participants (Average Age: 40.86 $\pm$ 12.08 years, 36.11% females) with T2D in Diabefly-Pro®program was analyzed. The program provided 90 days PGR based lifestyle management support via digital meal logging through mobile application and remote health coaching. CGM data was collected in week 1 and week 2 with a modified lifestyle plan being introduced from week 2 of the program. All the parameters were analyzed for week 1 (baseline) and week 2 of the program. Net area under the curve (AUC) for 0-24h was calculated using trapezoidal rule. The incremental area under the curve (iAUC) was calculated at 1h-post breakfast. Paired t-test and spearman correlation method was used for statistical analysis with $P < 0.05$ considered as significant.
Results
A significant reduction in AUC by 44.71 $\pm$ 17.40 % was observed from an average week 1 AUC of 7328.59 $\pm$ 4265.79 mg/dl*h ($P < 0.0001$). iAUC post breakfast showed a significant reduction by 42.33 $\pm$ 22.90 % from a baseline average of 340.52 $\pm$ 202.19 mg/dl*h ($P < 0.0001$). The comparison of dietary recall in week 1 and week 2 showed that participants showed reduction in intake of calories (70.29 kcal; $P=0.04$) and carbohydrate (12.68 g; $P=0.002$). The percent reduction in AUC showed a significant correlation with the reduction in the amount of carbohydrate intake ($\rho = 0.24$, $P=0.01$). Time-in-range (TIR) improved significantly from a baseline of 67.35 $\pm$ 25.56 % to 70.05 $\pm$ 25.55 % ($P=0.03$) in week 2. Time-above-range (TAR) reduced significantly from a baseline of 27.13 $\pm$ 27.64 % to 22.13 $\pm$ 27.25 % ($P < 0.0001$). Reduction in TAR showed significant correlation with percent reduction in AUC ($\rho = 0.32$, $P < 0.001$).
Conclusion
Diabefly-Pro® program led to significant reduction in postprandial hyperglycemia while improving TIR and dietary behavior in people with diabetes after 7 days of modified lifestyle plan. PGR-based coaching can play an important role in achieving better glycemic control in the long-term.

DOI: 10.1530/endoabs.81.P326

P327

Retrospective observational study of Italian patients with diabetes mellitus in Covid-19 era: a big data approach

Carla Greco[1,2], Tommaso Pirotti[3], Giulia Brigante[1,2], Tommaso Filippini[4], Chiara Pacchioni[2], Tommaso Trenti[3], Manuela Simoni[1,2] & Daniele Santi[1,2]
[1]University of Modena and Reggio Emilia, Modena, Italy, Unit of Endocrinology, Department of Biomedical, Metabolic and Neural Sciences, Modena, Italy; [2]Azienda Ospedaliero-Universitaria of Modena, Italy, Unit of Endocrinology, Department of Medical Specialties, Modena, Italy; [3]Azienda USL of Modena, Italy, Department of Laboratory Medicine and Anatomy Pathology; [4]University of Modena and Reggio Emilia, Modena, Italy., Environmental, Genetic and Nutritional Epidemiology Research Center (CREAGEN), Department of Biomedical, Metabolic and Neural Sciences, Modena, Italy

Introduction
The prevalence of diabetes mellitus (DM) in patients with coronavirus disease (COVID)-19 varies widely, depending on population characteristics, country, age and disease severity. Moreover, pre-existing DM seems to double the risk of both critical COVID-19 and mortality.
Aim
To evaluate incidence and mortality risk of COVID-19 in a large diabetic population in Northern Italy.
Methods
A retrospective, observational, big data cohort study was carried out, including subjects with type 1 and type 2 DM living in the Province of Modena, submitted to at least one swab for SARS-CoV-2 between March 2020 and March 2021. Data were extracted from the Hospital data warehouse.
Results
9553 diabetic patients were enrolled (age 68.8 + 14.1 years). COVID-19 was detected in 2302 patients (24.1%) with death in 8.9% of cases. No differences in COVID-19 prevalence were detected considering sex. Mean age (67.6 + 13.7 *vs* 69.8 + 14.1 years) was significantly lower in infected than uninfected patients and COVID-19 was more frequent in youngest people, according to quartile of age ($P<0.001$) and retirement age of 65 years ($P<0.001$). Moreover, DM duration was lower in infected than uninfected patients (11.2 + 6.6 vs 11.8 + 6.7 years, $P<0.001$), but higher HbA1c was found in infected compared to uninfected patients (58.7 + 16.7 vs 56.7 + 15.9 mmol/mol, $P<0.001$). Accordingly, COVID-19 was less frequent in patients treated with anti-diabetic drugs compared to those not treated ($P<0.001$). Logistic analysis confirms these results and identifies 3 risk factors for COVID-19: age (odds ratio-OR 1.013, 95% confidence interval-CI:1.008-1.017), DM duration (OR 1.007, 95%CI:1.001-1.013), and HbA1c (OR 1.009, 95%CI:1.002-1.016). As regards COVID-19 mortality, logistic analysis demonstrated that death was predicted by DM duration (OR 1.010, 95%CI: 1.005-1.015) and HbA1c (OR 1.005, 95%CI:1.002-1.009). Three ROC analyses were generated setting death as test variable, showing that the worse prognosis could be predicted by DM duration longer than 10.9 years (AUC = 0.639, 95%CI:0.601–0.676) and age older than 74.4 years (AUC = 0.797, 95%CI:0.767–0.827).
Conclsion
Our big data analysis confirms the correlation between COVID-19 mortality and DM. In particular, although COVID-19 was more frequently detected in youngest patients, a poor glycemic control worsens outcomes, confirming the importance of strict glyco-metabolic control, especially in older diabetic people with long DM duration. Thus, diabetic patients should undergo careful monitoring of blood

glucose. In particular, patients with DM and COVID-19 should be followed carefully when older than 74 years and with long DM duration.

DOI: 10.1530/endoabs.81.P327

P328

DKA registry: A step towards harmonising management of diabetes-related ketoacidosis in the United Kingdom-initial findings

Catherine Cooper[1], Lakshmi Rengarajan[2], Amy Birchenough[3], Haaziq Sheikh[4], Meghnaa Hebbar[5], Carina Synn Cuen Pan[5], Parijat De[3], Parth Narendran[6] & Punith Kempegowda[6]

[1]Walsall Manor Hospital, Walsall, United Kingdom; [2]Birmingham Heartlands Hospital, Birmingham, United Kingdom; [3]Sandwell and West Birmingham Hospitals, Birmingham, United Kingdom; [4]Haberdashers' Adams' Grammar School, United Kingdom; [5]University of Birmingham Medical School, Birmingham, United Kingdom; [6]Queen Elizabeth Hospital Birmingham, Birmingham, United Kingdom

Background

Diabetes-related ketoacidosis (DKA) is a common and potentially life threatening complication in people with diabetes. Despite national and international guidelines, interhospital guideline variation and mismanagement during admission are important contributory factors to increased DKA duration and length of stay.

Aim

To establish a common DKA registry to identify gaps in management, assess outcomes and share best practises across centres.

Methods

Retrospective analysis of all DKA admissions between 1st January 2021 to 1st December 2021 across six hospitals in the United Kingdom was undertaken. People aged <18 years, admission pH >7.3 or self-discharged before treatment completion were excluded. Information on fluid and insulin prescriptions, glucose and ketone monitoring, DKA duration and length of hospitalisation was collected. Comparison between hospitals was performed using the Independent-Samples Kruskal-Wallis Test. Data was analysed using SPSS version 27.0 and presented in median interquartiles, frequencies and proportion as appropriate.

Results

Since the objective is to identify best practice and not to compare, hospital names are coded A to F to ensure anonymity. A total of 465 DKA episodes across the six hospitals were included. There were differences observed in the DKA duration (median in hours; A- 13.1, B-11, C-9.7, D-15.7, E-19.5, F-15.2; P value < 0.001) and length of hospitalisation (median in days;A-4.6, B-5.4, C-2, D-3.9, E-4.5, F-3.5; P value < 0.001) across hospitals. Similarly, variations were noticed in appropriateness of glucose monitoring(A- 110.9%, B- 86.3%, C- 95.9%, D-89.1%, E- 92.6%, F- 117.8%; P value <0.001), appropriateness of ketone monitoring (A- 61.3%, B- 83.6%, C- 91.5%, D- 67.3%, E- 62.6%, F- 69.6%; P value <0.001) and fluid prescription (A- 83.6%, B- 80.0%, C- 102.8%, D- 100%, E- 100%, F- 133.3%; P value <0.001). No significant differences were noted in the appropriateness of fixed rate intravenous insulin infusion (A- 100%, B-100%, C- 1008%, D- 98.8%, E- 98%, F- 100%; P value: 0.156).

Conclusion

With the exception of fixed rate intravenous insulin infusion, significant inter-hospital variation in other individual parameters were observed. A centralised DKA registry can abet identifying gaps in DKA management and dissemination of best practises across centres to aid improved patient outcomes.

DOI: 10.1530/endoabs.81.P328

P329

The relationship between clinically significant neonatal hypoglycemia and cord blood c-peptide levels in neonates of mothers with type 1 diabetes

Genya Aharon-Hananel[1,2], Keren Levi[1], Rina Hemi[3], Ehud Barhod[3], Oshrit Kordi-Patimer[3], Shali Mazaki-Tovi[2,4], Rakefet Yoeli-Ullman[2,4] & Tali Cukierman-Yaffe[1,5]

[1]The Chaim Sheba Medical Center, Tel Hashomer, Division of Endocrinology, Diabetes and Metabolism, Ramat Gan, Israel; [2]Tel Aviv University, Sackler School of Medicine, Tel Aviv, Israel; [3]Chaim Sheba Medical Center, Tel-Hashomer, Israel, Endocrine Laboratory, Division of Endocrinology, Diabetes and Metabolism, Ramat Gan, Israel; [4]Sheba Medical Center, Tel-Hashomer, Department of Obstetrics and Gynecology, Israel; [5]Tel Aviv University, Epidemiology D., Sackler School of Medicine, Tel Aviv, Israel

Introduction

Neonate of patients with type I diabetes (T1D) are at increased risk for neonatal hypoglycemia. It is hypothesized that this is a result of maternal hyperglycemia and subsequent fetal hyperinsulinemia.

Aim

The aim of this study was to determine the relationship between clinically significant neonatal hypoglycemia (CS-hypo) and cord-blood c-peptide (CBCP) concentrations in patients with T1D.

Materials and methods

This was a prospective cohort study including patients with T1D followed at a single tertiary center. Clinical variables and glucose control data during pregnancy were prospectively recorded. Cord-blood of neonates was collected, and CBCP concentration was determined. The correlation between CS-hypo (neonatal hypoglycemia requiring IV glucose treatment) and CBCP concentrations was determined.

Results

This analysis pertains to 54 pregnancies. Mothers to neonates that experienced CS-hypo had longer diabetes duration (19 vs. 13 years, $P=0.023$), higher HbA1c at conception (7.3 [6.3–8.8] vs. 6.5 [6.0–7.0], $P=0.042$) and higher rates of caesarian section (73.3% vs. 28.2%, $P=0.005$) than mothers to neonates who did not. No differences were observed between the groups in BMI, age, and other maternal complications, nor in glucose control indices (Table 1). CBCP levels were significantly higher in neonates with CS-hypo than in those who did not (3.3 mg/l vs 1.9 mg/l, $P=0.002$). After adjustment for age at conception, BMI, diabetes duration, neonatal birth weight and 3rd trimester HbA1c, every 1 unit higher in CBCP level was associated with a 1.46 (1.02–2.09, $P=0.035$) fold greater risk CS-hypo.

Conclusion

In neonates of patients with T1D, higher CBCP levels are associated with a higher risk for neonatal hypoglycemia.

Table 1

	Neonatal – CS-hypo	No neonatal CS-hypo	P for comparison	Total
Maternal Age (Median, [IQR])	30.0 [26.0–34.0]	29.0 [25.7–35.2]	0.905	
BMI (Median, [IQR])	23.1 [21.2–30.1]	25.4 [23.1–27.8]	0.333	
Duration of T1D (Median, [IQR])	19.0 [13.0–23.0]	14 [9.5–18.0]	0.023*	
A1C at conception (Median, [IQR])	7.3 [6.3–8.8]	6.5 [6.0–7.0]	0.042*	
A1c at 1st trimester (Median, [IQR])	6.7 [5.5–7.3]	5.9 [5.5–6.4]	0.136	
A1c at 2 nd trimester (Median, [IQR])	5.8 [5.2–6.1]	5.5 [5.2–6.0]	0.347	
A1c at 3rd trimester (Median, [IQR])	5.7 [5.3–6.0]	5.7 [5.3–6.1]	0.969	
Mean average blood-glucose (Median, [IQR])	126 [119.7–156.7]	127 [111.5–138-3]	0.591	

Mean average glucose-Sensor (Median, [IQR])	118.0 [103.1–130.6]	115 [106.7–126.4]	0.785	
PET (Number, [%])	3 [20.0]	2 [5.1]	0.124	5 [9.3%]
Cesarian section (Number, [%])	11 [73.3]	11 [28.2]	0.005*	22 [40.7%]
Preterm delivery (Number, [%])	6 [40.0]	6 [15.4]	0.06	12 [22.2%]
LGA (Number, [%])	0 [0.0]	3 [7.7]	0.5	3 [5.6%]

DOI: 10.1530/endoabs.81.P329

P330

Time of gestational diabetes diagnosis and neonatal outcomes

Paola S. Morpurgo[1], Laura F. Peverelli[1], Andrea M. Bolla[1], Alessandra Gandolfi[1], Michele Vignali[2], Giovanna Spadaccini[2] & Paolo Fiorina[1]
[1]ASST Fatebenefratelli-Sacco, Milano, Italy, SSD Diabetologia, MILANO, Italy; [2]ASST Fatebenefratelli-Sacco, Milano, Italy, UOC Ginecologia e Ostetricia, P.O. Macedonio Melloni, MILANO, Italy

Background
The incidence of gestational diabetes mellitus (GDM) is increasing worldwide, with considerable impact on the health of both mother and newborn. There is no doubt that screening for GDM between 24 and 28 gestational weeks (GWks) is important to reduce the risk of adverse outcomes; however, there is no clear consensus about the diagnosis and treatment of GDM in early pregnancy.
Aims
To evaluate the effect of time of GDM diagnosis (early onset (EO, 16–18 GWks) vs late onset (LO, 24–28 GWks)) on fetal outcomes.
Materials and methods
We retrospectively evaluated 1369 women with GDM followed at our Center. Diagnosis of GDM was performed by an oral glucose tolerance test (OGTT) at 16–18 GWks ($n=321$) or at 24–28 GWks ($n=1048$). Neonatal outcomes were macrosomia, neonatal intensive care unit (NICU) admission, neonatal hypoglycemia and neonatal cardiac hypertrophy. Self-monitoring of blood glucose (SMBG) data and insulin therapy at last visit were also assessed.
Results
No differences between groups were found in the need for insulin therapy (EO 48,5% vs LO 33,4%, $P=$NS) or in SMBG parameters. Considering all pregnancies, 18,3% were complicated with macrosomia; 10,7% of newborns had neonatal hypoglycemia and 20,5% had cardiac hypertrophy, while no NICU admission was observed in either group. In both groups, neonatal hypoglycemia correlated with poor glucose control at the last visit (less than 50% of SMBG measurements in target). In the LO group, we found a higher risk to develop macrosomia ($+38.6\%$, $P<0.003$) or cardiac hypertrophy ($+31.4\%$, $P<0.01$) compared to EO group. Interestingly, we observed that 23% of women in LO group presented the risk factors suggesting to perform an early OGTT, that was lost for different reasons. In this subgroup, 63% of women had at least one neonatal adverse outcome.
Conclsions
High risk women should be screened as early as possible and an early treatment may have a significant effect to improve fetal outcomes.

DOI: 10.1530/endoabs.81.P330

P331

Increasing overrepresentation of diabetes in non-traumatic lower limb amputations

Sindre Eik-Nes[1], Susanna Valland[1], Ove Talsnes[2], Kristin Østlie[3], Kristin Holvik[4] & Trine Elisabeth Finnes[1,2,5]
[1]Innlandet Hospital, trust. Hamar, Department of Internal Medicine, Hamar, Norway; [2]University of Oslo Faculty of Medicine, Institute of Health and Society Studies, Oslo, Norway; [3]Innlandet Hospital Trust, Department of Physical Medicine and Rehabilitation, Ottestad, Norway; [4]Norwegian Institute of Public Health, Department of Chronic Diseases and Ageing, Oslo, Norway; [5]Oslo University Hospital, Aker, Department of Endocrinology, Morbid Obesity and Preventive Medicine, Oslo, Norway

Background and Aim
Recent international studies indicate a secular decrease in the proportion of patients with diabetes who undergo lower limb amputations (LLA), and the same trend is observed in the national quality indicator. The validity of electronic databases and quality indicators are limited by multiple discharges and precision of coding. Furthermore, amputation codes included in the quality indicator do not include all amputations. We therefore aim to investigate the recent incidence of LLA in the catchment area of a middle-sized Norwegian hospital, and to compare it with data collected during 1990–99.
Methodes
Medical records for all patients identified with LLA by the electronic discharge registers at Innlandet Hospital, Elverum, from 2013 through 2019 were retrieved. All codes for amputations and exarticulations were included, and amputations were verified by manual review by two of the authors. Traumatic and cancer-related amputations were excluded. Both minor and major amputations were included in further analyses. Diabetes was defined by the WHO criteria. The prevalence of diabetes was calculated using data from the Norwegian Prescription Database and Statistics Norway.
Results
We identified 169 non-traumatic, non-cancer related amputations in 127 patients, of which 77 had diabetes. The proportion of amputees with diabetes had increased from 44% in the previous period to 61% in the recent data. Ten percent had type 1 diabetes compared to 4% during 1990–99. We estimated that 0.23% of individuals on antidiabetic drugs in the catchment area, underwent an amputation per year in the period 2013–19, compared to 0.31 % in 1990–99. The average absolute number of diabetics undergoing an LLA per year was 11 in both periods. Multiple amputations were common both in persons with and without diabetes and was present in 26% of the amputees, even though a high proportion in both groups underwent vascular surgery before amputation. Detailed information and further results will be provided.
Conclusion
Our findings suggest that the proportion of diabetics among patients undergoing non-traumatic, non-cancer related lower limb amputations has increased over the past decades. Multiple amputations are still common, despite comprehensive preoperative investigations and other surgical interventions.

DOI: 10.1530/endoabs.81.P331

P332

COVID-19 pneumonia patients with 25(OH)D levels lower than 12 ng/ml are at increased risk of death

Juraj Smaha[1], Martin Kužma[2], Kristína Brázdilová[2], Samuel Nachtmann[2], Martin Jankovský[2], Katarína Pastírová[2], Andrea Gažová[3], Peter Jackuliak[2], Zdenko Killinger[2], Ján Kyselovič[2], Tomáš Koller[2], Neil Binkley[4] & Juraj Payer[2]
[1]Comenius University Faculty of Medicine, 5th Department of Internal Medicine University Hospital Bratislava, Bratislava, Slovakia; [1]Comenius University Faculty of Medicine, 5th Department of Internal Medicine University Hospital Bratislava, Bratislava, Slovakia; [3]Comenius University Faculty of Medicine, Institue of Pharmacology and Clinical Pharmacology, Bratislava, Slovakia; [4]University of Wisconsin Medical Sciences Center, Department of Medicine Geriatrics Faculty, Madison, Wisconsin, United States

Objectives
There is no consensus about specific serum 25(OH)D levels associated with higher risk of severe outcome in COVID-19 patients. According to the literature patients with serum 25(OH)D levels $<$ 12 ng/ml are clearly deficient at all ages.

Our aim was to assess COVID-19 mortality in the settings of severe 25(OH)D deficiency.
Methods
A cohort study of 357 COVID-19 patients was conducted. Subjects were monitored until discharge or in-hospital death. At admission, severity parameters (CRP, IL-6, Charlson Comorbidity Index etc.) were assessed. These parameters were compared regarding 25(OH)D levels threshold 12 ng/ml, where values below 12 ng/ml were considered absolute vitamin D deficiency.
Results
25(OH)D levels at the time of admission were independently associated with mortality ($P<0.05$). Non-survivors ($n=168$) had lower 25(OH)D levels, SO2, higher age, CRP, viral load, and Charlson Comorbidity Index in comparison to survivors. Patients with serum 25(OH)D levels $<$ 12 ng/ml had higher mortality (55% vs. 45 %), viral load (21.5 vs 23.1) and Charlson Comorbidity Index (5.3 vs 4.4) in comparison to those with serum 25(OH)D levels >12 ng/ml ($P<0.05$).
Conclusions
COVID-19 patients with serum 25(OH)D levels $<$ 12 ng/ml have higher mortality. Among other factors, severe vitamin D deficiency likely leads to poor outcome.

DOI: 10.1530/endoabs.81.P332

P333

REAL Life study of SEMaglutide in Patients with Type 2 diabetes in SPain (REALSEM-SP): Retrospective clinical study on the efficacy, adherence, and safety with Semaglutide

Jersy Jair Cardenas Salas[1,2], Roberto Miguel Sierra Poyatos[3,4], Bogdana Luiza Luca[3], Begoña Sánchez Lechuga[3], Naiara Modroño Mostoles[2], Teresae Montoya Alvarez[2], María De La Paz GóMez Montes[2], Raquel Sanchez-Lopez[3], Carlos Casado[3] & Clotilde Vazquez Martinez[2,3,4]
[1]Hospital Universitario Fundación Jiménez Díaz, Endocrinology, Madrid, Spain; [2]Hospital Universitario Infanta Elena, Spain; [3]Hospital Universitario Fundación Jiménez Díaz, Madrid, Spain; [4]General Hospital Villalba, Spain

Introduction
Real-world data on glucose and weight control effectiveness in patients with Type 2 diabetes mellitus (T2DM) on treatment with semaglutide is scarce. We aim to assess it in a cohort of patients from a real-world setting in Spain.
Materials and methods
We identified 830 patients with T2DM that were prescribed Semaglutide once-weekly since May 2019 to December 2020, in 4 hospitals in Madrid-Spain. At 6 $\pm$ 3 months, 435 GPL1-naïve and 317 GLP1-experienced patients continued on treatment. Semaglutide withdrawal ocurred in 78 patients(9.4%), mainly due to gastrointestinal adverse events. At 12 $\pm$ 3 months, 317 GPL1-naïve and 265 GLP1-experienced patients continued on treatment. Semaglutide withdrawal ocurred in 24 patients (3.3%), mainly due to gastrointestinal adverse events. The changes in HbA_{1c}, weight, fat-mass and skeletal-muscle-mass at 6 and 12 months of follow up, adjusted by basal HbA_{1c}, age, T2DM duration, BMI, sex, and change in Metformin, DPP-4, SGLT-2, Sulfonylurea, Repaglinide, Insuline and Thiazolidinedione status was assessed (multiple linear regression model).
Results
Baseline characteristics and T2DM treatments are shown in Table 1. There was a significant reduction in HbA_{1c}, weight, and fat mass after Semaglutide treatment at 6 and 12 months of follow-up (Table 2). The proportion of patients that achieved a $HbA_{1c} \leq 7\%$ was significant higher in boths groups. After adjusment the baseline-HbA_{1c} was the only predictor for HbA_{1c} change at 6 and 12 months.
Conclusion
Treatment with semaglutide once-weekly is an effective glucose and weight lowering treatment in GLP1-naïve and GLP1-experienced patients with T2DM.

Table 1.

	GLP1-naïve	GLP1-experienced
Male: (%)	55.6	56.8
Age: (years)	59.6(10.5)	61.3(9.1)
T2DM duration(years)	9.0(7.5)	11.3(6.8)
Weight: (kg)	99.9(19.3)	98.2(16.2)
BMI: (kg/m2)	36.4(5.5)	35.6(5.4)
Baseline-HbA1c	7.8(1.5)	7.3(1.2)
Baseline-eFGR (ml/min1.73 m2)	85.9(20.8)	82.9(20.1)
HbA1c $\leq$7%	36.6	43.9
T2DM-treatment(%)		
– Metformin	82.8	91.1
– DPP-4 inhibitor	40.7	2.2
– SGLT2 inhibitor	31.5	48.9
– Sulfonylurea	9.9	5.7
– Repaglinide	7.4	11.4
– Insuline	31.5	42.6
– Thiazolidinediona	0.6	0.6
– GLP1 agonist	0	100 (SD)

Table 2.

		GLP1-naïve		GLP1-experienced	
		6 m	12 m	6 m	12 m
HbA1c change	Total	-1,24**	-1.22**	-0.42**	-0.32**
	$<$0.5 mg	-1.18**	-1.14**	-0.34**	+0.01
	1.0 mg	-1.42**	-1.29**	-0.49**	-0.40**
Weight Change (%)	Total	-4.93**	-6.71**	-1.92**	-3.06**
	$<$0.5 mg	-4.71**	-6.49**	-1.05**	-2.03**
	1.0 mg	-5.70**	-6.90**	-2.72**	-3.30**
% with HbA1c $\leq$7%		70.85**	74.75**	62.69**	62.86**
% with Weight loss $\geq$5%		44.3**	55**	18.3**	33.1**
% with Weight loss $\geq$10%		14.8**	26.3**	5.1*	8.3**
Fat mass(%) **change**		-2.02**	-3.1**	-0.27*	-0.93*
Skeletal muscle mass(kg) **change**		-0.48**	-0.89**	-0.47*	-0.53*

** $P<0.01$; * $P<0.05$; m = months

DOI: 10.1530/endoabs.81.P333

P334

Health outcomes following engagement with a digital health tool GroHealth app amongst people with type 2 diabetes

Farah Abdelhameed[1], Elle Pearson[2], Petra Hanson[1], Thomas Barber[1], Arjun Panesar[3], Charlotte Summers[4] & Michaela de la Fosse[5]
[1]Warwickshire Institute for the Study of Diabetes, Warwick Medical School, University of Warwick, Endocrinology and Metabolism, University Hospitals Coventry and Warwickshire, Coventry, United Kingdom; [2]Warwick Medical School, University of Warwick, Coventry, United Kingdom; [3]Founding CEO and Head of AI, DDM Health Ltd, Coventry, United Kingdom; [4]Founding Chief Operations Officer, DDM Health Ltd., Coventry, United Kingdom; [5]Operations Manager, DDM Health Ltd., Coventry, United Kingdom

Introduction
Diabetes is a chronic condition causing morbidity and mortality globally, with a growing economic burden on healthcare systems. In the UK, 1 in 14 people have diabetes, with type 2 accounting for 90% of cases (1). Complications from poorly controlled diabetes are associated with increased socioeconomic costs and a reduced quality of life. Research has shown education and self-management are crucial in helping diabetic patients achieve metabolic control (1). Smartphones

have become an influential platform providing feasible tools such as health-apps to deliver tailored support to enhance diabetic patients' ability for self-management. GroHealth is a NHSX-certified digital health tool used to deliver educational and monitoring support to facilitate the development of skills and practices for maintaining good health.
Objectives
To assess self-reported outcomes of the GroHealth app amongst diabetic and prediabetic users.
Method
The EuroQol-5D (EQ-5D) questionnaire is a standardised tool used to measure health status for clinical and economic appraisal. GroHealth users completed the EQ-5D at baseline and 6 months after using the app. Users provided informed consent for use of their anonymised data for research purposes. Health index scores (HIS) and visual analogue scale (VAS) scores were calculated at baseline and 6 months for individuals with prediabetes and type 2 diabetes (T2DM). Descriptive statistics and multiple-regression models were utilised to assess changes in outcome measures and determine the driving variables for change in HIS.
Results
HIS are average values that reflect people's preferences about their health state (1 = full health, 0 = moribund). There was a significant and clinically meaningful increase in mean HIS amongst app users between baseline (0.746 [SD 0.234]) and follow-up (0.792 [SD 0.224], $P < 0.001$). The greatest change was observed in mean VAS score with percentage change of 18.3% improvement (*baseline*:(61.7 [SD 18.1]), *follow-up*:(73.0 [SD 18.8]), $P < 0.001$). These VAS score improvements remained significant across age, gender, ethnicity, income, and diagnosis (prediabetes/T2DM). Baseline HIS, ethnicity and education variables were associated with significant changes in follow-up HIS ($P < 0.001$).
Conclsion
This study provides evidence of significant positive effect on self-reported quality of life amongst people living with T2DM engaging with a digital health intervention. The improvements in the five dimensions of health, as described by the EQ-5D, are facilitated through access to education and monitoring support tools within the app. This provides an opportunity for healthcare professionals to incorporate NHS certified digital tools, such as GroHealth as part of the holistic management of patients.
References
(1) Bene. BA *et al*. BMJOpen2019;9:e025714
DOI: 10.1530/endoabs.81.P334

P335

Prevalence of amputation in a group of long-standing type 1 diabetic patients

Emna Bornaz, Haifa Abdesselem, Imene Sebai, Amal Meherzi, Kamilia Ounaissa, Fatma Boukhayatia, Asma Ben Brahim, Rim Yahiaoui & Chiraz Amrouche
National Institute of Nutrition, Outpatient Department and Functional Explorations, Tunis, Tunisia

Background
Amputation is the major complication of diabetic foot. The aims of our study were to assess prevalence of amputation in a group of long-standing type 1 diabetic patients and to determine its risk factors.
Methods
We conducted a cross-sectional study including type 1 diabetic patients followed at the National Institute of Nutrition of Tunis. All patients had a duration of diabetes $\geq$ 20 years. Clinical and biological data were collected from medical observation records.
Results
One hundred and fifty five patients with mean age 39.7 $\pm$ 9.8 years were included in the study. About 30% of them were male. Age at diagnosis of diabetes was 12.7 $\pm$ 7.47 years. Mean duration of diabetes was 27.33 $\pm$ 6.38 years. The average of the last four glycated hemglobin (A1c) was 9.45 $\pm$ 1.62%. The prevalence of amputation was 7.1%. It was associated with low socioeconomic status ($P = 0.002$), low level of education ($P = 0.045$), unemployment ($P = 0.012$), age at diagnosis of diabetes ($P = 0.039$) and anemia ($P = 0.031$).
Conclsion
Amputation is a serious complication of diabetes. It is more associated with socioeconomic factors than with diabetes-related factors.
DOI: 10.1530/endoabs.81.P335

P336

Is there a relationship between nonalcoholic fatty liver disease (NAFLD) and atheroma disease?

Josep León Mengíbar[1,1], Carolina Lopez, Marta Zorzano, Ana Gloria Soler Beunza, Maricruz De La Fuente, Fernando Herrerias, Felip Vilardell, Maite Santamaria & Albert Lecube
Hospital Universitari Arnau de Vilanova, Lleida, Spain

Introduction
Over the last few years, there are some studies that suggests a close connection between Nonalcoholic Liver Disease (NAFLD) and increased cardiovascular (CV) risk in population with obesity. Indeed, these two conditions share common drivers, most notably insulin resistance and other elements of the metabolic syndrome. Notwithstanding the above, this affirmation does not have solid scientific evidence. The proliferation of Vasa Vasorum (VV) in the adventitial layer of the carotid is proposed as an early alteration of atheromatous disease, which precedes the intima-media thickness. However, there is not any study that evaluates the association between NAFLD and VV.
Methods
A cross-sectional study was performed with 54 subjects undergoing bariatric surgery. Before surgery, all patients were subjected to a contrast-enhanced ultrasound study to evaluate carotid density of VV, to measure the thickness of intima-media and to verify the presence of atheromatous plaque. Whilst surgery a liver biopsy was performed.
Results
From liver biopsy, we regarded that 42 subjects had simple steatosis and 12 had steatohepatitis. The mean density of VV was similar between subjects with steatosis and subjects with steatohepatitis (0.742 $\pm$ 0.173 vs. 0.781 $\pm$ 0.136 arbitrary units (AU), $P = 0.481$). In addition, there were no difference in carotid intima-media thickness (0.742 $\pm$ 0.173 vs. 0.781 $\pm$ 0.136 AU, $P = 0.481$). We did not find any significative lineal correlation between mean density of VV and the carotid intima-media thickness ($r = 0.036$, $P = 0.799$), as well as there was not correlation with clinical parameters such as age ($r = -0.128$, $P = 0.346$), BMI ($r = 0.066$, $P = 0.627$), fasting plasma glycaemia ($r = 0.118$, $P = 0.390$), HbA1c ($r = 134$, $P = 0.342$), the 'fatty liver index' ($r = 0.024$, $P = 0.863$) nor levels of GOT ($r = 0.067$, $P = 0.623$), GPT ($r = 0.009$, $P = 0.945$) and GGT ($r = -0.099$, $P = 0.467$). From the multivariate analysis, we did not observe any clinical or analytic variable that correlates with the adventitial VV density in an independent way. Nevertheless, when carotid intima-media thickness was the dependent variable, we found that age correlated independently in the multivariate study, whilst the other variables did not correlate.
Conclusion
NAFLD disease is a comorbidity associated with severe obesity almost inevitably. However, there is insufficient evidence to suggest that NAFLD plays a key role in the initial development of obesity-associated cardiovascular disease.
DOI: 10.1530/endoabs.81.P336

P337

Roux-en-Y gastric bypass and vertical sleeve gastrectomy showed similar efficacy in achieving cardiometabolic composite target in subject with type 2 diabetes undergoing bariatric surgery

Lavinia Monte[1], Dario Tuccinardi[1], Giovanni Rossini[1], Mikiko Watanabe[2], Paolo Pozzilli[†], Nicola Napoli[2] & Silvia Manfrini[1]
[1]Campus Bio-Medico University of Rome, Rome, Italy., Unit of Endocrinology and Diabetes Department of Medicine, Rome, Italy; [2]Sapienza University of Rome, Rome, Italy., Department of Experimental Medicine, Section of Medical Pathophysiology, Food Science and Endocrinology, Rome, Italy

Introduction
The American Diabetes Association (ADA) produced a triple composite outcome that summarizes the therapeutic targets of the three most prevalent complications of obesity: type 2 diabetes (T2D), hypertension and dyslipidemia (HbA1c $< 7.0\%$; LDL cholesterol < 100 mg/dl and systolic blood pressure < 130 mmHg). The present study primarily investigates the difference between VSG and RYGB in achieving the composite target one year after the surgery. The secondary outcome assessed the success rate in achieving the separate components' target at months 6, 12 and 24 post-surgery, the 2-year remission of DT2 and postoperative adverse events.
Methods
This retrospective observational study evaluated 103 patients with obesity and T2D (75/28 F/M). Sixty-two (60%) underwent VSG and 41 (40%) RYGB. Patient data

were collected before surgery and subsequently during the follow-up visits at 6, 12 and 24 months post-surgery. At each visit, anthropometric measurements were recorded, and the metabolic and lipid profile was evaluated. Pharmacological therapies for diabetes, hypertension, dyslipidemia and any adverse events were also collected.

Results

Twelve months after surgery, patients undergoing RYGB did not show a significant difference compared to those undergoing VSG in achieving the composite target [RYGB vs VSG OR 2.21 (95% CI: 0.61–8.05), $P = .57$]. Patients undergoing RYGB showed greater LDL target achievement (< 100 mg/dl) at 6 months post-surgery than the VSG group ($P = .005$). Total cholesterol and LDL cholesterol were significantly reduced over time (months 6–12-24 post-surgery) in the RYGB compared to the VSG group ($P = .023$ and $P = .010$ respectively). No significant differences were observed in the T2D remission rate and the use of antidiabetic, cholesterol-lowering and antihypertensive drugs between the two groups at months 6–12-24 post-surgery. There was a significant increase in the frequency of constipation episodes in the VSG compared to the RYGB group ($P = .002$).

Conclusion

Roux-en-Y Gastric Bypass and Vertical Sleeve Gastrectomy showed similar efficacy in reaching the cardiometabolic ADA composite target in subject with T2D undergoing bariatric surgery. Patients undergoing RYGB showed a greater achievement of the LDL target < 100 mg/dl at 6 months after surgery and also a significant reduction over time in LDL and total cholesterol compared to the VSG group. More extended randomized studies are needed to evaluate the effectiveness of the two surgical procedures in the improvement and remission of cardiovascular risk factors associated with obesity.

DOI: 10.1530/endoabs.81.P337

P338

Effect of dietary protein source on body composition and cardiometabolic risk in young adults with obesity during anti-inflammatory weight management program

Gordana Kendel Jovanovic[1], Sanja Klobučar Majanović[2,3], Ines Mrakovcic Sutic[4] & Dario Rahelic[5,6,7]

[1]Teaching Institute of Public Health of Primorsko-goranska County, Department of Health Ecology, Rijeka, Croatia; [2]Clinical Hospital Centre Rijeka, Department of Endocrinology, Diabetes and Metabolic Diseases, Rijeka, Croatia; [3]University of Rijeka, Faculty of Medicine, Rijeka, Croatia; [4]University of Rijeka, Faculty of Medicine, Department of Physiology, Immunology and Pathophysiology, Rijeka, Croatia; [5]Merkur University Hospital, Vuk Vrhovac University Clinic for Diabetes, Endocrinology and Metabolic Diseases, Zagreb, Croatia; [6]Croatian Catholic University, School of Medicine, Zagreb, Croatia; [7]Josip Juraj Strossmayer University, School of Medicine, Osijek, Croatia

Introduction

Many studies have shown that dietary protein content may play a role in weight management. Moreover, it has been found that diets high in protein (either animal or plant) significantly reduced markers of insulin resistance and hepatic necroinflammation independently of body weight change. This study aimed to examine the effect of dietary protein source on body composition and cardiometabolic risk factors in young adults with obesity during anti-inflammatory weight management program.

Methods

A total of 56 participants (93% female, mean age 44 years, mean BMI 35.4 kg/m2) were enrolled in the study, and 42 of them completed the 24-week anti-inflammatory weight management program in the Obesity Outpatient Clinic at the Clinical Hospital Centre Rijeka, Croatia. Dietary protein intake was estimated from six three-day food diaries. The inflammatory potential of diet was assessed with the Dietary Inflammatory Index (DII®). Body composition parameters were assessed by bioelectrical impedance analysis (Seca® mBCA 515, Hamburg, Germany). Serum concentrations of glucose, insulin, total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides, and high sensitivity C-reactive protein from fasting blood samples were measured and their correlation with dietary protein intake from animal or plant origin was examined.

Results

On average, participants lost 7.1 kg ($P < 0.01$) over the 24-week period, and reduced high sensitivity C-reactive protein concentration by 30% ($P < 0.01$). The inflammatory potential of their diet was significantly improved toward more anti-inflammatory potential ($P < 0.01$). The total ($P < 0.01$), animal ($P < 0.01$) and plant ($P = 0.01$) protein intakes were significantly reduced, but its energy fraction was significantly increased ($P < 0.01$). The plant protein intake was strongly negatively correlated with serum triglycerides ($r = -0.99$, $P = 0.02$) at the beginning of the program, and total body fat mass ($r = -0.99$, $P = 0.02$) after its completion. There was no correlation between animal protein intake with any of the considered parameters.

Conclusion

The study results suggest that change of the dietary protein source toward plant origin can improve body composition and cardiometabolic risk profile in young adults with obesity.

DOI: 10.1530/endoabs.81.P338

P339

Autoimmune thyroiditis: What impact on diabetic retinopathy ?

Emna Bornaz, Haifa Abdesselem, Ghofrane Hkiri, Kamilia Ounaissa, Fatma Boukhayatia, Imene Sebai, Asma Ben Brahim, Rim Yahiaoui & Chiraz Amrouche

National Institute of Nutrition, Outpatient Department and Functional Explorations, Tunis, Tunisia

Introduction

Data from literature suggest that combination of autoimmune diseases may have a major physical and psychological impact on type 1 diabetic patients. The aim of our study was to assess the impact of autoimmune thyroiditis on diabetic retinopathy.

Methods

We conducted a descriptive observational retrospective study of type 1 diabetic patients, followed at the National Institute of Nutrition and Food Technology of Tunis, between December 2019 and April 2021. All included patients had a diabetes duration of more than 20 years. Clinical and biological data were collected from medical observation records. The diagnosis of diabetic retinopathy was based on fundus examination, associated with retinal angiography in case of abnormality.

Results

The study included 155 patients. The mean age of patients was 39.7 ± 9.8 years. The sex ratio M/F was 0.49. Mean duration of diabetes was 27.33 ± 6.38 years with extremes ranging from 20 to 48 years. Autoimmune diseases associated with type 1 diabetes were dominated by autoimmune thyroiditis (22.4%) followed by celiac disease (6.8%) and adrenal insufficiency (4.3%). Diabetic retinopathy was present in 74.3% of the participants with a mean duration of 22 ± 5.9 years. The univariate study showed that autoimmune thyroiditis was present in 16.3% of patients with diabetic retinopathy compared with 35.1% of those with a normal fundus ($P = 0.016$).

Conclsion

Our study highlights the possible protective effect of autoimmune thyroiditis on diabetic retinopathy. Further research are needed to confirm this effect and determine the factors involved in this association.

DOI: 10.1530/endoabs.81.P339

P340

Excellent disease control in Berardinelli Seip type 1 patient through dietary therapy alone: only an exception?

Carolina Cecchetti[1], Elisabetta Belardinelli[1], Paola Dionese[1], Rita Teglia[1], Ilaria Di Cintio[1], Maria Rosaria D'apice[2], Uberto Pagotto[1] & Alessandra Gambineri[1]

[1]IRCCS Azienda Ospedaliero - Universitaria di Bologna - Department of Medical and Surgical Sciences (DIMEC), Alma Mater Studiorum, University of Bologna, Division of Endocrinology and Diabetes prevention and Care, Bologna, Italy; [2]Azienda ospedaliera universitaria Policlinico Tor Vergata, Laboratory of Medical Genetics, Tor Vergata Hospital, Rome, Italy

Background and Objective

Severe metabolic complications generally manifest at an early age in Berardinelli – Seip congenital lipodystrophy (BSCL) and their management is especially

challenging, often requiring prompt pharmacological treatment with insulin-sensitizers, lipid lowering drugs, insulin and eventually metreleptin. Nutritional intervention with low lipid personalized diets is considered by experts a fundamental tool in handling the disease when associated with medical therapy, but little is known about the beneficial effect of diet intervention alone. This report aims to underline the importance of a well-structured low-fat diet in BSCL patients, by presenting a rare case of successful long-term disease control with the use of a low-fat diet only.
Methods and Results
A BSCL male patient strictly followed a personalized hypolipemic diet since clinical diagnosis at one year of age, with daily intake divided into 25 % lipids, 20% proteins and 55% carbohydrates. Interestingly, pharmacological intervention was not required at any point during follow up. At 16 – years old, age of transition from Paediatric to our Division, the patient weighed 40 kg and had a height of 162 cm (BMI 15,24 kg/m2), P5/B5 Tanner stage, 135/75 blood pressure, 12 % total body fat and normal BMD for age (evaluated by DEXA). Biochemistry, evaluation of thyroid function and sex hormones, 75 mg oral glucose tolerance test, cardiac evaluation and abdominal ultrasound were performed, revealing no abnormalities and therefore an excellent control of the syndrome by an exclusive dietary therapy. Genetic analysis and leptin dosage were carried out, confirming the diagnosis of BSCL type 1 (homozygosity for c.493–1G>C pathogenic variant in AGPAT2 gene) and showing undetectable circulating levels of leptin (< 0.2 mg/l).
Conclsions
This report proves how a personalized low-fat diet is of great help in the management of BSCL and its complications; furthermore, a specific hypolipemic diet may be used alone as an effective long-term treatment in selected cases with high compliance and, probably, a milder phenotype.
DOI: 10.1530/endoabs.81.P340

P341

Impact of the mode of insulin delivery on the quality of life of type 1 diabetes patients

Lilian Tzivian[1], Jelizaveta Sokolovska[1], Anna E. Grike[2], Agate Kalcenaua[3,4], Abraham Seidmann[5,6], Arriel Benis[7,8], Martins Mednis[4], Ieva Danovska[4], Ugis Berzins[4], Arnolds Bogdanovs[4] & Emil Syundyukov[4,9]
[1]University of Latvia, Faculty of Medicine, Riga, Latvia; [2]University of Latvia, Faculty of Humanities, Riga, Latvia; [3]Riga Stradins University, Faculty of Medicine, Riga, Latvia; [4]Longenesis Ltd, Riga, Latvia; [5]Boston University, Questrom Business School, Boston, United States; [6]Boston University, Digital Business Institute, Health Analytics and Digital Health, Boston, United States; [7]Holon Institute of Technology, Faculty of Industrial Engineering and Technology Management, Holon, Israel; [8]Holon Institute of Technology, Faculty of Digital Technologies in Medicine, Holon, Israel; [9]University of Latvia, Faculty of Computing, Riga, Latvia

Background
Insulin pump therapy is an alternative to multiple daily injections and can improve glycemic control and quality of life (QoL) in Type 1 diabetes mellitus (T1DM) patients. The aim of this study was to assess the differences and factors related to the T1DM-specific QoL of T1DM patients in Latvia.
Methods
87 adult patients with T1DM were included. Of them, 20 were pump users and 67 were users of injections. All recruited patients participated in the quantitative part of the study; 8 pump users and 13 injection users participated in the qualitative part. Patients were invited to participate using a dedicated digital platform. Specially developed questionnaires adapted to Latvian conditions were used for assessment of QoL and self-management habits. Association between social and self-management factors and patients' QoL was investigated using multiple logistic regression models. Qualitative analysis of answers was performed according to major theme of transcripts.
Results
Compared to injection users, insulin pump users were younger (median age pump users 20.0 (18.2 – 22.0) years, injection users 31.0 (25.0 – 40.0) years, $P<0.01$) and reported higher T1DM expenses. There were no differences in self-management and HbA1c level between the groups; Total QoL differed at the 0.1 significance level. In fully adjusted multiple logistic regression models, the most important factor that increased Total QoL was lower T1DM-related expenses (odds ratio, Or=7.02 [95% confidence interval 1.29; 38.0]). Men and those with more years of living with T1DM had better QoL (Or=9.62 [2.20; 42.1] and Or=1.16 [1.05; 1.29], respectively), but the method of administration was not significantly associated with QoL (Or=7.38 [0.87; 62.9]). Qualitative data supported the results of quantitative analysis.
Conclsions
QoL was the main reason to use an insulin pump, while the expenses were the main reason to avoid the use of it or to stop using it. Reimbursement policies thus should be considered to enable patients to choose the more convenient method for themselves.
Acknowledgements
Children's Clinical University Hospital in Riga, Latvia, Latvian Association of Endocrinology, and Latvian organizations of patients with diabetes.
DOI: 10.1530/endoabs.81.P341

P342

IGF1-zSDS in patients suffering from obesity with or without metabolic syndrome: a cross-sectional study in 2032 subject

Davide Masi[1], Renata Risi[1], Rossella Tozzi[2], Elena Gangitano[1], Mariaignazia Curreli[1], Mikiko Watanabe[1], Stefania Mariani[1], Lucio Gnessi[1] & Carla Lubrano[1]
[1]Sapienza University of Rome, Department of Experimental Medicine, Section of Medical Pathophysiology, Food Science and Endocrinology, Roma, Italy; [2]Sapienza University of Rome, Department of Molecular Medicine, Roma, Italy

Background
Metabolic syndrome (MS) is associated with increased mortality, and the key factors predictive of its development among patients with obesity are still unclear. We recently demonstrated with a machine learning approach that Insulin-like Growth Factor 1 (IGF-1) is a novel marker of metabolic health and that in individuals with obesity, lower IGF-1 levels are associated with increased metabolic deterioration. However, the interpretation of IGF-1 serum measurement is limited by a poor standardization of its normal values, as they vary significantly with sex, age and BMI.
Objective
To calculate a surrogate marker of serum IGF-1 concentration, normalized for age and sex, expressed as IGF-1 standard deviation score (IGF1-zSDS), in a cohort of 2032 individuals with obesity and to investigate its association with the presence of MS.
Methods
We conducted a cross-sectional study on adult Caucasian patients entering our third-tier obesity centre from 2010 to 2022. Anthropometric parameters, routine laboratory assessments, markers of glycolipid metabolism and serum IGF-1 levels were obtained. Adult treatment panel III criteria were adopted for the clinical diagnosis of MS. IGF1-zSDS was calculated both in men and in women age-grouped as follows: 18–22; 23–30; 31–50; 51–65; >65 years, according to the equation IGF-1 zSDS=(IGF-1 – mean)/SD. Student's t-test was used to assess differences between patients with MS and groups of obese patients without MS (noMS) matched for age. A multinomial logistic analysis (MLA) was performed to assess the association between IGF1-zSDS and the probability of being diagnosed with MS.
Results
A total of 2032 patients (1551 females and 481 males) were enrolled. IGF-1 means and SDs obtained were specific for the obese population. Overall, male subjects had both a higher BMI (39.1±7.2 vs 37.8±7.1, $P=0.001$) and a higher prevalence of MS (64.7% vs 45.7%, $P<0.0001$) than their female counterpart, suggesting that women may seek medical attention earlier or may be less likely to develop MS. The IGF1-zSDS in the overall population was 0.13±0.8 and was significantly lower in patients with MS than in noMS. A MLA showed that for each decrease in IGF1-zSDS units, the chance of having MUO increased by 30%.
Conclsion
In a large population with obesity, lower IGF1-zSDS is associated with a higher chance of suffering from MS. Our results obtained with classical statistical analysis confirm preliminary results proposed by artificial intelligence. We suggest to use specific IGF-1 reference values to calculate IGF1-zSDS in obese Caucasic patients
Keywords
metabolic syndrome, insulin-like growth factor 1
DOI: 10.1530/endoabs.81.P342

P343

Exposing the crosstalk between obesity and prostate cancer: miR-191-5p as personalized diagnostic and therapeutic tool

Francisco Porcel-Pastrana[1,2,3], Vicente Herrero-Aguayo[1,2,3,4], Prudencio Sáz-Martínez[1,2,3,4], Juan M. Jiménez-Vacas[1,2,3,4], Julia Carrasco-Valiente[3,5,6], José López-Miranda[3,5,7], Enrique Gómez-Gómez[3,5,6], Andrá Sarmento-Cabral[1,2,3,4], Manuel D. Gahete[1,2,3,4] & Raúl M. Luque[1,2,3,4]
[1]University of Cordoba, Department of Cell Biology, Physiology and Immunology, Córdoba, Spain; [2]Maimonides Institute of Biomedical Research of Cordoba (IMIBIC), GC27 'OncoObesity and Metabolism', Córdoba, Spain; [3]Reina Sofia University Hospital (HURS), Córdoba, Spain; [4]CIBER Physiopathology of Obesity and Nutrition (CIBERobn), Córdoba, Spain; [5]Maimonides Institute of Biomedical Research of Cordoba (IMIBIC), Córdoba, Spain; [6]Reina Sofia University Hospital (HURS), Urology Service, Córdoba, Spain; [7]HURS, Lipids and Atherosclerosis Unit, Internal Medicine Unit, Córdoba, Spain

Prostate cancer (PCa) is one of the most common causes of cancer-related deaths in men worldwide. Therefore, more specific non-invasive diagnostic biomarkers as well as novel therapeutic targets are urgently needed. As miRNAs have been proposed as promising elements for the identification of novel diagnostic and therapeutic tools for different pathologies, including cancer, we investigated the miRNA landscape in PCa patients and explored their putative diagnostic/therapeutic utility. Specifically, the miRNome of plasma samples from healthy ($n=18$) and PCa patients ($n=19$) was initially determined using an Affymetrix-miRNA array. The main changes were validated in an independent cohort ($n=295$) by quantitative real-time PCR. Additionally, *in silico* and *in vitro* assays in normal and tumor prostate cell lines were performed. Results from the array revealed that the expression of 104 miRNAs was significantly altered ($P<0.01$) in plasma samples from PCa patients compared with healthy controls. Of note, 6 of these miRNAs also exhibited a significant ROC curve to distinguish between healthy and PCa patients with an AUC = 1. The validation using an independent cohort of patients demonstrated that miR-191–5p was one of the most profoundly altered miRNAs in PCa ($P<0.0001$) exhibiting an AUC = 0.67. Remarkably, miR-191–5p significantly outperformed the ability of prostate specific antigen (PSA) to distinguish between control and PCa patients, especially in the 'grey zone', which represents the range where PSA levels are less accurate to diagnose PCa. Interestingly, the diagnostic capacity of miR-191–5p was even stronger in obese patients (BMI > 30). Furthermore, we found that miR-191–5p levels were also dysregulated in PCa cells (compared to non-tumor cells). Moreover, *in vitro* overexpression of miR-191–5p significantly increased cell proliferation and migration in DU145 and PC-3, two of the most aggressive PCa cell models. Finally, these functional effects were associated with the alteration in key cellular elements that are critical in PCa and obesity pathophysiology. Altogether, our data demonstrate that miR-191–5p might represent a novel and useful personalized diagnostic biomarker in PCa, especially in patients with obesity, as well as a potential therapeutic tool in PCa.

Fundings
MINECO (PID2019–105564RB-I00/PRE2020–094225/FPU16–06190/FPU17–00263), ISCIII (PI16–00264/PI17–02287), Junta de Andalucía (PI-0094–2020, P20_00442, BIO-0139) and CIBERobn.

DOI: 10.1530/endoabs.81.P343

P344

Case Report: A triad of Diabetic Ketoacidosis, hypertriglyceridaemia and acute pancreatitis as a first presentation of diabetes mellitus

Ebo Dadey[1], Jesmith Perumbalath[1], David Leonard[1] & Gideon Mlawa[2]
[1]King George Hospital, United Kingdom; [2]Queen's Hospital, United Kingdom

Objective
We present a case of hypertriglyceridemia induced acute pancreatitis (HTG-AP) and concurrent diabetic ketoacidosis (DKA) as a first presentation of Diabetes Mellitus in an adult patient. This uncommon triad has been previously described in the literature, however, it is rare to be observed in a previously undiagnosed patient with diabetes. The purpose of this poster is to describe the potential mechanisms for this and discuss management strategies.
Case Presentation
A previously fit and well 30-year-old South Asian man presented to the emergency department with a 3-day history of vomiting and abdominal pain. He had a BMI of 36 kg/m^2 and there was a maternal history of Type 2 Diabetes Mellitus. His initial panel of investigations demonstrated severe metabolic acidosis with ketonaemia. Admission venous blood gas showed a pH of 7.152, glucose 20.4 mmol/l, lactate 1.3 mmol/l, bicarbonate (HCO_3^-) 5.8 mmol/l as well as blood ketones of 6 mmol/l. A subsequent CT scan showed acalculous acute pancreatitis (severity = Glasgow Score 2, Balthazar Score 2). Diabetic antibodies (GAD65, IA-2, ZnT8) were negative for Latent Autoimmune Diabetes of Adulthood (LADA). Triglycerides were 44.22 mmol/l and Haemoglobin A1C (HbA1C) was 118 mmoll/mol. He was treated in a high dependency unit with aggressive fluid resuscitation, intravenous and subcutaneous insulin as well as fibrates.
Conclusion
While acute pancreatitis (AP) and DKA are common presentations in the Emergency Department, it was unusual as a de novo diabetic presentation and required Multidisciplinary Team discussion with the Diabetology team as well as the Intensive Care team. AP is a complication in around 11% of patients with DKA and hypertriglyceridaemia (HTG) commonly occurs as a result of inhibition of lipoprotein lipase. It has been hypothesised that DKA could be the inciting event leading to HTG and ultimately AP. The correction of DKA is the crux of management, involving aggressive fluid repletion, intravenous insulin infusion and diligent monitoring of glucose, ketones and electrolytes. In the case of severe hypertriglyceridemia, clinicians should be aware of interventions such as fibrates or therapeutic plasma exchange.

DOI: 10.1530/endoabs.81.P344

P345

Understanding and improving the management of hyperosmolar hyperglycaemic state

Carina Synn Cuen Pan[1], Emily Warmington[1], Lakshmi Rengarajan[2], Catherine Cooper[3], Megan Owen[3], Haaziq Sheikh[4], Anjitha Anilkumar[1], Ketan Dhatariya[5], Jonathan Webber[6] & Punith Kempegowda[6]
[1]University of Birmingham Medical School, College of Medical and Dental Sciences, Birmingham, United Kingdom; [2]Birmingham Heartlands Hospital, Birmingham, United Kingdom; [3]Walsall Manor Hospital, Walsall, United Kingdom; [4]Haberdashers' Adams' Grammar School, Newport, United Kingdom; [5]Norfolk and Norwich University Hospital, Norwich, United Kingdom; [6]Queen Elizabeth Hospital Birmingham, Birmingham, United Kingdom

Background
Hyperosmolar hyperglycaemic state (HHS) is an acute metabolic complication of diabetes that can lead to significant morbidity and mortality if managed incorrectly. With <1% prevalence, there is limited published literature available on HHS and most management guidelines worldwide are based solely on expert advice and opinions.
Aims
To study the precipitating causes and identify baseline practises of HHS management, to highlight areas for improvement.
Methods
This retrospective study included all patients who meet the diagnostic criteria of HHS from May to November 2021 in six hospitals across the West Midlands region of the United Kingdom. The criteria for HHS diagnosis was defined as serum osmolality >320 mOsmol/kg and glucose >25 mmol/l whereas HHS resolution was defined as either serum osmolality <300 mOsmol/kg, when fixed rate intravenous insulin infusion (FRIII) was stopped or when the clinical team documented resolution time, whichever came earliest. Osmolality was calculated using the formula: [(2x sodium) + (2x potassium) + glucose + urea, all values in mmol/l]. Data regarding precipitating causes, insulin and fluid administration, glucose and osmolality measurements, total duration of HHS and length of admission were collected. The data was then analysed using SPSS 28.0 and results were presented as frequencies, median and interquartile range (IQR) where appropriate.
Results
A total of 31 HHS episodes were identified. From these, 64.5% had the diagnosis of HHS documented in hospital records and 48.4% had serum osmolality measured. The most common precipitating causes were intercurrent illness (38.7%), suboptimal compliance to treatment (12.9%) and new onset of diabetes (9.7%). The median calculated serum osmolality at diagnosis was 343.2 mOs mol/kg (IQR: 330.1–363.9). Patients with HHS received a median of 4500 ml (IQR: 1825–8574) of fluid until resolution. 38.7% of patients had FRIII commenced within the first hour of diagnosis and 54.8% were given basal insulin alongside FRIII. The median duration of HHS was 26.7 hours (IQR: 6.7–46.8) and these people were admitted for a median of 9.0 days (IQR: 4.7–11.8). While the length of stay was similar for HHS across included hospitals, there was a significant difference in HHS duration between sites ($P<0.001$).
Conclusion
Our findings suggest there is an unmet need to improve the awareness of HHS identification and its management. With the difference in HHS duration between

hospitals, there is scope to identify and share best practises to provide improved, uniform clinical care for people with HHS across all centres.

DOI: 10.1530/endoabs.81.P345

P346

Combination study of apoptosis gene polymorphisms in mitochondrial diabetes: Potential role in the pathogenesis of mitochondrial diabetes

Faten Haj Kacem Akid[1], Mohamed Abdellahi Mohamed Ahmed[1], Dhieb Nesrine[1], Youssef S[2], Mkaouar-Rebai E[2], Fakhfakh F[2], Mouna Mnif[1] & Mohamed Abid[1]
[1]Department of Endocrinology and Diabetology CHU Hedi Chaker Sfax, Tunisia; [2]Laboratory of Molecular and Functional Genetics, Faculty of Science, University of Sfax, Tunisia

Introduction
Mitochondrial diabetes (DM) is a monogenic form of maternal transmission diabetes that is caused by mutations in the mitochondrial genome. These mutations affecting mitochondrial function may be the cause of initiation of the phenomenon of apoptosis itself having an aggravating role of the phenotype in patients with mitochondrial diabetes.
Materials and Methods
This study involved 43 patients with mitochondrial diabetes (20 non-syndromic and 23 syndromic) for whom mutations were identified in the mitochondrial genome in addition to 100 controls of the general Tunisian population. An analysis of apoptosis was carried out on muscle biopsy using TUNEL, immunohistochemistry and western blot cytochrome C expression. The analysis of 11 SNPs in 10 apoptosis genes (TP53, BCL2, BAX, BAK1, FASL, CASP8, CASP10, CASP3, CASP7) was carried out by genotyping on the DNA of patients and controls.
Results
Our results confirmed the presence of apoptosis by the TUNEL approach on muscle biopsy and by the study of the expression of the cytochrome C protein by western blot. This apoptosis is most accentuated in patients with a severe phenotype suggesting possible involvement of genetic factors. To study this hypothesis, we carried out a genotyping analysis of 11 functional SNPs in 9 genes involved in the pathways of apoptosis to evaluate their association with the development of apotosis in patients with DM compared with controls. Results showed that mitochondrial (TP53) apoptosis and effector pathway (PSAP3) SNPs were significantly associated with a high risk of developing apoptosis (TP53 rs 1042522 OR 3.57, PSAP3 rs1405937 OR 4.33). In addition, this risk is increased (TP53 rs 1042522 OR 6.07, CASP3, rs1405937 OR 4.8) in patients with syndromic DM and pathogenic mitochondrial mutations.
Conclusion
apoptosis initiated by mtDNA mutations is aggravated by SNPs of the apoptosis genes in particular Tp53, and CASP3 in patients with DM in comparison with controls of the general population.

DOI: 10.1530/endoabs.81.P346

P347

Uncommon side effect of a common drug: doxycycline induced hypoglycaemia

Elohor Ijete[1], Moustafa Hosni[1], Ebo Dadey[1], Khash Nikookam[1], Hassan Rehmani[1] & Gideon Mlawa[1]
[1]Queen's Hospital, London, United Kingdom

Introduction
Doxycycline is a broad-spectrum antibiotic that is used to treat gram negative, gram positive and atypical bacterial infections. It is a member of the second-generation tetracycline class of antibiotics.
Case
We describe a case of a (non-diabetic) male patient who developed hypoglycaemia following treatment with doxycycline. A 73-year-old male presented to the emergency department following a witnessed collapse at 9am on the 4thof September 2021. He was found to have a blood glucose level of 2.6 mmol/l with the London Ambulance Service. He had a past medical history of asthma, prostatic cancer, GORD and spondylosis. He had recently been prescribed doxycycline by his GP for treatment of a possible lower respiratory tract infection. He took an initial dose of 200 mg of doxycycline followed by 100 mg once daily for 11 days. It was on day 11 that he collapsed. During admission he received a Computed Tomography (CT) Head scan due to head injury which was reported as normal. His cortisol levels were normal at 346 nmol/l and he did not have any further episodes of hypoglycaemia after stopping doxycycline. Following discharge, he was reviewed at an endocrine clinic and endocrine causes of hypoglycaemia were investigated with a prolonged fasting glucose (15 hours) showed normal glucose and a repeat hormonal profile for IGF-1, IGF-2 and cortisol all of which were normal.
Discussion
Medications can frequently cause hypoglycaemia especially in the elderly. Anti-diabetic medications are usually the culprit however many other non-diabetic medications used routinely can also cause hypoglycaemia and the list of these medications is expanding. Doxycycline has a number of side effects. Commonly known side effects include gastrointestinal irritation such as vomiting, diarrhoea and oesophageal ulceration. It is also known to cause photosensitivity and photo-onycholysis. A rare side effect of doxycycline that is not well known is hypoglycaemia A Study of the FDA Adverse Event Reporting System (FAERS) on hypoglycaemia associated with antibiotics alone and in combination with sulfonylureas and meglitinides showed that many patients developed hypoglycaemia while on antibiotics with or with sulfonylureas and meglitinides.
Conclsion
Hypoglycaemia due to doxycycline is rare. The mechanism for doxycycline-induced hypoglycaemia is still unclear but it may be related to augmented insulin sensitivity, direct hepatotoxicity, inhibition of insulin degradation in the liver as well as inhibition of glycogenolysis. Paying attention to this potential adverse event is important as this medication is commonly prescribed antibiotic, especially in outpatient setting.

DOI: 10.1530/endoabs.81.P347

P348

The effect of intermittently scanned continuous glucose monitoring on the glycemic control and treatment satisfaction in Korean type 2 diabetic patients

Junghoon Lee
Chuncheon Sacred Heart Hospital, Endocrinology and Metabolism, Chuncheon, Rep. of South Korea

Background
In recent years, continuous glucose monitoring (CGM) has emerged as a method for the assessment of glycemic control. Also CGM enables diabetic patients to understand their own blood glucose status and change their lifestyle.
Aims
We investigated the effect of CGM on the glycemic control in Korean type 2 diabetic patients.
Methods
We enrolled type 2 diabetic patients who met all the following criteria: 1) use of oral antidiabetic drug (OAD) or lifestyle change for diabetes control, 2) no change of OAD before the previous 3 months, 3) HbA1c levels, 7.0–8.9%, and 4) age, 30 to 75 years old. After informed consent, we applied the CGM (FreeStyle Libre) to the participants for 2 weeks. Participants were asked to record their diet and exercise while wearing the CGM on the apps. We educated the participants how to interpret the glucose profile and manage glucose. The participants were randomly assigned CGM or CGM + short message service (SMS) group. We sent educational feedback message for the each CGM glucose profile and lifestyle to the CGM + SMS group We compared the change of HbA1c, lifestyle, and diabetes treatment satisfaction questionnaire after 10 to 12 weeks.
Results
Fifty seven diabetic patients consented to the study. But 11 participants did not apply the CGM (no wearing CGM group). Twenty four were assigned to the CGM group. Twenty two were assigned to the CGM + SMS group. There were no differences in age (56.4 ± 7.8 vs 58.5 ± 7.3 years, $P = 0.429$), DM duration (12.5 ± 7.0 vs 12.4 ± 6.5 years, $P = 0.946$), baseline HbA1c (8.0 ± 0.5 vs 8.0 ± 0.3%, $P = 0.926$) between wearing CGM (CGM and CGM + SMS group) and no wearing CGM group. The deltaHbA1c of CGM, CGM + SMS, no wearing CGM group was -0.35 ± 0.65%, -0.32 ± 0.73%, and -0.04 ± 0.78% ($P = 0.478$). There was no difference in the scan frequency per day (11.2 ± 5.8 vs 10.9 ± 4.8, $P = 0.825$) and in walking time per week (219 ± 170 vs 302 ± 180 minutes, $P = 0.159$) between CGM and CGM + SMS group. The self-care for diabetes was improved in both CGM and CGM + SMS group, especially in diet, exercise, and glucose monitoring. The DTSQ score was also improved in CGM (delta 4.0 ± 7.6) and CGM + SMS group (delta 4.1 ± 5.6). In the logistic regression analysis, time in range in CGM results was related to the prediction of glycemic control in this study.
Conclusions
CGM can be used as a motivational tool for diabetes management when integrates with diabetes education. It is presumed that the intuitive ambulatory glucose profile had an effect on diet and diabetes management.

DOI: 10.1530/endoabs.81.P348

P349

User acceptance and satisfaction with the eversense XL CGM in patients with type 1 diabetes

Francisco Javier Martinez Martin, Alba Hernandez-Lazaro, Ricardo de Leon-Durango, Agnieszka Kuzior, Claudia Arnas-Leon & Carmen Acosta-Calero
Hospital Universitario de Gran Canaria Dr. Negrin, Endocrinology and Nutrition, Las Palmas de Gran Canaria, Spain

Objectives
Eversense XL is a fully implantable sensor for continuous glucose monitoring (CGM) that lasts for up to 180 days. Our objective was to perform a survey on user acceptance and satisfaction among our type 1 diabetic patients who had been using the Eversense XL CGM for at least 3 months.
Methods
A questionnaire was devised in which the patients were asked about their experience with the Eversense XL CGM, including:
-Comparison with blood glucose strips and previously used glucose sensors if available
-Perceived accuracy, comfort and ease of use.
-Perceived changes in quality of life, and ability to perform their daily activities including sports
-Overall satisfaction with the device
Visual analogue scales were used for quantitative data. The questionnaires were collected anonymously and with informed consent from the patients. All our type 1 diabetic patients who had been using the Eversense XL monitor for at least 3 months gave their consent and fulfilled the questionnaire
Results
Thirteen patients were included in the survey, mean age 34 $\pm$ 5 years, 61.5% male. Five of them (38.5%) had previously used a glucose monitor (Abbott FreeStyle Libre in all cases). All patients were more satisfied with the Eversense XL than with blood glucose strips (by 49.3 $\pm$ 11.4%) and their previous glucose monitor (by 13.4 $\pm$ 2.5%) 9 patients (69.2%) perceived the Eversense XL as more accurate than blood glucose strips (change 13.6 $\pm$ 5.8%) and 3 patients (60%) as more accurate than the previous sensor (change 7.3 $\pm$4.7%). The Eversense XL increased the perceived overall quality of life of 11 patients (84.6%, change 23.2 $\pm$ 7.3%), and the perceived ability to perform their daily activities in all patients (change 32.7 $\pm$ 9.6%); all the 9 patients who regularly performed sports activities improved their ability to do so (by 63.7 $\pm$ 15.6%). The overall satisfaction with the device was rated 79.6 $\pm$ 12.8%. Comfort was rated 73.3 $\pm$ 15.5%, and ease of use 45.8 $\pm$ 29.7%.
Conclsions
The user acceptance and satisfaction with the Eversense XL CGM was high among our type 1 diabetic patients. The general impression was an improvement in their quality of life, and in their perceived ability to perform their daily activities. In particular, their ability to perform sport activities was markedly enhanced.

DOI: 10.1530/endoabs.81.P349

P350

Prevalence of autoantibodies in paediatric and adult patients with type 1 diabetes mellitus – study of a Portuguese cohort

Ines Cosme[1], Catarina Silvestre[1], Daniel Nunes[2], Carlos Lemos[2], Maria João Bugalho[1] & Helena Proença[2]
[1]Centro Hospitalar Universitário Lisboa Norte, Serviço de Endocrinologia, Diabetes e Metabolismo, Portugal; [2]Centro Hospitalar Universitário Lisboa Norte, Serviço de Patologia Clínica, Portugal

Introduction
Almost all type 1 diabetes mellitus (T1DM) patients have autoantibodies (ab) at disease onset. These ab prevalence varies according to patients' age, origin and disease duration.
Aim
Determine diabetes mellitus ab prevalence in a paediatric and adult T1DM Portuguese according to their age on diagnosis, gender and diabetes duration.
Methods
Retrospective review of T1DM ab (glutamic acid decarboxylase 65 autoantibodies – GAD, islet cell autoantibodies – ICA, insulin autoantibodies - IAA, tyrosine phosphatase–like insulinoma antigen-2 antibodies - IA2) evaluated from 2018 to 2021. Considering the age at ab assessment, patients were divided into prepuberty (0–12 years) or postpuberty ($\geq$ 13 years) and further subdivided into G1 and G2 when the assessment was at diagnosis or during follow-up, respectively.
Results
Included 156 patients (56.4% men; mean age 21.9$\pm$15.5 years). Of these, 101 (64.7%) belonged to G1 and 55 (35.3%) to G2 (mean age at diagnosis 15.1$\pm$10 vs. 20.7$\pm$12.1 years;$P=0.004$). In G1, 65 (64.4%) were men and 45 (44.6%) were prepubertal. In G2, 23 (41.8%) were men and T1DM mean duration was 13.4$\pm$14.2 years. The overall prevalence of positive ab was 83.2% in G1 and 69.1% in G2 ($P=0.042$), without differences between genders. There was a higher prevalence of GAD ($P=0.23$), IA ($P=0.009$) and ICA ($P=0.006$) in G1 and IAA ($P=0.17$) in G2. In G1, the mean number of positive ab was 1.6 and in G2 was 1.1 ($P=0.017$). In prepubertal G1 patients, positive ab prevalence was 88.9% (highest rate between 6–12 years) and in postpubertal was 78.6%, without significant difference regarding each ab prevalence in pre or postpuberty. In G2, patients diagnosed in postpuberty had a higher prevalence of ab, with a significant difference for GAD ($P=0.011$) and ICA ($P=0.025$). Patients with all ab negative (30.9%) had a T1DM duration of 19.2$\pm$13.1 years, while patients with at least 1 positive ab (69.1%) had T1DM duration of 10.7$\pm$14 years ($P=0.039$). Spearman's correlation test indicated that there was a negative and moderate correlation between the number of positive ab and the diabetes duration (rs=-0.5, $P=0.001$).
Conclsions
In our cohort, more than 80% of T1DM patients had positive ab at diagnosis. GAD and IA were the most prevalent ab, contributing to T1DM diagnosis both in pre and postpubertal patients. There was no difference between genders and ab prevalence. The number of positive ab decreased with disease duration.

DOI: 10.1530/endoabs.81.P350

P351

Glucokinase (GCK) diabetes

Mona Abouzaid, Jean MacLeod & Naveen Aggarwal
North Tees and Hartlepool NHS Foundation Trust, Diabetes & Endocrinology Department, Stockton on Tees, United Kingdom

Background
Glucokinase (GCK) is a gene which plays an important role in recognising how high the blood glucose is in the body. It acts as the glucose sensor for the pancreas. Changes in the GCK gene can lead to increases in blood glucose and affected people may be diagnosed with diabetes although this rise in blood glucose is mild and does not need treatment. Glucokinase diabetes is one of familial diabetes types that called MODY (maturity onset diabetes of the young). We report a case was diagnosed with type 1 diabetes during her second pregnancy in 2006 and she was on insulin since. However, her genetic test in 2021 confirmed Diabetes - MODY2 – Heterozygous mutation in GCK.
Case report
50-year-old female diagnosed with type 1 diabetes during her second pregnancy in 2006 and at that time her ketone levels were high and therefore she was started on insulin. She was commenced on a basal bolus regime during her pregnancy. After pregnancy, she was only on Insulatard twice a day. Her insulin requirements were low so the type of diabetes was revisited in 2010 and at that time the islet cells antibodies were positive and therefore it was agreed to continue to treat her as type 1 diabetes. She was on a small dose of Insulatard and still having hypos and therefore the insulin was stopped in January 2020. Before that she had another set of blood tests done in November 2019 and at that time her islet cell, IA2 and GAD antibodies were all negative. The C peptide level was still in the middle of the range at 0.76 nmol/l. Her HbA1c remained between 39 and 47 mmol/mol since 2009. When she was monitoring blood sugars for a few months after coming off insulin, they were always in the normal range. Her MODY probability score shows the probability of MODY being 15.1%. Her genetic test results show a pathogenic GCK missense variant consistent with MODY2. Her daughter genetic test also confirmed the same variant. It was explained to her that there is no need for any treatment.
Conclusion
Patients with GCK gene variants generally have a mildly raised fasting blood glucose (typically 5.5- 8 mmol/l) and small increment at 2 hours ($<$4.5 mmol/l) on 75g oral glucose tolerance test (OGTT). Clinicians need to be aware of GCK gene variant and its implications.

DOI: 10.1530/endoabs.81.P351

P352

The effects of an acute metreleptin injection on hepatic lipid metabolism in patients with lipodystrophy

Marianna Beghini[1], Matthaeus Metz[1], Peter Wolf[1], Magdalena Bastian[1], Martina Hackl[1], Sabina Baumgartner-Parzer[1], Alexandra Kautzky-Willer[2], Michael Trauner[3], Rodrig Marculescu[4], Michael Krebs[1], Jürgen Harreiter[1],

Martin Wabitsch[5], Julia von Schnurbein[5], Stephanie Brandt-Huenemann[5], Michael Stumvoll[6], Konstanze Miehle[6], Ferruccio Santini[7], Giovanni Ceccarini[7], Silvia Magno[7], Caterina Pelosini[8], Martin Krssak[1,9], Lorenz Pfleger[9], Herbert Stangl[10], Clemens Fürnsinn[1] & Thomas Scherer[1]
[1]Division of Endocrinology & Metabolism, Department of Medicine III, Medical University of Vienna, Vienna, Austria; [2]Medical University of Vienna, Department of Medicine III, Division of Endocrinology & Metabolism, Vienna, Austria; [3]Division of Gastroenterology and Hepatology, Department of Internal Medicine III, Medical University of Vienna, Vienna, Austria; [4], Department of Laboratory Medicine, Medical University of Vienna, Vienna, Austria; [5]Center for Rare Endocrine Diseases, Division of Paediatric Endocrinology and Diabetes, Department of Paediatrics and Adolescent Medicine, Ulm University Medical Centre, Ulm, Germany; [6]Medical Department – Endocrinology, Nephrology, Rheumatology, Lipodystrophy Center Leipzig, University of Leipzig, Leipzig, Germany; [7]Obesity and Lipodystrophy Research Center, Endocrinology Unit, Department of Clinical and Experimental Medicine, University Hospital of Pisa, Pisa, Italy; [8]Chemistry and Endocrinology Laboratory, Department of Laboratory Medicine, University Hospital of Pisa, Pisa, Italy; [9]High Field MR Center, Department of Biomedical Imaging and Image-guided Therapy, Medical University of Vienna, Vienna, Austria; [10]Institute of Medical Chemistry, Center for Pathobiochemistry and Genetics, Medical University of Vienna, Vienna, Austria

Objective
Treatment with metreleptin ameliorates hepatic steatosis in patients with lipodystrophy. The anti-steatotic effect of metreleptin is partially independent of its anorexic action, which suggests a direct effect of metreleptin on hepatic lipid metabolism. However, this mechanism is unknown. Based on previous findings in rodents, we hypothesized that metreleptin reduces hepatic lipid content by stimulating very-low density lipoprotein triglyceride (VLDL1-TG) secretion, a key mechanism that protects the liver from steatosis.
Methods
In this randomized, placebo-controlled, crossover trial we investigated the effects of a single acute subcutaneous metreleptin injection (0.1 mg/kg body weight) in overnight-fasted patients with lipodystrophy on VLDL1-TG secretion (primary outcome) and hepatocellular lipid content (HCL%, secondary outcome). VLDL1-TG secretion rate was assessed using an intralipid infusion test combined with density gradient ultracentrifugation. Changes in HCL% were measured by H^1-magnetic resonance spectroscopy before and 3hrs after metreleptin or placebo injection. Patients previously on metreleptin treatment suspended injections for 14 days prior to the study. A two-sided paired t-test and the Wilcoxon signed rank test were used to analyze the differences after placebo vs. metreleptin injection in VLDL1-TG secretion and HCL%, respectively (statistical significance $P < 0.05$).
Results
We recruited 5 patients with familial partial lipodystrophy: 4 females and 1 male; age range 27.9–58.6yrs; BMI 25.8 ± 2.8 kg/m^2 (mean ± SD); all Caucasian; LMNA mutations confirmed in 2 cases; 2 previously on metreleptin treatment. An HCL > 5% was detected in 3 patients. Hepatic VLDL1-TG secretion rate was higher after metreleptin in 5 out of 5 patients (mean ± SD: 366 ± 146 mg/h vs. 588 ± 108 mg/h; placebo vs. metreleptin;$P = 0.019$), whereas no statistically significant difference was observed in HCL% fold change within 3hrs post injection (median[IQR]: 1% [-7%;5%] vs. -6%[-11%;0%]; placebo vs. metreleptin;$P = 0.23$)
Conclusion
Metreleptin markedly increases hepatic VLDL1-TG secretion in patients with lipodystrophy. This effect may play a role in the longterm antisteatotic action of metreleptin.

DOI: 10.1530/endoabs.81.P352

P353

Evaluating obesity among second and third age premature children

R K Jha[1] & A K Chandra[2]
[1]DMCH, Darbhanga, India; [2]Kurji Holi Family Hospital, Patna, India

Introduction
Premature newborns are defined as babies born before 37 weeks of pregnancy and after 22 weeks of pregnancy as a viability limit. This study aimed to analyse growth characteristics at the age of second and third age and the prevention of metabolic diseases that may occur in adult age at an early phase.
Methods
This study was conducted as a retrospective cohort study between May 2021 and October 2021 in 18 different Outpatient Clinics in Patna, Bihar. All participants were at least 3 years old and their follow-up visits were made by the same family physicians for 3 years.
Results
The findings showed that 55% of the babies were males and 46% of them were females i.e., 123 participants were males and 102 participants were females. The evaluation of the body mass index showed that 19.8% were overweight (43 babies), 16% of the participants were obese (36 babies) at the age of 2. 20% of the participants were overweight (45 babies), 13.33% of the participants were obese (30 babies) at the age of three. Mean Hb levels of the mothers showed that those mothers whose children were obese at the age of two were statistically low as compared to those who were not obese'.
Conclusion
The worldwide prevalence of childhood obesity and overweight was 6.70% in the year 2010. In 2020, it was expected to reach 9.10%. When reasons for high obesity and overweight were searched, not much significant difference had been seen between feeding patterns and maternal factors. A significant relationship was however seen between maternal anaemia and obesity or overweight.

DOI: 10.1530/endoabs.81.P353

P354

Higher glucocorticoid receptor sensitivity is associated with less favorable body composition in patients with obesity

Robin Lengton[1,2], Anand Iyer[1,2], Eline van der Valk[1,2], Bibian van der Voorn[1,2] & Elisabeth van Rossum[1,2]
[1]Erasmus MC, University Medical Center Rotterdam, Department of Internal Medicine, Division of Endocrinology, Rotterdam, Netherlands; [2]Erasmus MC, University Medical Center Rotterdam, Obesity Center CGG, Rotterdam, Netherlands

Background
Mounting evidence points to an association between increased glucocorticoid (GC) action and weight gain. However, the response to GCs is not only determined by GC serum concentrations, but also by individual differences in tissue-specific sensitivity, influenced by genetic and acquired (e.g. disease-related) factors. The extent to which differences in GC sensitivity may influence development of (abdominal) obesity, or vice versa, is poorly understood. In this study we investigate the relation between GC sensitivity and (abdominal) obesity.
Methods
Anthropometric data (BMI, weight, waist circumference and dual-energy X-ray absorptiometry (DXA) scans) and peripheral blood mononuclear cells (PBMCs) were obtained at baseline (T0) and completion of 10 weeks of treatment (T1) from 16 patients with obesity (BMI $\geq$ 30 kg/m^2) undergoing a combined lifestyle intervention with cognitive behavioral therapy. The half maximal effective concentration of dexamethasone (DEX), mediating the transactivation (EC50) or transrepression (IC50) of responsive genes GC-induced leucine zipper (GILZ) or interleukin (IL)-2 and IL-6 respectively in PBMCs, was used as a measure of GC sensitivity. The associations of EC50 and IC50 with BMI, weight, waist circumference, DXA fat mass and DXA leans mass, were analysed using linear regressions.
Results
A lower IC50 of DEX-mediated transrepression of IL-6 at inclusion (higher sensitivity) was associated with higher DXA fat mass (% of total body mass) (β = -0.52, 95%CI = -0.86 to -0.19) and lower DXA lean mass (% of total body mass) (β = 0.52, 95%CI = 0.18 to 0.86). Interestingly, the lower the IC50 for DEX-mediated transrepression of IL-6 at inclusion, the higher was the weight loss in the first 10 weeks of lifestyle intervention (T1, β = 0.32, 95%CI = 0.04 to 0.60). Similar, but non-significant, associations were observed for IL-2. However, there were no associations between EC50 of DEX-mediated transactivation of GILZ and any of the above-mentioned anthropometrics variables.
Conclusion
This study suggests that increased GC sensitivity is associated with a less beneficial body composition in patients with obesity. Although, increased GC sensitivity at baseline was associated with weight loss at T1, further analysis of the data is in progress to determine whether this seeming contradiction is related to changes in GC sensitivity after lifestyle intervention.

DOI: 10.1530/endoabs.81.P354

P355

GLP-1 receptor agonists and erectile dysfunction in diabetic men with and without hypogonadism: a 1- year retrospective observational study

Giuseppe Lisco[1], Maria Isabella Ramunni[2], Giovanni De Pergola[3], Emilio Jirillo[4], Edoardo Guastamacchia[1], Vincenzo Triggiani[1] & Vito Angelo Giagulli[1]

[1]University of Bari Aldo Moro, Interdisciplinary Department of Medicine-Section of Internal Medicine, Geriatrics, Endocrinology and Rare Diseases, University of Bari 'Aldo Moro', School of Medicine, Policlinico, Bari, Italy; [2]Local Health Bari, Outpatients Clinic of Endocrinology and Metabolic Disease, Conversano Hospital, Conversano, Italy; [3]Hospital Saverio De Bellis, Castellana Grotte, Italy

Background
Erectile dysfunction affects nearly half of men with type 2 diabetes (T2DM), and one-third of diabetic men have hypogonadism[1]. As an add-on to TRT in hypogonadal men with T2DM, Liraglutide may improve erectile function[2], and dulaglutide decreased the incidence of moderate and severe ED in T2DM[3].
Study aims
To assess the GLP-1RA effect in T2DM men complaining of ED treated with both liraglutide and dulaglutide as an add-on to metformin.
Design overview
This was a 1-year retrospective observational study. Patients with established type 2 diabetes mellitus, serum HbA1c $<$ 8.5%, two or more additional cardiovascular risk factors were included. Men with estimated glomerular filtration rate (eGFR) $<$ 60 ml/min per 1.73 m^2 were excluded. As per protocol, men with HbA_{1c} $<$7.2 % received metformin (2000 mg per day) while those with serum HbA1c $>$7.2% received a GLP-1RA as in add-on to metformin (52% liraglutide, 1.2 mg/day; 48% dulaglutide, 1.5 mg/week) for one year. ED was diagnosed and classified by the International Index of Erectile Function 5 (IIEF5) score. Hypogonadal men were identified according to standardized parameters from the European Male Aging Study (EMAS).
Results
Forty-eight men with hypogonadism (HP) and 62 eugonadal individuals (EP) complaining of ED were retrospectively eligible for analyses. Mean age ranged 51–64 years; T2DM evolution ranged from 5–10 years. Around 6% of participants had established cardiovascular disease. Twenty-eight HP were on metformin plus a GPL-1RA (HPs), and 20 HP were on metformin alone (HPc); thirty-eight EP received metformin plus a GPL-1RA (EPs), and 30 were on metformin alone (EPc). After 12 months of treatment, both HPs and EPs significantly reduced serum HbA_{1c} compared to baseline (-0.7 $\pm$ 0.3 %; $P<0.001$). HPc and EPc slightly increased HbA_{1c} (0.4 $\pm$ 0.2). IIEF 5 score increased from baseline (all $P<0.01$) in HPs and EPs.
Conclsione
Liraglutide and dulaglutide seem to have a favorable effect on ED in T2DM men with and without baseline hypogonadism. Further controlled studies are needed to confirm those preliminary results.
References
1. Kouidrat Y *et al*., Diabet Med. 2017, 34(9), 1185–92.
2. Giagulli VA, *et al*., Andrology. 2015, 3(6), 1094–103.
3. Bajaj HS *et al*., Lancet Diabetes Endocrinol. 2021, 9(8), 484–90
DOI: 10.1530/endoabs.81.P355

P356

Prevalence and awareness of complications in type 2 diabetes mellitus : a hospital based comparative cross-sectional study

Uttar Kumar Mainali[1], Laxmi Narayan Kamat[1], Sanjeep Khatri[2] & Den Prasad Acharya[1]
[1]Koshi Hospital, Medicine, Biratnagar, Nepal; [2]Koshi Health Institute, Public Health, Biratnagar, Nepal

Introduction
Diabetes Mellitus appears to be globally pandemic and is drawing attention as a major public health concern. Chronic complications of this disease can lead to poor quality of life with significant financial burden to family and country as well. The current study aims to assess prevalence of such complications and its awareness in type 2 diabetes population.
Methods
This descriptive cross-sectional study was conducted during one year period in Endocrinology Outpatient Department of Koshi Hospital, Biratnagar, Nepal from 1st January 2021 to 31st December 2021. Consecutive sampling was applied and face to face interview was conducted to collect the information after informed verbal consent. Various factors related to awareness level were noted and compared.
Results
Out of 495 participants, 294 (59.4%) were male and 201 (40.6%) were female. The mean age of the participants was 52.07 $\pm$ 11.35 years. Of total patients 49.7 percent had diabetes related complications. Out of them 30.9 percent had one, 13.9 percent had two, 4.2 percent had three and 0.6 percent had four complications pertaining to their primary condition i.e. Diabetes Mellitus. Peripheral neuropathy was high (27.5%) followed by Diabetic retinopathy (17.6%), Diabetic Kidney Disease (16.2 %), Ischemic Heart Disease and/or Heart failure (4.8%), sexual problems (3.8 %) and Cerebrovascular disease (3.4%). Regarding awareness, only 45.5 percent had good awareness on microvascular and macrovascular complicatons related to Diabetes. Among the 49.7 percent patients who had complications, only 48.3 percent patients with retinopathy were aware that their retinopathy was secondary to Diabetes Mellitus. Similarly it was 75 percent awareness in case of cardiovascular complications, 52.9 percent with Cerebrovascular disease, 43.8 percent with Diabetic Kidney Disease, 43.4 percent with neuropathy and 31.6 percent with sexual problems. Participants of older age, male gender, longer duration of disease, higher literacy status and having other diabetic patient in family were more aware about the complications of type 2 diabetes than their counterparts.
Conclsion
This study revealed that there is lack of awareness in diabetic population on micro and macrovascular complications even them having considerable prevalence of such complications. The primary care physicians, diabetes educators and public health program implementers all have an important role in educating diabetics on chronic complications and measures to prevent them so that patients' morbidity and financial burden to family and country can be reduced or prevented.
DOI: 10.1530/endoabs.81.P356

P357

Assessment of risk of foot ulceration in a group of long-standing type 1 diabetic patients

Emna Bornaz[1], Haifa Abdesselem[1], Manel Dridi[1], Yosra Hasni[2], Kamilia Ounaissa[1], Fatma Boukhayatia[1], Imene Sebai[1], Asma Ben Brahim[1], Rim Yahiaoui[1] & Chiraz Amrouche[1]
[1]National Institute of Nutrition, Outpatient Department and functional explorations, tunis, Tunisia; [2]Farhat Hached Hospital, Department of Endocrinology, Tunisia

Background
Diabetic foot represents a serious complication due to its prevalenceas well as its impact on functional and vital prognosis of the diabetic patient. The aim of our study was to assess the risk of foot ulceration in a group of long-standing type 1 diabetics.
Methods
We conducted a descriptive observational cross-sectional study including type 1 diabetic patients who had diabetes for more than 20 years, followed at the National Institute of Nutrition of Tunis. The risk of foot ulceration was determined according to the International Working Group of the Diabetic Foot (IWGDF) grading. Then, we devided patients into two groups: patients with low podiatric risk (grade 0 or 1) and patients with moderate to high podiatric risk (grade 2 or 3).
Results
Sixty patients were included in this study. The mean age was 38.92 $\pm$ 8.17 years. The mean duration of diabetes was 26.98 $\pm$5.95 years [ext : 20–48 years]. A history of amputation and plantar puncture was found in two patients. Foot deformity was noted in 31.7% of participants. Thirty-eight percent of the patients had sensory neuropathy. Obliterative arteriopathy of the lower limbs was diagnosed in 5% of the patients. According to the IWGDF classification; 53.3%, 23.3%, 20% and 3.4% of patients had grade 0,1,2 and 3 respectively. Univariate analysis showed that risk of foot ulceration was associated with age ($P=0.001$) and duration of diabetes ($P=0.004$). Only the association with age persisted after multivariate analysis ($P=0.013$).
Conclsion
Our study highlights the importance of screening of diabetic foot as well as prevention of foot abnormalities, particularly in long-standing type 1 diabetics.
DOI: 10.1530/endoabs.81.P357

P358

Long-standing type 1 diabetes and female sexuality : Is there impact ?

Emna Bornaz, Haifa Abdesselem, Amal Salem, Kamilia Ounaissa, Fatma Boukhayatia, Imene Sebai, Asma Ben Brahim, Rim Yahiaoui & Chiraz Amrouche
National Institute of Nutrition, Outpatient Department and Functional Explorations, Tunis, Tunisia

Background
While sexual dysfunction in men with type 1 diabetes is well known, sexual dysfunction in women remains a neglected issue. The aim of this study was to

assess the sexual quality of life (SQOL) of women with long-standing type 1 diabetes.
Methods
We conducted a cross-sectional study of women followed at the National Institute of Nutrition and Food Technology of Tunis. We included women with type 1 diabetes for 20 years or more. Women who were not sexually active and those who were pregnant or breastfeeding were not included. The Audit Diabetes Dependent Quality of Life score was used to assess quality of life. This scale assesses overall quality of life, quality of life without diabetes and 19 life domains, includingsexual life. SQOL was impaired if its relative score was less than (-3).
Results
We included 39 patients with mean age 40.77 ± 7.9 years [ext :29–60 years]. Participants had been sexually active for a mean of 11 ± 8.9 years. All women included had only one partner. The mean glycated hemoglobin (A1c) was 9.3 ± 1.3%. The mean QOL score was (-3) ± 3 with extremes ranging from (-9) to 0. SQOL was impaired in 64.1% of the population. Univariate study showed that impaired SQOL was associated with history of in utero fetal death ($P = 0.012$) and number of abortions ($P = 0.015$). SQOL was associated with quality of life without diabetes ($P = 0.012$). Overall quality of life, glycaemic control, and chronic complications of diabetes were not associated with SQOL.
Conclsion
The results of our study highlight the impact of previous pregnancies on the SQOL of long-standing type 1 diabetic patients. Hence the importance of psychological support for all these women, especially those who has experienced an early or late abortion.

DOI: 10.1530/endoabs.81.P358

P359

New insights into obesity treatment provided by smart technologies and telemedicine

Iva Jakubíková[1], Kristýna Štolbová[2], Peter Novodvorský[1], Iveta Dvořáková[3], Barbora Doležalová[1], Szabolcs Kalina[4], Petr Raška[4], Josef Kautzner[2] & Martin Haluzík[1]
[1]Institute for Clinical and Experimental Medicine, Diabetes Centre, Prague, Czech Republic; [2]Institute for Clinical and Experimental Medicine, Department of Cardiology, Prague, Czech Republic; [3]Institute for Clinical and Experimental Medicine, Centre for Experimental Medicine, Prague, Czech Republic; [4]Institute for Clinical and Experimental Medicine, Information Technologies Department, Prague, Czech Republic

Introduction
Obesity represents a major public health challenge and is linked with increased risk of multiple medical conditions including atrial fibrillation (AF). We have recently published the study protocol of the '*The Effect of complex weigHt-reducing interventiOns on rhythm control in oBese subjects wITh Atrial Fibrillation*' (HOBIT-AF) trial. Here we communicate the preliminary results with the focus on the use of smart technologies and telemedicine.
Methods
HOBIT-AF is a single-blinded, parallel-group, randomised controlled trial with 18-month follow-up to assess the effect of complex weight-reducing interventions supported by the use of smart technologies on the arrhythmia burden in obese individuals following catheter ablation for AF. Participants are randomised in a 1:1 fashion to undergo a structured weight reduction programme and optional sleeve gastrectomy aiming to achieve greater than 10% weight reduction (intervention group) or standard post-ablation medical care (control group). All participants are provided with the Apple Watch Series 5 and iPhone (Apple Inc, Cuppertino, CA, USA). Daily initial settings for the intervention group are as follows: 5000 steps, 30 minutes of physical activity, energy expenditure of 300 kCal, home self-monitoring of blood pressure, heart rhythm, body weight, waist circumference etc. Control group have no goals set and use smart technologies solely for the heart rhythm monitoring. Individual patient goals and settings are monitored by healthcare team by a custom made software IKEMOnlineFit.
Results
Thus far 75 patients have been enrolled into the trial of which 50 are male. Mean baseline characteristics are as follows: age 56 years, weight 118 kg, BMI 37 kg/m2, waist circumference 128 cm. 69 % patients suffer from paroxysmal AF, the rest of persistent. No statistically significant differences in baseline characteristics were detected between the groups at randomization time. Thus far, participants in the intervention group lost 6 % in weight, walked on average 8300 steps per day, performs 32 active minutes daily, energy expenditure of 900 kCal daily. Control group have lost 0,4% in weight so far, walked 3700 steps per day, and had energy expenditure of 600 kCal daily. In intervention group,1 patient underwent sleeve gastrectomy, the rest cut down on weight by life-style intervention or were provided by a GLP-1 receptor analogue liraglutide from the 9thstudy month onwards. All participants use smart technologies.
Conclusion
This time calls for wider usage of smart technologies and telemedicine. Our preliminary results are very promising in relation to their usage in the management of obesity.

DOI: 10.1530/endoabs.81.P359

P360

Functional analysis of melanocortin-4 receptor variants linked to obesity

Alejandra Virginia, Rodriguez Rondon[1,2], Martin Huisman[1,2], Mila Welling[1,2,3], Erica van den Akker[2,3], Elisabeth van Rossum[1,2], Patrick Delhanty[1,2] & Jenny Visser[1,2]
[1]Erasmus MC, Department of Internal Medicine, Rotterdam, Netherlands; [2]Obesity Center CGG, Erasmus MC, Rotterdam, Netherlands; [3]Erasmus MC, Department of Pediatrics, Rotterdam, Netherlands

Introduction
Melanocortin-4 receptor (MC4R) is a G-protein-coupled receptor expressed in regions of the hypothalamus regulating appetite and energy expenditure. Extensive evidence from genetic and biological studies show that MC4R is a key player in the homeostatic regulation of body weight. MC4R loss of function (LoF) variants are the most common cause of monogenic obesity. We have identified 13 heterozygous MC4R variants in patients with obesity at our academic Obesity Center CGG, Erasmus MC. However, it is unknown whether these variants affect MC4R signaling and are causing obesity. Here, we functionally characterized these variants by analyzing the effects on cell surface expression, MSH-induced cAMP production and β-arrestin 2 (βarr2) recruitment.
Methods
HEK293 cells were transiently transfected with expression plasmids encoding WT or variant MC4R and stimulated with MSH. cAMP response was measured using GloSensor cAMP bioluminescence assay, NanoBiT complementation luminescence assay was used to measure βarr2 recruitment, and the cell surface expression was measured using HiBiT Detection System.
Results
Thirteen variants were identified by sequencing the *MC4R* gene of adult and pediatric patients with obesity using an obesity gene panel. Eight of these variants have not been previously reported in literature. The median age of onset obesity for the adult patients was 1.0 year and for the pediatric patients was 1.9 years. Furthermore, the median BMI of the adult patients was 48.8 kg/m^2(range 36 - 58.8) and the median BMI-SD of the pediatric group was +4.2 SD (range +3 SD - +7 SD). Eleven out of 13 patients presented with hyperphagia. MC4R variants had differential effects on cAMP production, βarr2 recruitment and cell surface expression. Eight of the 13 MC4R variants caused partial or complete LoF for both cAMP production and βarr2 recruitment; out of those eight variants, three showed no cell surface expression. Surprisingly, two of the 13 MC4R variants resulted in a gain of function for cAMP production, and two other variants showed a normal cAMP response as well as βarr2 recruitment.
Conclsion
We show that the MC4R variants identified in our patients with obesity affect MC4R signaling differently, through modulation of cell surface expression, cAMP and/or βarr2 signaling pathways. Therefore, this study demonstrates the value of examining different aspects of MC4R signaling to understand possible biased effects of mutations on these pathways. Overall, our results show the clinical importance of assessing the function of MC4R variants as these studied variants are likely to be causative of obesity.

DOI: 10.1530/endoabs.81.P360

P361

Comparison of glycemic variability in type 2 diabetes mellitus patients on oral anti diabetic drugs (OAD) with and without insulin using ambulatory glucose profile (AGP)

Sidharth S[1], Ramesh Aggarwal[1], Anupam Prakash[1], L H Ghotekar[1] & Meenakshi Aggarwal[2]
[1]Lady Hardinge Medical College, Medicine, New Delhi, India; [2]Kalawati Saran Children's Hospital, Microbiology, New Delhi, India

Introduction
Assessment of diabetes with daily blood glucose fluctuations including peaks and nadirs forms the crux of the modern management. Use of glycemic variability

(GV) as a parameter to assess these fluctuations is emerging. Diabetes mellitus patients follow different clinical trajectories which can be traced by the ambulatory glucose profile (AGP) obtained from flash glucose monitoring system (FGMS).
Methodology
This comparative observational study enrolled 106 adult (>18 years) type 2 diabetes patients with HbA1c<8% from a tertiary care hospital in India. Patients were divided into two groups (group A & group B) with 53 patients each. Group A included patients on OAD's with insulin and Group B included patients on OAD's without insulin. The patients were put on FGMS for 14 days and their AGP was analysed. Indices of glycemic variability like Mean, MAGE (Mean amplitude of glycemic excursion), SD (Standard deviation), COV (Coefficient of variation), time in target (TIT), time above target (TAT), time below target (TBT), MODD (Mean of daily differences) were computed using Mann Whitney test.
Results
Median (25th-75th percentile) of glycemic variability parameters - Mean(mg/dl), MAGE(mg/dl), SD(mg/dl), time above target(%), MODD in group A {Insulin} was {139, 145, 44.68, 40, 38.47} respectively which was significantly higher as compared to group B{OAD} {111, 123, 33.31, 18, 26.31} respectively ($P<0.05$). Time in target (%) depicting time in glucose range of 70–180 mg/dl and time below target was achieved more with group B{OAD} (54% & 12%) as compared with group A {Insulin} (39% & 7%) respectively ($P<0.05$). No significant difference was found for COV between the groups. Amongst the OAD's used in patients taking insulin {group A}, glycemic variability was higher with sulfonylurea as compared with DPP-4 inhibitors for the parameter of mean(mg/dl) and MODD (217.5 & 52.4 vs 126.5 & 31.38 respectively). DPP-4 inhibitors achieved higher time in target (53%) as compared with sulfonylurea (11%) ($P<0.005$). No significant difference in glycemic variability was found in subgroup analysis of group B (OAD) in our study. Group A patients had significantly higher (29.99%) total number of hyperglycemic episodes than with group B (9.08%) (p value<0.0001).
Conclusion
Our study showed that the glycemic variability was found to be significantly higher in patients taking OAD's with insulin (group A) as compared with patients who were taking OAD's without insulin (group B). DPP-4 inhibitor was found to achieve more time in target range with less glycemic variability as compared with sulfonylurea.

DOI: 10.1530/endoabs.81.P361

P362

Morphofunctional assessment of cancer patient's nutritional status receiving systemic treatment and oral nutritional supplements

Soraya León-Idougourram, Mireia García-Ramírez, Carlos Manuel Alzás-Teomiro, Gregorio Manzano-García, Concepción Muñoz-Jiménez, Alfonso Jesús Calañas-Continente, Rosa Rodríguez-Alonso, Maria José Molina-Puerta, María Ángeles Gálvez-Moreno & Aura Dulceida Herrera-Martínez
Hospital Universitario Reina Sofia, Endocrinología, Córdoba, Spain

Introduction
Disease-related malnutrition is one of the main factors associated with morbidity and mortality in cancer patients. Furthermore, maintaining and improving muscle mass and function are important to achieve an optimal nutritional status. In this sense, the role of leucine-enriched essential amino acids supplementation for the therapeutic approach to the promotion of muscle anabolism stands out.
Methods
46 cancer patients with malnutrition receiving systemic treatment were randomized to receive for three months leucine-enriched essential amino acids supplementation or standard supplements. Patients were evaluated before and after three months. Nutritional assessment was performed using bioelectrical impedance analysis (BIA), dynamometry, ultrasound of rectus femoris muscle and subcutaneous fat tissue, functional tests and laboratory parameters.
Results
54% women. Mean age: 65 years. Median BMI: 24 kg/m2. 19,6% with colorectal cancer. Regardless of primary tumor origin, 63% of patients received combined modality therapy consisting of surgery along with chemotherapy and/or radiotherapy. 80% of patients were classified as malnourished according to the GLIM criteria and 67% of patients presented decreased standardized phase angle (SPA) in the first morphofunctional assessment (Median 4.5° IQR 3.6–5.9). Positive correlation between 'Timed-Up-and Go' test (TUG), dynamometry and SPA was demonstrated ($P<0.05$). Nutritional supplementation increased prealbumin levels and decreased CRP values. Malnutrition was resolved three months later in 16% of patients. There were no significant differences between nutritional supplements in ultrasound parameters, body composition, functional test or prevalence of malnutrition after intervention.
Conclusion
In a third of patients disease-related malnutrition was resolved despite being in treatment with combined therapy. There were no differences between nutritional supplements, probably because of the short duration of nutritional treatment.

DOI: 10.1530/endoabs.81.P362

P363

Evaluation of the Ankle-brachial index in a group of long-standing type 1 diabetic patients

Emna Bornaz[1], Haifa Abdesselem[1], Hajer Moalla[1], Nesrine Souissi[1], Kamilia Ounaissa[1], Fatma Boukhayatia[1], Imene Sebai[1], Feyka Ben Mami[2] & Chiraz Amrouche[1]
[1]National Institute of Nutrition, Outpatient Department and Functional Explorations, Tunis, Tunisia; [2]National Institute of Nutrition, Department of Diabetology and Therapeutic Dietetics, Tunis, Tunisia

Background
Lower extremity artery disease (LEAD) is a common complication of diabetes, with increasing prevalence with duration and/or the coexistence of other cardiovascular risk factors. The Ankle-brachial index (ABI) is the first diagnostic step after clinical examination, for screening and diagnosis of LEAD. The aim of our study was to evaluate the ABI in a group of long-standing type 1 diabetic patients.
Methods
We conducted a cross-sectional study at the National Institute of Nutrition of Tunis. We included type 1 diabetic patients who had diabetes for more than 20 years. We measured the brachial systolic pressure using the tourniquet and the Doppler probe and the posterior tibial systolic pressure. A high ABI (>1.30) suggests the presence of mediacalcosis. An ABI ≤0.90 indicates the presence of LEAD.
Results
We included 155 type 1 diabetic patients with mean age39.7±9.8 years. The population was predominantly female (67.1%). Mean duration of diabetes was 27.33±6.38 years [ext : 20–48 years]. Mean glycatedhemoglobin (A1c)was 9.45±1.62%. The mean ABI was 1.22 ± 0.25 with extremes ranging from 0.76 to 2.18. The majority had an ABI between 0.9 and 1.3. An ABI > 1.3 was found in 18.6% of patients. Only 5.2% of patients had an ABI < 0.9. The ABI was correlated with age ($r=0.360$; $P<0.001$) and duration of diabetes ($r=0.398$; $P<0.001$). It was inversely correlated with insulin dose ($r=-0.279$; $P=0.006$).
Conclsion
Most patients with LEAD are asymptomatic. Patients with diabetes are at higher risk of chronic limb-threatening ischaemia as the first clinical manifestation of LEAD, supporting regular screening with ABI measurement for early diagnosis.

DOI: 10.1530/endoabs.81.P363

P364

Acute hemolytic anemia due to glucose-6-phosphate dehydrogenase deficiency during treatment of diabetic ketoacidosis in an African American patient diagnosed with Ketosis-prone diabetes

Panagiotis-Nikolaos Tsakalomatis, Vasiliki Daraki, Rodanthi Vamvoukaki, Maria Mytilinaiou, Eleni-Konstantina Syntzanaki, Kalliopi Kontolaimaki, Maria Chrysoulaki, Maria Sfakiotaki, Vasiliki Venetsanaki, Katerina Bouki, Grigoria Betsi & Paraskevi Xekouki
University General Hospital of Heraklion, Endocrinology and Diabetes Clinic, Heraklion, Crete, Greece

Background
Diabetic ketoacidosis (DKA) has been associated with severe hemolysis in patients with Glucose-6-phosphate dehydrogenase (G6PD) deficiency after restoration of euglycemia. Less than 30 cases have been reported so far. The exact mechanism is not fully understood.
Case presentation
A 35-year-old African American man presented to the emergency department with polyuria, polydipsia, abdominal pain and weight loss the last 15 days. Physical examination revealed an afebrile man with severe dehydration, tachypnoea and tachycardia. Diagnosis of DKA was confirmed by laboratory tests. Remarkably, he had no previous history of precipitating factors but he reported use of cannabis twenty days ago, which was confirmed by toxicological testing. He was treated with hydration and intravenous insulin infusion, with a remarkable clinical and biochemical improvement. One day after he was switched to subcutaneous insulin therapy, a significant reduction in hemoglobin (9.2 g/dl)

accompanied by an increase in indirect bilirubin (1.59 mg/dl) was observed. Direct Coombs was negative and haptoglobin was <7.38 (20–200) mg/dl. Examination of peripheral blood smear revealed blister cells, indicative of hemolysis. Medical history was negative for common hemolytic causes. Considering that African American men are commonly affected with G6PD deficiency, with a prevalence of approximately 10%, deficiency of this enzyme was suspected and confirmed by its low level (3 IU). Hemolysis was resolved after several days, and the patient left the hospital on intensive insulin regimen. During follow up, gradual reduction of total daily insulin requirements was observed, with permanent discontinuation 10 weeks later. C-peptide stimulation test, showed a peak c-peptide up to 1.1 mg/dl, suggesting residual pancreatic b-cell function. Antibodies to insulin, islet cell, glutamic acid decarboxylase and protein tyrosine phosphatase were negative. The diagnosis of Ketosis-prone diabetes (KPD) A-β+ subtype was established. During annual follow up, patient was euglycemic without any antidiabetic treatment.
Discussion
KPD is a heterogeneous syndrome characterized by varying degrees of insulin deficiency. It is classified into four subgroups according to Aβ classification system. 'A' is referring to the presence or absence of islet autoantibodies and 'β'is referring to the presence or absence of b-cell functional reserve, measured 6–8 weeks after DKA episode. Recent data suggest that alterations in genes controlling both insulin secretion and G6PD-mediated antioxidant defenses may contribute to the predisposition to KPD in West Africans with G6PD deficiency. The occurrence of hemolysis in these patients during treatment of DKA is increased and should be investigated.

DOI: 10.1530/endoabs.81.P364

P365

Flash glucose monitoring in patients with DM3c

Ángel Rebollo-Román, Soraya León-Idougourram, Carlos Manuel Alzás Teomiro, Paloma Moreno-Moreno & Maria Angeles Galvez Moreno
Hospital Universitario Reina Sofía, UGC Endocrinología y Nutrición, Córdoba, Spain

Objective
Flash glucose monitoring (FGM) allows non-invasive glucose level assessment. Since November 2020 the use of this system is subsidized in patients with type 3c diabetes (DM3c) Our objective was to describe the characteristics of these patients and their glycemic control expressed as times in range.
Methods and patients
Observational longitudinal clinical study between January 2021 and December 2021 in patients with DM3c in which FGM implementation was subsidized
Results
26 patients included. Mean age: 59.27 ± 12.22 years, with DM diagnosed with a mean age of 51.85 ± 12.19 years. 30.8% women. 76.9% use of pancreatic enzymes in these patients. FGM metrics: A mean use of 91.17 ± 8.57%. 74.83 ± 16.12% time in range, 16.91 ± 11.82% time between 180–250 mg/dl, 5.35 ± 7.50% time above 250 mg/dl, 2.65 ± 2.99% time between 54–70 mg/dl, 0.13 ± 0.34% time below 54 mg/dl. Glycemic CV 31.59 ± 6.61%. 39.1% of patients achieved all clinical targets for FGM metrics.
Conclusion
- The main cause of DM3c in our series was surgical pancreatic resection (38.5% of patients)
- In our series of patients with DM3c and FGM, metabolic control was adequate using the same clinical targets as in DM1. 39.1% of patients achieved all clinical FGM targets.

Table 1.

Cause of DM3c	n	%
Chronic pancreatitis (CP) due to alcohol abuse	4	15.4
CP w/o alcohol abuse	4	15.4
Pancreatic surgery (Tumour)	3	11.5
Pancreatic surgery (Non tumoral)	10	38.5
Cystic fibrosis	1	3.8
Others	3	11.5

DOI: 10.1530/endoabs.81.P365

P366

Impact of glucose monitoring on quality of life

David Veríssimo, Catarina Ivo, Vitória Duarte, Ana Cláudia Martins, Joao Silva, Luis Lopes, Dolores Passos, J Jácome Castro & Mafalda Marcelino
Portuguese Armed Forces Hospital, Endocrinology Department, Lisboa, Portugal

Introduction
The quality of life (QoL) of patients with Diabetes has been the subject of several studies worldwide. In Portugal, studies have shown that patients under intensive insulin therapy had worse results in QoL questionnaires. The introduction of interstitial glucose monitoring (IGM) appears to reduce the impact of insulin therapy on QoL.
Objective
To assess whether IGM changes the quality of life of patients with diabetes, compared to the assessment of glycemia and its impact on glycemic control of patients.
Methods
Retrospective cohort study of patients with diabetes under intensive insulin therapy and IGM system. The 'Appraisal of Diabetes Scale' (ADS) questionnaire was used, which consists of a set of 7 items summed to reflect the patients' self-appreciation of their diabetes management. A 0 score indicates good management, with minimal impact on quality of life and 35 worse management and a negative impact on quality of life. The ADS was completed in two stages: a questionnaire applied at the time they used blood glucose monitoring and a questionnaire applied when using IGM systems.
Results
29 patients, 80.6% male, mean age 61 years, 58.6% with type 2 diabetes and 41.4% with type 1 diabetes. At the implementation of the IGM system, the mean duration of diabetes was 19.3 +/- 11.2 years, with HbA1c of 8.4 +/- 1.5% and 4.5 +/- 2.6 daily capillary blood glucose tests, on average. The ADS result reported to this date averaged 19 +/- 5 points. After the introduction of IGM, for an average period of 13.9 +/- 10.6 months, the mean ADS value was 16 +/- 4, corresponding to a significant reduction of 17% ($P<0.0001$). The mean HbA1c was 7.8 +/- 1.2%, corresponding to a 7% reduction ($P=0.03$), with an increase in the number of glucose measurements (12 +/- 11 IGM measurements per day ($P=0.004$). ADS and HbA1c results were independent of time of IGM use ($P=0.2$ and$P=0.4$) and number of daily glucose measurements ($P=0.7$ and$P=0.9$).
Discussion
The results demonstrate that the use of IGM, regardless of the number of measurements or the date of placement, has a positive impact both on diabetes control and on patients' perception of their disease management, with a consequent improvement in QoL.

DOI: 10.1530/endoabs.81.P366

P367

Metformine: anti-fibrotic molecule?

Dayssem Khelifi[1], Ibtissem Ben Nacef[1], Kahena Bouzid[2], Imen Rojbi[1], Youssef Lakhoua[1], Nadia Mchirgui[1] & Karima Khiari[1]
[1]Charles Nicolle University Hospital, Endocrinology's Department, Tunisia; [2]Charles Nicolle University Hospital, Clinical Biochemistry Department, Tunisia

Background and aims
Diabetes causes tissue fibrosis by still poorly understood mechanisms which involve glycation products. Galectin-3 (Gal-3) is an emerging key player in metabolic disorders and a powerful factor in the development and progression of the fibrotic process in target organs in diabetic patients. The plasma level of Gal-3 increases during diabetic cardiomyopathy and diabetic nephropathy. We have studied the correlation between serum Gal-3 level and anti-diabetic treatment.
Methods
We carried out a cross-sectional study with an analytical aim. This work was carried out on type 2 diabetic patients followed in our department whose age range between 35 years and 80 years.
Results
On the therapeutic level, 11 patients (4.2%) were under hygieno-dietetic rules alone, 131 patients (50.4%) on oral anti-diabetics alone, 30 patients (11.5%) on insulin therapy alone and 88 patients (33.8%) on oral anti-diabetics and insulin therapy. For the oral treatment class, 207 patients (79.8%) were on metformin, 64 patients on sulfonylureas (24.6%), 13 patients (5%) on acarbose, 2 patients (0.8%) on glinide. We found a significant negative correlation of Gal-3 with metformin treatment ($r=-0.042$; $P=0.028$).

Conclsions
We observed a significant inverse correlation between Gal-3 and metformin treatment and this effect was independent of BMI, HbA1c and CRP. Metformin reduces oxidative stress and the formation of AGEs (advanced glycation products). This may help lower serum Gal-3 levels. Metformin has also been shown to reduce Gal-3 in human adipocytes and monocytes indicating a direct effect of metformin against fibrosis. Metformin has been argued to exert a nephroprotective effect by attenuating renal fibrosis, as well as as an effect on reducing cardiac remodeling.

DOI: 10.1530/endoabs.81.P367

P368

Comparative analysis of clinical, obstetric and perinatal characteristics of pregnant women according to serum levels of vitamin D

Víctor José Simón Frapolli, Andrea Fernández Valero, Miguel Damas Fuentes, María Molina Vega, María José Picón César & Francisco José Tinahones Madueño
Hospital Universitario Virgen de la Victoria, Endocrinology and Nutrition, Málaga, Spain

Introduction
Vitamin D is considered a fat-soluble vitamin and a fundamental prohormone in mineral and bone metabolism, with an immunoregulatory, cardiovascular and neuroprotective effect, among others. Vitamin D can be found as vitamin D2 or ergocalciferol and vitamin D3 or cholecalciferol. The main source of vitamin D comes from ultraviolet radiation in sunlight, but it is also obtained through food. Vitamin D deficiency is very prevalent in Europe, with a significant peak in Spain among the pregnant and infant population, being associated with adverse maternal-fetal effects such as gestational diabetes mellitus (GDM), deficit of bone mineralization in the newborn and increased risk of preeclampsia.
Material and method
Retrospective observational study that analyzes the data of 148 pregnant women, with a mean age of 33.32 ± 5.29 years, who came to our service to undergo 100g-SOG as a diagnostic test for GDM. Pregnant women were classified into 3 categories based on serum vitamin D levels (≤20 ng/ml, 20–29.99 ng/ml, ≥30 ng/ml), and different clinical, obstetric and perinatal variables were compared. In addition, the correlation of these variables with vitamin D levels was studied.
Results
No statistically significant differences were observed between serum vitamin D levels and the prevalence of GDM, BMI prior to pregnancy, blood pressure, HOMA-IR, total cholesterol, LDL, triglycerides, or newborn weight, among others. However, an elevation of HDL is observed in the pregnant group with higher levels of vitamin D, and an inverse correlation is observed between vitamin D and BMI prior to pregnancy, but not with the rest of the variables.
Conclsion
In our population, no differences were found between clinical, perinatal and obstetric parameters according to vitamin D levels. Vitamin D levels were only inversely correlated with BMI prior to pregnancy.

DOI: 10.1530/endoabs.81.P368

P369

A role for somatostatin in regulating weight regain after bariatric surgery in mice

Doron Kleiman, Yhara Arad, Anna Permyakova, Joseph Tam, Rachel Ben-Haroush Schyr & Danny Ben-Zvi
Hebrew University of Jerusalem, Jerusalem, Israel

Somatostatin is a hormone and neuropeptide expressed in the pancreas, gastrointestinal tract, hypothalamus, and other tissues. It regulates directly the secretion of insulin, glucagon, many of the gastrointestinal hormones, and growth hormone. It is therefore surprising the somatostatin knockout (sst-ko) mice have a very mild phenotype. We subjected sst-ko mice and heterozygous siblings which served as controls to a high-calorie diet, and confirmed that sst-ko mice gain weight normally and have slightly more adipose tissue. Continuous glucose measurement of these mice has shown they have lower glycemia than controls. both groups of mice lost weight and regained weight at the same rate after a short transition to a normal chow diet. However, sst-ko mice did not regain weight following sleeve gastrectomy (SG), a common bariatric surgery. Sst-ko mice maintained low weight 90 days after surgery, while fed on a high-calorie diet and were leaner than heterozygous siblings that had the same procedure. SG operated sst-ko mice had low fasting insulin levels, and very rapid glucose clearance. Mechanistically, SG sst-ko mice had an exaggerated post-prandial Glp1 secretion. Post-prandial Glp1 levels were higher than in heterozygous controls that had the same surgery. Sham-operated sst-ko mice did not display an elevation in Glp1 secretion. In conclusion, by performing sleeve gastrectomy on sst-ko mice we were able to expose a role for somatostatin in regulation glycemia and weight gain, in part via regulating postprandial Glp1 secretion.

DOI: 10.1530/endoabs.81.P369

P370

Differential localisation of the A-ring reductases in human hepatocytes: implications for substrate preference and utilisation

Tom Potter[1], Ismael da Conceição[2], Nikolaos Nikolaou[2], Nellie Loh[2], Jeremy Tomlinson[2] & Laura Gathercole[1]
[1]Oxford Brookes University, Department of Biological and Medical Sciences, Oxford, United Kingdom; [2]University of Oxford, Radcliffe Department of Medicine, Oxford Centre for Diabetes, Endocrinology & Metabolism, Oxford, United Kingdom

The 5-reductases are steroid metabolising enzymes that saturate the C4=C5 bond of the steroid A-ring, and their substrates include androgens, glucocorticoids, and bile acids. 5β-reductases (SRD5A1 & SRD5A2) convert testosterone to the more potent androgen 5β-dihydrotestosterone, and carry out the first step in glucocorticoid clearance, generating 5β-dihydrocortisol from cortisol. 5β-reductase (AKR1D1) is also able to carry out the first step of glucocorticoid clearance, converting both cortisol and cortisone to 5β-dihydrocortisol and 5β-dihydrocortisone but, in contrast to 5β-reductases, it converts testosterone to a low activity intermediate, 5β-dihydrotestosterone. In addition, it catalyses an essential step in bile acid synthesis. The subcellular localisation of steroid metabolising enzymes is thought to have a role in determining their activity and substrate preference. In this regard, hepatic SRD5A1 is reported to be

$n=148$	Vit D ≤20 ng/ml ($n=45$)	Vit D 20–29.99 ng/ml ($n=71$)	Vit D ≥30 ng/ml ($n=32$)	Chi^2, ANOVA (p)	Pearson correlation (p)
GDM	12 (26.7%)	17 (23.9%)	13 (40.6%)	0.234	
BMI prior to pregnancy (kg/m^2)	28.22 ± 8.1	27.36 ± 6.3	24.94 ± 4.1	0.107	**-0.2 (0.03)**
Systolic blood pressure (mmHg)	110.2 ± 11.8	110.6 ± 12.9	110.6 ± 17.1	0.988	0.006 (0.94)
Diastolic blood pressure (mmHg)	71.78 ± 9.4	71.92 ± 8.4	69.97 ± 10.4	0.587	-0.001 (0.99)
HOMA-IR	2.33 ± 2.2	2.38 ± 1.3	2.06 ± 1.4	0.670	-0.07 (0.39)
Total cholesterol (mg/dl)	258.7 ± 46.1	256.37 ± 47.7	243.39 ± 35.3	0.303	-0.12 (0.14)
HDL (mg/dl)	77.53 ± 15.9	78.9 ± 16.7	70.19 ± 15.0	**0.042**	-0.13 (0.10)
LDL (mg/dl)	143.44 ± 40.2	136.85 ± 38.6	134.58 ± 32.4	0.542	-0.10 (0.22)
Triglycerides (mg/dl)	203.64 ± 77.2	194.93 ± 49.1	193.42 ± 45.3	0.677	-0.05 (0.54)
Newborn weight (kg)	3.18 ± 0.4	3.17 ± 0.4	3.17 ± 0.4	0.990	
Delivery (week of pregnancy)	39.35 ± 1.6	38.82 ± 1.6	38.61 ± 2.5	0.403	

localised in either the nucleus, cytoplasm or both. However, evidence for the subcellular localisation of SRD5A2 and AKR1D1 in hepatocytes is lacking. To determine whether SRD5A2 and AKR1D1 are localised to the nucleus or cytoplasm, nuclear and cytoplasmic fractions were isolated from HepG2 hepatoma cells. The purity of the fractions was confirmed by Western blot, using Lamin A/C as a nuclear and β-tubulin as a cytosolic marker. Similar to SRD5A1, SRD5A2 was detected in both cytoplasmic and nuclear fractions. In contrast, AKR1D1 was detected only in the cytoplasmic fractions. Further work is required to determine whether the localisation of SRD5A1 and 2 impact on their substrate preference, and to determine the localisation of AKR1D1 within the cytoplasm.

DOI: 10.1530/endoabs.81.P370

P371

Body composition in patients undergoing liver transplantation

Maria Argente Pla[1], Katherine Garcia-Malpartida[1], Regina Lopez-Gironás[1], Silvia Martín-Sanchis[1], Andrea Mico-Garcia[1], Eva Gasco[1], Angela Dura-De Miguel[1], Lorena Hernandez[1], Elena Vera[1] & Juan Francisco Merino Torres[1]
[1]La Fe Universitary Hospital, Endocrinology and Nutrition, Spain

Rationale
Liver cirrhosis frequently leads to changes in body composition consisting of a loss of lean mass, increased body water and variable alterations of fat mass. Changes in body composition may occur after liver transplantation (LT). Our aim was to study the changes that occur in body composition after LT (in the postoperative period after LT as well as 1 month later).
Methods
A body composition study was carried out using the bioimpedance InBody S10® in patients undergoing liver transplantation, postoperatively and 1 month after discharge. Several markers were analyzed: appendicular skeletal muscle mass (ASM), percentage of body fat, phase angle (PA) and extracellular water ratio (ECW ratio). Low muscle mass was considered when the ASM/height^{2}was <7 kg/m^{2}in men or <5.5 kg/m^{2}in women; normal PA according to the standardized tables by age and sex and using the cut-off value of 4^o; normal ECW ratio between 0.360–0.390; and normal fat mass in men between 10–20% and in women between 18–28%. Means comparison was carried out using the T-student test for paired samples and the comparison of proportions using the McNemar test.
Results
60 patients(78.3% men) were included. The age was 60.8(7.5) years. The median stay was 10.5(5–88) days. The time elapsed between both evaluations was 32.8(11.1) days. The assessment of body composition before and 1 month after discharge from transplantation is shown in the following table. Sarcopenia was present in 2.1% and 12.7% of men at the first evaluation and 1 month later, respectively($P<0.001$). No women presented sarcopenia in the immediate post-transplant period vs 23% at one month. Table-2 shows SMI and PA.

Variable:	Baseline	1 month	p-value
Body Mass Index(kg/m2)	25.3(3.6)	23.8(3.3)	**<0.001**
Fat mass(%)	23.2(7.6)	23(7.9)	0.69
Visceral fat area(cm)	79.2(30)	74.2(29.4)	0.07
Extracellular water ratio	0.40(0.1)	0.39(0.1)	**<0.001**
Body cell mass(kg)	34.3(8)	32.8(5.8)	**0.038**

	ASM/height^2 (baseline vs 1 month, *P*-value)	PA (baseline vs 1 month, *P*-value)
Men:	8.2(1.4) vs 7.8(1.0), **$P<0.001$**	4.2(0.9) vs 4.4(1.4), **$P<0.001$**
Women:	7.2(1.2) vs 6.3(0.8), $P=0.082$	3.5(0.8) vs 4.3(0.6), **$P=0,02$**

Conclusion
Alterations in body composition in patients with LT are very frequent. One month after LT, there was a decrease in BMI, ASM, cell mass and body water, and an increase in PA. The worsening of muscle mass indicates that this period is critical in these patients. It would be interesting to assess body composition in the longer term. Since impedance metry is altered by excess extracellular water, these findings could be compared with other techniques for assessing body composition.

DOI: 10.1530/endoabs.81.P371

P372

Impact of diabetes mellitus on patients' quality of life

David Veríssimo, Catarina Ivo, Vitória Duarte, Ana Cláudia Martins, Joao Silva, Luis Lopes, Dolores Passos, J Jácome Castro & Mafalda Marcelino
Portuguese Armed Forces Hospital, Endocrinology Department, Lisboa, Portugal

Introduction
Diabetes is a disease with great psychosocial impact and reduced quality of life (QoL), and psychosocial factors seem to be excellent predictors of clinical outcomes.
Objective
Assess the relationship between the patient's perception of diabetes management and its impact on QoL.
Methods
Interview of patients with type 1 (T1D) and type 2 diabetes (T2D), using the 'Appraisal of Diabetes Scale' (ADS), a questionnaire composed of 7 items that are summed to reflect the patients' self-appreciation of their diabetes. A 0 score indicates good management, with minimal impact on QoL and 35 a worse management and a negative impact on QoL. Analysis of the association between the ADS result and the following factors: type of treatment, duration and control of diabetes, chronic complications (assessment of the number and severity using the 'Diabetes Complications Severity Index' (DCSI)), daily number of blood glucose measurements and number of consultations in the last year.
Results
165 patients, 86.2% male, mean age 65 +/- 11 years, 92.1% with T2D and 7.9% with T1D, with a mean duration of 13.5 +/- 10.5 years. 64.8% of patients were on oral antidiabetic drugs (OAD), 5.5% on daily injectable GLP-1 agonists (aGLP-1), 14.5% on basal insulin and 15.2% on basal-bolus insulin regimen. The mean HbA1c was 7.1 +/- 1.4% and the DSCI result was 2 +/- 2, corresponding to 1 +/- 1.2 complications per patient. Daily glycaemia measurements were on average 1+/-2 and the average medical visits per year was 3.5 +/- 1.7. The ADS result was 16 +/- 4 in the OAD and aGLP-1 groups, 18 +/- 4 in the basal insulin group, and 19 +/- 5 in the basal-bolus insulin group, with a significant difference between groups ($P=0.018$). Higher HbA1c values correlated with worse ADS results ($P=0.009$), but the same was not observed with the number and severity of diabetic complications (DSCI) ($P=0.58$), nor with the duration of diabetes ($P=0.5$). A greater number of daily blood glucose measurements and annual medical visits correlated with worse results in the ADS ($P=0.02$ and$P=0.03$).
Discussion
The results demonstrate that patients' perception of diabetes management was adequate for their actual control and that the introduction of insulin regimens or stricter follow-up (greater number of blood glucose tests or consultations per year) are correlated with worse QoL. However, the impact of diabetic complications is undervalued by patients, which reinforces the need to raise awareness about them.

DOI: 10.1530/endoabs.81.P372

P373

Auto-immune diabetes associated with systemic scleroderma: a case report

Hind Ouakrim, Bilihi Natacha, Sana Rafi, Ghizlane El Mghari & Nawal El Ansari

Mohammed VI University Hospital, Department of Endocrinology, Diabetes, Metabolic diseases and Nutrition, Marrakech, Morocco

Introduction

The association of multi-organ autoimmune diseases is described. We report a case of association between Latent autoimmune diabetes in adults (LADA) and systemic scleroderma (SSc), which remains a rarely reported entity in the literature.

Observation

38-year-old female patient, followed for systemic scleroderma with digestive and pulmonary involvements. The patient presented a dysphagia to solids with dyspnea installed in the last 2 months, with general state alteration. No polyuro-polydipsic syndrome, no diabetic heredity. A generalized cutaneous sclerosis was objectified at the clinical examination. A standard workup showed fasting blood glucose at 1.69 g/l with HbA1c: 8.6%, the patient is treated with insulin-therapy. Immunology typing test of diabetes: anti GAD, anti Znt8: positive Skin biopsy: Morphological aspect compatible with scleroderma.

Discussion

Cases of coexistence of autoimmune diabetes with systemic sclerosis are rare. The pathogenesis of this association is not yet well understood. Interferon seems to play a major role as an immunomodulator and inhibitor of collagen production, and hypotheses suggest that it is also involved in the pathophysiology of several autoimmune diseases, including diabetes. And it is well known that autoimmune diseases with the presence of organ-specific antibodies such as autoimmune diabetes or autoimmune thyroiditis can coexist with other non-organ-specific autoimmune diseases such as SSc. In addition, autoimmune diabetes has been shown to be more likely to occur in first-degree relatives of patients with SSc.

Conclsion

The association of autoimmune diabetes and systemic scleroderma could be at the origin of a difficulty to assure insulin injections, which may be responsible for an important blood glucose unbalance.

Bibliography

1. Divaker Choubey, **Interferons in Autoimmune and Inflammatory Diseases: Regulation and Roles**. JOURNAL OF INTERFERON & CYTOKINE RESEARCH Volume 31, Number 12, 2011 2. Caterina Ferreli1, **Cutaneous Manifestations of Scleroderma and Scleroderma-Like Disorders: a Comprehensive Review**. Clinic Rev Allerg Immunol 3. Yannick Allanore, **Physiopathologie de la sclérodermie systámique**. medecine/sciences 2016; 32: 83–91 4. Ewa Wielosz1, **Coexistence of diabetes mellitus type 1 with diffuse systemic sclerosis**: **case report and literature review**. Reumatologia 2017;55(2): 104–107 5. Koumakis E, Dieude P, Avouac J, *et al*. **Familial autoimmunity in systemic sclerosis- results of a French-based case controlfamily study**. J Rheumatol 2012; 39: 532–538. 6.Hála Zeglaoui, **Type 1 diabetes mellitus, celiac disease, systemic lupus erythematosus and systemic scleroderma in a 15-year-old girl**. Rheumatol Int (2010) 30:793–795

DOI: 10.1530/endoabs.81.P373

P374

Threshold value of galectine-3 in a Tunisian diabetic population

Dayssem Khelifi[1], Ibtissem Ben Nacef[1], Kahena Bouzid[2], Imen Rojbi[1], Youssef Lakhoua[1], Nadia Mchirgui[1] & Karima Khiari[1]
[1]Charles Nicolle University Hospital, Endocrinology's Department, Tunisia; [2]Charles Nicolle University Hospital, Clinical Biochemistry Department, Tunisia

Background and aims

Plasma Galectin-3 (Gal-3), mediator of fibrogenesis and inflammation, has been implicated in many diseases. Particularly in diabetics, this lectin directly mediates transdifferentiation in collagen-producing cells thus leading to fibrosis of target organs and accelerating the development of complications. The objective of our study was to determine a cut-off value for Gal-3 in our population.

Methods

We conducted a cross-sectional, analytical study including 260 type 2 diabetic patients. For statistical purposes, we solicited a second control group of non-diabetic patients. For the determination of the discriminating threshold of the quantitative variable, we established ROC curves (Receiver Operating Characteristics).

Results

In our series, the mean serum Gal-3 level in our diabetic patients was in the order of 14.24 ng/ml $\pm$ 7.32 (range: 3.30 and 69.30 ng/ml). The median concentration was 12.4 ng/ml. The mean Gal-3 value in the control group was 11.80 ng/ml $\pm$ 3.75 (range: 4.4 and 25.5 ng/ml) and a median of 10.9 ng/ml. A statistically significant increase in serum Gal-3 ($P<0.001$) in the diabetic group was observed. We carried out an ROC curve which allowed us to define a value of Gal-3 at 11.25 ng/ml as the best threshold of sensitivity and specificity. The area under the ROC curve was 0.61 (Confidence Interval: CI95 [0.55–0.67], $P=0.001$).

Conclsions

The level of Gal-3 differs from study to study. This could be explained by the fact that the plasma levels of Gal-3 are influenced by socio-demographic, anthropometric, clinical and biological factors. Hence the need to determinate a specific serum threshold for each population.

DOI: 10.1530/endoabs.81.P374

P375

More than 20 years after diagnosis of type 1 diabetes: what about the quality of life?

Emna Bornaz, Haifa Abdesselem, Chaima Sdiri, Kamilia Ounaissa, Fatma Boukhayatia, Imene Sebai, Asma Ben Brahim, Rim Yahiaoui & Chiraz Amrouche
National Institute of Nutrition, Outpatient Department and Functional Explorations, Tunis, Tunisia

Background

Long-standing type 1 diabetes, had many complications which have an impact on both life expectancy and quality of life of these patients. The aims of our study were to evaluate the quality of life of a group of Tunisian patients with type 1 diabetes evolving for more than 20 years as well as to determine the factors associated with its alteration.

Methods

We conducted a descriptive observational cross-sectional study including type 1 diabetic patients who had diabetes for more than 20 years, followed at the National Institute of Nutrition. Quality of life was assessed using the version 19 of the Audit of Diabetes Dependent Quality of Life (ADDQOL-19), translated into Tunisian dialect; which includes, in addition to two general questions, 19 questions specifically assessing 19 life domains. From these 19 questions, a weighted composite score was calculated. We considered that quality of life was impaired if this score was $\leq$-3.

Results

A total of 155 patients with a mean age of 39.7 $\pm$ 9.8 years were included in the study. The diabetes had progressed for 27.33 $\pm$ 6.38 years. The sex ratio M/F was 0.49. More than half of the population (53.4%) had an impaired quality of life with a mean composite score of -3.22 $\pm$ 2.19. Of the nineteen life domains assessed, thirteen had a mean score $\leq$-3. Fear of the future, physical ability and freedom to eat, were the most impaired life dimensions. Their mean scores were -4.39$\pm$3.4, -4.09$\pm$2.9 and -3.91$\pm$3.2, respectively. Univariate analysis showed that impaired quality of life was associated with unemployment ($P=0.02$), low level of education ($P=0.049$), low socioeconomic status ($P=0.009$), frequency of hypoglycemia ($P<0.001$), complicated retinopathy ($P=0.037$), peripheral neuropathy ($P=0.012$), disorders of the lower urinary tract ($P=0.047$) and category of risk of foot ulceration ($P=0,028$).

Conclsion

Our study highlights that after more than 20 years of the diagnosis of type 1 diabetes, the quality of life is often impaired. Prevention of chronic complications, psychological management, and adoption of therapeutic techniques that preserve dietary autonomy, could improve the QOL of long-standing type 1 diabetic patients.

DOI: 10.1530/endoabs.81.P375

P376

Diabetic retinopathy and erectile dysfunction: is there a relationship ?

Emna Bornaz, Haifa Abdesselem, Skander Msolly, Kamilia Ounaissa, Boukhayatia Fatma, Imene Sebai, Asma Ben Brahim, Rim Yahiaoui & Chiraz Amrouche

National Institute of Nutrition, Outpatient Department and Functional Explorations, Tunis, Tunisia

Background
Erectile dysfunction impairs the quality of life of men with type 1 diabetes. Many factors are involved in this complication. According to the literature, diabetic microangiopathy is associated with erectile dysfunction. The aim of our study was to evaluate the impact of diabetic retinopathy on erectile dysfunction in a group of long-standing type 1 diabetics.
Methods
We conducted a cross-sectional study that included male patients with type 1 diabetes for 20 years or more and followed at the National Institute of Nutrition of Tunis. Diagnosis and severity of erectile dysfunction were assessed by the short version of the International Index of Erectile Function (IIEF-5), translated and validated in Arabic. Diabetic retinopathy (DR) and its degree of severity were diagnosed by fundus examination and retinal angiography if abnormalties.
Results
A total of 51 men with a mean age of 41 ± 9.7 years wereincluded in the study. Diabetes was diagnosed at the age of 14.8 ± 7 years. Mean duration of diabetes was 26.4 ± 6 years. Only one-fifth (21.1%) of the population did not have DR on fundus examination. Two patients had permanent blindness. DR was minimal, moderate and severe in 18.4%, 21.1% and 15.8% of participants, respectively. It was proliferative in 10.5% of patients and complicatedin 7.9%. Mean IIEF-5 score was 15.3 ± 5.3. Erectile dysfunction was diagnosed in 85% of participants. It was mild in 39.1%, moderate in 43.5% and severe in 17.4% of cases. Univariate analysis showed a significant association between DR and erectile dysfunction ($P = 0.014$). Severity of DR was associated with severity of erectile dysfunction ($P = 0.034$).
Conclsion
Erectile dysfunction remains under-diagnosed and untreated in many diabetic patients. However, as our study showed, systematic screening in all patients with DR, especially in the advanced stages, should be recommended.

DOI: 10.1530/endoabs.81.P376

P377

Diabesity showcases the need for intensive care for COVID-19

Ak Das[1], Shaibal Guha[2], Subhash Kumar[2] & Anand Shankar[2]
[1]Diabetes, Muzaffarpur, India; [2]Diabetes, Patna, India

Background
Old age is proven to be one of the greatest danger factors for intensively dealing with COVID-19 patients. Stoutness and diabetes are enhancers of dangers among COVID-19 patients. In any case, there exists restricted proof for the modifiable danger components, for example, bodyweight which is an indicator of the Intensive Care Unit and its need among type 2 diabetes patients. In this review, the subject of body weight as an indicator of ICU confirmations will be investigated.
Methods
A total of 127 Type 2 DM patients were selected. These patients had recovered from COVID-19, on follow up for diabetes care, from eight diabetes clinics that had the association of the metabolic risk factors with the need for intensive care. Descriptive statistics and Fisher's exact test were performed.
Results
100 hypertensives and 104 patients had recovered without intensive care. The mean age was 6 (±14, minimum 11, maximum 94, range 83, 95% CI 55 to 58), BMI (kg/m^2) was 27 (±4.7, minimum 17, maximum 44, range 83, 95% CI 27 to 28), and HbA1c (%) was 8.1 (±1.6, minimum 4.8, maximum 15, range 10, 95% CI 7.9 to 8.4). 10 patients at follow-up, for diabetes consultation, post COVID-19 had good glycaemic control with less than 7% of HbA1c. 23 patients needed ICU care. The higher proportion with BMI $\leq$ 25, 27% required ICU as compared to 20% out of the 62 patients who had BMI $<$ 25 kg/m2.
Conclusion
ICU admission risk had heightened for both the obese patients and the elderly patients among the Type-2 DM patients who were diagnosed with COVID-19. The findings of this study reveal that obesity needs to be managed for reducing the severity of COVID-19, bodyweight needs to be reduced to lessen the need for ICU care.

DOI: 10.1530/endoabs.81.P377

P568

Study of musculoskeletal manifestations in type 2 diabetes mellitus

Biswajit Payra[1], Sachin K. Jain[1], Anupam Prakash[1], Alok Sud[2], Ritika Sud[1] & Ramesh Aggarwal[1]
[1]Lady Hardinge Medical College, Medicine, New Delhi, India; [2]Lady Hardinge Medical College, Orthopaedics, New Delhi, India

Introduction
Musculoskeletal manifestation is one of the leading cause of morbidity and disability among type 2 diabetics. Also management of these conditions with steroids and non-steroidal anti-inflammatory drugs, adversely impact the glycaemic control of diabetics. Our study aims to look for prevalence of different musculoskeletal manifestation among type 2 diabetes.
Methodology
Our study is a cross-sectional observational study and it is comprised of 200 type 2 diabetics (>1 year duration) and 200 non-diabetic adult (>18 years) populations. All the cases were subjected to GALS screening (Gait, Arm, Leg and Spine). Patients with positive GALS screening were evaluated by REMS (Regional Examination of Musculoskeletal systems). Radiological examinations were done where needed.
Results
Prevalence of musculoskeletal manifestations was 55% ($n = 1110$) among diabetics compared to 22.5% ($n = 44$) among non-diabetics ($P < 0.001$). 8% of diabetic patients with musculoskeletal manifestations were asymptomatic and detected by GALS screening. According to prevalence most common musculoskeletal manifestation among diabetics was cheiroarthropathy (21.5%; $n = 43$) followed by osteoarthritis (19%; $n = 38$), Adhesive capsulitis (11.5%; $n = 23$), dupuytren's contracture (6.5%; n-13), flexor tenosynovitis (2%; $n = 4$), Charcot joint (2%; $n = 4$) and carpal tunnel syndrome (1.5%; $n = 3$). Presence of musculoskeletal manifestations is found to be significantly associated with long duration of diabetes, glycaemic control and presence of one or more microvascular complications.
Conclusion
Our study showed that the musculoskeletal manifestations are more prevalent among type 2 diabetics compared to non-diabetes population. A significant proportion of diabetics have these manifestations asymptomatically. Early diagnosis of these manifestations and good glycaemic control are important for the management.

DOI: 10.1530/endoabs.81.P568

P569

Metabolic dysfunction–associated fatty liver disease and cardiovascular risk characterization

Carolina M. Perdomo[1], Jorge Nuñez[2], Ana Ezponda Casajús[3], Francisco J. Mendoza[3], Gorka Bastarrika Alemañ[3], Gema Fruhbeck[1,4,5] & Javier Escalada[1,4,5]
[1]Clínica Universidad de Navarra, Endocrinology and Nutrition, Pamplona, Spain; [2]Clínica Universidad de Navarra, Research Support Service, Central Clinical Trials Unit; [3]Clínica Universidad de Navarra, Radiology; [4]IdiSNA, Pamplona, Spain; [5]CIBERObn

Objectives
Metabolic dysfunction–associated fatty liver disease (MAFLD) is a new nomenclature for fatty liver disease (FLD). The clinical impact of the change in nomenclature on the ability to identify individuals at risk for cardiovascular disease (CVD) has not yet been elucidated. The aim of this study is to describe the cardiovascular risk and subclinical CVD of the different MAFLD subtypes.
Methods
Retrospective analysis of patients who attended a medical check-up at Clínica Universidad de Navarra between June 2003-December 2006 who had whole-body CT scan and analytics. Exclusion criteria included cerebral vascular diseases, heart disease, excessive alcohol consumption, advanced liver diseases and malignant disease. The cardiovascular risk was assessed through visceral adipose tissue (VAT)/subcutaneous adipose tissue (SCAT) Ratio. The presence of subclinical CVD was assessed by quantifying epicardial adipose tissue adjusted for body surface area (EATi) and Coronary Calcium according to Visual Scale (CAC-V).
Results
A total of 374 patients were included in the analysis: 154 without FLD and 220 with FLD. Mean age was 57.9 ± 9.3 years and 71.4% (267/374) of the cohort were men. Of the FLD cohort: 12.7% (28/220) were patients without metabolic

dysfunction (non-MD FLD), 69.5% (153/220) were patients with MAFLD due to the presence of overweight/obesity (MAFLD-overweight), 3.2% (7/220) were patients with MAFLD due to the presence of two metabolic abnormalities (MAFLD-MD) and 14.5% (32/220) were patients with MAFLD due to the presence of T2D (MAFLD-T2D). Compared with patients without FLD, patients with FLD had increased HOMA-IR, a more detrimental lipid profile, worse kidney and liver function ($P<0.001$) and a higher prevalence of metabolic syndrome disorders ($P<0.001$). MAFLD-T2D had significantly higher subclinical cardiovascular disease markers and cardiovascular risk, followed by MAFLD-overweight with metabolic dysfunction (MD) (VAT/SCAT Ratio: 1.070 ± 0.456 and 0.889 ± 0.291 [$P<0.001$]; EATi: 113.3 ± 42.5 $cm^2$and 108.2 ± 46.9 cm^2[$P<0.001$]; CAC-V: 3.3 ± 3.4 and 1.87 ± 2.61 [$P<0.001$], respectively) . MAFLD-overweight without MD, MAFLD-MD, non-MD FLD and non-FLD had similar subclinical cardiovascular disease markers and cardiovascular risk (VAT/SCAT Ratio: 0.807 ± 0.327, 0.794 ± 0.420, 0.695 ± 0.359 and 0.615 ± 0.382 [$P>0.05$]; EATi: 82.3 ± 33.5 cm^2, 78.6 ± 39.9 cm^2, 57.1 ± 27.0 $cm^2$and 67.7 ± 38.1 cm^2[$P>0.05$]; CAC-V: 1.04 $\pm$1.8,9, 1.14 ± 1.77, 1.21 ± 2.57 and 1.28 ± 2.25 [$P>0.05$], respectively).

Conclusions

MAFLD–T2D and MAFLD–overweight with MD had the highest subclinical CVD and risk for CVD. Changing to the MAFLD criteria may help to stratify CVD risk and, therefore, aid clinicians in the task of reducing cardiovascular risk. Omitting a small fraction of individuals with metabolically uncomplicated FLD apparently does not confer an issue regarding heart outcomes.

DOI: 10.1530/endoabs.81.P569

P570

When and How to Screen for Glucose Dysregulation (GD) in patients with β-Thalassemia Major (β-TM): A retrospective study by The International Network of Clinicians for Endocrinopathies in Thalassemia and Adolescent Medicine (ICET-A)

Vincenzo De Sanctis[1], Ashraf Soliman[2], Shahina Daar[3], Ploutarchos Tzoulis[4], Mehran Karimi[5], Salvatore Di Maio[6] & Christos Kattamis[7]

[1]Quisisana Hospital, Ferrara, Italy; [2]Hamad Medical Center, Pediatrics, Doha, Qatar; [3]College of Medicine, Sultan Qaboos University, Muscat, Oman; [4]Department of Diabetes and Endocrinology, Whittington Hospital, University College London, London, UK;, United Kingdom; [5]Hematology Research Center, Shiraz University of Medical Sciences, Shiraz, Iran, Shiraz, Iran; [6]Children's Hospital 'Santobono-Pausilipon', Pediatrics, Naples, Italy; [7]National Kapodistrian University of Athens 11527, Greece, Pediatrics, Athens, Greece

To investigate the best criteria and time to diagnose dysglycemia in β-TM patients, the ICETA performed a retrospective study on glycemic abnormalities (GD) in 397 with β-TM patients (aged 5–40 years; 56.3% males) followed between 1988 to 2021 in a single centre (by VDS) (40 years).

Methods

Fasting blood glucose (FPG) and standard oral glucose tolerance test (OGTT) results were collected over 40 years of follow up and results were categorized following ADA and WHO criteria.

Results

Based on the FPG data, using the ADA criteria, the prevalence of isolated IFG was 23.6 %, while increasing the threshold value of FPG to 110 mg/dl according to WHO criteria, decreased the prevalence to 15.3%. β-TM patients showed a higher prevalence of GD mainly in the second to third decade of life. Based on the OGTT, 44 of 234 β-TM patients presented with IFG (18.8%), 3 (1.2%) with IGT and 1 with a new diagnosis of thalassemia related DM (Th-RD). In patients with IFG the probability of diagnosing IGT was higher (46.1%) in subjects with FPG between 100 and 109 mg/dl compared to subjects with FPG between 110 and 125 mg/dl ($P=0.0071$). Both ADA and WHO criteria for IFG missed the diagnosis of Th-RD in 4 of 91 patients (4.3%) and 11 of 59 patients (18.6%), respectively. The number of patients with a new diagnosis of diabetes, after OGTT, increased progressively starting from the age of 11 years (Table).

Conclusion

Many β-TM patients who have a normal FPG may present with GD after OGTT. Dysglycemia may occur in very young patients. OGTT screening seems to be cost-effective. ADA criteria used for the diagnosis of IFG identified an additional group of patients with dysglycemia. Diagnostic value of FPG and OGTT in detecting Th-RD in 384 patients with β-TM aged 5–40 years.

Table 1. Comparative characteristics of 2019 and 2020 groups

(FPG)	5–10 years N (%)	11–20 years N (%)	21–30 years N (%)	31–40 years N (%)
FPG < 100 (mg/dl) ($n=40$)	0/63 (0 %)	0/78 (0 %)	0/53 (0 %)	3/40 (7.5%)
IFG_{low}: 100–109 mg/dl ($n=33$)	0/11 (0 %)	0/47 (0 %)	2/19 (10.5%)	2/14 (14.2%)
IFG_{high}: 110–125 mg/dl ($n=55$)	0/4 (0 %)	1/25 (4%)	6/23 (26.0%)	4/7 (57.1%)
New Th-RD PG after OGTT: ≥ 200 mg/dl	0/78 (0 %)	1/150 (0.6 %)	8/95 (8.4 %)	9/61 (14.7 %)

DOI: 10.1530/endoabs.81.P570

P571

Glycogen hepatopathy- a rare and frequently misdiagnosed hepatic complication of diabetes mellitus

Swayamsidha Mangaraj

IMS and SUM Medical College and Hospital, Endocrinology, Bhubaneswar, India

Introduction

Glycogenic hepatopathy(GH) refers to excessive intrahepatic glycogen accumulation in patients with poorly controlled diabetes mellitus especially type 1 diabetes mellitus. It is a rare and frequently misdiagnosed complication of diabetes mellitus. The patients present with non-specific pain abdomen may be incidentally detected during evaluation of deranged liver function tests(LFT).

Case report

A 15 years old female presented with pain abdomen, nausea and lethargy for last ten days. She was a known case of type 1 diabetes mellitus for last two years and was currently on multiple daily subcutaneous insulin injection regimen. However, her glycemic control was very poor due to poor compliance and she had three episodes of diabetic ketoacidosis(DKA) in the past. Clinical evaluation revealed presence of lethargy and dehydration. Hepatomegaly(palpable 5 cm below costal margin) was also seen. Blood investigations revealed presence of DKA. Blood gas analysis showed arterial pH 7.1 and bicarbonate level of 12 meq/l. Her random blood glucose at the time of hospitalization was 435 mg/dl and HbA1c was 12.9 %. Urine analysis confirmed presence of ketonuria (urine ketone 3+). Renal function tests including serum electrolytes were normal. LFT revealed aspartate aminotransferase (AST) 208 IU/ml, alanine aminotransferase (ALT) 186 IU/ml and alkaline phosphatase (ALP) 198 U/l. The patient was managed with intravenous fluids, insulin infusion and other supportive measures as per DKA treatment protocol. After three days of treatment, the patient improved and she was transitioned to subcutaneous basal bolus insulin regimen. However, despite improvement in all other metabolic parameters, LFT derangement persisted. Abdominal ultrasonography showed hepatomegaly with gross hepatosteatosis without any other organ abnormality. Contrast enhanced computerized tomography also showed significant hepatomegaly with diffuse fatty infiltration. A thorough screening for liver disease markers including viral markers, autoimmune panel, coeliac disease, hemochromatosis and Wilson's disease was negative. Subsequently, a liver biopsy as per advice of treating gastroenterologist was done and it confirmed presence of classical glycogen hepatopathy. The parents were counseled regarding nature of disease and advised to maintain strict glycemic control. Subsequently after three months post discharge, revaluation confirmed regression of hepatomegaly and significant normalization of liver function tests.

Conclusion

GH is a very rare metabolic complication of poorly controlled type 1 diabetes mellitus. It may be frequently missed or misdiagnosed if clinical vigil is not high. The treatment of choice for management of GH includes strict glycemic control, periodic follow up and prevention of DKA episodes recurrence.

DOI: 10.1530/endoabs.81.P571

P572

Telephone support program for patients with type 2 diabetes under treatment with insulin glargine 300 u/ml (t-coach) in the area of cadiz (spain)

Jesus Manuel Cornejo Dominguez[1], Esteban Sanchez Toscano[1], Maria Isabel Mateo Gavira[1], Lourdes Garcia Garcia-Doncel[2] & Florentino San Laureano Carral[3]
[1]Hospital Universitario Puerta del Mar, Cádiz, Spain; [2]Hospital Universitario De Jerez, Jerez de la Frontera, Spain; [3]University Hospital of Puerto Real, Puerto Real, Spain

Introduction
The T-Coach® telephone support program for patients with type 2 diabetes (DM2) treated with insulin glargine 300 u/ml, facilitates dose adjustments of basal insulin therapy through regular telephone consultations and offers diabetes education in order to improve empowerment of the patient. Objective: To assess the usefulness of the T-Coach® program in metabolic control and degree of satisfaction in patients with T2DM.
Patients and methods
Observational, descriptive, retrospective, multicenter study, including patients with type 2 Diabetes (T2DM) included in the T-coach® program from October 2016 to December 2020, attended in Endocrinology in the province of Cádiz. Demographic data, baseline clinical and laboratory parameters, 3 and 6 months after inclusion in the program are analyzed. The degree of patient satisfaction and evolution of the level of knowledge with the use of the platform are evaluated.
Results
286 patients are included, 50.2% ($n=143$) women, age 66.05 ± 11.62 years and T2DM evolution time 15.4 ± 8.2 years. 45.4% ($n=71$) had microangiopathy and 24.5% ($n=70$) macroangiopathy. 19% started long-acting insulin. Average of 7.2 calls per patient. At baseline long-acting insulin dose was $25.5 \pm 16{,}34$ U/day after 6 months $36.2 \pm 19{,}26$ U/day. At baseline *Fasting plasma glucose* $188.5 \pm 76{,}45$ mg/dl after 6 months 119 mg/ ($P<0.001$). The initial mean HbA1c was $9 \pm 1{,}42$ % and at 6 months $7.30 \pm 1{,}38$ % ($P<0.001$). The level of knowledge raises from 5.2/8 to 7.7/8 points at 3 months. The degree of patient satisfaction was high, with scores above 9/10 in most of the items evaluated.
Conclsions
In our setting, the T-Coach® program is shown to be a useful tool for adjusting the dose of long-acting insulin, with the consequent improvement in glycemic control in these patients. The degree of patient satisfaction with the support for insulin dose adjustment is high and the level of knowledge improves with telephone reinforcement of diabetes education.

DOI: 10.1530/endoabs.81.P572

P573

Total daily dose of insulin at the beginning of treatment with Continuous Subcutaneous Insulin Infusion system: which is the best formula?

Vânia Benido Silva, Susana Garrido, Joana Vilaverde, Sofia Teixeira & Maria Helena Cardoso
Centro Hospitalar Universitário do Porto, Endocrinology, Diabetes and Metabolism, Porto, Portugal

Introduction
Several formulas are described to calculate the Insulin Dose to start insulin pump therapy. However, there are no data demonstrating their effectiveness in achieving good glycemic control.
Aim
To assess the Total Daily Dose of Insulin (TDDI) at 3 months after beginning an insulin pump, and determine which formula most closely matches the TDDI required in cases where good glycemic control is achieved after that period.
Methods
Retrospective study including individuals with type 1 diabetes who started treatment with an insulin pump between 1st of January of 2019 and 30th of September of 2021 at our center. Patients were frequently evaluated until glycemic control was achieved. Glycemic control was assessed at 'time zero'(T0) and 'time 3 M'(T3 M) through the HbA1c value, % time in target range(%TIR), % time above(%TAR) and below the target range(%TBR). The TDDI at T3 M months was compared with the insulin dose calculated by the different formulas at T0: F1-mean TDDI of the 7 days preceding the beginning of treatment;F2-TDDI calculated by weight(0.5xweight);F3-obtained by 90% of the mean of F1 and F2 ([F1 + F2]/2x0.9).
Results
Of the 62 individuals who started treatment, 52 were included(30[57.7%] women; median age 39 years [minimum-maximum:19–70 years]), with a mean of 22 ± 13.28 years of disease progression. At T3 M, the median %TIR was 63.5%(IQR 24%), the median %TAR 32%(IQR 31), the median %TBR 3%(IQR 6) and the median HbA1c 7.1%(IQR 1.3). The median TDDI at T3 M was 42 UI (IQR 21.5UI) and was similar to TDDI at T0 by F1(40.5UI[IQR 19.2], $P=0.723$) but with a significantly lower percentage of basal insulin(38%vs.49.3%, $P<0.001$). The median TDDI at T3 M was significantly superior than TDDI obtained by F2(42UI[IQR 21.5UI]vs.32.5UI[IQR 12.3], $P<0.001$) and by F3(34.1UI[IQR 13.3], $P<0.001$). In the 19 patients with %TIR > 70% at T3 M, the median TDDI at T3 M was not different from the TDDI at T0 calculated by F1($P=0.268$) and F2($P=0.427$), but major differences were found comparing with F3(37.0UI[IQR 23.8]vs.29.4[IQR 12.2], $P=0.05$).
Conclusion
The TDDI in use 3 months after the beginning of an insulin pump in this work was quite similar to the mean TDDI of the 7 days preceding the starting of this treatment. This result was similar in patients with TIR above or below 70% at T3 M. The main difference at T3 M was the percentage of basal insulin which decrease significantly from almost 50% to 40%. These results suggest that the mean TDDI of the 7 days preceding the starting of this treatment can be the best option to begin the insulin pump.

DOI: 10.1530/endoabs.81.P573

P574

Impact of whatsapp based Communication on insulin adherence and glycemic control in patients with Diabetes in Indian population

Bharat Saboo[1], Abhishek Shrivastav[2], Banshi Saboo[3] & Aniket Inamdar[4]
[1]Prayas Diabetes Center, INDORE, India; [2]R R Hormone Clinic, Jabalpur, India; [3]Dia Care - Diabetes Hormone Clinic, Ahmedabad, India; [4]Samarpan Clinic, Omerga, India

Introduction
Diabetes treatment requires the involvement of people with diabetes in the form of medication adherence. Insulin treatment is an important aspect of diabetes therapy. Regular and timely insulin therapy is necessary for good glycaemic control and complications prevention. Newer follow-up techniques, such as WhatsApp based communication are now finding their way into diabetes care and treatment. It can assist diabetes patients to maintain a regular treatment schedule and drug adherence.
Materials and Methods
A total of 342 Diabetic patients aged 15–65 years were selected by random sampling. Inclusion Criteria : 1. Known case of Diabetes mellitus 2. Consent to take part in study. 3. Ability to use WhatsApp messaging Exclusion criteria: 1. Inability to use WhatsApp 2. Not consenting to be a part of the study. They were randomly allocated to two groups of 171 people each. In the first group, the participants were added to a WhatsApp group and were asked to regularly answer a question about whether they have taken insulin or not on that particular day to the clinic over WhatsApp. The other group was treated as usual. The participants were monitored for HBA1C and insulin adherence at 3 and 6 months. The results were analysed using SPSS.
Result
After excluding 4 droupouts the analysis of data shown : HBA1C reduction in the WhatsApp group was 1.8 % as compared to 0.8 % in the routine care group. At the end of 3 months and was 2.3 % in the WhatsApp group and 1.3 % at the end of 6 months. The number of patients achieving the target goal of 7% HBA1C was better in the WhatsApp group (54%) as compared to the routine group (38%) at the end of 3 months and in the WhatsApp group (72%) as compared to the routine group (53%) at the end of 6 months. 82 % of patients in the WhatsApp group were insulin compliant compared to 63 % in the routine group.
Discussion
The strategies and means of communicating with patients have improved with the emergence of modern modes of communication. This has paved the door for the development of innovative messaging systems such as WhatsApp that enable more patient-centric communication. When utilized properly, these tools can help

reduce in-person follow-ups while increasing the connection between caregiver and patient. Additionally, this can result in improved patient outcomes, as well as fewer complications and financial repercussions.

DOI: 10.1530/endoabs.81.P574

P575

Maturity-onset diabetes of the young in a large portuguese cohort

Sílvia Santos Monteiro[1], Liliana Fonseca[1], Tiago S. Santos[1], Guilherme Assunção[1], Ana M. Lopes[1], Diana B. Duarte[1], Ana Rita Soares[2], Francisco Laranjeira[3], Maria João Oliveira[4], Teresa Borges[4] & Maria Helena Cardoso[1]

[1]Centro Hospitalar Universitário do Porto, Department of Endocrinology, Diabetes and Metabolism, Porto, Portugal; [2]Centro Hospitalar Universitário do Porto, Department of Medical Genetics, Porto, Portugal; [3]Centro Hospitalar Universitário do Porto, Department of Genetic Biochemistry, Porto, Portugal; [4]Centro Hospitalar Universitário do Porto, Department of Pediatric Endocrinology, Porto, Portugal

Introduction

Monogenic forms of diabetes that develop with autosomal dominant inheritance are classically aggregated in the maturity-onset diabetes of the young (MODY) categories. Despite increasing awareness, its true prevalence remains largely underestimated.

Aim

o evaluate the clinical and molecular characteristics of patients with MODY.

Methodology

This single-center retrospective cohort study enrolled patients with positive genetic testing for MODY between 2015 and 2021, followed at our Pediatric and Adult Endocrinology Outpatient Clinic. Clinical and molecular characteristics were described.

Results

Eighty-two patients were included, mostly female (51.2%), with a median age at diabetes diagnosis of 23 years (interquartile range [IQR] 23). The most frequent mutation was in the *HNF1A* gene (43.9%, $n=36$), followed by *GCK* (32.9%, $n=27$), *HNF4A* (12.2%, $n=10$), *HNF1B* (4.9%, $n=4$), *PDX1* (2.4%, $n=2$), *INS* (2.4%, $n=2$) and *APPL1* (1.2%, $n=1$). The mean number of family generations affected was 2.3 ± 0.7. The following table summarizes the main characteristics of the four most frequent types of MODY within our sample:

Conclusion

Mutations of *HNF1A* gene were the most common within our cohort, followed by *GCK*. This study highlights the need to increase accuracy in the diagnosis and characterization of monogenic forms of diabetes. This strategy may contribute to a better understanding of this type of diabetes and a more personalized clinical management and follow-up of these individuals and their families.

Table 1

MODY	Age at diagnosis years)**	Symptoms of insulin deficiency	Kidney malformations	Non-insulin hypoglycaemic agents	Insulin	HbA1c at diagnosis (%)*	C-peptide (ng/ml)**	Atual HbA1c (%)*	Follow-up (months) **	Diabetes-related complications
HNF1A	30 (23)	5.6%	None	75%	30.6%	8.7±2.5	1.7 (1.46)	7.1±0.9	27 (115)	27.8% microvascular 8.3% macrovascular
GCK	10 (8)	None	None	22.2%	None	6.2±0.4	1.4 (0.7)	6.2±0.4	15 (41)	None
HNF4A	22 (29)	10%	None	50%	20%	6.1±1.6	1.1 (0.7)	6.1±0.8	17 (62)	20% microvascular 10% macrovascular
HNF1B	11.5 (13)	50%	100%	None	75%	6.8±1.5	2.6	6.9±1.4	36.5 (173)	50% microvascular

*Results shown in mean ± standard deviation
**Results shown in median (interquartile range)

DOI: 10.1530/endoabs.81.P575

P576

Ketosis prone type 2 diabetes in covid times - a missing link?

Bhavna Sharma & Mushtaqur Rahman
Northwick Park Hospital, United Kingdom

Traditional literature agrees that Diabetic Ketoacidosis is typically associated with Type 1 Diabetes Mellitus, but can be associated with stress including infections in Type 2 diabetics. The authors did a restrospective evaluation of diabetic ketoacidosis presenting to a large district hospital in London. 343 patients were admitted with diagnosis of Diabetic Ketoacidosis during the COVID peaks from January 2020 to January 2021. 57% of these were Type 1 diabetics and 43% were found to be Type 2 diabetics. 23% of the patients admitted with Type 2 diabetes and DKA did not have a previous presentation with ketosis. 68% of both Type 1 and Type 2 diabetics tested negative for COVID 19 on first/second swab (accounting for hospital exposure). 56% of Type 2 diabetics with DKA tested positive for COVID-19 on first/second swab. 32% of Type 2 diabetics were new diagnosis of diabetes. Initial studies agreed a significant increase in ketosis prone DKA in Type 2 diabetics during COVID times however were unable to establish a clear correlation with COVID infection. Our Initial studies did suggest a possible extrapolation with widespread vaccination of a possible emerging cohort of ketosis prone type 2 diabetes. We therefore evaluated the incidence of ketosis prone type 2 DKA in vaccinated individuals with a total of 178 admissions with diabetic ketoacidosis evaluated between August 2021 and December 2021. 58.7% of patients admitted with diabetic ketoacidosis were Type 2 diabetics. 23% of patients presenting with diabetic ketoacidosis were new diagnosis of diabetes (19% Type 1 Diabetes). An overall increase in monthly admissions over five months was noted when compared to previous one year evaluated was noted. The authors suggest that exposure/immunity to COVID 19 may be a contributing factor to increase in ketosis prone diabetic ketoacidosis. Several etiologies may be suggested including viral destruction of beta cells in patients with widespread subclinical infection or possible role of antibodies in vaccinated individuals. More research is needed for the same particularly with emergence of variants and widespread vaccination as this has potential to change the understood epidemiology of Type 2 Diabetes.

DOI: 10.1530/endoabs.81.P576

P577

Covid-19, Dexamethasone and Diabetes(CODED) study: a single centre experience

Noha Meneissy, Scott Waring, Umme Farhana, Sarah Kasigwa, Yishan Wang, Tasfia Rashid, Sohee Kim, Shanta Paul, Htet Myat Hlaing,

Sukuta Darego, Sadia Siddika, Olga Nachas, Lamis Fahal, Bashir Mahamud & Gideon Mlawa
Queen's Hospital, Romford, United Kingdom

Coronavirus (COVID-19) caused by severe acute respiratory syndrome (SARS)-CoV-2, which leads to multi-organ disease. Covid-19 high mortality and morbidity arising from autoimmune destruction of the lungs due to pro-inflammatory cytokines storm, has enabled worldwide collaborative studies aimed at elucidating potential management strategies in order to overcome pandemic. The RECOVERY trial, a multi-centred trial involving 175 United Kingdom based hospitals. The results from this trial revealed that using dexamethasone lowered 28-day mortality rate for patients receiving either invasive mechanical ventilation or oxygen but had no effect on patients not receiving respiratory support. Using dexamethasone can cause manifestation of hyperglycaemia or induce Diabetes mellitus in previously non-diabetic patients. In the present study, we looked at 100 patients (both diabetics and non-diabetics) with COVID 19 on dexamethasone and we monitored their glucose levels.
Aims
1. To assess doctors' and nurses' knowledge of dexamethasone related hyperglycaemia and diabetes.
2. To assess doctors' awareness of guidelines for management of patients with COVID-19 who started on dexamethasone and whether they were using it.
3. To assess if patients who had hyperglycaemia and/or hyperglycaemia related complications were seen by diabetes team when appropriate
4. To improve doctors and nurses' awareness of proper management of patients with COVID-19 who need to be started on dexamethasone
Methods
Retrospective analysis of paper notes, case notes & electronic records of patient reported outcome (EPRO). Single centre study 100 randomly selected patients with RT-PCR COVID-19 treated with dexamethasone admitted to Queens hospital.
Results
100 COVID-19 positive given dexamethasone treatment. 18 patients were known T2DM, 82 were non-diabetic. Of the 100 patients, only 87 had regular glucose monitoring, 67 had monitoring as per BHRUT guidelines. Out of the monitored patients (87) 30 patients had hyperglycaemia which was more frequent in T2DM patients (9; 50%). Of those who developed hyperglycaemia 11 (37%) patients had their hyperglycaemic episodes treated as per national guidelines and 10 diabetic patients (56%) with T2DM required up titration of their medications. One of non-diabetic patients started on insulin.
Discussion/conclusion
Dexamethasone can be associated with hyperglycaemia in non-diabetic and known diabetic mellitus increasing their mortality and morbidity risk. Thus, it is important that these patients be monitored and managed according to national and local guidelines. Therefore, we intend to create new proformas to keep doctors and nurses up to date with the guideline of management of COVID 19 patients on dexamethasone.

DOI: 10.1530/endoabs.81.P577

P578

Inflammatory markers in patients with type 1 diabetes and diabetic kidney disease

Aleksejs Fedulovs[1], Kaspars Jekabsons[1], Lıga Kunrade[1], Irena Puzirevska[1], Inese Folkmane[1,2] & Jelizaveta Sokolovska[1]
[1]University of Latvia, Faculty of Medicine, Riga, Latvia; [2]Pauls Stradins Clinical University Hospital, Riga, Latvia

Background
Inflammation is involved in the pathogenesis of complications of type 1 diabetes (T1DM). We aimed to assess the differences in the markers of endotoxaemia and faecal calprotectin in patients with T1D different status of diabetic kidney disease (DKD).
Methods
31 generally healthy adults (control) and 74 patients with T1DM and were included. Of the latter, 13 had DKD (defined as microalbuminuria, macro-albuminuria, estimated glomerular filtration rate (eGFR) below 60 ml/min/1.73^2, end stage kidney disease). In serum, lipopolysaccharide (LPS) activity was measured by Limulus Amebocyte Lysate assay, lipopolysaccharide binding protein (LPB), endogenous anti-endotoxin core antibodies (EndoCAb IgG and IgM), high sensitivity C reactive protein (hsCRP) and faecal calprotectin were measured by ELISA.
Results
The mean age in the T1D group was 42.3 ± 15.2 years and in the healthy participant group 37.3 ± 10.6 years. In the T1D group, the mean diabetes duration was 23.1 ± 12.2 years, the mean HbA1c was 8.2 ± 1.9%. Patients with and without DKD did not differ in age, anthropometric measures, prevalence of cardiovascular hard endpoints. Patients with DKD had longer T1D duration ($P = 0.04$); higher prevalence of arterial hypertension ($P = 0.08$); severe retinopathy ($P = 0.010$); end-stage renal disease ($P = 0.029$), and previous gastrointestinal surgery ($P = 0.02$). The levels of EndoCAb IgG and IgM did not differ between T1D and control. Compared to control group, patients with T1D had statistically significantly lower LPS (LPS: T1D 0.23 ng/ml (0.22;0.31) control 0.38 ng/ml (0.32;0.56), $P = 0.009$) and hsCRP (T1D 894.57 ng/ml (1255.91; 1990.92), control 313.29 ng/ml (368.82; 1173.07), $P = 0.01$). LPB was higher in T1D, compared to control, but the difference did not reach statistical significance (T1D: 11444.50 ng/ml (11076.45;13058.45), control 9776.60 ng/ml (8991.34; 12911.32)). None of the markers differed between DKD groups. The level of calprotectin did not differ neither between controls and T1D, nor between T1D patients with and without DKD. Within patients with T1D and DKD, LPS correlated positively strongly with serum creatinine and albuminuria; LPB correlated with HbA1c. In the whole cohort, LPS correlated weakly positively with faecal calprotectin.
Conclsions
In patients with T1D and DKD, markers of serum inflammation are associated with kidney function and HbA1c.
Acknowledgements
Postdoctoral project Nr. 1.1.1.2/VIAA/3/19/525 'Intestinal inflammation as a potentially modifiable risk factor for complications in type 1 diabetes' and a grant in Biomedicine and Pharmacy 'Research of biomarkers and natural substances for acute and chronic diseases' diagnostics and personalized treatment' by the University of Latvia. MikroTik donation administered by Foundation of the University of Latvia.

DOI: 10.1530/endoabs.81.P578

P579

Association between clinical and genetic factors and glycemic and weight loss response to liraglutide in patients with type 2 diabetes

Artemis Kyriakidou[1], Angeliki V. Kyriazou[1], Theocharis Koufakis[1], Yiannis Vasilopoulos[2], Maria Grammatiki[1], Eirini Mellidou[1], PANTELITSA RAKITZI[1], Georgios Karaliolios[1], Dimitrios Goulis[3], Pantelis Zebekakis[1] & Kalliopi Kotsa[1]
[1]AHEPA University Hospital, Division of Endocrinology and Metabolism - Diabetes Center, 1st Department of Internal Medicine, Medical School, Aristotle University of Thessaloniki, Thessaloniki, Greece; [2]University of Patras, Department of Biology, Section of Genetics, Cell Biology and Development, Patras, Greece; [3]Medical School, Aristotle University of Thessaloniki, Unit of Reproductive Endocrinology, 1st Department of Obstetrics and Gynecology, Thessaloniki, Greece

Background
Previous research suggests an association between specific genetic variations and interindividual variability in response to treatment with glucagon-like receptor agonists (GLP-1 RAs) in patients with type 2 diabetes mellitus (T2DM). We aimed to evaluate the role of *CTRB1/2* rs7202877 (T > G) polymorphism in glycemic control and weight loss response to liraglutide among Greek patients with T2DM and to identify clinical factors related to prediction of response to liraglutide administration.
Methods
The medical records of 116 adults with T2DM [51% female, mean Body Mass Index (BMI) 35.4 ± 6.4 kg/m^2], who had been on treatment with liraglutide for at least 6 months and were genotyped for *CTRB1/2* rs7202877 (T > G) polymorphism, using real-time PCR, were evaluated. Clinical and laboratory parameters were measured at baseline, 3 and 6 months after initiation of liraglutide treatment. The good glycemic response was defined as one of the following: i) achievement of glycated hemoglobin (HbA_{1c}) < 7%, either at 3 or 6 months after treatment initiation ii) reduction of the baseline HbA_{1c} by ≥ 1% after

3 or 6 months of liraglutide use, and iii) maintenance of HbA_{1c} <7% that a patient had before switching to liraglutide, after 3 or 6 months of treatment. Weight loss responders were defined as subjects who lost ≥3% of their baseline weight after 3 or 6 months of liraglutide administration.
Results
97 (84%) patients were homozygous for the wild type rs7202877 T allele (TT) and 19 (16%) patients carried one polymorphic G allele (TG). 81 (70%) and 77 (66%) individuals were classified as glycemic control and weight loss responders, respectively. Heterozygotes had similar responses to liraglutide treatment in terms of glycemic control [odds ratio (OR): 1.25, 95% confidence interval (CI): 0.4, 3.8, $P=0.69$] and weight loss (OR: 1.12, 95% CI: 0.4, 3.2, $P=0.84$). In the multivariable analysis, higher baseline HbA_{1c} (adjusted OR: 1.45, 95% CI: 1.05, 2.1, $P=0.04$) and lower baseline weight (adjusted OR: 0.97, 95% CI: 0.94, 0.99, $P=0.01$) were associated with better glycemic response to liraglutide, while higher baseline weight was associated with worse weight response (adjusted OR: 0.97, 95% CI: 0.95, 0.99, $P=0.02$). Both glycemic responders and non-responders demonstrated a significant reduction in weight and BMI from baseline to 6 months ($P<0.0001$). Both weight responders and non-responders significantly reduced HbA_{1c} after administration of liraglutide ($P<0.0001$ and $P=0.008$, respectively).
Conclusion
Specific patient features can predict glycemic and weight loss response to liraglutide in patients with T2DM.

DOI: 10.1530/endoabs.81.P579

P580

Hypoglycemia and impared hypoglycemia awareness: frequency and relevance in type 1 diabetes under continuous subcutaneous insulin infusion

MafaldaMartins Ferreira, Ana Carreira, Inês Vieira, Luísa Barros, Miguel Melo, Dírcea Rodrigues, Patrícia Oliveira, Carla Baptista, Carolina Moreno & Isabel Paiva
Centro Hospitalar e Universitário de Coimbra, Endocrinologia, Diabetes e Metabolismo, Coimbra, Portugal

Introduction
Continuous subcutaneous insulin infusion (CSII) therapy in type 1 diabetes (T1D) reduces the risk of hypoglycemia. Hypoglycemia remains a treatment-limiting factor. Impared hypoglycemia awareness (IHA) occurs in 25% of T1D cases and seems to be underestimated by continuous glucose monitoring (CGM). Glycemic variability (GV) is a increasingly valued parameter as a predictor of hypoglycemia and risk of chronic complications.
Objective
Analysis of the relationship between impared hypoglycemia awareness (IHA) and new metrics of glycemic control [estimated A1C (A1Ce), time in hyper- and hypoglycemia, GV] in T1D patients on CSII and CGM.
Methods
Cross-sectional, observational study of patients with T1D under CSII and intermittent-scanning GCM FreeStyle Libre® (active >70% of the time). Glycemic control assessed by the 30-day GCM (AGP report). IHA was defined by a score ≥4 on the Clarke Questionnaire (CQ).
Results
43 cases were analyzed: 61.5% were female; mean age of 33.3±12.7 years. Mean onset of CSII at 26.9±12.2 years. The mean duration of T1D was 20.5±9.3 years. The mean A1Ce was 7.1±0.7% and glycemic variability was 39.3±8.0%. The time spent in hyperglycemia was 35.2±18.7% (8.5 hours/day): 24.0±11.5% between 180–250 mg/dl and 11.2±9.4% above 250 mg/dl. Time spent in hypoglycemia was 7.0±5.9% (1.7 hours/day): 4.6±3.3% between 54–70 mg/dl (level 1) and 2.4±3.2% <54 mg/dl (level 2). From the Clarke Questionnaire, we obtained a prevalence of 14.3% of IHA and 9.3% of ≥1 level 3 hypoglycemia per year. There was a moderate to strong correlation between glycemic variability and time in hypoglycemia ($r=0.72$; $P<0.001$), as opposed to time in hyperglycemia which showed no significant correlation ($P=0.41$). GV did not show correlation with T1D duration but approached statistical significance ($P=0,06$). In patients with A1Ce < 7% medians of time in hypoglycemia were significantly higher – 7.0(4)% vs 3.0(3)%. Impared hypoglycemia awareness occurred in patients with lower A1Ce values (6.9±0.7% vs 7.2±0.7%) but without significant difference. There was no significant difference in time in hypoglycemia at 30 days in these cases.
Conclusion
Hypoglycemia occurred in a higher frequency than the goals especially for more demanding glycemic controls, correlating with the increase in glycemic variability (GV). GV was higher than desirable in most cases, underlining the difficulty of its optimization. Impared hypoglycemia awareness in this population had a lower prevalence than the overall estimated prevalence in T1D and did not show a significant correlation with the GCM data, highlighting the complexity of its pathophysiology and its possible undervaluation by glycemic control metrics.

DOI: 10.1530/endoabs.81.P580

P581

Comparing global rating scores from simulation-based diabetes and endocrine scenarios between healthcare professionals of high- and low- and middle-income countries

Zakee Abdi[1,2], Dengyi Zhou[3], Kashish Malhotra[4], Anisah Ali[3], Jameela Sheikh[3], Pavithra Sakthivel[3], Emily Warmington[3], Carina Synn Cuen Pan[3], Wentin Chen[3], Harjeet Kaur[3], Rachel Nirmal[3], Vina Soran[3], Isabel Allison[3], Nia Evans[5], Dwi Delson[6], Meri Davitadze[7], Punith Kempegowda[3,8] & Simba Simulation[3,8]
[1]Medical University of Plovdiv, Plovdiv, Bulgaria; [2]School of Medicine, Barts and The London School of Medicine and Dentistry, Queen Mary University of London, London, UK; [3]College of Medical and Dental Sciences, University of Birmingham, Birmingham, UK; [4]Dayanand Medical College and Hospital, Punjab, India; [5]Royal Glamorgan Hospital, Cwm Taf Morgannwg University Health Board, Rhondda Cynon Taff, UK; [6]School of Medicine, University of Dundee, Dundee, UK; [7]Georgian-American Family Medicine Clinic 'Medical House', Tbilisi, Georgia; [8]Institute of Metabolism and Systems Research, College of Medical and Dental Sciences, University of Birmingham, Birmingham, UK

Background
Simulation via Instant Messaging - Birmingham Advance (SIMBA) is an online simulation learning modality designed to recreate clinical scenarios, allowing participants to increase their confidence in a safe environment without compromising patient safety. The global rating scale (GRS) is a commonly used assessment tool in medical schools to assess participant competence and skills. Following SIMBA sessions, an independent assessor anonymously scores participants' performance of their simulated case using an adapted version of the GRS.
Objective
To study the pattern of GRS score across various domains of endocrine scenarios and the variation by country of residence.
Methods
We included all diabetes and endocrine SIMBA sessions conducted from July 2020 to October 2021. The participants' responses were divided into various domains and each domain was scored from 1 (poor) to 5 (excellent). Data were pooled during analysis and findings are reported as frequencies. Chi-square test was used to compare the differences between participants' performance across various domains. Participants were further grouped by the country's income according to the country of residence based on the 2022 World Bank Report: high-income countries (HICs) and low- and middle-income countries (LMICs).
Results
293 healthcare professionals participated in six SIMBA sessions (thyroid, pituitary, diabetes, metabolic bone, gonadal, and diabetic microvascular complications). The median (IQR) GRS scores for domains are as follows: history-taking: 4.0 (3.0–5.0), physical examination: 4.0 (3.0–4.6), investigations requested: 3.3 (3.0–4.0), results' interpretation: 2.6 (1.6–3.3), clinical judgement: 3.3 (2.6–4.0) and management and follow-up: 2.6 (2.0–3.3). HICs and LMICs (31.2%, $n=91$) scored similarly in history-taking (HIC: 3.81 vs LMIC: 3.79;$P=0.05$), physical examination (HIC: 3.67 vs LMIC: 3.68;$P=0.19$), investigations requested (HIC: 3.35 VS LMIC: 3.33;$P=0.27$), and results' interpretation (HIC: 2.63 vs LMIC: 2.61;$P=0.74$). HICs scored better in clinical judgement (HIC: 3.23 vs LMIC: 3.18;$P=0.008$) and providing management and follow-up plans (HIC: 2.66 vs LMIC: 2.64;$P=0.001$).
Conclusion
All participants, particularly those from LMICs, scored lower in the categories of investigations, clinical judgement, and management skills. This demonstrates the need for targeted educational programmes which can be both cost-effective and beneficial to all participants independent of country of residence.

DOI: 10.1530/endoabs.81.P581

P582

Diabetic foot association with premature cardiovascular mortality in a single centre prospective of study of people with diabetes

Dragan Tesic[1], Dragica Andric[2], Miroslav-Tomislava Tomic[3], Stefan Andric[4] & Mirjana Tomic[5]
[1]Clinics of Internal Diseases, Clinic of Endocrinology, Diabetes and Metabolic Disorders, Novi Sad,; [2]Institute for Cardiovascular Diseases, Clinic of Cardiology, Sremska Kamenica, Serbia; [3]Intiturte for Surgery, Clinic for Plastic Surgery, Novi Sad,; [4]Institut for Cardiovascular Diseases, Clinic of Cardiology, Sremska Kamenica,; [5]Clinics of Internal Diseases, Clinic of Hematology, Novi Sad

Background and aims
In many developing countries, diabetic foot is considered as a problem only when the patient develops a wound on the foot. Until that moment, the detection of changes in the neurovascular condition of the feet is rarely applied. The aim of this prospective, single centre study was to define factors associated with early cardiovascular mortality in diabetes.
Materials and methods
1345 patients under age 75 were included who were undergoing assessment of their diabetes between January 2008 and May 2010 as part of standard practice in a specilaist clinic at a regional teaching hospital in Serbia. Peripheral artery disease (PAD) and peripheral neuropathy was assessed. Evidence of other comorbidities was also collected. Outcome was determined in 2021 and baseline characteristics were compared between those who had and had not suffered cardiovascular death under age 75 years within 10 years of review in two casually selected cohorts.
Results
Those who died ($n2=70$) were more frequently male (60 vs. 45.3%, $P=0.08$), younger (66.4 $\pm$ 7.4 vs. 79.9 $\pm$ 3.4, $P<0.000$), had a shorter period of follow-up (3.6 $\pm$ 2.3 vs. 11.2 $\pm$ 1.7 years, $P<0.000$) when compared to those still alive ($n1=75$). Those who died were also significantly ($P<0.01$) more likely to have had PAD (48.6 vs. 9.3%), diabetic foot ulcer (25.7 vs. 9.3%), major amputation (17.1 vs. 1.3%) at baseline. Minor amputations were significantly more likely (8.6 vs. 1.3%, $P<0.04$). Following multivariable logistic regression analysis significant differences between groups remained for only creatinine (123 $\pm$ 45 vs. 88.9 $\pm$ 16.9 mmol/l, $P<0.003$) and vibration perception threshold <5 (7.8 [95% CI: 3.7-16.4)], $P=0.008$), estimated maximum lifetime BMI (3.4 [95% CI: 1.7-6.8)], $P<0.000$), alcohol usage (4.7 [95% CI: 1.5-14.7)], $P=0.005$), smoking habit (2.2 [95% CI: 1.1-4.3)], $P<0.03$) and earlier age of diabetes onset (43.4 $\pm$ 12.5 vs. 49.2 $\pm$ 9.9, $P=0.0029$). When the 72 patients with impaired vibration sense were compared with 73 with VPT >6 and there were significant differences in and PAD (3.9 [95% CI: 1.8-8.8)], $P<0.001$) and estimated maximum lifetime BMI (9.4 [95% CI: 3.4-25.7), $P<0.000$). Those who had had a previous MI at baseline ($n=46$) was associated with increased death rate (3.2[95% CI: 1.5-6.6)], $P=0.002$) and PAD (2.9[(1.3-6.1)], $P=0.007$).
Conclusion
Decreased VPT, the presence of PAD on clinical testing and higher maximum estimated lifetime BMI are strongly associated with premature cardiovascular death. Early detection of independent markers of greater risk of reduced life expectancy might improve management of their diabetes.

DOI: 10.1530/endoabs.81.P582

P583

Waist-to-height ratio is a predictor of weight loss with Gelesis200 treatment for people with overweight or obesity having prediabetes or type 2 diabetes in the LIGHT-UP study

Livio Luzi[1], Frank Greenway[2], Sam Miller[3], Erika Matejkova[4], Barry McLean[5], Witold Zmuda[6], Pawel Bogdanski[7], Malgorzata Arciszewska[8], Anders Sjödin[9], Judith Salz[10], Anna Bochenek-Mularczyk[11], Lorena Lewy-Alterbaum[12], Michael Butcher[13], Gyorgy Paragh[14], Yvonne Davis[15], John Wilding[16], Howard Golub[17], Harry Leider[18], Yishai Zohar[18], Alessandro Sannino[18], Henry Calderon[18] & Hassan Heshmati[18]
[1]University of Milan, Milan, Italy; [2]Pennington Biomedical Research Center, Baton Rouge, Louisiana, United States; [3]SAM Clinical Research Center, San Antonio, Texas, United States; [4]Health & Care, sro, Prague, Czech Republic; [5]Central Alabama Research, Birmingham, Alabama, United States; [6]Medicome Sp z o o, Oswiecim, Poland; [7]Poznan University of Medical Sciences, Poznan, Poland; [8]NZOZ Specjalistyczny Osrodek Internistyczno - Diabetologiczny, Bialystok, Poland; [9]University of Copenhagen, Frederiksberg C, Denmark; [10]Wake Research - Clinical Research Center of Nevada, LLC, Las Vegas, Nevada, United States; [11]Centrum Badawcze Wspolczesnej Terapii, Warszawa, Poland; [12]ALL Medical Research, LLC, Cooper City, Florida, United States; [13]Sterling Research Group, Ltd, Cincinnati, Ohio, United States; [14]Debreceni Egyetem Klinikai Kozpont, Debrecen, Hungary; [15]Coastal Carolina Research Center, North Charleston, South Carolina, United States; [16]Aintree University Hospital, Liverpool, United Kingdom; [17]Care-Safe LLC, Boston, Massachusetts, United States; [18]Gelesis, Inc, Boston, Massachusetts, United States

Introduction
Methods to predict clinically meaningful weight loss can help tailor treatment for people with overweight or obesity. LIGHT-UP (NCT03058029), is a multicenter, double-blind, randomized, placebo-controlled study over 25 weeks including 254 people with prediabetes or type 2 diabetes (127 each in the Gelesis200 and placebo arms) with a body mass index between 27 and 40 kg/m^2, which demonstrated that Gelesis200 offers a compelling new potential approach in the management of overweight and obesity. A stepwise logistic regression analysis was conducted on data from the LIGHT-UP study to identify variables at baseline that reliably predict body weight (BW) Responders and Super-Responders ($\leq$ 5% BW loss and $\leq$ 10% BW loss, respectively, from baseline at Week 25).
Methods
Two stepwise logistic regression analyses were conducted for each study arm (Gelesis 200 placebo). The dependent variables were the percentage of participants who were Responders and Super-Responders. The independent baseline variables included in the models were the ones hypothesized to potentially predict BW loss at Week 25 [e.g., gender, age, BW, body mass index, height, waist circumference, waist-to-height ratio (WHR), fasting plasma glucose, and fasting serum insulin].
Results
After WHR was included in the model, there were no other variables that were significant in the prediction of Responders or Super-Responders. The final regression model shows that for a 0.1 change in the WHR (e.g., from 0.6 to 0.7), the probability for a Responder increases from 53% to 66%, and the probability for a Super-Responder increases from 24% to 39%. For a 0.2 change in the WHR (e.g., from 0.6 to 0.8), the probability for a Responder increases from 53% to 78%, and the probability for a Super-Responder increases from 24% to 56%. None of the independent variables was a significant predictor of Responders or Super-Responders in the placebo arm.
Conclusion
The results of this study suggest that a higher baseline WHR is predictive of an increased rate of Responders and Super-Responders. It is well known that WHR is strongly correlated with fat mass and insulin resistance. With respect to weight loss, it can be speculated that Gelesis 200 is more effective in people with higher insulin resistance. If the findings of the LIGHT-UP study are replicated in larger clinical studies, baseline WHR would become a simple tool for clinicians to identify individuals likely to achieve meaningful weight loss on Gelesis200.

DOI: 10.1530/endoabs.81.P583

P584

Gastroesophageal lesions after bariatric surgery: a controlled study

Catarina Ivo, David Veríssimo, Vitória Duarte, Ana Cláudia Martins, João Silva, Luís Lopes, Dolores Passos, João Jácome Castro & Mafalda Marcelino
Armed Forces Hospital - Lisbon, Endocrinology Department, Lisboa, Portugal

Introduction
Obesity is a multifactorial and chronic disease. Bariatric surgery (BS) is the most effective treatment. A prevalence of 45% of esophagitis and 40%-70% of gastritis after BS has been reported. We analysed the presence of gastroesophageal lesions in patients who underwent BS (By-pass Roux-en-Y(BP) and gastric sleeve(GS)) in our centre.
Methods
Patients submitted to BS between 2018-2020 were included. We retrospectively analysed clinical data, upper gastrointestinal endoscopy (UGE) and histologic results preoperatively and 12 months(M) after surgery. All patients underwent UGE and helicobacter pylori(HP) was eradicated if present. Protons pump inhibitors (PPI) were prescribed to all patients, until 6 M post-op. and maintained if upper gastric

symptoms(UGS). Endoscopic esophageal and gastric lesions were categorised based on Los Angeles and Sydney classification.
Results
32 patients (56% males) were included with mean age of 52±8.5 years-old and BMI of 41±4.4 kg/m^2. Mean follow-up was 29.4±9.3 M. 71.9% patients performed BP and 28% GS. At pre-op.:53% had positive HP, 21.9% had UGS and 21% were on PPI treatment. Class A or B esophagitis was diagnosed in 15.7% and erythematous gastritis in 78% of patients. Histologic results confirmed gastritis in 68.8%. 12 M after BS patients had a mean BMI of 28±3.7 kg/m^2 and 81.3% had no UGS. UGE revealed a total of class A or B esophagitis of 25%, in which 75% of the cases was "*de-novo*" lesion (83% submitted to GS and 33% had UGS). A significant reduction in erythematous gastritis was achieved in the corpus (18.8%; $P=0.05$) but not in the antrum (25%;$P=0.22$). 15.6% presented with "*de-novo*"ulcer (all of them underwent BP). Biopsy confirmed gastritis in 43.7%($P=0.85$). 1 case of Barrett's esophagus was diagnosed but no cases of dysplasia. No significant association was found between histologic result($P=0.537$) or PPI use ($P=0.654$), and BS procedure.
Conclusion
This study illustrates the importance of endoscopic follow-up of patients after BS, even if no UGS are present. After 12 M esophagitis was more prevalent, suggesting it was appropriate to maintain PPI use, in particular in those submitted to GS. A tendency to reduction was identified in gastric lesions.

DOI: 10.1530/endoabs.81.P584

P585

Improvements in physiological and psychological status of patients with obesity in response to a combined lifestyle intervention with cognitive behavioral therapy are not necessarily related to successful weight loss

Mostafa Mohseni[1], Susanne Kuckuck[1], Renate Meeusen[1], Robin Lengton[1], Eline van der Valk[1], Anand M. Iyer[1], Corjan de Groot[2], Sjoerd van den Berg[3] & Elisabeth F.C. van Rossum[1]
[1]Erasmus MC, University Medical Center Rotterdam, Internal Medicine, Division of Endocrinology, Rotterdam, Netherlands; [2]Erasmus MC, University Medical Center Rotterdam, Obesity Center CGG, Sophia Children's Hospital, Department of Pediatric Endocrinology, Rotterdam, Netherlands; [3]Erasmus MC, University Medical Center Rotterdam, Department of Clinical Chemistry, Rotterdam, Netherlands

Background
Obesity (BMI $\leq$ 30 kg/m^2) is a chronic and relapsing disease, associated with numerous co-morbidities. Lifestyle intervention is the cornerstone of treatment of obesity, and is considered effective when weight loss of $\leq$ 5% is achieved. Here, we describe changes in physiological, psychological and behavioral health outcomes in response to a multidisciplinary combined lifestyle intervention (CLI).
Methods
In this longitudinal study we evaluated 97 adult subjects with obesity (74 women; mean age: 42 years; mean BMI: 40.1 kg/m^2). The 1.5 year CLI comprised physical activity, cognitive behavioral therapy and dietary advise tailored to promote a healthy normocaloric diet. We measured changes in physiological health (anthropometrics, metabolic and immune parameters), and used questionnaires to assess psychological health (HADS, SCL-90, PSS, FNAES, RSE), quality of life (IWQoL-Lite), eating behavior (DEBQ, EDE-Q, FCQ-T) and physical activity (IPAQ). In a subset of participants, DEXA-scans ($n=37$) were also performed to assess body composition. Linear regressions were used to investigate the association between weight loss and changes in physiological and psychological health outcomes, corrected for sex and age.
Results
After 1.5 years, there was a mean 5.1% weight loss ($P<.001$) along with a 6.1% decrease in waist circumference ($P<.001$). Total fat mass (-9.8%) and abdominal fat (-13.9%) decreased (both $P<.001$), while fat free mass did not. Fasting insulin, HOMA-IR, HbA1c, triglycerides and LDL-C decreased significantly (all $P<.01$), and HDL-C increased ($P<.05$). Levels of the immune parameters IL1ra, VEGF, sIL2R, sMR decreased (all $P<0.05$). Moreover, HADS scores ($P<.01$) and SCL-90 total score ($P<.05$) decreased, indicating lower psychological symptomatology. IWQoL-Lite scores were increased at 1.5 years ($P<.001$), indicating higher quality of life. Changes in DEBQ, EDE-Q and FCQT scores showed decreases in problematic eating behaviors ($P<.05$) while physical activity increased significantly ($P<.05$). Metabolic improvements correlated with the amount of weight loss ($P<.05$), except for LDL ($P>.05$). However, changes in most immune parameters, parameters of psychological health, and eating behavior did not correlate with the amount of weight loss, except for changes in IL1ra ($P>.001$), IWQoL, PSS (both $P<.05$) and EDE-Q total score ($P<.01$).
Conclsion
We show that the value of a multidisciplinary treatment approach for patients with severe obesity is not only limited to successful weight loss and improvements of body composition itself, but also includes the wide range of improvements in metabolic parameters, immunological, psychological, psychosocial, dietary, and behavioural improvements that may occur independently of weight loss.

DOI: 10.1530/endoabs.81.P585

P586

Weight loss variability with SGLT2 inhibitors, GLP-1 receptor agonists and repetitive Transcranial Magnetic Stimulation in Type 2 Diabetes and Obesity: results of a retrospective, comparative study

Anna Ferrulli[1,2], Stefano Massarini[1], Daniele Cannavaro[2], Paolo Perilli[2], Ileana Terruzzi[1,2], Pamela Senesi[1,2] & Livio Luzi[1,2]
[1]IRCCS MultiMedica, Department of Endocrinology, Nutrition and Metabolic Diseases, Sesto San Giovanni, Italy; [2]University of Milan, Department of Biomedical Sciences for Health, Milano, Italy

Weight loss in individuals with Obesity (O) and Type 2 Diabetes (T2D), may improve glycaemic control and weight-related comorbidities, and in some cases, induce diabetes remission. However, body weight control is generally an unmet aim in this population. Thus, there is an increasing need to consider pharmacological approaches to assist weight loss in diabetes-obesity. Glucose-lowering agents as the sodium-glucose co-Transporter 2 inhibitors (SGLT2i) and GLP-1 Receptor Agonist (GLP1-RAs) have been proved to be capable to simultaneously control body weight and glucose levels, and their use has been recommended in individuals with O and T2D. Recently, we demonstrated the efficacy of repetitive Transcranial Magnetic Stimulation (rTMS) in inducing weight loss up to 1 year in O individuals with and without T2D.
Aim of this study was to compare retrospectively the efficacy of SGLT2i, GLP1-RAs and rTMS in long-term (up to 1 year) body weight reduction in patients with O and T2D. Data obtained from 31 patients with O and T2D were retrospectively analysed: 11 subjects (bw 98.1±18.3 Kg, BMI 36.8±5.7 Kg/m2) were treated for O with High Frequency rTMS for 5 weeks, 8 subjects (93.4±13.1 Kg, 33.6±3.1 Kg/m2) were treated for T2D with SGLT2i for 1 year, and 12 individuals (98.1±18.3 Kg, 36.8±5.7 Kg/m2) were treated for T2D with GLP1-RA for 1 year. Data relating to bw, BMI, glucose, glycated hemoglobin, cholesterol and triglycerides variations in the 3 groups have been analyzed with ANOVA, after 6 months (FU1) and 1 year (FU2) from the start of treatment. Body weight variation (%) between the 3 groups was significant both at F1 [-3.2±1.8% (SGLT2i) vs -3.5%±1.5% (GLP1-RA) vs -6.3±4.0% (rTMS);$P=0.026$] and FU2 [-2.1±2.1% (SGLT2i) vs -2.1±4.2% (GLP1-RA) vs −6.7±4.7% (rTMS);$P=0.017$]. As expected, glycated hemoglobin variation was significantly higher in SGLT2i and GLP-1 RA groups both at FU1 [-11.7±25.1% (SGLT2i) vs -11.9%±13.2% (GLP1-RA) vs -8.9±10.4% (rTMS);$P=0.922$] and FU2 [-15.9±24.2% (SGLT2i) vs -7.8±11.9% (GLP1-RA) vs -5.6±9.0% (rTMS);$P=0.116$], although not statistically significant. In this study, rTMS revealed to be a more effective intervention than SGLT2i and GLP1-RAs in promoting long-term weight loss in a population with O and T2D, probably due to a prevalent effect of rTMS on controlling food craving and appetite at the level of meso-cortico-limbic system. These findings lay groundwork for a potential use of dTMS as an add-on intervention for the treatment of T2D and O.

DOI: 10.1530/endoabs.81.P586

P587

GLP-1 and glucagon depict complementary actions on visceral adipose tissue that could mediate metabolic shifts towards catabolism

Tiago Morais[1], Alexandre Seabra[1], Barbara Patrício[1], Marta Guimarães[1,2], Mário Nora[1,2], Pedro Oliveira[3], Marco Alves[1] & Mariana Monteiro[1]

[1]UMIB - Unidade Multidisciplinar de Investigação Biomédica, ICBAS - Instituto de Ciências Biomédicas Abel Salazar, Universidade do Porto, Porto, Portugal; [2]Centro Hospitalar de Entre o Douro e Vouga, Department of General Surgery, Santa Maria da Feira, Portugal; [3]QOPNA/LAQV - University of Aveiro, Department of Chemistry, Aveiro, Portugal

Visceral adipose tissue (VAT) metabolic fingerprints differ according to the individual's BMI and glycemic status. GLP-1 and Glucagon are two hormones that participate in energy homeostasis and glycemic control. Dual GLP-1/Glucagon agonists are a drug class under development for obesity and diabetes treatment. Although the pancreas and the liver are considered major GLP-1 and glucagon targets, these hormones act in other tissues, which could contribute for its effects on glucose balance. Thus, our purpose was to assess how GLP-1 and Glucagon influence VAT metabolic fingerprints according to the individual's BMI and glycemic status. Subjects ($n=19$) undergoing elective abdominal surgery for non-infectious nor oncologic conditions were included in this study. Subjects were allocated into 4 experimental groups according to BMI and glycemic status, namely with obesity and euglycemia (Ob+NGT, $n=5$), obesity and pre-diabetes (Ob+Pre-T2D, $n=5$), obesity and T2D (Ob+T2D, $n=5$). Subjects without obesity or dysglycemia were used as controls (Non-Ob, $n=4$). VAT harvested during the surgical procedure was kept in culture media supplemented with insulin (100 nM) and exposed for 48 h to GLP-1 or glucagon at different concentrations (1, 10 or 100 nM). Culture media was then collected for proton nuclear magnetic resonance (^{1}H-NMR) analysis. In VAT of Non-Ob controls, GLP-1 decreased acetate production (-25.20 %, $P<0.05$), while in Ob+NGT glucagon increased valine consumption (76.6%, $P<0.05$). In VAT of subjects with Ob + Pre-T2D, GLP-1 decreased isoleucine consumption (-99.6%, $P<0.05$), but increased alanine (32.6%, $P<0.05$) and lactate (43.8%, $P<0.01$) production. Glucagon decreased the consumption of isoleucine (-55.2%, $P<0.05$) and valine (-169.2%, $P<0.01$), as well as the production of alanine (-28.0%, $P<0.05$) and lactate (-54.4%, $P<0.05$), while increasing pyruvate consumption (10.9%, $P<0.05$). VAT of Ob+T2D subjects depicted no changes in metabolite profile after exposure to GLP-1 or glucagon. GLP-1 and glucagon are able to modify VAT metabolic profile, particularly in obesity and pre-diabetes. GLP-1 shifts VAT metabolic profile by decreasing isoleucine consumption and increasing alanine/lactate production, which suggests decreased gluconeogenesis. Glucagon lowers isoleucine and valine consumption, coupled with the decrease in lactate and alanine production, whilst increases pyruvate consumption, which suggests an increase in oxidative phosphorylation. Overall, out data suggests that dual GLP-1/Glucagon agonists' action in VAT could also play a role in mediating its glucose lowering and catabolic effects.

Funding: Fundação para a Ciência e Tecnologia (FCT), Portugal (PTDC/MECMET/32151/2017, UIDB/00215/2020 and UIDP/00215/2020). T. Morais funded by FCT (SFRH/BD/123437/2016).

DOI: 10.1530/endoabs.81.P587

P588

Influence of diabetes and metabolic risk factors on the outcomes of COVID-19 Vaccination: Scoping Review of the Observational Studies

Shailesh Trivedi[1], Renu Trivedi[2] & Akta Trivedi[3]
[1]Anand Hospital, Baroda, India; [2]Anand Hospital, India; [3]Anand Neurology Hospital, India

Introduction

Obesity and diabetes are the known risk factors for severity and susceptibility to severe COVID-19 with a poor prognosis. However, there is limited evidence for the implications and association of metabolic factors on COVID-19 vaccination.

Methods

We systematically searched PubMed/Medline and Cochrane library till January 28, 2022, using: ("diabetes OR BMI OR weight OR glucose OR obesity OR metabolic" and "COVID OR Coronavirus OR SARS-Cov-2" and "vaccine OR immunization OR vaccination"). Two independent researchers assessed the literature and conducted the review according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis guidelines for Scoping Reviews (PRISMA-ScR).

Results

We evaluated four studies (3 from Italy) with cumulative 1380 patients. The mean number of patients was 345 (±521, minimum 21, maximum 1123). One study ($n=84$) was only among healthcare workers. COVAC-DM cohort study suggests that humoral immune response to COVID-19 vaccination in diabetes is age dependent but is independent of type of diabetes and glycaemic control. CAVEAT study suggests that hyperglycaemia at the time of vaccination worsens the immunological response and, achieving adequate glycaemic control during the postvaccination period improves the immunological response. Evaluation of the protocols suggests that patients with higher BMI ≤ 30 kg/m^2 are significantly under-represented in most of the trials. Modulation of the diet to hypocaloric, very-low-carbohydrate diet one week before the mRNA vaccine and blood glucose reduction has a significant positive corelation on the adaptive humoral (anti-SARS CoV-2 S antibodies) and cell-mediated responses (IFN γ). Higher waist circumference, smoking, systemic hypertension and dyslipidaemia are independent confounding variables that lead to lower antibody titres. Diabetes and metabolic risk factors can modulate the immunogenicity of COVID-19 vaccine. Omission or under-representation of participants with higher BMI may cause poorer vaccine coverage for people with higher weight and contribute to greater health inequities.

Discussion

Obesity and hyperglycemia are associated with a reduced adaptive response to a COVID-19 mRNA vaccine. However, weight loss and metabolic−glycemic improvement may reverse the effect. Inclusion of higher BMI individuals in vaccine trials would yield a comprehensive evidence and help mitigate health inequities and potentially add value for substantial subgroup analysis based on the metabolic parameters and appropriately titrate vaccine dose regimes or earlier vaccine boosters, evaluate safety, and ensure equitable protection for higher weight people against COVID-19.

DOI: 10.1530/endoabs.81.P588

P589

Utility of webinars with case-based learning approach in teaching endocrinology to undergraduate medical students during the COVID-19 pandemic

Kashish Goyal[1], Kashish Malhotra[1], Rohin Kansal[1], Mahima Marwah[1], Ravikant Goyal[2], Harry Goyal[3] & Anmol Galhotra[4]
[1]Dayanand Medical College and Hospital, Ludhiana, India; [2]Government Medical College, Amritsar, India; [3]All India Institute of Medical Sciences, New Delhi, India; [4]Pandit BD Sharma PGIMS, Rohtak, India

Background

Conventional methods of one-way teaching may not involve the integration of clinical skills and may become more inefficient and passive [1]. During the COVID-19 pandemic, limited patient interaction and shift to online lectures greatly reduced the clinical exposure and opportunity of developing interpersonal skills for junior medical students. In this study, we hosted online webinars with case-based teaching for medical students so that they can amalgamate clinical skills with patient-based care and systems-based practice.

Methods

Six free webinars were hosted at one-month intervals covering various endocrine topics for first and second-year medical students of Punjab, India. Each webinar started with three endocrine case vignettes containing the patient's chief complaints, history of present illness, and their clinical course. These anonymised clinical scenarios were derived from real-life patient transcripts. It was followed by a lecture explaining the pathophysiology of that system along with a clinical discussion. Then, students were divided into multiple breakout rooms where the instructors discussed the case vignettes and answered any further queries. Pre-webinar and post-webinar assessment were done using multiple-choice questions which were clinically oriented. Follow-up assessment was also done one month after each webinar to estimate the retention of knowledge by students. Students' attitudes regarding the usage of webinars and case-oriented teaching as compared to conventional training were ascertained using Likert scale (1=low, 5=high) and open-ended questions. Analysis was done using SPSS Statistics v26.0.

Results

72 students filled all the surveys and were included in the analysis. Significantly higher ($P<0.001$) improvement in student's post-session scores after attending each webinar and 1-month follow-up assessment were observed compared to pre-test scores. No significant differences were seen in post-webinar results and one-month follow-up results which is indicative of good retention of knowledge. The majority of the students (67, 93.1%) either strongly preferred or preferred case-based learning model compared to conventional one-way teaching. In thematic analysis, the key strengths of our model were simulating clinical scenarios and providing engaging and focused training with an emphasis on doubt-solving.

Conclusions

Webinars with a case-based learning approach provide an important utility in simulating endocrinological clinical scenarios and may be used

as an adjunct/alternative when compared to the traditional one-way teaching methods.

Reference

[1] Nandi, P.L., *et al*. Undergraduate medical education: comparison of problem-based learning and conventional teaching. Hong Kong Medical Journal, 6(3), pp.301–306.

DOI: 10.1530/endoabs.81.P589

P590

Type 1 diabetes on continuous subcutaneous insulin infusion: impact of glycaemic control on quality of life

Ana Carreira, Mafalda Ferreira, Inês Vieira, Mariana Lavrador, Luísa Barros, Carla Baptista, Carolina Moreno, Miguel Melo & Isabel Paiva
Centro Hospitalar e Universitário de Coimbra, Department of Endocrinology, Diabetes and Metabolism, Coimbra, Portugal

Background

In type 1 diabetes (T1D), quality of life (QoL) and the effectiveness of treatment influence each other. QoL has been associated with glycaemic control assessed by HbA1c in T1D on continuous subcutaneous insulin infusion (CSII), but data on the relationship between Continuous Glucose Monitoring (CGM) metrics and QoL are scarce.

Objectives

To assess QoL and the association between CGM metrics and QoL in T1D on CSII.

Methods

Transversal observational study of adults with T1D on CSII and CGM. Patients with active CGM time $<70\%$, age >65 years and severe unrelated illness were excluded. QoL was assessed by the 34-item ViDa1 questionnaire, between July-December/2021, after its translation and validation. ViDa1 is divided in 4 independent subscales: 2 positively related with QoL (self-care, wellbeing) and 2 negatively related (interference with life [IWL], concern about the illness). Each score is presented in percentage (0-100%).

Results

56 cases were analysed, with mean age of 34.5 ± 12.6 years, 6.5 ± 5.5 years of CSII and 20.6 ± 10.0 years of diabetes duration. 12.7% had diabetes complications. Mean Glucose Management Indicator (GMI) was $7.2\pm0.7\%$ (5.8-8.6), Time in range (TIR) $57.7\pm14.9\%$, above range (TAR) $35.2\pm17.1\%$ and bellow range (TBR) $7.1\pm5.5\%$, with mean Coefficient of Variation (CV) of $39.8\pm7.7\%$. The obtained QoL subscale's scores were $71.7\pm17.0\%$ for self-care, $60.6\pm19.7\%$ for wellbeing, $27.8\pm20.4\%$ for IWL and $70.2\pm20.1\%$. for concern. When questioned, 69.1% reported having overall good QoL. Self-care correlated negatively with GMI ($r=-0.42$, $P=0.001$) and TAR ($r=-0.40$, $P=0.003$) and positively with TIR ($r=0.38$, $P=0.004$), with higher self-care associated with higher TIR. Wellbeing had similar correlations ($r=-0.33$, $P=0.011$; $r=-0.34$, $P=0.012$ and $r=0.34$, $P=0.012$), with higher TIR associated with higher wellbeing. Mean IWL differed significantly across GMI range ($P=0.027$), scoring $45.5\pm20.1\%$ for GMI $>8\%$ vs $27.7\pm20.0\%$ and $21.9\pm18.3\%$ for GMI 7-8% and $<7\%$, respectively. Concern was associated with GMI and TAR, with levels of concern $\leq70\%$ showing significantly higher mean GMI ($7.3\pm0.7\%$ vs $6.9\pm0.6\%$, $P=0.034$) and TAR ($39.1\pm9.0\%$ vs $28.5\pm13.8\%$, $P=0.027$). QoL didn't differ significantly based on TBR or CV. In brief, patients with lower GMI and higher TIR had higher self-care and wellbeing, patients with lower GMI showed lower interference with life and patients with higher GMI and TAR showed higher concern about the illness.

Conclusions

T1D patients on CSII displayed overall satisfactory glycaemic control and QoL. Patients with better glycaemic control displayed better QoL. TBR wasn't associated with QoL. These results show that QoL may be more influenced by hyperglycaemia than by hypoglycemia.

DOI: 10.1530/endoabs.81.P590

P591

Systematic review of ongoing clinical trials assessing the comparative therapeutic efficacy and safety of insulin glargine 300 u/ml with insulin degludec

Saibal Chakravorty[1], Aditya Chakravorty[2] & Monica Belagodu[1]
[1]Metro Multispeciality Hospital, Noida, UP, India; [2]School of Medical Sciences & Research - Sharda University, Greater Noida UP, India

Introduction

To systematically evaluate the study designs and the outcomes being analysed in the ongoing trials evaluating the efficacy and safety of Insulin Glargine 300 U/ml with insulin degludec

Methods

We reviewed contemporary protocols of trials that are currently ongoing through WHO-ICTRP (www.who.int/ictrp/search/en), www.clinicaltrials.gov trials registry database. Latest evaluation was on January 28, 2022 with key word 'insulin galrgaine U 300', degludec, for the trials initiated over the last two years (2019-2021). Two researchers independently extracted the protocols and analysed the outcomes.

Results

We evaluated clinical parameters to improve metabolic control and lower risk of hypoglycaemia. We analysed the protocols of the six ongoing trials including, the landmark trials namely PREMIER INSULIN (perioperative non-ICU, $n=180$), ULTRAFLEXI1 (T1DM) are cumulatively recruiting 1416 patients; across Japan (4 trials) and Austria (1 trial) and 1 trial as global multicentric (North America and Europe). The study designs include randomised, parallel, cross-over, designed studies. Three trials are evaluating the comparative efficacy patients in T1DM ($n=110$) and other three in T2DM ($n=1306$). Insulin glargine U300 along with insulin degludec is being compared with Insulin icodec - a novel once-weekly basal insulin analog. The comparative trials include age range from 7 to 90 years, including a dedicated trial in elderly ($n=30$). The mean number of participants being enrolled is 236 (SD $\pm$ 425, maximum 1096, minimum 25, 95% CI -210 to 682). The trial duration range from 1 day in post-operative non-ICU setting to 52 weeks. Trials evaluate the glycemic control (HbA1c), time spent in hypoglycaemia in post exercise regimen, mean amplitude of glycemic excursion, nocturnal glucose fluctuation index by flash glucose monitoring, and frequency of hypoglycemia.

Conclusion

We evaluated emerging outcomes based on clinical, comparative glycemic indices including CGM based precise evaluation parameters, qualitative non-glycemic and quality of life parameters, patient reported outcome comparing Insulin glargine U300 with insulin degludec.

DOI: 10.1530/endoabs.81.P591

P592

Risk of developing type 2 diabetes in young adults with a psychiatric disorder: a nationwide population-based cohort study

Lee Min-Kyung[1], Seo-Young Sohn[1], Jiyeon Ahn[1], Kyungdo Han[2] & Jae-Hyuk Lee[1]
[1]Myongji Hospital, Hanyang University Medical Center, Division of Endocrinology and Metabolism, Department of Internal Medicine, Rep. of South Korea; [3]Soongsil University, Department of Statistics and Actuarial Science, Rep. of South Korea

Objective

Having a psychiatric disorder may increase the risk of developing type 2 diabetes (T2D) and we aimed to determine whether young adults with a psychiatric disorder have an increased risk of developing T2D.

Research Design and Methods

We conducted a nationwide cohort study to evaluate the association of different psychiatric disorders with the risk of T2D in the young population. Records of 6.457.991 adults aged $20-39$ years without a history of T2D were retrieved from database of the South Korean National Health Insurance between 2009 and 2012. Service and followed up for incident T2D cases until December 2018. Five categories of psychiatric disorders were included: schizophrenia, bipolar disorder, depressive disorder, anxiety disorder, and insomnia. Hazard ratios (HRs) and confidence interval (CI) for developing T2D were estimated using Cox proportional hazards regression models.

Results
Over a median follow-up period of 7.59 years (range 6.47-8.23), a total of 122.603 patients with newly diagnosed T2D were identified. Cumulative incidence of T2D significantly increased with all five psychiatric disorders ($P < 0.001$). The multivariable-adjusted HRs was 1.146 (95% CI 1.106−1.189) for depression; 1.517(95% CI 1.319−1.745) for schizophrenia; 1.594 (95% CI 1.413−1.798) for bipolar; 1.226 (95% CI 1.183−1.271) for insomnia; and 1.134 (95% CI 1.07−1.62) for anxiety disorder.
Conclusions
All five psychiatric disorders were associated with increased risk of incident T2D in the young population. There was most significant increased risk of T2D in young adults with schizophrenia and bipolar disorders.

DOI: 10.1530/endoabs.81.P592

P593

Hyperglycemia, but not previous diagnosis of diabetes mellitus, is an independent indicator of poor outcome in patients hospitalized for severe COVID-19

Elisa Eletto[1], Alessandra Dei Cas[1], Antonio Nouvenne[2], Andrea Ticinesi[1], Beatrice Prati[2], Valentina Spigoni[1], Raffaella Aldigeri[1], Gloria Cinquegrani[1], Silvia Schirò[1], Livia Ruffini[3], Nicola Sverzellati[1], Tiziana Meschi[1] & Riccardo C. Bonadonna[1]
[1]University of Parma, Department of Medicine and Surgery, Parma, Italy; [2]Azienda Ospedaliera-Universitaria di Parma, Department of General and Specialistic Medicine, Parma, Italy; [3]Azienda Ospedaliera-Universitaria di Parma, Department. of Medical Imaging, Parma, Italy

Background
Both diabetes mellitus and hyperglycemia are reported to be strong risk factors for poor outcome(s) in patients hospitalized for COVID-19. However, their relative roles in affecting patient prognosis are under debate.
Aims
To evaluate the independent influence of known diabetes mellitus and hyperglycemia on death/admission to intensive care unit (ICU) in patients hospitalized for COVID-19 during the first wave of SARS-Co-V2 pandemic.
Experimental Design
We retrieved the clinical data/records of the patients admitted with COVID-19 between 23rd February 2020 and 31st March 2020 to the Covid-1 macro-unit of the University Hospital of Parma. Known diabetes was defined by self-reported history, electronic medical records or ongoing medications. The readout of hyperglycemia was fasting plasma glucose at admission. The primary outcome (follow-up: 6 weeks) was a composite of transfer to the Intensive Care Unit or death. Logistic regression analysis was used to identify independent risk indicators of the primary end-point by univariable and multivariable models. We used Receiver Operating Characteristic (ROC) curves to assess the overall predictive power of the different regression models.
Results
757 subjects were included, 143 of whom (19.2%) had known diabetes. Patients with diabetes were older and had more frequently comorbidities associated. The primary outcome occurred in 61.5% of patients with diabetes compared to 43.1% in those without (log-rank test < 0.001). Among variables associated with COVID-19 severity, age, obesity, arterial hypertension, previous CV event, eGFR, glucose levels at admission (but not known diabetes), C-reactive protein and HR-CT visual score of pneumonia extension, were independent risk indicators of poor outcome in logistic regression models undergoing progressively more and more adjustments for potential confounders. The ROC curves showed remarkably good accuracy (up to AUC = 0.89) in predicting the primary composite end-point in all models, including the one which used the simplest, most immediate clinical parameters.
Conclusions
Known diabetes indicated poor COVID-19 outcomes, but not when adjusted for other baseline clinical variables and comorbidities, suggesting that its impact was mostly driven by concomitant factors and complications. Fasting hyperglycemia was a powerful and independent predictor of poor outcomes, together with age and biomarkers of inflammation (CRP) and lung tissue damage (HR-CT visual score). The molecular mechanism(s) underlying the tight association between high glucose and poor COVID-19 outcome remain(s) to be elucidated.

DOI: 10.1530/endoabs.81.P593

P594

Circulating levels of endothelial progenitor cells (EPCs) and sexual function in fertile women with type 1 diabetes

Antonietta Maio[1], Maria Tomasuolo[2], Chiara Porcellini[3], Annalisa Sarnataro[2], Vlenia Pernice[1], Laura Castellano[3], Paola Caruso[3] & Katherine Esposito[3]
[1]University of Campania "L. Vanvitelli", Department of Advanced Medical and Surgical Sciences, University of Campania "Luigi Vanvitelli", Naples, Italy, [2] University of Campania "L. Vanvitelli", PhD in Translational Medicine, Department of Experimental Medicine, University of Campania "Luigi Vanvitelli, Naples, Italy, [3] University of Campania "L. Vanvitelli", Division of Endocrinology and Metabolic Diseases, University Hospital "Luigi Vanvitelli", Naples, Italy

Introduction
Female sexual dysfunctions (FSD) are complex conditions characterized by impairment of the female sexual cycle. Higher prevalence of FSD has been found in women with diabetes, as compared with matched healthy controls. Endothelial progenitor cells (EPCs) are circulating mononuclear cells participating in the neo-angiogenesis. There is evidence that circulating levels of EPCs are reduced in diabetic patients compared with age-matched subjects. The relationship between EPCs and sexual function during menses in women with diabetes has never been investigated.
Aim
The aim of this study is to assess circulating levels of EPCs in different phases of the menses in young women with type 1 diabetes. The relationship between EPCs levels and sexual function will be also investigated.
Matherials and methods
Sexually active women, aged 18-30 years, with type 1 diabetes (T1D) and age-matched healthy controls with a stable couple relationship and no oral contraceptive use were included in the study. Blood samples were drawn in the follicular, ovulatory and luteal phases of the same menses to assess sexual hormones levels, including FSH, LH, progesterone and estradiol. EPCs were quantified by flow cytometry. Sexual function was investigated using the Female Sexual Function Index (FSFI) and the Female Sexual Distress Scale (FSDS) during the three phases of menstrual cycle; FSD was diagnosed by a FSFI score $<$ 26.55 and a FSDS score $>$15. Women with hypogonadism, polycystic ovarian syndrome or irregular menses were excluded.
Results
A total of 18 women with T1D and 8 healthy controls were enrolled. Mean age was 25 years and mean BMI was 23.4 Kg/m2. In the overall population FSD prevalence was 7%. There were no differences in sexual hormone levels during the different phases of menses in the 2 groups. The FSFI total score as well as the scores related to desire, arousal, lubrication and pain were lower in diabetic women as compared with those of control subjects. Moreover, circulating levels of CD34+ and CD34+KDR+ cells EPCs were significantly lower in the ovulatory phase ($P = 0.03$) and ovulatory/luteal phases ($P = 0.04$;$P = 0.02$) respectively in women with diabetes as compared healthy controls. No significant difference was observed in the other EPCs phenotypes.
Conclsion
Young fertile diabetic women showed a worse sexual function and lower levels of EPCs as compared with healthy age-matched women during the different phases of menstrual cycle.

DOI: 10.1530/endoabs.81.P594

P595

Somatostatin analogue treatment for hyperinsulinemic hypoglycemia with glucokinase activating mutation (GCK), c.295T>C (p.Trp99Arg)

Anna Boguslawska, Ewelina Rzepka, Lukasz Kluczyński, Alicja Hubalewska-Dydejczyk & Aleksandra Gilis-Januszewska
Department of Endocrinology, Endocrine Oncology and Nuclear Medicine, Jagiellonian University Medical College, Cracow, Poland

Somatostatin analogues (SSA) are used to treat different forms of hyperinsulinemic hypoglycemia (HH) in children and adults and therapeutic effect is achieved by suppressing insulin secretion from pancreatic β-cells by complex mechanisms. These treatments might be associated with several side effects, can even cause the worsening of severity of hypoglycemia. This is a report of the treatment of HH with SSA in patient with Activating Mutation (GCK), c.295T>C (p.Trp99Arg). We

present a 58-year-old male with HH, which was diagnosed at the age of 20 years. However, symptoms of hypoglycemia were present from the postnatal period. Fasting was mainly the trigger for hypoglycemia episodes. Additionally, epilepsy was diagnosed at the age of 10 years and he is currently treated with carbamazepine. At the age of 54 years, the patient underwent genetic testing and a heterozygous variant in Glucokinase (*GCK)* c.295T>C was confirmed. The severity of hypoglycemia ranged from mild to serious with the lowest glucose of 1.88 mmol/l during fasting. In early adulthood, the patient did not consent to pancreatectomy. At the age of 20 years, diazoxide treatment was introduced. It resulted in decreased both the number and severity of hypoglycemic episodes, however, poor patient compliance was observed in terms of regular medical follow-ups and regular diazoxide intake. In 11.2021 SAA treatment was introduced at the age of 57. At that time, his HbA1c level was 4.1%, fasting glucose level 2.59 mmol/l with c-peptide level 2.1 ng/ml, and insulin level 7 uU/ml. Initially patient received 10 mg short-acting octreotide with a good response. He is now treated with 20 mg octreotide monthly. In self-monitoring mean fasting and after meal glycemia values increased by 20-30 mg%. His most recent 4-h oral glucose tolerance test (OGTT), performed after three months of treatment with SSA, showed fasting glucose level 3.22 mmol/l with insulin level 3.82 uU/ml and c-peptide 1.1 ng/ml. The lowest glucose level (1.58 mmol/l) was observed in 180 min in OGTT. Currently, the patient reports no symptomatic and self-monitored hypoglycemia as well as no side effects of SSA. The SSA treatment of HH with activating *GCK* mutation, c.295T>C improved both fasting and after meal glucose levels by 20-30 mg% with complete remission of hypoglycemia. However, hypoglycemia during OGTT suggests that glucose load is a very strong trigger of insulin oversecretion despite SSA treatment. Therefore efficient treatment with SSA analogues should be combined with the low glycemic diet.

DOI: 10.1530/endoabs.81.P595

P596

Transient Refractory Hyperinsulinemic Hypoglycemia

John Berquist & Matthew Wahl
University of Utah Hospital, Endocrinology, Salt Lake City, United States

Fasting hypoglycemia in the setting of hyperinsulinemia typically is persistent and often progressive. We present a case where fasting hypoglycemia with hyperinsulinemia was transient in nature over a fortnight. This occurred in the setting of recurrent seizure-like activity. Seizures are a well known sequela of hypoglycemia; however, the reverse is not nearly as well documented. A 20 year old male with a history of developmental delay, chronic PEG tube, and nonverbal at baseline presented for breakthrough seizures after a 17 year seizure-free period. On day 3 of admission, his fasting glucose levels fell to less than 65 mg/dl. He required D10 infusion, and experienced return of hypoglycemia when D10 was stopped. Labs obtained during a hypoglycemic episode showed blood glucose 47 mg/dl, insulin 12 uU/ml, beta-hydroxybutyrate 0.07 mmol/l, C-peptide 7.9/ml, sulfonylurea screen negative, and negative insulin antibodies. Octreotide was started in addition to D10 for persistent hypoglycemia. MRI abdomen did not reveal pancreatic lesions and 68 Gallium-DOTATAE PET scan showed normal pancreatic structure. Over a two week period, octreotide and D10 infusion were slowly weaned off without return of hypoglycemia. During his admission, he underwent EEG assessment, which showed a moderate degree of diffuse or possibly multifocal cerebral dysfunction warranting clinical correlation. True hypoglycemia needs to fulfill Whipple's Triad: Documented venous hypoglycemia, symptoms consistent with hypoglycemia, and resolution of symptoms with correction of hypoglycemia. In this case, the triad was presumed to be positive based on laboratory evaluation and a report of behavioral changes with hypoglycemia from patient's parents. Laboratory assessment met criteria for endogenous hyperinsulinemia. Imaging did not reveal a source for excess insulin. He went from requiring D10 and octreotide to being euglycemic off both medications. Critical illness is also implicated in fasting hypoglycemia, particularly in end-organ failure or sepsis. The patient did not have any organ damage to this degree, but there was recurrent seizure-like activity. Status epileptics causes a massive release of catecholamines, which increases serum glucose. The latter then leads to a large insulin release from the pancreas, which can lead to a period of hypoglycemia. Although clear epileptiform activity was not noted on EEG, the patient's clinical presentation with seizures raises the possibility that the hypoglycemia was related to recurrent seizures. This case highlights the need to consider epiletiform activity as a cause of hyperinsulinemic hypoglycemia.

DOI: 10.1530/endoabs.81.P596

P597

The impact of changes to Joint British Diabetes Societies' diabetes-related ketoacidosis management guidelines on trends of complications and outcome

Gobeka Ponniah[1], Amy Birchenough[2], Megan Owen[3], Carina Synn Cuen Pan[4], Shamanth Soghal[4], Emily Warmington[1], Haaziq Sheikh[5], Muhammad Ali Karamat[6], Sanjay Saraf[7] & Punith Kempegowda[4]
[1]University of Birmingham Medical School, Birmingham, United Kingdom; [2]Sandwell and West Birmingham Hospitals NHS Trust, Birmingham, United Kingdom; [3]Walsall Manor Hospital, Walsall, United Kingdom; [4]Queen Elizabeth Hospital, Birmingham, United Kingdom; [5]Haberdashers' Adams' Grammar School, Newport, United Kingdom; [6]Heartlands Hospital, Birmingham, United Kingdom; [7]Good Hope Hospital, Birmingham, United Kingdom

Background
Serious complications of diabetes-related ketoacidosis (DKA) and its management with fixed rate insulin infusion (FRIII) include hypoglycaemia, hyperkalaemia and hypokalaemia. Revised Joint British Diabetes Societies for Inpatient Care (JBDS) guidelines in July 2021 recommended a reduced rate FRIII of 0.05 units/kg/hour from 0.1 units/kg/hour once blood glucose levels fall to $\leq$14.0 mmol/l to alleviate the risk of these complications.
Aim
To study the impact on trends of hypoglycaemia, hyperkalaemia, and hypokalaemia in DKA prior to and following the JBDS guideline update.
Method
We performed a retrospective analysis of all DKA admissions between February and November 2021 across six hospitals in the UK. Three out of the six hospitals have updated their management guidelines to reflect the new national recommendations. The trends in hypoglycaemia, hyperkalaemia, and hypokalaemia episodes pre- (February to June) and post-guideline update (July to November) was compared.
Results
220 (February-June) and 188 (July-November) DKA admissions were identified. 23 (10.5%) patients experienced hypoglycaemic episodes prior to the guideline update compared to 29 (15.4 %) patients post-guideline update ($P=0.116$). 55 and 58 episodes of hypoglycaemia were identified pre- and post-guideline update, respectively. 82 (37.3%) admissions pre-guideline update experienced episodes of hyperkalaemia compared to 51 (27.1%) admissions post-guideline update ($P=0.306$). Additionally, 67 (30.5%) patients experienced hypokalaemic episodes pre-guideline update compared to 72 (38.3%) patients post-guideline update ($P=0.033$). Overall, 141 and 142 episodes of hypo- and hyperkalaemia were identified pre-guideline update in comparison to 189 and 72 hypo- and hyperkalaemic episodes post-guideline update. The median DKA duration was 13.5(IQR9.0-20.6) hours in February-June vs 14.1(IQR 9.6-19.7) hours in July-November ($P=0.424$). Median length of stay was 4.4(IQR 2.3-8.2) days in February-June vs 3.4(IQR 2.0-6.7) days in July-November ($P=0.58$) respectively. Lack of awareness and understanding was listed as the reason for minimal changes in complications and outcome post-guideline update.
Conclusion
With an exception a higher number of hypokalaemic episodes was observed after the guideline revision, there was no significant changes in the complications or outcomes of DKA. These findings suggest more work needs to be done in implementing and educating the end-user to improve the anticipated outcomes from the revised guidelines.

DOI: 10.1530/endoabs.81.P597

P598

Impact of Bariatric Surgery on the liver - An adolescent cohort

Madalena von Hafe[1], Joana Chaves[1], João Sérgio Neves[2], Marta Borges-Canha[2], Catarina Vale[1], Inês Lourenço[1], Susana Corujeira[3] & Miguel Campos[4]
[1]Faculdade de Medicina da Universidade do Porto, Departamento de Cirurgia e Fisiologia, Porto, Portugal; [2]Centro Hospitalar Universitário de São João, Serviço de Endocrinologia, Diabetes e Metabolismo, Porto, Portugal; [3]Centro Hospitalar Universitário de São João, Serviço de Pediatria, Porto, Portugal; [4]Centro Hospitalar Universitário de São João, Serviço de Cirurgia Pediátrica, Porto, Portugal

Introduction
Obese patients are at an increased risk of develop nonalcoholic fatty liver disease. Evidence supports that bariatric surgery might have an important impact on hepatic profile in obese adults. Literature suggests that bariatric surgery in adolescents might decrease the prevalence of some comorbidities, but information about its impact on liver profile and steatosis and fibrosis risk remains scarce.
Aim
To evaluate the impact of bariatric surgery on liver parameters and on Hepatic Steatosis Index (HSI, predictor of hepatic steatosis) and AST to Platelet Ratio Index (APRI, predictor of hepatic fibrosis) in adolescents.
Material and methods
We conducted an observational retrospective cohort study in obese adolescents who underwent sleeve gastrectomy in our center between 2013 and 2021. Clinical and laboratorial parameters were evaluated before surgery, and at 6 months, 12 months, and 24 months after surgery. The variation after surgery of anthropometric parameters, lipid profile, liver parameters, HIS and APRI were evaluated with paired t-tests.
Results
The population included ($n=22$) had an average age of 18.0 [17.0; 18.0] years at the time of the surgery, a body mass index of 47.0 ± 5.4 Kg/m^2 and 70.4% were female. In the pre-operative study, 44.4% used metformin, 37.0% had hypertension, and 48.1% dyslipidemia. Six months after the surgery, there was a clinically significant decrease in weight (127.8 ± 17.5 vs 96.6 ± 16.3 Kg, $P<0.01$), body mass index (46.9 ± 5.3 vs 34.9 ± 5.2 Kg/m^2, $P<0.01$), and percentage of fat mass (47.7 ± 7.6 vs 38.0 ± 12.1 %, $P<0.01$). There was also a decrease in GGT (34.0 ± 22.5 vs 20.0 ± 12.0, $P<0.01$). HSI score, which predicts hepatic steatosis, was also markedly decreased (60.0 ± 6.7 vs 45.5 ± 7.6, $P<0.01$). One year after surgery, there was still a noticeable decrease in weight, body mass index, percentage of fat mass and HSI score. There was also an increase of HDL ($P=0.03$) and a decrease of triglycerides (116.4 ± 57.6 vs 81.7 ± 36.8 mg/dl, $P<0.01$). After a two-year follow-up period years after the surgery, the reduction of HSI, weight, body mass index, and percentage of fat mass remained significant ($P<0.01$). There were no statistically significant differences in the hepatic fibrosis score (APRI), AST, ALT, FA, total bilirubin, direct bilirubin, total cholesterol, and LDL levels during follow-up.
Conclusions
Among severely obese adolescents, sleeve gastrectomy is associated with an improvement of steatosis and triglycerides levels, and this might have a long-term impact on the progression of nonalcoholic fatty liver disease.

DOI: 10.1530/endoabs.81.P598

P599

Effect of bariatric surgery on metabolic profile − a pediatric cohort

Madalena von Hafe[1], Joana Chaves[1], João Sérgio Neves[2], Marta Borges-Canha[2], Catarina Vale[1], Susana Corujeira[3] & Miguel Campos[4]
[1]Faculdade de Medicina da Universidade do Porto, Serviço de Pediatria, Porto, Portugal; [2]Centro Hospitalar Universitário São João, Serviço de Endocrinologia, Diabetes e Metabolismo, Porto, Portugal; [3]Centro Hospitalar Universitário de São João, Serviço de Pediatria, Porto, Portugal; [4]Centro Hospitalar Universitário de São João, Serviço de Cirurgia Pediátrica, Porto, Portugal

Introduction
Obesity is a complex multifactorial disease and its prevalence in pediatric age has increased. Obesity prejudices the individual metabolic profile due to the adipotoxicity involved in this condition. Bariatric surgery improves the weight of obese patients along with metabolic comorbidities, being today one of the most effective treatments for obesity. Time of exposure to adipotoxicity appears to be an important risk factor for the development of metabolic complications.
Objective
To assess the impact of bariatric surgery in the metabolic profile of adolescents.
Methods
Observational cohort study in obese adolescents selected to the criteria for sleeve surgery between 2013 and 2021. Clinical and laboratory parameters were evaluated before retro surgery and at 6 and 12 months after surgery. The effects of surgery were used to test the functioning test and the McNemmar test.
Results
The population included ($n=24$) had a mean age of 17.5 [17.0; 18.0] years at the time of surgery and 70.8% were female. The mean body mass index (BMI) at the time of surgery was 46.0 ± 6.0 kg/m2; 45.8% arterial hypertension, 50.0% dyslipidemia and 54.2% used metformin. After 6 months of follow-up, there was a significant reduction in weight (127 ± 20.5 vs 96.2 ± 17.3 kg, $P<0.001$), BMI (46.7 ± 5.7 vs 35.6 ± 5.4 Kg/m2, $P<0.01$) and percentage of fat mass (47.6 ± 8.3 vs 39.0 ± 12.0%, $P<0.001$). At the end of one year, the decrease in weight gain, BMI and percentage of fat mass remained statistically significant. Glycated hemoglobin levels significantly decreased compared to baseline (5.4 ± 0.2%), at 6 (5.2 ± 0.3%, $P=0.01$) and 12 months ($5.2\pm0.0.3$%, $P=0.01$). Also, a significant reduction in HOMA-IR was observed, compared to the initial value (5.7 ± 2.6 mg/dl), at 6 (2.3 ± 0.9 mg/dl, $P<0.001$) and at 12 months (2, 1 ± 1.2, $P=0.002$) after surgery. These changes culminated in a reduction in metformin use, from 54% to 6% ($P=0.05$), 6 months after surgery.
Conclusion
These results evidence that bariatric surgery has a beneficial effect on the metabolic profile. Knowing the cumulative effects of obesity, performing this surgery earlier will reduce the time exposed to adiposity and glucotoxicity, and may mitigate the long-term consequences of obesity. Longer follow-up is needed to assess these benefits.

DOI: 10.1530/endoabs.81.P599

P600

Esr1 and Esr2 estrogen receptors have different functions in Glut4 expression of 3t3-l1 cells

Caroline Pancera Laurindo, Karen Cristina Rego Gregorio & Ubiratan Fabres Machado
University of São Paulo, Department of Physiology and Biophysics, Institute of Biomedical Sciences, São Paulo, Brazil

Diabetes mellitus (DM) is an important cause of morbidity and mortality on a global scale. The pathophysiology of DM involves insulin resistance, even in insulin-treated type 1 DM, which in turn is related to the amount of glucose transporter GLUT4 (*Slc2a4* gene). Estrogen activity can be mediated by two distinct receptors (ESR1 and ESR2) and may involve genomic and non-genomic mechanisms. Estrogen has been described as involved in glycemic homeostasis, but the related mechanisms are only now beginning to be investigated. Previous studies conducted by our group have demonstrated that estradiol (E2) can modulate the *Slc2a4*/GLUT4 expression in muscle and adipose cells and have suggested that the ESR1- or ESR-mediated effects may be different. The present study seeks to demonstrate the ESR1- and ESR2-induced effects upon the *Slc2a4*/GLUT4 expression in adipose cells. Differentiated 3T3-L1 adipocytes were treated with 10 nM E2, 10 nM PPT (ESR1 agonist), 1μ MPP (ESR1 antagonist) and 100 nM DPN (ESR2 agonist) alone, or E2 + PPT, E2 + MPP and E2 + DPN (in the same concentrations), for 24h. Oil Red (OR) staining for analysis of cell differentiation, RT-qPCR for *Slc2a4* mRNA quantification and Western blotting for GLUT4 protein quantification were used. Differentiation of 3T3-L1 cells was successfully achieved and similarly preserved after the treatments. E2 and PPT promoted a similar increase (2 to 3 folds, $P<0.05$) in *Slc2a4*/GLUT4 expression; and their association did not induce any additional effect. The presence of MPP or DPN in E2-treated cells abrogates the E2 enhancer effect upon the *Slc2a4*/GLUT4 expression ($P<0.05$). Curiously, MPP alone was capable of reducing ($P<0.01$) the *Slc2a4*/GLUT4 expression as compared to that of control cells (cultivated without E2), suggesting some enhancer effect of ESR1 even in the absence of the ligand. Therefore, E2 increases the *Slc2a4*/GLUT4 expression in adipocytes by an ESR1-mediated mechanism; an effect that can be counterbalanced by the hyperactivation of ESR2. These data indicate that the E2-induced and ESR1-mediated effects increase the GLUT4 expression, contributing to the improvement of cellular glucose uptake, which can explain a beneficial effect of estrogen upon glycemic homeostasis. On the other hand, the hyperactivity of ESR2, by repressing the GLUT4 expression, may play a diabetogenic effect

DOI: 10.1530/endoabs.81.P600

P601

Isoflavones genistein and daidzein enhance the expression of Slc2a4 mRNA and GLUT4 protein in adipocytes

Karen Cristina Rego Gregorio, Caroline Pancera Laurindo & Ubiratan Fabres Machado
University of São Paulo, Department of Physiology and Biophysics, Institute of Biomedical Sciences, São Paulo, Brazil

According to the world Health Organization, about 422 million people worldwide have diabetes mellitus (DM), and this number is growing rapidly. DM, mainly type 2, is associated with insulin resistance, which involves reduced expression of glucose transporter GLUT4 (*Slc2a4* gene). It is known that estrogen can modulate glycemic homeostasis and seems to involve changes in the *Slc2a4*/GLUT4 expression. There has been an increased interest in plant-derived phytoestrogens, which can bind to estrogen receptors (ESR1 and ESR2), mimicking or inhibiting some estrogen effects. It is believed that these compounds have beneficial health properties, acting against various diseases, however, that must be carefully analyzed. Phytoestrogens can have different affinity for ESR1 or ESR2 and can reveal variable estrogen or antiestrogen effects. Little is known about the effect of phytoestrogens upon the GLUT4 expression, and about their possible role in cellular glucose disposal. The present study investigates the effects of some abundant phytoestrogens, isoflavones genistein (G) and daidzein (D), as compared to estradiol (E2), upon the *Slc2a4* mRNA and GLUT4 expression (respectively by RT-qPCR and Western blotting), in isolated adipocytes. Differentiated 3T3-L1 cells were cultivated for 24 h with 10 nM of E2, G and D, alone or in combination. Alone, E2, G and D showed a similar increase (by ~50%, $P<0.05$) in the expression of both *Slc2a4* mRNA and GLUT4 protein, as compared to untreated cells. Besides, in combination with E2, both G and D promoted an additional increase ($P<0.005$) in the *Slc2a4* mRNA, which was not accompanied by a similar increase in GLUT4, suggesting the presence of a posttranscriptional regulation. Based on these results, we conclude that phytoestrogens genistein and daidzein can increase *Slc2a4*/GLUT4 expression as efficiently as estradiol does. These results indicate that, concerning the adipocyte capacity of glucose uptake, the isoflavones studied can effectively substitute estradiol.

DOI: 10.1530/endoabs.81.P601

P602

Mediterranean Diet and 12 months weight loss result in complex serum metabolomic and fecal metaproteomic changes in paediatric obesity

Daniele Spadaccini[1], Virginia Vita Vanella[2], Elettra Barberis[2], Roberta Ricotti[3], Simonetta Bellone[3], Elisa Bona[4], Valentina Antoniotti[3], Marina Caputo[1], Valentina Mancioppi[3], Ivana Rabbone[3], Marcello Manfredi[2] & Flavia Prodam[1]
[1]University of Piemonte Orientale, Department of Health Sciences, Novara, Italy; [2]University of Piemonte Orientale, Department of Translational Medicine, Novara, Italy; [3]University of Piemonte Orientale, SCDU of Pediatrics, Department of Health Sciences, Novara, Italy; [4]University of Piemonte Orientale, Department of Sciences and Technological Innovation, Alessandria, Italy

Background
The relationship between composition and function of microbiota, obesity and nutrition has been increasingly studied and is still a challenge.
Aims
To test whether in a group of 12 pediatric patients with obesity the treatment with a structured hospital and in-home Mediterranean Diet intervention had an impact on gut microbiota composition, function, and metabolite production, including Short chain fatty acids (SCFAs).
Methods
An untargeted metaproteomics analysis through nano-LC chromatography coupled to high-resolution mass spectrometer (Triple TOF 5600+, Sciex), for the identification of phyla, and GC-MS for the analysis of SCFA and small molecules in serum and stools were carried out. All identified peptides were annotated (UniProtKB database, KEGG) and their functions were identified by UniPept software. Phylogenetic analysis was also performed. Subjects were evaluated at baseline, and after 6 and 12 months.
Results
At metaproteomic, we identified more than 250000 peptides, and 70000 proteins. We were able to identify common features between patients from the same time group. We detected changes associated with an improvement of the gut inflammatory state directly dependent on the diet. Bacterial phylogenetic and functional changes were observed in relation to the dietary intervention, BMI reduction, and adherence to the Mediterranean diet. Both after 6 and 12 months, patients lost weight and contemporarily showed a reduction of fecal SCFA (acetic, butanoic, pentanoic, and propanoic) and an increase of the Bacteirodetes/Firmicutes ratio. Acetic acid and butyric acid were also decreased in serum after 6 and 12 months. Functionally, we observed an increase in pectin catabolism. We also identified fecal sugars and amino acid changes associated to the dietary intervention.
Conclusions
This preliminary data confirm that also pediatric obese individuals losing weight reverse their microbiota, increasing their Bacteirodetes/Firmicutes ratio. At the same time, most SCFA were found to be reduced both after 6 and 12 months after the intervention. Obese individuals could have an impaired utilization of SCFA that translates into a higher lipogenic effect compared to lean individuals who might better take advantage of the anti-inflammatory role. More intervention studies should be performed in this promising area by utilizing similar innovative techniques.

DOI: 10.1530/endoabs.81.P602

P603

Ghrelin deficiency sex-dependently alters food intake, locomotor activity, and white adipose tissue gene expression in a binge-eating mouse model

Karina Prins, Patrick Delhanty, Martin Huisman, Rosinda Mies, Anke McLuskey & Jenny Visser
Erasmus MC, Department of Internal Medicine, Rotterdam, Netherlands

Binge-eating disorder is the most prevalent eating disorder diagnosed, affecting three times more women than men. It is characterised by binge-eating episodes: the rapid consumption of a large amount of food, without needing the calories. The gut hormone ghrelin stimulates appetite and reward signalling, and loss of its receptor reduces binge-eating behaviour in male mice. We aimed to examine the influence of ghrelin itself on binge-eating behaviour in mice of both sexes. 5-week-old wild-type (WT) and ghrelin-deficient (GKO) mice were housed individually in an indirect calorimetry system for 9 weeks. Binge-like eating in mice given *ad libitum* chow was induced by time-restricted access to Western-style diet (WD; 2h access, 3 days/week) in the light phase (BE); control groups received *ad libitum* chow (CO), or *ad libitum* access to both diets (CW). Food intake, locomotor activity, body composition, and white adipose tissue (WAT) gene expression were assessed. All groups of BE mice showed binge-eating behaviour, eating up to 60% of their 24h intake during the WD access period. Subsequent dark phase chow intake was decreased by 12.4% in GKO mice ($P=0.029$) and remained similarly decreased, especially in GKO females, on non-binge days ($P=0.015$). As a result, on binge days, chow comprised a smaller portion of the 24h caloric intake of GKO BE ($48\pm4\%$) compared with WT mice ($60\pm2\%$;$P=0.02$). This reduction in chow preference was also observed in CW mice (GKO: $3\pm1\%$; WT: $8\pm2\%$;$P=0.029$). Compared to males on the same diet, dark phase locomotor activity was increased by 97.6% in CO females ($P<0.0001$), 107.0% in CW females ($P<0.0001$), and, on binge days, by 46.0% in BE females ($P=0.003$). Interestingly, on non-binge days, locomotor activity remained increased in WT females but was reduced to the level of the males in GKO females (interaction:$P=0.03$). Upon sacrifice, GKO BE mice weighed 7.8% less ($P=0.001$) and had a 2.2% lower lean body mass percentage than WT BE mice ($P=0.014$). In inguinal white adipose tissue of BE and CW groups, ghrelin deficiency and female sex were associated with suppression of macrophage polarization-regulatory genes, and increased expression of genes that modulate thermogenesis. We conclude that, in contrast to ghrelin receptor deficiency, ghrelin deficiency does not hamper the development of binge-like eating. Moreover, ghrelin deficiency sex-dependently alters food intake timing, locomotor activity, and inguinal white adipose tissue function. These results add to the growing body of evidence that ghrelin signalling is sexually dimorphic.

DOI: 10.1530/endoabs.81.P603

P604

Glucocorticoids enhance browning and thermogenic functions of mouse and human white adipocytes

Ramesh Kasarla[1], Iacopo Gesmundo[1], Noemi Congiusta[1], Greta Sabbia[1], Barbara Pardini[2], Maria Alessandra Bocchiotti[3], Ezio Ghigo[1] & Riccarda Granata[1]
[1]Division of Endocrinology, Diabetes and Metabolism, Department of Medical Science, University of Turin, Turin, Italy; [2]Italian Institute for Genomic Medicine (IIGM), Candiolo, Italy, Candiolo, Italy; [3]Department of Clinical and Biological Sciences, University of Turin, Turin, Italy

White adipose tissue (WAT) stores excess energy as triglycerides, while brown adipose tissue (BAT) dissipates energy through heat, acting as a defence against cold and obesity and as a positive regulator of metabolic functions. BAT thermogenic functions are mainly induced by mitochondrial uncoupling protein-1 (UCP-1), which induces uptake of lipids and glucose to sustain oxidation and thermogenesis in both brown and beige adipocytes. Beige/brite adipocytes arise in WAT depots and morphologically and functionally resemble to brown adipocytes. The glucocorticoid receptor (GR) agonist dexamethasone plays an important role in energy homeostasis, regulation of insulin sensitivity, lipid metabolism and adipose tissue distribution. Indeed, *in vivo* studies suggest that Dex increases the effects on UCP-1 mRNA expression in BAT. However, the role of Dex in adipose browning and BAT function is yet not fully known. Thus, we aimed to assess the role of Dex on browning of white adipocytes and brown adipocyte thermogenic functions. 3T3-L1 murine preadipocytes and human mesenchymal stem cells (hMSCs), isolated from bariatric surgery of lean subcutaneous and visceral adipose tissues, were differentiated into white adipocytes for 9 and 21 days respectively. Browning was induced for 72 h with rosiglitazone (Rosi) and insulin, in the presence or absence of Dex. Our results showed that in 3T3-L1 adipocytes Dex increased both mRNA and protein expression of BAT markers UCP-1, PRDM16, and PGC-1α. Moreover, the GR antagonist RU486 completely blocked Dex-induced mRNA expression of *Ucp-1*, indicating the involvement of GR on these effects. Dex also strongly enhanced the mRNA expression of the beige markers transmembrane protein 26 (TMEM26) and sirtuin 1(SIRT1), while inhibited the WAT marker *C/ebpα*. Interestingly, oil red O staining revealed that Dex increased the number of small lipid droplets and enhanced Iso-induced lipolysis, promoting the expression levels of adipose triglyceride lipase (ATGL) and hormone sensitive lipase (HSL). Furthermore, Dex enhanced mitochondrial biogenesis, determined by staining with Mito-Tracker dye, increased the expression of the fat oxidation marker *CPT1*, and modulated the oxygen consumption rate (OCR), assessed by Seahorse analysis, in transdifferentiated 3T3-L1 adipocytes. Finally, Dex increased the mRNA levels of browning genes in transdifferentiated adipocytes obtained from hMSCs of both subcutaneous and visceral human adipose tissues. Overall, these findings indicate that Dex enhances the differentiation of 3T3-L1 and human white adipocytes into beige adipocytes, by regulating the expression of genes characteristics of browning and increasing beige thermogenic functions.

DOI: 10.1530/endoabs.81.P604

P605

The effects of Long-term (five years) prednisone therapy in frequently relapsing nephrotic syndrome of childhood: impact on glycemia and the different components of the metabolic syndrome (MetS)

Mostafa Elbaba[1], Noor Hamed[1], Ashraf Soliman[1], Fawzia Alyafei[1], Maya Itani[1,2], Fatima Al-Naimi[1,2], Doaa Al Yousef[2] & Mona Shaat Dalees[2]
[1]Hamad Medical Center, Pediatrics, Doha, Qatar; [2]Hamad Medical Center, Nutrition and Dietitic Department, Doha, Qatar

Although widely prescribed for their anti-inflammatory and immunosuppressive properties, glucocorticoids have various common metabolic side effects including hypertension, dysglycemia and diabetes.

Aim

This study was carried out to investigate the prevalence of different metabolic components and dysglycemia in children with steroid sensitive nephrotic syndrome (SSNS) with multiple relapses for 5 years in relation to the cumulative dose of steroids.

Methods

Data of 30 children with SSNS was analysed retrospectively. They received prednisolone only in the standard dose for the initial episode at 2 mg/kg/day for six weeks followed by 1.5 mg/kg on alternate days for six weeks and relapses were treated with 2 mg/kg/day till remission followed by 1.5 mg/kg/day for four weeks. The cumulative dose of steroids over the period of 5 years was calculated for each child. The growth data was recorded along the treatment period. The different metabolic criteria including impaired fasting glucose (IFG), high LDL and cholesterol, lower HD and high blood pressure for age and sex were studied over this period of time.

Results

The mean cumulative prednisone = 125 +/- 28 mg /kg/year given over an average duration of 5 years. Obesity (OB) and overweight (OW) increased from 25% pre-treatment to 59.2% after 5 years of treatment. After 3 and 5 years of treatment IFG was found in 24 and 36 % respectively, high LDL in 89% and 80% respectively, high cholesterol in 85% and 100% respectively. Hypertension was detected in 12.5% and 23% of patients after 3 and 5 years of treatment. The mean serum cholesterol and LDL levels were significantly higher than normal in treated children after 3 and 5 years of treatment.

Conclusion

Long term prednisone therapy (for 5 years) with a mean cumulative dose of prednisone = 125 +/- 28 mg/kg/yr. was associated with increased prevalence of OW and obesity as well as with higher risk of developing hypertension and dyslipidemia.

Table 1

Variables	Beginning	3 yr	5 yr	*P* value
Number	30	30	30	
IFG (FBG > 5.6 mmol/l	15.93%	24.14%	35.71%	0.1
LDL > 2.7 mmol/l	88.89%	88.89%	80.00%	0.35
HDL < 1.03 mmol/l	10.53%	10.00%	0.00%	0.07
TG >1.7 mmol/l	77.27%	33.33%	60.00%	0.23
Cholesterol > 4.5 mmol/l	100.00%	85.71%	100.00%	1
Hyperten-sion BP > 95th centile for age	23.30%	12.50%	23.00%	0.9

DOI: 10.1530/endoabs.81.P605

P606

The ecology of the microbiome in children with congenital generalized lipodystrophy type 4 (CGL4) is quickly modified after metreleptin treatment

Tommaso Daffara[1], Valentina Mancioppi[2], Marina Caputo[1], Simonetta Bellone[2], Nadia Massa[3], Alice Caramaschi[3,4], Flavio Mignone[3,5], Martina Romanisio[1], Ivana Rabbone[2], Mara Giordano[6], Gianluca Aimaretti[1,6], Elisa Bona[3,4] & Flavia Prodam[1,6]
[1]Novara, Endocrinology Unit, Department of Translational Medicine, Novara, Italy; [2]Novara, SCDU Pediatrics, Department of Health Sciences, Novara, Italy; [3]Alessandria, Department of Sciences and Technological Innovation, Alessandria, Italy; [4]Vercelli, Department for Sustainable Development and Ecological Transition, Vercelli, Italy; [5]Novara, SmartSeq s.r.l., spin-off of the Università del Piemonte Orientale, Novara, Italy; [6]Novara, Department of Health Sciences, Novara, Italy

Introduction

Lipodystrophy syndromes are characterized by a progressive metabolic impairment secondary to adipose tissue dysfunction and genetic background. The role of microbiota is still uninvestigated.

Objective

Evaluate the gut microbiome ecology in relation to dietary and clinical parameters in two infant siblings with congenital generalized lipodystrophy type 4 (CGL4) before and after treatment with recombinant leptin.

Methods
Two siblings (male, 5.5 years; female 2.5 years) with CGL4 caused by a new homozygous PTRF mutation (NM_012232 eson1:c T21A:p. Y7X) were identified and followed after the starting of leptin treatment. We collected auxological, metabolic, nutritional parameters, and stool samples at baseline and every 3 months. Two baseline stool samples were pooled. DNA was extracted directly from 0.25 g of stool using the QIAamp PowerFecal Pro DNA Kit. DNA was amplified with primers for the V3 and V6 regions of 16S rDNA tagged with Multiplex Identifier sequences using Microbiota Solution B Kit optimized for Illumina Miseq sequencing. Raw FastQ sequences were analyzed using MicrobAT Software. Statistical analyses were performed using MicrobiomeAnalyst and R software.
Results
At baseline, reduced subcutaneous fat, muscular hypertrophy, distinct facial features, myopathy, atlantoaxial instability were observed. Stature and BMI were normal. Blood tests showed elevated CK, mildly elevated levels of liver enzymes and triglycerides, low leptin and adiponectin levels. Fasting glucose and HbA1c were normal; HOMA-IR was mildly elevated in the female, and continuous glucose monitoring often detected glucose higher than 180 mg/dl after meals in male. They were hyperphagic, mainly for foods rich in fats and sugars. The 2 subjects showed a Bacteroides enterotype (F/M): 46%/44% Bacteroidetes, 49%/42% Firmicutes, 0.02%/0.04 other Bacteria, 3.2%/1.9% Actinobacteria, 0.7%/0.4% Proteobacteria; 0%/11%Verrucomicrobia. Treatment with metreleptin was started at standard dose according to age and weight. All the metabolic parameters and hyperphagia improved, and they were more adherent to dietary indications. The male subject lost 0.8 kg after 3 months, female weight was stable. We present microbiome ecology after 3 months of treatment, before starting also medium-chain triglyceride oil formulas. Alfa-diversity increased in both children. Ecology was modified ($P<0.06$) with a reproducible signature with decreased and increased relative abundance of species linked to metabolic homeostasis.
Discussion
These preliminary results highlight as dietary adherence and leptin treatment were soon followed by improvements in metabolic alterations and changes in microbiome ecology. Whether microbiota composition and function have a role in the lipodystrophy phenotype needs further investigation. Our preliminary data should be validated in a wide cohort.

DOI: 10.1530/endoabs.81.P606

P607

An audit of management of severe hyperlipidaemia in secondary and primary care services in greater london area

Bhavna Sharma & Anees Fatima
Northwick Park Hospital, United Kingdom

Hyperlipidaemia services in the UK are guided by National Guidance for Lipid Management for primary and secondary prevention of cardiovascular disease. Our audit studied a total of 71 patients in primary and secondary care in the greater London area with total Cholesterol levels greater than 7.5 mmols/l. In patients admitted to hospital ($n=22$); 27.8% patients were ITU admissions with 56% being under surgical team for acute pancreatitis. Only 45.4% of these patients were reviewed by the diabetes/endocrine team (most reviews being for management of diabetic ketoacidosis). 54.5% of patients were initiated and continued on insulin therapy (11% were on IV insulin only for management of hyperlipidaemia). 9% of patients had to have plasmapheresis. With regards to work up only 9% of these patients received lifestyle advice or screening for further co-morbidities. 45.5% were referred onwards to a lipid clinic. None of the acute admissions had inpatient investigations sent to screen for familial causes. Selected Patients attending GP practice ($n=49$) had an average total cholesterol level of 11.28 mmols/litre. About 70% of these patients received formal lifestyle advice. 18.3% of these patients were referred to a dietician. Around 77% of these patients were on statins and 67% of these patients were on two or more medications. 33.7% of these patients were diabetic and under follow up with Endocrine. 18.3% of these patients were classified as increased cholesterol secondary to alcohol use (it was unclear whether these patients were always referred to alcohol liaison services). Only 4% of these patients were referred to endocrine after screening for diabetes highlighting a significant gap in secondary screening. 34.7% of these patients underwent screening for familial hypocholesteraemia and were referred to a specialised lipid clinic. Our audit highlighted the gap in management of patients getting followed up in primary care vs being admitted in the hospital. The authors felt that dual guidelines emphasising on discharge based planning from hospital and a more secure safety net for patients with significant cardiovascular risk is needed. A GP guided approach with early referrals to lipid clinic/endocrine may achieve positive outcomes in such cases.

DOI: 10.1530/endoabs.81.P607

P608

Dysregulation of cytochrome P450 oxidoreductase (POR) in NAFLD and hepatocellular carcinoma; evidence from clinical, rodent and cellular models

Ismael da Conceição[1], Nikolaos Nikolaou[2], Laura Gathercole[3], Shelley Harris[1], Niall Dempster[1], Ahmad Moolla[1], Leanne Hodson[1] & Jeremy Tomlinson[1]
[1]University of Oxford, Oxford Centre for Diabetes, Endocrinology and Metabolism, Oxford, United Kingdom; [2]University of Cambridge, Department of Pathology, Cambridge, United Kingdom; [3]Oxford Brookes University, Department of Biological and Medical Sciences, Oxford, United Kingdom

The incidence of non-alcoholic fatty liver disease (NAFLD), the hepatic manifestation of the metabolic syndrome, continues to rise. NAFLD is associated with significant liver-specific and cardiovascular morbidity and mortality, including hepatocellular carcinoma (HCC). Currently, there are no licensed therapies, highlighting the importance of understanding the pathogenic mechanisms that drive the condition. Cytochrome p450 oxidoreductase (POR) plays an essential role in activation of all microsomal cytochrome p450s (CYPs) by electron transfer. Rodent models of POR deletion develop hepatic steatosis, but the underpinning mechanisms remain poorly understood. The role of POR in human models to modulate hepatic metabolic phenotype has not been explored in detail. We have tested the hypothesis that POR contributes to NAFLD progression through dysregulation of major metabolic pathways using clinical samples from patients with NAFLD and HCC, *in vivo* rodent models (American Lifestyle-Induced Obesity Syndrome, ALIOS) and human hepatoma cells. In liver biopsies of NAFLD patients, relative POR mRNA expression was significantly lower compared to non-NAFLD controls ($P<0.01$). In addition, POR activity as measured by the analysis of urine steroid metabolites, decreased with advancing NAFLD severity (control vs F0-F2, $P<0.0001$; control vs F3-F4, $P<0.0001$). In patients with cirrhosis or HCC, POR activity was also decreased when compared to healthy controls ($P<0.0001$). Mice fed the ALIOS diet (12-months) developed significant hepatic steatosis and fibrosis. In both male and female ALIOS mice, POR mRNA expression was significantly decreased in comparison with normal chow-fed animals ($P=0.01$, FDR$=0.04$). In human hepatoma cells (HepG2), lipid loading was associated with decreased POR expression. To determine the cellular impact of decreased POR expression, siRNA knockdown experiments were performed. RNA-sequencing analysis combined with real-time PCR identified multiple metabolic pathways that were dysregulated. Changes in fatty acid metabolism were indicative of futile cycling with increased expression of fatty acid synthesis (AMPK, ACC, FASN) and oxidation (*CPT1A*) markers. These findings were endorsed with biochemical analysis demonstrating increased triacylglycerol ($P<0.01$) and 3-hydroxybutyrate ($P=0.03$) levels in cell culture media, and increased rates of *de novo* lipogenesis in cellular triacylglycerol ($P<0.01$). Moreover, there were significant changes in glucose metabolism suggesting increased gluconeogenesis and reduced glucose uptake. Finally, bile acid synthesis was impacted with increased expression of rate limiting synthetic enzymes and altered cellular bile acid production. Altered POR expression and activity has the potential to contribute to the complex metabolic phenotypes associated with NAFLD. Further studies are needed to determine whether this represents a putative cause or consequence of disease.

DOI: 10.1530/endoabs.81.P608

P609

Modern method of diagnosing of cerebral microangiopathy in patients with diabetes mellitus type 2 by doppler ultrasound

Madina Adkhamova, Dilfuza Karimova & Rakhshona Mirzaeva
Tashkent Medical Academy, Department of Endocrinology, Tashkent, Uzbekistan;

Background
To identify opportunities for Doppler ultrasound in the diagnosis of cerebral microangiopathy in patients with diabetes mellitus type 2 and hypertension.
Methods
The study included the diagnosis of 72 patients with type 2 diabetes and hypertension who were hospitalized in the 2 and 3 clinics TMA. The control group consisted of 25 patients aged 61.9 $\pm$ 2.6 years, suffering from type 2 diabetes. The study group included 47 patients (19 men and 28 women), older age groups with diagnosed type 2 diabetes and hypertension history, besides the patients of the second group were divided into two groups - those with diabetes complications flow - 23 patients without microvascular complications - 24 patients. Time monitoring of patients ranged from 3 to 8 years. All patients underwent Doppler ultrasound of the main arteries of the head and neck - the internal carotid artery. Evaluated the speed of blood flow indices, the PI index (which determines the stiffness and elasticity of the arteries), the RI index (reflecting peripheral resistance), systolic and diastolic index (the ISD), assessed cerebrovascular reactivity (according to tests with breath-holding and hyperventilation).
Results
Changes dopplerographic index in the BCA were observed in 19 patients in the subgroup with diabetes complications compared with 2 patients of the subgroup without complications. In the subgroup with diabetes complications 21 patients had signs of nephropathy and in 18 of them were identified changes in dopplerographic indicators BCA, which may indicate vascular remodeling processes in the body of patients with type 2 diabetes. Significant moderate and strong correlation LED current duration of type 2 and the presence of diabetic retinopathy and nephropathy, altered dopplerographic indices PI and RI. So a critical increase in the ICA RI index was observed after 6.8 years after the diagnosis of type 2 diabetes. It was revealed that the predictors of microcirculatory disorders in patients with type 2 diabetes mellitus were the duration of 8 years. It is shown that microcirculatory disorders, diagnosed by means of ultrasound diagnostics, develop an average of 7 years after the onset of diabetes. Changes in dopplerographic indices were observed mainly in patients with type 2 diabetes complications. At the same time in all patients with a diabetes study group for the duration of 2 years, more than 7 marked changes in cerebrovascular reactivity by reducing vasodilatation reserve.
Conclusions
These results suggest that Doppler ultrasound diagnoses cerebral microangiopathy in patients with type 2 diabetes.

DOI: 10.1530/endoabs.81.P609

P610

Impact of the COVID-19 pandemic on diabetic foot

Sara Ragbi, Mjabber Amal, Nassim Essabah Haraj, Siham El Aziz & Asma Chadli
Uhc Ibn Rochd, Endocrinology and Metabolic Disorders, Casablanca, Morocco

Introduction
The COVID-19 pandemic has presented many challenges in the management of diabetics around the world. While many people can be managed using new methods such as tele-consulting, the diabetic foot presents unique challenges due to the frequent need for "face-to-face" consultation and treatment. The pandemic has thus made the management of diabetic feet, already complex, even more difficult. This study aims to assess the impact of the COVID-19 pandemic on the diabetic foot.
Methods and results
It's a retrospective study conducted at the endocrinology and diabetology department of the Ibn Rochd University Hospital, including patients who consulted in the emergency room for diabetic foot ulcer starting from the announcement of confinement in March 2020 until September 2021. Our study included 340 patients. The average age was 59 years, 62.35% were male and type 2 diabetics accounted for 93.23% with an average duration of diabetes of 12.3 years. Among the patients, 64.7% were on insulin, 22.6% on ADO and 7.3% on mixed treatment. Patients at very high cardiovascular risk represented 46.7% of which 6.9% were followed for ischemic cardiomyopathies and 40.8% for peripheral arterial disease. About microangiopathy, 27.3% had diabetic retinopathy and 25.3% diabetic kidney disease. Compared to the years 2018-2019, the number of patients who consulted was 1.9 times higher, the number of ulcers and cellulitis was 32.9% each, i.e. 6.8% more ulceration and 4% more cellulitis. The percentage of necrotizing fasciitis also increased by 18.4% as well as dry gangrene (22.6% vs 17%). 39.7% had to be referred for immediate surgical management due to the advanced stage of the lesions, which was 5.7% higher than in previous years. This increase in the number of emergencies was contrasting with a decrease in the number of outpatient consultations because of confinement.
Conclsion
The severity and increasing of the diabetic foot ulcers observed during the period of COVID-19 confirms the need for appropriate and rapid management to avoid dramatic results. Telemedicine and the use of new technologies are needed to provide optimal wound care while minimizing the exposure risk.

DOI: 10.1530/endoabs.81.P610

P611

Influence of dopamine receptor d2 and dopamine transporter polymorphisms in angiopathy in patients with type 2 diabetes mellitus

Marta Neves[1], Ana Carolina Santos[1,2], Joana Ferreira[1,2], João F. Raposo[3], Ana Valente[4] & Manuel Bicho[1,2]
[1]Faculty of Medicine, University of Lisbon, Genetics Laboratory, Ecogenetics and Human Health Group, Institute for Environmental Health, Lisbon, Portugal; [2]Scientific Research Institute Bento da Rocha Cabral, Lisbon, Portugal; [3]Associação Protectora dos Diabéticos de Portugal, Lisbon, Portugal; [4]Atlântica - Escola Universitária de Ciências Empresariais, Saúde, Tecnologias e Engenharia, Barcarena, Oeiras, Portugal

Introduction and Aim
Dopamine receptor D2 (DRD2) polymorphism (rs1800497) appears to be associated with increased susceptibility to the development of type 2 diabetes mellitus (T2DM). The dopamine transporter (DAT) determines dopamine signalling, responsible for the reuptake of its active form from the synapse. Polymorphism in the DAT gene (rs2836317) can increase dopamine reuptake in the synaptic cleft. However, its association with T2DM is still controversial.
This study aimed to evaluate the relationship between genetic polymorphisms of DAT and DRD2 and the susceptibility to the development of angiopathy in T2DM and its influence on the biochemical parameters.
Design and Methods
150 patients with T2DM were divided into: G1-75 patients with angiopathy and G2-75 patients without angiopathy. The DRD2 and DAT polymorphism were determined by endpoint analysis method and PCR, respectively. Blood levels of malondialdehyde (MAD), ascorbic acid, homocysteine and cysteine, vitamins B6 (vit.B6), B12 (vit.B12) were measured by HPLC methods, and standardized methods determined the other biochemical parameters. Statistical analysis was performed using SPSS with statistical significance for $P<0.05$.
Results
There were differences only in the DRD2 polymorphism between G1 to G2 ($P=0.016$). Carriers of allele A of DRD2 had a 3.18-fold increased risk to angiopathy (OR = 3.18 [1.40-7.21], $P=0.006$). Analyzing the relationship of biochemical parameters between groups was found an increase in systolic blood pressure (SBP) ($P=0.023$), MAD ($P=0.010$) and retinol ($P=0.011$) in G1. Regarding DRD2 polymorphism, there was an increase in HDL cholesterol (HDL-C) ($P=0.035$) for genotype GG and of vit.B12 in carriers of the allele G ($P=0.013$). For DAT polymorphism, it was found an increase in weight ($P=0.042$) and waist circumference ($P=0.050$) and a decrease in ascorbic acid ($P=0.039$) for genotype 10/10 and an increase in LDL cholesterol (LDL-C) ($P=0.027$) in genotype 9/10. Biochemical parameters were compared between groups, but dividing the population by the studies polymorphisms, for DAT it was found higher values of SBP ($P=0.014$), triglycerides ($P=0.019$) and retinol ($P=0.031$) and lower HDL-C values ($P=0.050$) for carriers of allele 10 in G1; for DRD2 it was found in carriers of the allele A, higher values of homocysteine ($P=0.038$), cysteine ($P=0.035$) and retinol ($P=0.007$) and in the genotype GG higher values of SBP ($P=0.020$) and triglycerides ($P=0.011$) in G1.
Conclusions
DRD2 polymorphism appears to influence susceptibility to angiopathy in T2DM patients directly. DAT and DRD2 polymorphism may modulate disease-associated biochemical parameters.

DOI: 10.1530/endoabs.81.P611

P612

An Experience of Insulin Basal Titration in Lombardy (Italy) during the Pandemic

Olga Eugenia Disoteo[1], Alessandro Roberto Dodesini[2], Bruno Solerte[3], Paolo Desenzani[4], Paolo Erpoli[5], Roberto Manfrini[6], Laura Molteni[7] & Antonio Carlo Bossi[8]
[1]ASST Grande Ospedale Metropolitano Niguarda, SC Diabetologia, Milano, Italy; [2]ASST Papa Giovanni XXIII, UO Malattie Endocrine e Diabetologia, Bergamo, Italy; [3]Istituto Di Riabilitazione E Di Cura Santa Margherita Asp Pavia, Uo Geriatria, Pavia, Italy; [4]PO Montichiari ASST Spedali Civili, SD Diabetologia, Bresca, Italy; [5]ASST Valle Olona Ospedale Sant Antonio Abate, SSD Endocrinologia e Diabetologia, Gallarate, Italy; [6]ASST Santi Paolo e Carlo, UD di Diabetologia e Malattie Metaboliche, Milano, Italy; [7]Ospedale Sacra Famiglia Fatebenefratelli, Centro Diabetologico, Erba, Italy; [8]Humanitas Gavazzeni, Ambulatorio Diabetologia, Bergamo, Italy

Introduction
Correct titration of basal insulin is one of the most important conditions allowing Type 2 Diabetes Mellitus patients to reach correct and personalised fasting plasma glucose. The persistence of the pandemic, together with the persistence of the SARS-CoV2 virus made titration process more complex, and pushed the Lombardy diabetologists to develop solutions which could be handled by the patient independently, or with the remote online assistance of diabetes team.
Patients, materials and methods
The Lombardy diabetologists participating in a training program shared their titration experiences of degludec basal insulin and its association with liraglutide (iDegLira). These physicians collected aggregated data of 387 subjects with T2DM (W:60%; M: 40%); homogeneous distribution in age groups 50 and 65 (31%); 65 and 75 (32%), and over 75 (28%), with 9% of the patients below 50; duration of illness <5 years (15%), 5 and 10 years (17%), 10 and 20 years (39%), over 20 years (29%). The patients had not adequate glycaemic control (90% with HbA1c>7.0%) with overweight or obesity (84.5% with BMI>25 kg/m2). Degludec was introduced for 129 patients, iDegLira for 258, titration was set up through modifications recommended by the diabetes team (244 patients); through the program "Titolando" (www.titolando.it) (132 patients); with no education to titration (11 patients).
Results and discussion
Thanks to the diabetes centres support, the patients reached an adequate FPG (average 174.7 mg% at baseline; 122 mg% after 6.1 weeks of controlled titration, increase of basal insulin dose by 4.7 Ul/die); the self-titration with the program "Titolando" obtained overlapping results (average FPG 178.5 mg% at baseline; 127 mg% after 7 weeks of self-managed titration, increase of basal insulin dose equal to 7UI/die). Less satisfactory the evolution of FPG in those who have independently modified the dosages of basal insulins (average FPG 199 mg% vs 140 mg% at six months follow-up, with increase of 5.9 UI of daily doses). The main limit and drawback of this retrospective observation consists in the fact of not having collected hypoglycaemia episodes.
Conclsions
During the pandemic, the remote support by Lombardy diabetes centres allowed to obtain satisfactory FPG after introduction of Degludec or iDegLira. Similarly, the process of self-titration led by the "Titolando" program proved adequate, easy to understand and manage, and such as to offer a valid alternative in all the situations where it is not possible to provide clinical regular feedback to patients who are in therapy with basal insulins.

DOI: 10.1530/endoabs.81.P612

P613

Use of continuous glucose monitoring for treatment adjustment in type 2 diabetes patients

Tzvetelina Totomirova & Mila Arnaudova
Military Medical Academy, Clinic of Endocrinology and Metabolic Diseases, Sofia, Bulgaria

Continuous Glucose Monitoring (CGM) is proved to be useful for dose adjustment in patients treated with multiple insulin injection regimens or with continuous subcutaneous insulin infusion. CGM give precise information about glucose variability in type 1 diabetes but are rarely used in type 2 patients. We assessed continuous glucose monitoring systems (CGMs) as control assessment tool in patients with type 2 diabetes receiving different treatment regimens. We studied 85 patients (50 men, 35 women; mean age 43.93 ± 10.87 years, mean disease duration 21.91 ± 6.07 years) with type 2 diabetes (31 receiving non-insulin therapy, 33 treated with pre-mixed insulin, 21 on multiple insulin injections. Continuous glucose monitoring by using iPro^{TM} was performed for seven days and HbA1c was measured at the end of this period. High positive correlation was found between HbA1c (7.46 ± 1.19%) and average glucose level during CGM period (7.45 ± 1.57 mmol/l) ($r=0.73$), AUC above limit ($r=0.75$) and percentage of time spent with glucose above 7.8 mmol/l (38.26 ± 26.38%, $P<0.05$, $r=0.69$). There was similar but negative correlation between HbA1c and percentage of time within the limit 3.9-7.8 mmol/l for all groups (56.07 ± 24.28%, $P<0.05$, $r=-0.63$). Comparing CGM results in different treatment groups we found similar correlations of HbA1c and percentage of time spent within limit (non-insulin treated group 55.65 ± 25.99%, $phi_1=-0.48$; premixed insulin treated group 54.33 ± 24.85%, $phi_2=-0.67$; intensified insulin treatment group 59.62 ± 21.36%, $phi_3=-0.58$). No correlations were found between HbA1c and number of all, positive and negative excursions. These results do not differ for age and gender. We conclude that performing CGM in patients with type 2 diabetes could give more precise information about the overall control nevertheless short time reflected and could present details about glucose deviations and hypoglycemic episodes and thus be useful for current treatment adjustment.

DOI: 10.1530/endoabs.81.P613

P614

Dopaminergic system and adipose tissue: in vitro effect of cabergoline on white, brown and beige adipogenesis and lipogenesis processes

Mariarosaria Negri[1], Claudia Pivonello[1], Feliciana Amatrudo[1], Roberta Patalano[1], Tatiana Montò[1], Cristina de Angelis[1], Chiara Simeoli[1], Renata Simona Auriemma[1], Annamaria Colao[1,2] & Rosario Pivonello[1,2]
[1]Federico II University, Department of Clinical Medicine and Surgery, Naples, Italy; [2]Federico II University, UNESCO Chair for Health Education and Sustainable Development, Naples, Italy

Adipose tissue is an endocrine organ releasing adipokines and expressing specific markers and intracellular mediators, which regulate whole-body energy by balancing lipid accumulation and utilization through adipogenesis, the differentiation of preadipocytes into mature adipocytes associated with gradual lipid storage, and lipogenesis, the additional lipid accumulation in mature adipocytes. Adipogenesis and lipogenesis, strongly induced by insulin, occur in white adipocytes, specialized in excess energy storage as fat depots, and in brown and beige adipocytes, specialized in energy storage dissipation. Decreasing white and increasing brown and beige adipogenesis and lipogenesis, may represent therapeutic tools for obesity. This study aims at investigating the effects of the dopamine agonist cabergoline (CAB) on white, brown and beige adipogenesis as well as on basal and insulin-induced lipogenesis. At this purpose, CAB (10^{-10} -10^{-6} M) was administered in 3T3L1 preadipocytes induced to differentiate, in order to evaluate its effect on white, brown and beige adipogenesis, and in white, brown and beige mature 3T3L1, in order to evaluate its effect on lipogenesis. Adipogenesis and lipogenesis were investigated measuring lipid accumulation using Oil red O staining. Messenger and protein levels of leptin, adiponectin and PPARγ, as white lipogenesis markers and mediators, and of UCP1, PPARγ and PKA, as brown lipogenesis markers and mediators, were analyzed by RT-qPCR and/or WB. During white adipogenesis, CAB10^{-8} M and 10^{-6} M significantly inhibited lipid accumulation (27-37%; $P<0.05$) and lipogenesis in absence (63-64%; $P<0.001$) and presence (85-51%; $P<0.0001$) of insulin administration, compared to controls, with significant decrease of leptin protein and messenger levels ($P<0.01$), slight increase of adiponectin protein and slight decrease of PPARγ protein. During brown adipogenesis, CAB10^{-10} M-10^{-6} M slightly stimulated lipid accumulation (18-24%) and lipogenesis in presence of insulin (15-30%), compared to controls, with slight increase of UCP1 and PPARγ messenger and PPARγ and PKA protein levels. Finally, during beige adipogenesis, CAB10^{-10} M-10^{-6} M slightly inhibited lipid accumulation (34-38%) and lipogenesis (38-43%), with slight increase of UCP1 and PPARγ messenger levels. In conclusion, the current study demonstrated a novel CAB effect on adipose tissue modulation, defining a pivotal role of dopaminergic system in the obesity pathophysiology.

DOI: 10.1530/endoabs.81.P614

P615

Is age-related hepatic elevation of endogenous SERM 27-hydroxycholesterol associated with hepatocellular degeneration female-specific? – Results from Rat study

Branka Šošić-Jurjević[1], Ljubiša Jovanović[2], Ljiljana Marina[3], Natasa Ristic[4], Marko Miler[4], Vladimir Ajdžanović[4], Branko Filipović[4] & Dieter Luetjohann[5]

[1]University of Belgrade Institute for Biological Research "Siniša Stanković" National Institute of Republic of Serbia, Citology, Beograd, Serbia; [2]Clinical Center of Serbia, Faculty of Medicine, University of Belgrade, 11000 Belgrade, Serbia, Department of Pathology and Medical Cytology, Beograd, Serbia; [3]Clinical Center of Serbia, Faculty of Medicine, University of Belgrade, 11000 Belgrade, Serbia, Clinic for Endocrinology, Diabetes and Diseases of Metabolism, Beograd, Serbia; [4]Institute for Biological Research "Siniša Stanković" - National Institute of Republic of Serbia, University of Belgrade, Citology, Beograd, Serbia; [5]Institut für Klinische Chemie und Klinische Pharmakologie, Universitätsklinikum Bonn, Sigmund-Freud-Str. 25, D-53127 Bonn, Germany

The cholesterol oxidation product 27-hydroxycholesterol (27OHC) is enzymatically produced from cholesterol by CYP27A1 in an alternative pathway of cholesterol degradation to bile acids. This oxysterol also acts as an endogenous selective estrogen receptor modulator (SERM). In healthy humans its concentration in circulation increases in hypercholesterolemia and with age, and is associated with increased risk of atherosclerosis, cardiovascular diseases and breast cancer. Several drugs with SERM activity used for treatments of breast cancer or osteoporosis have been reported to have sporadic hepatotoxic effects. Women suffer from some liver diseases more commonly (acute liver failure, autoimmune hepatitis, benign liver lesions, or primary biliary cirrhosis). For all of these the incidence increases with advancing age. To the best of our knowledge, there is no information in the literature, clinical or experimental, relating changes in hepatic 27OHC with incidence of liver disease in the context of aging and sex. To address this problem, we examined the effect of age and sex on liver and serum concentrations of 27OHC, as well as the immunostaining pattern of CYP27A1 in the liver of four-month and 24-month-old Wistar rats (experiments were repeated twice with similar results, $n=5$-6 animals/group) using LC MS/MS and immunohistochemistry, respectively. Furthermore, we examined changes in total cholesterol and concentration in liver and serum, liver histopathology, as well as serum concentration of hepatic enzymes, alanine (ALT) and aspartate aminotransferase (AST). The effect of age ($P<0.05$) on increase of serum and hepatic 27OHC was obtained both in males and females ($P<0.05$) and followed the same pattern of age-related total cholesterol increase ($P<0.05$). However, the intrahepatic increase of 27OHC was dramatically more pronounced only in old-aged females ($P<0.0001$). CYP27A1 immunostaining intensity was similar in all experimental groups, being the strongest in the cytoplasm of centrilobular hepatocytes, but the immunopositivity was diffusely spread throughout the liver lobule. Histopathological analysis revealed age-related hepatocellular degeneration (swelling and hydropic degeneration, increased fraction of binuclear hepatocytes and focal fatty changes) only in females. Moreover, age-related elevation of alanine transaminase (ALT) was observed only in female rats ($P<0.01$). In conclusion, the obtained results confirmed age-related female-specific increase of hepatic 27OHC as well as hepatocyte degeneration obsereved only in the liver of rat females. These age-related adaptive changes in cholesterol metabolism may atenuate hepatoprotective estrogen-like effects in the liver.

DOI: 10.1530/endoabs.81.P615

P616

Ketogenic diet is protective against atherosclerosis development in Apolipoprotein E Knockout Mice

Vincenzo Marzolla[1], Caterina Mammi[1], Alessandra Feraco[1], Stefania Gorini[1], Andrea Armani[1,2] & Massimiliano Caprio[1,2]

[1]IRCCS San Raffaele Roma, Laboratory of Cardiovascular Endocrinology, Rome, Italy; [2]San Raffaele Roma Open University, Department of Human Sciences and Promotion of the Quality of Life, Rome, Italy

Objective

higher aldosterone (aldo) levels are associated with increased risk of cardiovascular ischemic events and mortality. It has been demonstrated that aldo accelerates the development of aterosclerosis in apolipoprotein E knockout mice (ApoE KO). Ketogenic diet (KD) positively impacts several cardiovascular risk factors, yet its effect on atherosclerosis, is elusive. We hypothesize that, KD protects from development of atherosclerotic plaques in ApeE KO mice, a murine model of atherosclerosis.

Methods

eight-week-old male ApoE KO mice were fed an *ad libitum* KD (90.5-fat, 0.4-carbohydrate, 9.1-protein; $n=12$) or a moderate high fat diet (HFD) (42-fat, 42.7-carbohydrate, 15.2-protein; $n=12$) and treated with aldo (6 μg/mouse per day) or vehicle through osmotic mini-pumps. Cholesterol content was comparable in KD and HFD. After 4 weeks of treatment, intraperitoneal glucose tolerance test was performed, and peripheral blood samples were collected and used to quantify beta-hydroxybutyrate (OH-But). At the endpoint, mice were euthanized and their cryosections of embedded aortic root were used to quantify the atherosclerotic plaque size, lipid and collagen content in all experimental groups. Vascular inflammation was assesed in speciments of thoracic aorta trough mRNA analisys of pro-inflammatory (ICAM-1, VCAM-1, IL-6, TNF-α and MCP-1) and anti-inflammatory (Arg-1, RETNLA, CCL5) genes.

Results

in ApoE KO mice treated with aldo, KD determined a significant improvements in glucose tolerance compared to mice fed a HFD without any significant effect on body weight. OH-But levels were always significantly higher in KD-mice than in AD-mice, confirming nutritional ketosis in KD-mice. Histological sections of aortic root showed that aldo treatment determined a significant increase in atherosclerotic plaque size and lipid content in HFD-mice. Such effects were significantly reduced in KD mice, suggesting a positive impact of ketosis in the prevention of atherosclerosis development. Plaque fibrosis, as measured by collagen content, did not differ among treatment groups. Finally, we observed a significant reduction in vascular inflammatory markers in KD-mice, when compared to HFD-mice. In particular, KD determined a significant reduction of gene expression of pro-inflammatory markers (ICAM-1, VCAM-1, IL-6, TNF-α and MCP-1) with the concomitant up-regulation of anti-inflammatory markers (Arg-1, RETNLA, CCL5), compared to AD.

Conclusion

the present study identifies KD as a potential non-pharmacological approach to prevent the development of atherosclerotic disease in subjects with high cardiovascular risk. Indeed, we demonstrated that KD determines decreased vascular inflammation and reduced atherosclerotic lesions in ApoE KO mice.

DOI: 10.1530/endoabs.81.P616

P617

place of plasma injections rich in autologous platelet in the management of diabetic foot ulcer (preliminary results)

Lionel Stève Kamgain Simeu, Mjabber Amal, Nassim Essabah Haraj, Siham El Aziz & Asma Chadli

Ibn Rochd University Teaching Hospital, Endocrinology, Diabetology, Metabolic Diseases and Nutrition, Casablanca, Morocco

Introduction

Diabetic foot ulcer (DFU) is one of the leading causes of non-traumatic lower extremity amputations worldwide. Conventional treatment is expensive and often requires a long hospital stay, placing a heavy burden on any healthcare system. Using autologous platelet-rich plasma (PRP), which is rich in various growth factors, can approximate the natural healing process.

Objective

Evaluate the place of PRP injections and its interest in the management of DFU.

Material and methodology

Prospective descriptive study including 21 patients hospitalized in the endocrinology department of the Ibn Rochd UTH in Casablanca for DFU, having received PRP injections, from September 2016 to September 2019. We excluded those with positive hepatic or HIV serologies and hemostasis disorders.

Results

The mean age was 56 years (34-75 years). A male predominance with an M/F sex ratio of 1.5. The average duration of diabetes was 13 years (3 to 30 years). The mean HbA1c was 10.9% (8.6-14.9%). The majority (86%) had grade 2 feet according to the TEXAS classification. The patients benefited from 4 to 7 sessions of PRP injections at the rate of one per week. The evolution was marked by good

healing in 92% of patients with budding and epidermization. No incident of blood or infection were noted.
Conclusion
PRP injections offer a promising alternative in the management of DFU. It is less expensive, less invasive, promotes safe and natural healing by reducing healing time. This is a method of the future taking place in the therapeutic arsenal of DFUs.

DOI: 10.1530/endoabs.81.P617

P618

Impact of teaching communication techniques to family member on quality of life score in patients with T2DM

Bharat Saboo[1], Shweta Saboo[1] & Aniket Inamdar[2]
[1]Prayas Diabetes Center, Indore, India; [2]Samarpan Clinic, Omerga, India

Introduction
Impact of teaching communication techniques to family member on quality of life score in people with T2DM.
Communication holds an important place in Diabetes management. People with diabetes usually have low self esteem. Proper communication with them can help in improving quality of life of people with diabetes. Family plays an integral part in Diabetes management. Benefits of proper communication has long been seen in various studies.
Aim
To see the Impact of teaching communication techniques to family member on quality of life score in people with T2DM.
Method
234 patient with diabetes were selected from Central India. They were divided in two groups of 117 each. Family members of one group were taught about communication techniques (called communication group)along with standard treatment while the second group was treated as such. The patients were surveyed for Quality of life and Depression at 30 days and 90 days. Results were analysed using MS excel.
Results
The Communication Group showed a decrease in Depression and improved quality of life score as compared with routine group. ($P<0.0001$), the communication group also showed better disease control (Target HBA1C <7 % in 72 % vs 43 % in routine group)
Conclusion
Communication is an integral aspect in Diabetes Care and most of the times it's with family members. The family members should be taught proper Communication techniques for better outcomes in terms of quality of life in patients with Diabetes. A guideline should be set in place to make communication a core part of overall Diabetes Management. The family members should be motivated to be a part of communication technique programs to improve their communication.

DOI: 10.1530/endoabs.81.P618

P619

Injection of epidermal growth factors in the treatment of diabetic foot ulcers

Sara Ragbi, Mjabber Amal, Nassim Essabah Haraj, Siham El Aziz & Asma Chadli
Uhc Ibn Rochd, Endocrinology and Metabolic Disorders, Casablanca, Morocco

Introduction
Diabetic foot ulcer (DFU) is one of the major complications of diabetes mellitus. It can be a cause of amputation. A multidisciplinary approach is essential to promote wound healing and decrease amputation rates. Epidermal growth factor (EGF) is used as an adjuvant to close the wound in addition to standard care in diabetic foot ulcers.
Methods
This is a prospective study carried out between February 2019 and April 2021 in the department of endocrinology and metabolic diseases, involving 7 patients admitted for DFU and who received intralesional EGF injections.
Results
The mean age was 51 years (4 men and 3 women). There were patients with type 1 and type 2 diabetes mellitus with a mean duration of 15 years. All the patients had high levels of HbA1c with an average of 8.5%. The ulcers were mainly located on the plantar aspect of the foot, complicated in 4 cases by osteitis, with an evolution ranging from 2 months to 3 years. The standard care included blood glucose regulation, debridement of necrotic tissues, treatment of infections and offloading. The patients received an average of 3 injections of EGF until a complete granulation response was achieved. There was a case of overgranulation causing treatment to be stopped. The average length of stay was 21 days. Complete granulation was achieved in 5 patients, with an average healing time of 65 days.
Conclusion
The intralesional application of EGF is an effective adjuvant treatment in addition to standard care. The clinical evolution of patients treated with intralesional EGF together with its safety make it a promising product to treat DFU.

DOI: 10.1530/endoabs.81.P619

P620

Diabetes and spontaneous miscarriage

Meriam Dalhoum, Zohra Hadj Ali, Ines Bani, Faika Ben Mami & Yosra Htira
National Institute of Nutrition, Department C, Tunis, Tunisia

Introduction
Early spontaneous miscarriage is common in diabetic women and has an unknown mechanism. This rate of spontaneous miscarriage is directly correlated to the glycemic control at the beginning of pregnancy.
Objective
To assess the frequency of spontaneous miscarriage in women with diabetes.
Patients and Method: This is a retrospective study including 50 diabetic women followed at department C of the National Institute of Nutrition of Tunis.
Results
The average age of our patients was 30 ± 7 years. The average duration of diabetes was 9 ± 7 years. Our population included: 46% type 2 diabetes, 42% type 1 diabetes and 12% gestational diabetes. the mean glycated hemoglobin (HbA1c) was 8.2%. The frequency of spontaneous miscarriage was 34% with a higher incidence in type 2 diabetics:82% vs 18% in type 1 diabetics. Patients with a history of spontaneous miscarriage had less controlled diabetes than others (mean hemoglobin glycated hemoglobin : 8.8% vs 7.9%).
Conclusions
Given the high frequency of spontaneous miscarriage in diabetic women, the practitioner is encouraged to provide adequate management of diabetic women before pregnancy.

DOI: 10.1530/endoabs.81.P620

P621

Phase angle, a raw bioelectrical impedance analysis (bia) variable, as a prognostic factor for mortality at 90 days in patients with covid-19

Isabel Cornejo-Pareja[1], Isabel M[a] Vegas-Aguilar[1], Jose Manuel Garcia-Almeida[1], Andrea Fernández Valero[1] & Francisco J Tinahones[1]
[1]Department of Endocrinology and Nutrition, Virgen de la Victoria Hospital (IBIMA), Malaga University, Malaga, Spain

Introduction
COVID-19 has taken on pandemic proportions. Phase angle (PhA) and Standardized phase angle (SPhA) have been related to mortality and severity in several diseases.

Objetives: To determine the predictive role of PhA and SPhA on 90 days survival of adults with COVID-19.
Methods
A longitudinal cohort study with 127 consecutive patients diagnosed with COVID-19. We collected PhA, SPhA, body composition (fat mass, fat free mass, hydration) and laboratory markers (CRP, D-dimer or albumin).
Results
COVID-19 patients in the lowest SPhA quartile (Q1) had increased ($P<0.001$) mortality and hospital stay ($P=0.009$). Q1 patients have hyperhydration status ($P<0.001$), decreased nutritional parameters [body mass cell index [BCMI ($P<0.001$)]and increased inflammation biomarkers [CRP ($P<0.001$), albumin ($P<0.001$), D-dimer ($P=0.002$)]. Multivariate analysis (Cox regression) revealed that PhA, adjusted for age, sex, BMI, and comorbidities (diabetes, hypertension, dyslipidaemia or heart disease), were associated ($P<0.001$) with increased mortality. The HR was 2.48 (95% CI, 1.60-3.84, $P< 0.001$). PhA $<3.95°$ was the cut-off for predicting mortality in acute COVID-19 with 93.8% sensitivity and 66.7% specificity. Non-surviving COVID-19 patients had significantly lower PhA and SPhA values ($P<0.001$) and increased hydration ($P<0.001$) compared to surviving patients.
Conclusions
PhA may play a role in assessing mortality risk in COVID-19, independently of age, sex, BMI, and comorbidities. The HR was 2.48 times for each degree that PhA decrease. SPhA quartiles are related to median survival (70 days in Q1 vs. more than 90 days in Q2 and Q3). PhA $<3.95°$ could be considered as a cut-off point for mortality risk prognosis in acute SARS-CoV2 infection.

DOI: 10.1530/endoabs.81.P621

P622

Disturbances in melatonin, leptin and ghrelin rhythms in women with metabolic syndrome with and without polycystic ovary syndrome

Presiyana Nyagolova[1], Mitko Mitkov[1], Vanya Peneva[2] & Dora Terzieva[2]
[1]Medical University Plovdiv, Endocrinology and Metabolic diseases, Plovdiv, Bulgaria; [2]Medical University Plovdiv, Department of Clinical Laboratory, Plovdiv, Bulgaria

Background
Polycystic ovary syndrome (PCOS) is a highly prevalent heterogeneous disease associated with ovulatory dysfunction and hyperandrogenemia. Recent data support a critical role of neuroendocrine dysfunction and metabolic disturbances in the pathophysiology of the syndrome, including hyperleptinaemia. Accumulating evidence suggests that circadian desynchrony is linked to obesity and metabolic syndrome (MetS). Both prevalence and incidence of the metabolic syndrome is very high in women with PCOS.
Objective
To examine daily fluctuations in serum levels of melatonin, leptin and ghrelin in women with PCOS and MetS
Patients and methods
The study included 12 women with PCOS and MetS and age-and BMI-matched 12 women with MetS without PCOS. The diagnosis PCOS was made according to the Rotterdam criteria. MetS was verified against IDF criteria (2009). Anthropometric measurements and circulating levels of melatonin, leptin and ghrelin at 3AM and 8AM, fasting insulin, fasting blood glucose, cholesterol, triglyceride, high-density lipoprotein (HDL) and low-density lipoprotein (LDL) levels were evaluated. Statistical analyses were performed using SPSS Ver. 26.0. A *P*-value less than 0.05 was considered statistically significant.
Results
Women with PCOS and MetS had significantly higher levels of 8AM leptin ($P=0.02$), fasting insulin ($P=0.05$) and HOMA-IR ($P=0.05$) compared to the patients with MetS only. In both groups we did not find significant difference between day and night melatonin and ghrelin levels. In women with PCOS and MetS we found significant difference between day and night leptin levels ($P=0.37$) while such difference was missing in women with MetS only. In both groups there was preserved cortisol rhythm.
Conclusions
Our results indicate that leptin is increased, but with preserved circadian rhythm in women with PCOS. Circadian misalignment of melatonin and ghrelin rhythms might be associated with metabolic dysregulation in women with PCOS and metabolic syndrome.
Key Words
PCOS, Metabolic syndrome, Leptin, Ghrelin, Melatonin Rhythm

DOI: 10.1530/endoabs.81.P622

P623

Metabolic Syndrome (MetS) Criteria in children with steroid-sensitive Nephrotic syndrome (SSNS) and frequent relapses treated with long-term prednisone therapy (LTPT) vs normal obese children

Ashraf Soliman, Mostafa Elbaba, Noor Hamed, Mona Shaat Dalees, Maya Itani & Fatima Al-Naimi
Hamad Medical Center, Pediatrics, Doha, Qatar

Steroid-associated adverse events (SAAE) include hypertension, hyperglycemia, and diabetes, overweight and obesity and short stature.
Aim
The goal of this study was to assess the occurrence of steroid-associated metabolic and clinical adverse events (SAAE) in patients with NS and frequent relapses treated with long-term prednisone compared to another high-risk group (obese children BMISDS $>$ 2)
Methods
Data of 30 children with SSNS was analysed retrospectively. They received prednisolone only in the standard dose for the initial episode at 2 mg/kg/day for six weeks followed by 1.5 mg/kg on alternate days for six weeks and relapses were treated with 2 mg/kg/day till remission followed by 1.5 mg/kg/day for four weeks. The cumulative dose of steroids over the period of 5 years was calculated for each child. The growth data was recorded along the treatment period. The different metabolic criteria including impaired fasting glucose (IFG), high LDL and cholesterol, lower HD and high blood pressure for age and sex were studied over this period of time and compared with the data for 66 age-matched obese non-nephrotic children.
Results
Comparison between the NS group treated for an average of 5 years with prednisone (cumulative dose$=$125 $+/-$ 28 mg/kg/yr.) and the non-nephrotic obese group showed that short stature (HtSDS $<$ -2), impaired fasting glucose (IFG), high cholesterol, triglycerides (TG) and LDL levels occurred more significantly in the NS group. Hypertension was detected in 28 % of the NS group vs 12.5% in the obese group. (Table)
Conclusion
In children with SSNS and frequent relapses, long-term steroid therapy was associated with higher rate of obesity, short stature as well as the occurrence of different MetS abnormalities including hypertension, dysglycemia, and dyslipidaemias compared to age matched obese children.

Table Metabolic risk factors among NS children on Long-term Prednisone therapy for $>$ 5 years vs age matched obese children.

Variables	NS on Pred $>$5 yr.	Obese 6-12 yr.
Number	30	66
Age	8.9+/-3.8	9.8 +/- 2.5
Overweight and obese	50%	100%*
Short stature HtSDS $<$-2	22%	6%
IFG$>$5.6 mmol/l	35%*	17.8%
LDL $>$ 2.7 mmol/l	77.7%*	8.0%
HDL $<$ 1.03 mmol/l	10%	20.8%
TG $>$1.7 mmol/l	33.3%*	8.0%
Cholesterol $>$ 4.5 mmol/l	80%*	20.8%
Hypertension BP $>$ 95th centile for age and sex	28.1%	12.5%

*p,0.05 NS vs Obese

DOI: 10.1530/endoabs.81.P623

P624

The action of WAY163909, central selective serotonin receptor, in obese and diabetic Wistar rats

Ivaylo Bogomilov[1], Vesela MIhneva[2], Ivona Daskalova[2], Rumen Nikolov[3] & Nadka Boyadjieva[3]
[1]Military Medical Academy-Sofia/Medical University-Sofia, Endocrinology/Pharmacology, Sofia, Bulgaria; [2]Military Medical Academy-Sofia, Endocrinology, Sofia, Bulgaria; [3]Medical University-Sofia, Pharmacology, Sofia, Bulgaria

Background and aims
Obesity can be cause because of reduction in energy expenditure and /or increased caloric intake. Total calorie intake has increased in recent decades and studies on eating behavior have reported increased intake of foods rich in fats and sugars. Many regulatory pathways for food intake, including those that use serotonin as a neurotransmitter, are affected by obesity or by hypercaloric diets. Summarizing the data known so far, it can be said that reduced serotonergic signaling and low availability of SERT are associated with hyperphagia and obesity. In addition, obesity has increased eating motivation and decreased D2/3 receptor binding, and lower DAT binding can be detected as well. Because of these facts, it is important to know brain serotonin mediation.
Materials and methods
WAY-163909 is a novel 5-hydroxytryptamine (HT)(2C) (serotonin) receptor-selective agonist that we used in our study. We used forty Wistar rats separate in 2 groups-rats with obesity and diabetes and healthy rats (control group). Each of this groups was separated in other 2 - one with daily intraperitoneal injection (i.p.) of WAY-163909 (for 1 mg/kg increasing till 32 mg/kg, 1 mg/kg per day) and one without. In 4 weeks period we were tracking blood glucose level, insulin secretion and rats weight. The differences in the mean values among the groups are greater than would be expected by chance; there is a statistically significant difference ($P = < 0.001$) using SPSS program.
Results
It was shown that after application of WAY-163909, the weight of the rats in diabetic and obese group rats decreased by 55.2% ($P < 0.05$), and by 25.3% ($P < 0.05$) in the control group using and no significant dynamic in the groups without daily intraperitoneal injection of WAY-163909. In the diabetic and obese rats group in which WAY-163909 was applied we had registered reduction of hyperglycemia (blood glucose over 7.0 mmol/l) by 35.4% ($P < 0.05$) compering the results before the start of using WAY-163909, which is greater in the rats which reduce more body weight. The research also shows decreasing of insulin resistance by 42.3 % ($P < 0.05$) in diabetic and obese rats group using WAY-163909.
Conclusion
Using WAY-163909 for treatment of obesity and obesity-induced diabetes in male Wistar rats, WAY-163909 significantly reduces body weightm hyperglycemia and peripheral insulin resistance. In the study was registered reducing of body weight not only in the obese and diabetic rats group, but also in the control group.

DOI: 10.1530/endoabs.81.P624

P625

The role of endocrine disruptors, obesity, and cytokines in PCOS

Michaela Duskova[1,2], Jana Vítků[1], Lucie Kolátorová[1], Jana Vrbíková[3], Michala Vosátková[3], Josef Včelák[3] & Marketa Šimková[1,4]
[1]Institute of Endocrinology, Department of Steroids and Proteofactors, Praha, Czech Republic; [2]General Teaching Hospital, Third Medical Department – Department of Metabolism and Endocrinology, Praha, Czech Republic; [3]Institute of Endocrinology; [4]University of Chemistry and Technology, Praha, Czech Republic

As genetic and environmental components contribute to the PCOS expression, we compared levels of endocrine disruptors, steroid hormones, cytokines, and metabolic parameters in twenty healthy, nine normal-weight PCOS women, and ten obese PCOS women. Steroid hormones, bisphenols (BPA, BPS, BPF, BPAF) and parabens (methyl-, ethyl-, propyl-, butyl-, benzyl-parabens) were measured by liquid chromatography-tandem mass spectrometry. Differences between the groups were assessed using the Mann-Whitney U test. Spearman correlation coefficients were calculated for the individual parameters relationship. Significantly higher levels of BPA, Anti-Müllerain hormone, lutropine, lutropine/folitropine ratio, testosterone, androstenedione, 7β-OH-epiandrosterone, and cytokines (IL-6, VEGF, PDGF-bb), were found in normal-weight PCOS women compared to controls. In PCOS women concerning the weight, there were no differences in hormonal, but in metabolic levels. Obese PCOS women had significantly higher insulin resistance, fatty-liver index, triglycerides, cytokines (IL-2, IL-13, IFN-γ). In healthy, but not in PCOS, women, there was a positive correlation of BPA with testosterone, SHBG with lutropine, and folitropine, while testosterone negatively correlated with SHBG. In obese women with PCOS, insulin resistance negatively correlated with SHBG and estradiol. No differences were observed in the paraben exposure. Levels of BPA were higher in PCOS women, indicating its role in the etiology. Obesity significantly worsens the symptoms.
Acknowledgements: This study was supported by the Ministry of Health of the Czech Republic (MZ ČR – RVO; Endokrinologický ústav - EÚ, 00023761).

DOI: 10.1530/endoabs.81.P625

P626

MODY 6: To be, or not to be, that is the question

Leonor Lopes[1], Catarina Roque[2], Carlos Bello[1], Maria Clotilde Limbert[1] & João Sequeira Duarte[1]
[1]Hospital Egas Moniz, Endocrinology, Lisboa, Portugal; [2]Hospital Fernando Fonseca, Endocrinology, Lisboa, Portugal

Introduction
Maturity-Onset Diabetes of the Young (MODY) is a rare cause of Diabetes Mellitus (<5%), resulting from autosomal dominant monogenic defects.
NEUROD1 gene is expressed in pancreatic and neuronal cells, being associated with MODY type 6. Mutations in NEUROD1 gene are reported in 20 families worldwide to date. Heterozygous variant c.616C>A, p.(His206Asn) has never been described.
Case Report
The authors report a case of a 38-year-old woman, with normal BMI, medical history of *Hashimoto*'s thyroiditis and family history of presumed Type 2 Diabetes (mother and maternal uncles), as well as pancreatic cancer (maternal grandmother). Patient presented with *de novo* Diabetes: A1C 7.2%, fasting glucose of 146 mg/dl and serum C-peptide 1.8 ng/ml. She did not complain about polydipsia, polyuria, or weight loss. Being a young adult, without classical clinical features of type 1 or type 2 diabetes, and with a strong family history, MODY gene panel was evaluated. An extremely rare mutation on NEUROD1 gene was documented – Heterozygous c.616C>A, p.(His206Asn) variant. Patient's mothers was also a carrier of the same mutation. Medical Genetics found the mutation pathogenicity doubtful and considered its clinical influence uncertain. The peculiarity of the case led to further analytical investigation: antibodies to GAD65 were positive (113.0 U/ml). Glycaemic control was achieved with a low dose of long-acting insulin (12 units glargine). It has been 4 years since the initial diagnosis and patient is metabolically stable (A1c 6.7%). Serum C-peptide was revaluated: 0.4 ng/ml (with fasting glucose of 98 mg/dl). The family is being genetically studied at the time of this report.
Conclusion
Current International guidelines consider the presence of antibodies GAD65 an exclusion factor for MODY's diagnosis. We present a case of a 38 year-old-woman with heterozygous mutation (c616C>A p.(His206Asn)) of the NEUROD1 gene and concomitant antibodies GAD65. Patient had detectable C-peptide at the diagnosis but after 4 years C-peptide is below the normal range. However, glycaemic control was achieved with a single daily dose of long-acting insulin. The most probable diagnosis is a type 1 diabetes with long "honey-moon period" being the genetic mutation in NEUROD1 gene an analytical incidentaloma.
Further genetic evaluation is necessary to define de main cause of metabolic disorder in this patient.

DOI: 10.1530/endoabs.81.P626

P627

Anxio-depressive disorders in diabetic pregnant women on the circumstances of the COVID 19 pandemic

Sara Charkaoui, Bensbaa Salma, Siham El Aziz, Nassim Essabah Haraj & Asma Chadli
Ibn Rochd University Hospital, Department of Endocrinology, Diabetology and Metabolic Diseases, Casablanca, Morocco

Introduction
The COVID 19 pandemic is causing a considerable degree of fear and concern among the general population. In diabetic pregnant women, this risk is even higher given the physiological and psychological changes that occur during pregnancy.
Goal of the study
To evaluate the prevalence and risk factors for the onset of anxiety-depressive disorders in pregnant women with diabetes during the COVID 19 pandemic in comparison with those followed outside this period.
Materials and methods
Case-control study on diabetic pregnant women followed in the endocrinology department of CHU Ibn Rochd (March 2020 - May 2021), based on the Hamilton anxiety and depression scale Arabic version.
Results
The study included 117 patients with an average age of 30.9 years. 60% had pregestational diabetes.70% were on insulin. Mean HbA1c was 8.7%. 19% had complicated diabetes. 18% reported an unwanted pregnancy. Only 15% of patients had planned their pregnancy. 30% of patients had a history of maternal-fetal complications. 31% had a history of SARS cov 2 infection. 31% of patients thought that the virus is more serious in diabetics and more than 50% had fears about the risk of materofetal transmission and the risk of fetal malformations. Anxiety was objectified in 74% of patients against 65% in controls and depression was found in 45% against 30% in controls. Anxio-depressive disorders were significantly associated with insulin therapy, the presence of maternal-fetal complications and the belief of patients vis-à-vis the virus. Depression was significantly associated with pregestational diabetes. Anxio-depressive disorders were less marked in patients with a history of SARS cov 2 infection.
Conclusion
Our study demonstrated a significant increase in the prevalence of anxiety-depressive disorders in diabetic pregnant women during the COVID 19 pandemic compared to the control group. This is mainly due to the beliefs of the patients vis-à-vis the virus. This justifies the need for screening and management of these disorders in this population during this period.

DOI: 10.1530/endoabs.81.P627

P628

Type 1 diabetes and autoimmune diseases

Meriam Dalhoum, Zohra Hadj Ali, Ines Bani, Yosra Htira & Faika Ben Mami
National Institute of Nutrition, Department C, Tunis, Tunisia

Introduction
Type 1 diabetes (T1DM) is an autoimmune disease in 90% of cases and is frequently accompanied by other autoimmune diseases.
Objective
To assess the frequency of autoimmune diseases in type 1 diabetics and study the particularities of this association.
Patients and Method
This is a retrospective study including 120 type 1 diabetic patients hospitalized in department C of the National Institute of Nutrition in Tunis.
Results
The mean age of our patients was 30± 12 years with a sex ratio M/F = 0.7. The average duration of diabetes was 12± 8 years. The mean glycated hemoglobin (HbA1c) was 10.3%. The frequency of autoimmune diseases was 20% with a higher incidence in women: 79% vs 21% men. Hypothyroidism topped the list with a frequency of 13.3%. The frequency of hyperthyroidism, celiac disease and Addison's disease was 4.3%, 3.3 % and 1.6% respectively. The frequency of Biermer's disease was the same as that of vitiligo : 0.83%. The following associations were noted: Hypothyroidism and celiac disease with a frequency of 0.83%. Hyperthyroidism and celiac disease with a frequency of 0.83%. Hypothyroidism, celiac disease and Addison's disease with a frequency of 0.83%. Diabetes type 1 preceded dysthyroidism in 85% of cases and other autoimmune diseases elicited in 100% of cases. Patients with associated autoimmune diseases were older (34.4 ± 12 vs. 29.1 ± 13 years; $P = 0.008$) and had older diabetes (14 ± 11 vs. 10 ± 9 years; $P = 0.005$).
Conclsion
The coexistence of autoimmune diseases in the type 1 diabetic patient is not rare, the practitioner is encouraged to screen them at least, as soon as diabetes is discovered and in front of evocative signs.

DOI: 10.1530/endoabs.81.P628

P629

Deep soft tissue masses as a manifestation of type 2 diabetes

Cristiana Gomes da Costa[1], Francisca Jácome Morgado[2] & Sónia Vale[1,3]
[1]Hospital Santa Maria, Lisbon, Portugal; [2]Centro Hospitalar e Universitário de Coimbra, Coimbra, Portugal; [3]Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal

Introduction
Xanthomas are defined as aggregates of lipid-laden histiocytes. They are generally present in superficial soft tissues such as skin and subcutis but can occasionally involve deep soft tissues. Xanthomas are classically associated with hyperlipidemia, that can be primary or secondary to numerous disorders such as diabetes. This case highlights an atypical manifestation of T2D.
Case report
A 61-year-old women was referred to our endocrinology outpatient clinic in July, 2020, due to new-onset diabetes. The patient mentioned weight loss, polyuria, polydipsia and blurred vision for 10 months before diagnosis. Importantly, she mentioned the appearance of several subcutaneous nodules on the buttocks, thighs and forearms 2 months before diagnosis. Her past medical history revealed hypertension controlled with metoprolol. There was no history of alcohol or tobacco use. Laboratory findings showed an elevated fasting blood glucose 444 mg/dl and HbA1c 15.2%, and an altered lipid profile (total cholesterol 249 mg/dl, HDL cholesterol 50 mg/dl, triglycerides 252 mg/dl). Other laboratory findings were unrevealing. On physical examination we outline the presence of multiple firm deep soft tissue masses, with irregular margins and no pain on palpation on the patient's gluteal region, thighs and forearm. She also had thin yellow to orange plaques on the left lower eyelid compatible with xanthelasma. Subsequent ultrasonography of these lesions revealed multiple hypoechogenic and heterogenous expansive lesions, with undefined borders, they were in touch with aponeurosis but did not infiltrate it, the biggest with the diameter of 56 mm in the gluteal region. The x-ray excluded bone involvement. She started glargine 10U/day with self-adjustment of dosage and metformin 500 mg tid. Three months after introduction of anti-diabetic therapy the masses started to reduce in size and after four months, they had totally disappeared. Biopsy was not performed due to the complete involution of masses. Furthermore, HbA1c decreased to 6% and the lipid profile had improved (total cholesterol 190 mg/dl, HDL cholesterol 58 mg/dl, triglycerides 96 mg/dl).
Discussion
Poor glycemic control has a negative impact on lipid profile. We report a unique case where deep soft tissue masses developed in association with newly diagnosed diabetes with spontaneous resolution after institution of anti-diabetic therapy. The fact that the patient had already a xanthelasma and the complete resolution of the nodules with glycemic and lipid profile improvement favours the diagnosis of deep soft tissue xanthomas.

DOI: 10.1530/endoabs.81.P629

P630

Dylipidemia in type 1 diabetic patients

Ines Bani, Zohra Hadj Ali, Meriam Dalhoum, Yosra Htira & Feika Ben Mami
National Institute of Nutrition of Tunis, Department C, Tunis, Tunisia

Introduction
Dyslipidemia in type 1 diabetic patients is a frequent situation and seems to be a risk factor for the occurrence of degenerative complications. The aim of this study is to evaluate the lipid profile of type 1 diabetic patients and to study the relationship between dyslipedmia and the occurrence of degenerative complications.
Method
This is a retrospective study conducted at the National Nutrition Institute of Tunis including 110 diabetic patients during the year 2021.
Results
The population consists of 45 men and 65 women, with mean age of 30+/- 12 years. The average duration of diabetes was 12 +/- 8 years. The majority of patients had poorly controlled diabetes with a mean HB1AC of 10.3 +/- 2%. Hypertriglyceridemia was present in 25.5% of patients. Moreover, hyper-LDL cholesterol and hypo-HDL cholesterol were noted in 42.7% and 32.4% of patients respectively. A significant association was noted between hypo-HDL cholesterol and diabetic nephropathy ($P = 0.035$), diabetic retinopathy ($P = 0.025$) and diabetic neuropathy ($P = 0.017$). In addition, hper LDL cholesterol was associated with diabetic nephropathy ($P = 0.003$). However, no association was found between hypertriglyceridemia and microangiopathic complications.

Conclusion
Dyslipidemia is common in type 1 diabetes and the lipid profile in type 1 diabetic patients influences the occurrence of degenerative complications of diabetes.

DOI: 10.1530/endoabs.81.P630

P631

Predictive factors of glycaemic control in type 2 diabetic patients during the COVID-19 crisis

Anis Grassa, Bel Hadj Sliman Chayma, Ameni Terzi, Nadia Khessairi, Meriem Yazidi, Ibtissem Oueslati & Melika Chihaoui
Rabta Hospital, Endocrinology, Tunisia

Introduction
Glycaemic control is still difficult to achieve despite advances in the pharmacotherapy of type 2 diabetes. Moreover, the COVID-19 crisis led to a disruption in medical consultations and in the access to medications. The aim of our study was to identify factors associated with poor glycaemic control in Tunisian type 2 diabetic patients during the COVID-19 crisis.
Methods
This is a cross-sectional study, carried out in December 2021, on type 2 diabetic patients followed up at the outpatient clinic of the department of endocrinology in Rabta University hospital. Three hundred patients with type 2 diabetes mellitus followed up for at least two years were included. Each patient underwent a clinical examination. Data on glycaemic control during 2019 and 2021 were collected from the medical file.
Results
Patients were 117 males and 183 females with a mean age of 61.6±9.7 years (22-91). One or more micro or macrovascular complications were present in 47.3%. Twenty-nine percent were previously infected with COVID-19 and 87% were vaccinated. More than half (52%) had poor socio-economic conditions and 46.7% were unable to buy their medications if unavailable in the public structures. The visits were irregular in one third of the patients, of whom 73.3% took regularly their medication. The mean annual HbA1c in 2021 was 8.2±1.8%. HbA1c was within the personalized targets in 42.7%. Uncontrolled diabetes was positively correlated with disease duration ($P=10^{-3}$), poly-medication ($P=0.031$), poor compliance to treatment ($P=0.002$), and the lack of drugs availability ($P=0.002$) . No correlation was found with the gender ($P=0.805$) or the occurrence of a COVID-19 infection ($P=0.204$). In multivariate analysis, independent risk factors were a duration of the disease longer than 6.5 years (OR=3.83; $P< 10^{-3}$), poor compliance to treatment (OR=2.37, $P=0.029$), and a mean annual HbA1c in 2019 higher than 7% (OR=9.09; $P< 10^{-3}$).
Conclsion
The management of diabetes should be patient-centred and multifactorial. It is therefore necessary to work on socio-economic factors and therapeutic education in order to improve the health status of our patients and limit the early onset of vascular complications.

DOI: 10.1530/endoabs.81.P631

P632

Assessment of glycaemic control in type 2 diabetic patients before and during the COVID-19 crisis

Chayma Bel Hadj Sliman, Anis Grassa, Ameni Terzi, Nadia Khessairi, Fatma Chaker, Ibtissem Oueslati & Melika Chihaoui
Rabta Hospital, Endocrinology Department, Tunis, Tunisia

Introduction
Chronic hyperglycemia in type 2 diabetic patients is associated with an increased risk of micro and macrovascular complications. Therefore, glycemic control is the cornerstone of its management. The aim of this study was to evaluate glycemic control in patients with type 2 diabetes before and during COVID-19 crisis.
Methods
A cross-sectional study was conducted during December 2021, in the outpatient clinic of the department of endocrinology in Rabta University hospital. The study included 300 patients with type 2 diabetes mellitus followed up for at least two years. Each patient underwent clinical examination and data on glycaemic control during 2019 and 2021 were collected from medical files.
Results
Patients were 117 men (39%) and 183 women (61%), with a mean age of 61.6 ± 9.8 years (22-91). The mean duration of the disease was 9.6±6.1 years (2-35). The main cardiovascular risk factors were smoking (21%), hypertension (56.7%) and dyslipidaemia (57.3%). Eighty-eight percent of the patients were treated with metformin as a monotherapy in one quarter of the cases and in combination with other oral antidiabetic agents, mainly sulfonylurea in 41% or insulin therapy in 35%. The mean number of medical visits per patient was 1.78±0.67 in 2019 and 1.9±0.74 in 2021 ($P=0.005$). A poor compliance with medication during the past three months was noted in 27% of the patients and was explained by a lack of availability of the drugs in 46.7%. Hypoglycemia was reported by 18% of the patients. It occurred more than once a week in one quarter of the cases and it was severe in 9.8% of them. The mean annual HbA1c was 8.1±1.7 % in 2019 and 8.2±1.8 % in 2021 ($P=0.12$). The mean annual fasting blood glucose was 1.71±0.56 g/l in 2019 and 1.79± 0.72 g/l in 2021 ($P=0.22$). Compared to 2019, glycaemic control in 2021 was stable in 36.4%, worsened in 33.6% with an increase in HbA1c of 0.11%, and improved in 30% of the patients.
Conclsion
Glycaemic control was not worsened during the COVID crisis despite the difficulties in the availability of the drugs.

DOI: 10.1530/endoabs.81.P632

P633

Metabolic emergencies during the month of Ramadan

Lionel Stève Kamgain Simeu, Nassim Essabah Haraj, Siham El Aziz & Asma Chadli
Ibn Rochd University Teaching Hospital, Endocrinology, Diabetology, Metabolic Diseases and Nutrition, Morocco

Introduction
Fasting in the month of Ramadan is one of the pillars of Islam. The diabetic subject, whether he practices it or not, if not prepared expose him to acute complications. The objective of our study was to determine the frequency of occurrence of acute complications during the month of Ramadan.
Objectives
To establish the epidemiological profile of diabetics seen in the emergency room during the month of Ramadan. Determine the frequency of occurrence of acute metabolic complications during this month.
Material and methodology
Descriptive observational study, conducted from April 13 to May 12, 2021, including 150 diabetic patients admitted to the emergency room of the Ibn Rochd UTH in Casablanca, for an acute metabolic complication during this sacred month.
Results
The mean age was 44.6 years (18-78). A female predominance with an M/F sex ratio of 2.22. T2DM was the majority (70%), the average duration of diabetes was 12 years (1-20), fasting was practiced by 44% of patients, including 9% of elderly subjects, degenerative complications of diabetes were present in 10% of patients, diabetic retinopathy was predominant (67%). Diabetic ketosis was the main reason for admission (57%), the frequency of hypoglycaemia remained low (2%). The mean HbA1c level was 12.4% (8.2-15.3), 64% of patients were on insulin. Forgetfulness of treatment was found in 51% of patients. Before Ramadan, 52% of T1DM patients and 64% of T2DM patients had not discussed with their healthcare professional, among them 93% of these T1DM patients ($P=0.0015$) and 50% of these T2D patients ($P=0. 07$), presented an acute complication.
Conclsion
Fasting during the month of Ramadan, if authorized in balanced patients, must be interrupted if diabetes is unbalanced. Therapeutic education and appropriate medical care are necessary to avoid acute complications.

DOI: 10.1530/endoabs.81.P633

P634

Determinants and consequences of nonadherence among patients with type-2-diabetes

Caroline Raun Hansen[1], Helena Zander Wodschouw[1], Hans Perrild[1], Tomas Møller Christensen[1], Torben Jørgensen[2,3] & Mette Zander[1]
[1]Bispebjerg-Frederiksberg Hospital, Department of Endocrinology, Copenhagen NV, Denmark; [2]Bispebjerg-Frederiksberg Hospital, Center for Clinical Research and Prevention, Frederiksberg, Denmark; [3]University of Copenhagen, Copenhagen, Denmark

Objective
To determine the cumulative incidence of nonadherent patients with type-2-diabetes from an outpatient clinic, and to examine determinants and consequences of premature discharge.
Research design and methods
A cohort comprising patients with type-2-diabetes referred to a Diabetes Clinic from 2009-2012 was assessed. Patients were categorized as nonadherent if discharged within two years of referral due to nonattendance and/or nonadherence to medication and control. Medication and biochemical values at baseline and two years later were assessed. Data regarding co-morbidity, mortality and socio-economics were extracted from national registers, and determinants and consequences of nonadherence were assessed.
Results
1072 patients were identified, and of these 1008 met the inclusion criteria. The cumulated incidence of patients classified as nonadherent was 20.3 %. Nonadherent patients were younger at time of type-2-diabetes diagnosis and had poorer glycaemic control at referral and two years later. Both non-western ethnicity and low education were determinants of nonadherence, but the effect of ethnicity became insignificant when adjusting for education, whereas the effect of education was less influenced by ethnicity. Cohabitation had no influence on adherence. Nonadherence was significantly associated with increased mortality also after adjusting for ethnicity and education, whereas the significance disappeared when adjusting for cohabitation.
Conclusions
Significant differences in glycaemic control, socioeconomics, and mortality were found between an adherent and a nonadherent group of type-2-diabetes patients. Low education seemed to be the principal determinant of nonadherence, while living alone was a mediator of increased mortality. To reach nonadherent patients and to reduce their risk of complications and reduced life expectancy, differentiated efforts should be considered.

DOI: 10.1530/endoabs.81.P634

P635

The importance of hepatocyte STAT5b, glucokinase and ChREBP in GH receptor-mediated regulation of steatosis and de novo lipogenesis is dependent on the nutritional state

Mari C. Vázquez-Borrego[1], Mercedes Del Rio-Moreno[1], Magdalena Wnek[1], Mariyah Mahmood[1], Jose Cordoba-Chacon[1], Michelle Puchowicz[2] & Rhonda Kineman[1,3]
[1]Department of Medicine, Section of Endocrinology, Diabetes, and Metabolism, University of Illinois at Chicago, United States; [2]Department of Pediatrics, Unversity of Tennessee Health Science Center, Memphis, United States; [3]Jesse Brown VA Medical Center, Research and Development Division, Chicago, United States

Fatty liver (steatosis) can progress to non-alcoholic fatty liver disease, increasing the risk of diabetes and cardiovascular disease. Growth hormone (GH) deficiency is associated with steatosis, while raising GH reduces steatosis. To date it remains to be determined how GH mediates this hepato-protective effect. To investigate the hepatocyte-specific actions of GH, a mouse model of adult-onset hepatocyte-specific GH receptor knockdown (aHepGHRkd) was generated by treating adult mice, homozygous for the GHR-floxed allele, with an adeno-associated viral vector expressing a thyroxin-binding globulin promoter driven Cre recombinase (AAV8-TBGp-Cre). Mice treated with an AAV8-TBGp-Null serve as GHR-intact controls. We reported that 7d-post aHepGHRkd, steatosis develops associated with enhanced expression of glucokinase (GCK), ketohexokinase (KHK) and *de novo* lipogenesis (DNL) genes, and increased rate of DNL which was measured by deuterated water labeling. New data demonstrate the aHepGHRkd-mediated alterations in liver phenotype persist under thermoneutral conditions (mice housed at 30C). Also, the increase in cytoplasmic GCK protein (active), but not KHK, occurs just 3d-post aHepGHRkd, suggesting enhanced glycolysis may be an initiating event to drive enhanced DNL, since the expression of KHK is upregulated by carbohydrate response element binding protein (ChREBP), a transcription factor activated by glycolytic metabolites. In fact, in preliminary studies we found that knockdown of hepatocyte ChREBP, in aHepGHRkd mice, prevented the rise in KHK, but did not prevent the rise in GCK or steatosis. Since GHR signals through JAK2/STAT5b to regulate many genes in hepatocytes, we sought to determine if restoration of STAT5b activity in aHepGHRkd would normalize the liver phenotype. To this end, we co-treated a subset of aHepGHRkd mice with an AAV expressing a constitutive active form of STAT5b (AAV8-TBGp-STAT5b^{CA}). Since regulation of hepatic lipid accumulation is dynamically mediated by multiple hormones and substrate availability, we compared the impact of aHepGHRkd, without or with STAT5b^{CA} under multiple nutritional conditions: natural fasting (10h after food withdrawal at 0600h), overnight fasting (16h), or overnight fasting with 6h refeeding. Data collected thus far show hepatocyte STAT5b, in the absence of GHR, can suppress GCK expression/activity, but this is not always associated with a reduction in steatosis or DNL, depending on the nutritional state. These findings imply that the GHR may signal independent of STAT5b to suppress DNL.

DOI: 10.1530/endoabs.81.P635

Endocrine-Related Cancer

P120

Novel panels of tissue microRNAs to diagnose adrenocortical malignancy based on artificial intelligence tools

Peter Turai[1], Zoltán Herold[2], Gábor Nyirö[1], Katalin Borka[3], Tamás Micsik[4], Judit Töke[1], Nikolette Szücs[1], Miklos Toth[1], Attila Patócs[5] & Peter Igaz[1,6]
[1]Semmelweis University, Department of Endocrinology, Department of Internal Medicine and Oncology, Budapest, Hungary; [2]Semmelweis University, Department of Internal Medicine and Oncology, Budapest, Hungary; [3]Semmelweis University, 2 nd Department of Pathology, Budapest, Hungary; [4]Semmelweis University, 1st Department of Pathology and Experimental Cancer Research, Budapest, Hungary; [5]National Institute of Oncology, Department of Molecular Genetics, Budapest, Hungary; [6]Semmelweis University, Deapartment of Endocrinology, Department of Internal Medicine and Oncology, Budapest, Hungary

Adrenocortical tumors are common, occuring in 5-7% of the population. Adrenocortical carcinoma (ACC) is rare (0.7-2/million/year) and it has a poor prognosis with a five-year survival of less than 30% in advanced stages. The histological differentiation of benign and malignant adrenocortical tumors is challenging.
Objectives
To explore the diagnostic utility of multiple microRNAs in various combinations as markers of adrenocortical malignancy by using artificial intelligence methods, based on machine learning and neural networks.
Materials and Methods
63 formalin-fixed, paraffin-embedded (FFPE) adrenocortical tissues were studied. The discovery cohort included 10 adrenocortical adenoma (ACA) and 10 ACC samples. An independent validation cohort encompassed another 21 ACC and 22 ACA samples. 16 microRNAs shown to be differentially expressed based on literature data were included. MicroRNA expression was studied by a 2-step TaqMan RT-qPCR. RNU48 was used as an internal, alongside with cel-miR-39 as an external control. Normalization of microRNAs was performed with the ΔCt method using R package NormqPCR. The order of microRNAs for the grouping of ACA and ACC samples was determined by the random forest classification method. The possibility of automatic classification of samples into ACA or ACC groups was tested by machine learning methods (R packages nnet and caret). Only models with more than 90% classification capability were selected for RT-qPCR validation and subsequent artificial intelligence-based classification. The best performing microRNA combinations (statistical models) were selected by neural network-based, 90-10% random learner-tester cross validation. 24 microRNA models were included in the validation performed in a blind manner.
Results
Hsa-miR-195, *hsa-miR-375, hsa-miR-483_3p, hsa-miR-483_5p* and *hsa-miR-503* were the best 5 microRNAs revealed by random forest algorithm to correctly classify the previously unkown samples. The following three, best performing statistical models were selected out of the former microRNAs: *hsa-miR-195 + hsa-miR-210 + hsa-miR-503*, *hsa-miR-210 + hsa-miR-375 + hsa-miR-503* and *hsa-miR-210 + hsa-miR-483-5p + hsa-miR-503* with sensitivity and specificity of 90.91-90.48; 90.91-90.48 and 90.91-95.24 %, respectively. The diagnostic performance of these three models was clearly superior over that of individual microRNAs.

Conclusion
We have established three microRNA combinations with outstanding diagnostic performance using artificial intelligence-based methods. These biomarker combinations can help histological analysis, and their use in small amount preoperative biopsy samples might also be envisaged.

DOI: 10.1530/endoabs.81.P120

P121

Abstract withdrawn

DOI: 10.1530/endoabs.81.P121

P122

Diagnostic evaluation of selected granin family proteins and INSM-1 (Insulinoma-associated protein 1) in patients with medullary thyroid carcinoma

Piotr Glinicki[1], Agnieszka Żyłka[2], Joanna Długosińska[2], Magdalena Ostrowska[1], Małgorzata Gietka-Czernel[1], Wojciech Zgliczyński[1] & Marek Dedecjus[2]
[1]Centre of Postgraduate Medical Education, Department of Endocrinology, Warsaw, Poland; [2]Maria Sklodowska-Curie National Research Institute of Oncology, Department of Oncological Endocrinology and Nuclear Medicine, Warsaw, Poland

Introduction
Medullary thyroid carcinoma (MTC) accounts for 3.5-5% of thyroid cancers. The biochemical diagnosis of MTC is based on the determination of concentration of a sensitive and specific biomarker - calcitonin (CT) as well as CEA and procalcitonin (PCT). Neuroendocrine cells have the ability to produce various proteins and neuropeptides (e.g. granin proteins and INSM-1), which are secreted into the circulation with calcitonin and can be measured in the blood as so-called circulating tumor markers.
Purpose
The aim of the study was to assess the usefulness of determining levels of selected granin family proteins and INSM-1 in the diagnosis of patients with medullary thyroid cancer.
Material and methods
34 patients with medullary thyroid carcinoma (MTC) were enrolled in the study. Patients were divided into 2 groups:
1. MTC – active form (7 patients with newly diagnosed MTC and 8 patients with distant metastases (4-15 years after thyroidectomy),
2. MTC – stable form, with no recurrence nor metastases ($n=19$).
Forty healthy individuals were the control group. The following levels were determined in all patients: calcitonin, procalcitonin, CEA, INSM-1, proSAAS, chromogranin B (CgB), chromogranin A (CgA) and derivates peptides: Pancreastatin/chromogranin A (250-301), Serpinin/prepro-chromogranin A (429-454), WE-14/prepro-chromogranin A (342-355) and Catestatin.
Results
In MTC-active patients levels of: CT, CEA, PCT, INSM-1, WE-14, Catestanin and Serpinin were significantly different vs. control group, with higher level in MTC patients. No significant difference was confirmed for CgA, CgB, pro-SAAS and Pancreastatin between MTC-active and the control group. For MTC-stable patients, only CEA, INSM-1 and Serpinin levels were significantly higher compared to the control group. In the group of patients with the active form of MTC, the following indicators of the diagnostic evaluation of the analyzed biomarkers were obtained: CT: 93% sensitivity and 100% specificity (AUC 0.968), PCT: 100% sensitivity and specificity, INSM-1: 100% sensitivity and 95% specificity (AUC 0.997), WE-14: 86.7% sensitivity and 87.5% specificity (AUC 0.922), Catestatin: 80% sensitivity and 85% specificity (AUC 0.899), Serpinin: 53% sensitivity and 95% specificity (AUC 0.764). In the group of MTC-stable form patients, the highest diagnostic usefulness was the determination of INSM-1 level: 57.9% sensitivity and 82.5% specificity (AUC 0.720) and Serpinin: 47.4% sensitivity and 90% specificity (AUC 0.737).
Conclsion
In patients with active MTC, the greatest diagnostic usefulness was found for the determination of CT, PCT and CEA levels as well as of new biomarkers: INSM-1 and selected peptides from the granin family: WE-14, Catestatin and Serpinin.

DOI: 10.1530/endoabs.81.P122

P123

The transcriptomic and methylomic landscape of POU1F1 pituitary tumors

Gloria Elena Silva Román[1,2], Ma Isabel Salazar[2], Keiko Taniguchi Ponciano[1], Juan Eduardo Peña Martínez[1], Sandra Vela Patiño[1,2], Sergio Andonegui Elguera[1], Erick Gomez Apo[3], Laura Chavez Macias[3,4], Etual Espinosa Cardenas[1], Claudia Ramirez Renteria[1], Aldo Ferreira Hermosillo[1], Ernesto Sosa[5], Moises Mercado[1] & Daniel Marrero-Rodríguez[1]
[1]Unidad de Investigación Medica en Enfermedades Endocrinas, Hospital de Especialidades, Centro Medico Nacional Siglo XXI, Instituto Mexicano del Seguro Social, Mexico City, Mexico; [2]Departamento de Microbiología, Escuela Nacional de Ciencias Biológicas, Instituto Politécnico Nacional, Mexico City, Mexico; [3]Área de Neuropatología, Servicio de Anatomía Patológica, Hospital General de México Dr. Eduardo Liceaga, Mexico City, Mexico; [4]Facultad de Medicina, Universidad Nacional Autónoma de México, Mexico City, Mexico; [5]Servicio de Endocrinología, Hospital de Especialidades, Centro Médico Nacional Siglo XXI, Instituto Mexicano del Seguro Social, Mexico City, Mexico

Pituitary adenomas (PA) are primarily benign lesions with monoclonal origins from the adenohypophyseal cells and represent 10-15% of all intracranial tumors. Tumors derived from POU1F1 cell lineage are GH-, TSH-, and PRL-secreting tumors that cause important syndromes such as acromegaly, hyperthyroidism, and sexual dysfunction, respectively. Surgical resection is the first line of treatment; the secondary treatment is pharmacological; despite having targets pharmacological in tumors derived of POU1F1 cell lineage, a high percentage of patient's present resistance to pharmacotherapy over time. The molecular alterations continue unclearly understood. We performed global transcriptome and methylome profiling in six non-tumoral pituitary glands and sixteen POU1F1 tumors distributed as follows ten GH-, four TSH- and two PRL-tumors identifying differentially expressed genes regulated by methylation, miRNA-mRNA regulation, and pathway alterations. Our results showed distinctive transcriptome and methylome profiles segregating control glands from tumor samples. The transcriptomic analysis further revealed better segregation clusters according to the hormone-secreting tumor. We identified up-regulated coding genes such as *DGKG*, *GRM5,* and *GPR173* common to the three tumors derived from the POU1F1 lineage. Interestingly, in each tumor identified up-regulated coding and non-coding genes such as *CDKA5R1*, *MET*, *GRIN3A* and *miR4771-1* in PRL-; *CHKA*, *TMEM233, miR95, LINC01347* and *LINC01524* in GH-; *NTRK3*, *GRIK4*, *miR4510, miR3925* and *LINC00662* in TSH-secreting tumors, that could serve for future specific targets for molecular therapy. In addition, inside up-regulated genes we also identified hypomethylated status genes such as *DGKG*, *miR590*, *miR4510*, *LINC00662*, *LINC01000*, *LINC01347*, *LINC01524*; DNA hypomethylation in CPG islands in these genes potentially participates in up-regulated gene expression. miRNA-target gene found an interaction between *miR590* with *ANXA1*, *S100A10*, *YAP1*, *STAT3*, *ATP13A3*, *PTPN14*, *PCDG11X* that also were identified down-regulated in our transcriptomic analysis. Pathway analysis revealed alterations in glycerophospholipids, phospholipase, and calcium signaling pathways. Overall, these results indicate potential molecular markers that could become specific targets for developing novel therapies.

DOI: 10.1530/endoabs.81.P123

P124

Hirsutism as the first manifestation of a mesonephric-like adenocarcinoma of the ovary: the first case with positive androgen receptors

Iciar Martín Timón, Beatriz Ugalde-Abiega, Mikaela Zubillaga, Inmaculada Moreno-Ruiz, Isabel Huguet, Olalla Meizoso-Pita, Vanessa Triviño Yannuzzi & Cristina Sevillano-Collantes
Hospital Universitario Infanta Leonor, Endocrinology, Madrid, Spain

Mesonephric adenocarcinoma (MA) is an uncommon gynecologic tumor that are thought to arise from embryonal remnants of the mesonephric ducts, also known as Wolffian ducts. Mesonephric-like adenocarcinoma (MLA), despite absence of Wolffian origin, have similar morphology and immunophenotype and exhibit molecular aberrations like MA. These tumors are generally negative for estrogen and progesterone receptor.

Case Report

An 83-year-old Spanish female was referred to our outpatient clinic of endocrinology to study hirsutism. She had a history of 4 uncomplicated pregnancies and experienced menopause at age 42 years. She had not taken hormone replacement therapy and she didn't experience uterine bleeding. A drug history excluded anabolic steroid use or exposure to exogenous androgens. In the anamnesis she referred a recent-onset hirsutism, less than 3 months, without signs of virilization and constitutional syndrome with asthenia and anorexia. Ferriman-Gallwey score was not calculable by depilation of facial and body hair; it was only visible the presence of excess terminal hair growth in the abdomen. She had no stries. Laboratory testing revealed the following levels: total testosterone 4.46 ng/ml (normal range, <0.25), androstenedione >10 ng/ml (normal range, 0.3-3.3), 17-hydroxyprogesterone 17.80 ng/ml, dehydroepiandrosterone sulfate (DHEA-S) 183 mg/dl. Abdominopelvic CT revealed two tumors in the pelvis of 11.5x9 cm and 8.5x5.5 cm. The largest one had necrotic degeneration. No significant adenopathies where shown and adrenal glands were normal. A laparoscopic bilateral salpingo-oophorectomy was performed. Histopathology revealed two tumors of 13x11x7 cm, of 851 gr of weight, and another one of 9x8x2 cm. The first one was solid with gray-white solid areas associated with areas of necrosis with admixture of growth patterns (ductal and tubular), as well as intraluminal eosinophilic colloid-like material resembling mesonephric remnants, and atypical nuclear cells. No evidence of mesonephric remnants or endometriosis were observed. The other one was a fibrous fragment which included the other ovary and fallopian tube. There was no neoplastic infiltration of other tissues, and the peritoneal fluid was positive for malignancy. By immunohistochemistry, tumor cells were positive for GATA3, CD10 and androgen receptor and negative for calretinin, PAX8, estrogen and progesterone receptors, TTF1 and CDX2. The final diagnosis was MLA of the ovary pT2aNx (TNM, 8^a edic), FIGO IIA. After the surgery, testosterone level was <0.20, androstenedione <0.3 ng/ml, 17-hydroxyprogesterone 0.3 ng/ml and DHEAS 34.3 mg/dl.

Conclusion

Here we describe the first case of mesonephric-like adenocarcinoma of the ovary with positive androgen receptors

DOI: 10.1530/endoabs.81.P124

P125

Elevated SGPL1 expression is associated with increased metabolic rate in cells and reduced survival in individuals with adrenocortical carcinoma

Jack Williams[1], Chris Smith[1], Charlotte Hall[1], Zakaa Khaled[1], Avinaash Maharaj[1], Ruth Kwong[1], James Pittaway[1], Josefina Casas[2], Laila Parvanta[3], Tarek Abdel-Aziz[4], Fausto Palazzo[5], Teng-Teng Chung[4], Leonardo Guasti[1], Louise Metherell[1] & Rathi Prasad[1]
[1]Queen Mary University Of London, Centre for Endocrinology, William Harvey Research Institute, London, United Kingdom; [2]IQAC-CSIC, Research Unit on BioActive Molecules (RUBAM), Department of Biological Chemistry, Madrid, Spain; [3]St Bartholomew's Hospital, Department of Surgery, London, United Kingdom; [4]University College London Hospitals NHS Foundation Trust, Department of Endocrinology, London, United Kingdom; [5]Imperial College London, Department of Endocrine and Thyroid Surgery, London, United Kingdom

Introduction

Sphingosine-1-phosphate lyase (SGPL1) catalyses the final step in sphingolipid metabolism, irreversibly degrading the lipid signalling molecule sphingosine-1-phosphate (S1P). The relative abundance of S1P compared to its precursors sphingosine and ceramide finely tunes signal transduction for a wide range of cellular pathways including proliferation, apoptosis, migration and calcium handling. Loss-of-function mutations in SGPL1 cause a spectrum of disorders, including primary adrenal insufficiency (PAI). Adrenocortical carcinomas (ACCs) are invasive tumours arising in the adrenal cortex, and steroidogenic tumours are associated with worse prognostic outcomes. Given that loss of SGPL1 expression causes PAI, we hypothesised increased SGPL1 expression might increase steroidogenesis and therefore be linked to increase disease severity in ACC.

Methods

We analysed two ACC cohorts with survival data and corresponding RNA-seq/Microarray transcriptomic data, focusing on SGPL1 and other genes in the sphingolipid pathway. *In vitro,* we generated isogenic SGPL1-knockout and stable SGPL1-overexpressing H295R adrenocortical cells to better analyse the role of SGPL1 in cell signalling in ACCs. To investigate the effect of these perturbations on cell signalling and function we conducted assays for proliferation, migration, lipidomics, calcium signalling, apoptosis, autophagy, metabolism and gene/protein expression.

Results

We found increased *SGPL1* expression correlated with reduced patient survival in two ACC cohorts, and a correlation in SGPL1 and Ki67 expression in a small cohort of ACC tissue samples. We also found a similar correlation in patient survival and sphingosine-1 kinase expression and the opposite correlation with patient survival and sphingosine-1-phosphatase expression. We noticed a marked increase in proliferation in SGPL1-overexpressing cells and a concordant decrease in proliferation in knockout cells. Similarly, overexpressing cells migrated faster while knockout cells were slower. SGPL1 overexpression significantly reduced levels of pro-apoptotic ceramides, although no reduction in apoptosis was observed. RNA-seq revealed a global increase in the expression of genes in the electron transport chain in overexpressing cells, correlating with increased aerobic respiration and glycolysis in these cells. Furthermore, the opposite phenotype was seen in cells lacking SGPL1. We subsequently found the increased proliferation is linked to metabolic substrate availability. We therefore propose that SGPL1-overexpressing ACC tumours reduce patient survival by increasing anabolism and energy availability for growth and invasion.

Conclusions

SGPL1 expression correlates with growth and migration rates in H295R cells, with knockout reducing steroidogenic capacity and overexpression increasing metabolism.

DOI: 10.1530/endoabs.81.P125

P126

Ultrasound and cytological features of thyroid nodules with aggressive behavior: from histology to clinic

Daniele Sgrò[1], Giuseppe Greco[2], Alessandro Brancatella[2], Nicola Viola[2], Mauro Casula[2], Liborio Torregrossa[2], Teresa Rago[2], Ferruccio Santini[2] & Francesco Latrofa[2]
[1]University of Pisa, Section of Endocrinology and Metabolic Disease, Department of Clinical and Experimental Medicine, Pisa, Italy; [2]University of Pisa, Section of Endocrinology and Metabolic Disease, Department of Clinical and Experimental Medicine, Pisa, Italy

Fine-Needle Aspiration Biopsy (FNAB) is the recommended diagnostic tool for differentiating malignant from benign thyroid nodules and provides indication for surgical decisions. According to the Italian system, thyroid nodules are classified as TIR 1/1C, TIR 2, TIR 3A, TIR3B, TIR4 or TIR5, which correspond to Thy I, Thy II, Thy III, Thy IV, Thy V and Thy VI categories of the Bethesda system. TIR 3 identifies the indeterminate nodules. Surgery is usually recommended for TIR 3B, TIR 4 and TIR 5 nodules. Among papillary thyroid carcinomas (PTC), the classic and follicular (CV-PTC and FV-PTC) are characterized by a good prognosis and require a less aggressive treatment, while the tall cell (TC-PTC) and the solid variants (SV-PTC) and others rarer (columnar, hobnail and diffuse sclerosing variants) have a worse prognosis. In addition, thyroid ultrasound often identifies thyroid nodules <1 cm, which are usually characterized by an indolent behavior and active surveillance may be advised. We aimed at identifying which ultrasound and cytological features enable to recognize, among TIR4-5 nodules, the aggressive variants and, among TIR3B nodules, the malignant ones. To this purpose we retrospectively analyzed the histopathological records of 1117 patients (for a total of 1668 nodules, 650 malignant) who underwent surgery in 2017 and who had previously undergone FNAB and thyroid ultrasound (available for 390 nodules). Of the 566 PTC, 18.7% were TIR3A, 20.7% TIR 3B and 51.6% TIR4-5, while of 50 FTC 42.0% were TIR3A, 42.0% TIR3B and 6.0% TIR4-5. Of

the 11 PDTC 54.5% had been diagnosed as TIR 3B. Of the 249 classic variant of PTC, 0.8% had resulted TIR3A, 14.1% TIR3B and 79.9% TIR4-5. Among 49 TC-PTC, none had resulted TIR3A, 2% had been diagnosed as TIR3B and 95.9% as TIR4-5. Of the 219 FV-PTC 42.0% had resulted TIR3A, 39.7% TIR3B and 12.3% TIR4-5. Among 34 SV-PTC, 32.4% had been diagnosed as TIR3A, 41.2% TIR3B and 0.6% TIR4-5. At ultrasound, blurred margins were the only feature associated with malignancy ($P=0.034$) in TIR3B category. The coexistence of hypoechogenicity and blurred margins in absence of microcalcifications were more common in the TC (7/28) compared to the CV (10/120) of PTC ($P=0.021$). In conclusion ultrasound helps to identify, among TIR4 and TIR5 nodules, the aggressive variants, and among TIR3B, the malignant ones, and therefore to choose the extent of surgical treatment and, when <1 cm, to confidently advise active surveillance.

DOI: 10.1530/endoabs.81.P126

P127

Role of DKK1 in growth and migration of prostate cancer cells

Letizia Rinella[1], Mara Compagno[2], Gloria Fiorentino[1], Nicoletta Fortunati[3], Emanuela Arvat[1,3] & Maria Graziella Catalano[1]
[1]University of Turin, Department of Medical Sciences, Turin, Italy; [2]Fondazione Edo ed Elvo Tempia, Molecular Oncology Laboratory, Biella, Italy; [3]AO Città della Salute e della Scienza di Torino, Oncological Endocrinology, Turin, Italy

Androgen deprivation therapy is the choice treatment of metastatic prostatic tumors. Unfortunately, very often, resistance occurs and chemotherapy is needed. Results are however disappointing with frequent side effects. Therefore, new therapeutic approaches for metastatic and advanced prostate cancer are necessary. DKK1, an inhibitor of the Wnt signaling pathway, is increased in different types of cancer. In prostate cancer patients with bone metastases, an increase of DKK1 is observed both in the serum and in the prostate tissue, suggesting that DKK1 might be considered as a new molecular target in the metastatic prostate cancer therapy. The aim of this study was to evaluate the role of DKK1 in growth and migration of prostate cancer cell lines (PC3 and DU145), expressing high levels of DKK1. To this end, we carried out DKK1 gene silencing and knockout in PC3 and DU145 cells. Silencing was obtained by specific siRNA to DKK1; permanent knockdown was performed using a CRISPR/CAS9 system. Real-Time PCR, Western Blotting analysis, and secretion levels by ELISA confirmed DKK1 silencing and knockout, respectively. The effects of silencing (PC3-siRNA and DU145-siRNA) and knockdown (PC3-KO and DU145-KO) were evaluated in terms of cell growth by colorimetric WST-1 test and cell migration by transwell migration assay. A significant reduction of mRNA, protein levels and secretion of DKK1 was observed in both cell lines where DKK1 was silenced or knocked-down. Functionally, DKK1 inhibition resulted in a reduction of cell growth and migration. In conclusion, our data support a key role of DKK1 in the growth and migration of prostate cancer cells. Based on our study, DKK1 may represent a specific target for a new therapy intended to specifically block its function in metastatic and advanced prostate cancer.

DOI: 10.1530/endoabs.81.P127

P128

Splicing machinery dysregulation in rare neuroendocrine tumors: pheochromocytomas and paragangliomas

María Trinidad Moreno Montilla[1,2,3], Ricardo Blázquez Encinas Rey[1,2,3], Ángel Mario Martínez Montes[4], Víctor García Vioque[1,2,3], Emilia Alors-Pérez[1,2,3], Federica Mangili[1,2,3,5], Antonio Agraz-Doblas[1,2,3], Mercedes Robledo[4,6], Justo P. Castaño[1,2,3,7] & Alejandro Ibañez Costa[1,2,3]
[1]Instituto Maimónides de Investigación Biomédica de Córdoba, Córdoba, Spain; [2]University of Cordoba, Department of Cell Biology, Physiology and Immunology, University of Cordoba, Córdoba, Spain; [3]Hospital Universitario Reina Sofia, Córdoba, Spain; [4]National Cancer Research Center, Madrid, Spain; [5]University of Milan, Department of Clinical Sciences and Community Health, Milano, Italy; [6]Centro de Investigación Biomédica en Red de Enfermedades Raras (CIBERER), Madrid, Spain; [7]CIBER Physiopathology of Obesity and Nutrition (CIBERobn), Madrid, Spain

Pheochromocytomas and paragangliomas (PPGL) are commonly benign catecholamine-producing neuroendocrine tumors (NETs); however, up to 25 % of patients develop distant metastases or aggressive behavior. The current classification of PPGL comprises pseudohypoxia-profile, MAPK-pathway alteration, and Wnt-pathway dysregulation clusters according to their genomic characterization. However, to date, there are no biomarkers to help stratify patients based on their prognosis. Alternative splicing is an emerging cancer feature that has been linked to a more aggressive phenotype in a variety of neoplasms, including NETs. In this context, we have recently discovered alterations in the splicing machinery in other NETs, such as pancreatic and lung NETs. The splicing process has not been studied in detail before in PPGL, but there are reasons to expect that it could be altered. Thus, the aim of this study was to assess the profile of the splicing machinery in PPGL and study its potential relationship with clinical-molecular features. To this end, we studied the expression of 313 splicing-related genes in the data available in the TCGA dataset, which includes 151 patients (29 paragangliomas, PGL, and 122 pheochromocytomas, PCC). Most splicing-related genes were found to be similar in PCC and PGL, but 16 genes, including *RBM22*, *CELF4*, and *PABPC1*, exhibited significant differences. Interestingly, a detailed analysis among the three genomic clusters revealed considerable differences, standing out 143 of 313 splicing-related genes, which were found over- or under-expressed. It is also worth noting that just the expression of *CELF4* and *API5* was sufficient to clearly distinguish the three clusters: low expression of both genes in pseudohypoxia cluster, high in kinase signaling, and *CELF4* high and *API5* low expression in Wnt-altered cluster. Furthermore, 27 genes were shown to be associated with aggressive PCC; in particular, categorizing PCC samples based on high or low expression of specific genes, such as *LSM4* or *SMC1A*, allowed us to predict aggressive/metastatic behavior. In addition, aggressive PGLs had differential expression of 25 genes. Altogether, our findings show that the splicing machinery is disrupted in PPGL, which encourage us to explore the splicing process in a larger cohort of PPGL samples and investigate the functional importance of these splicing-related genes *in vitro*.

Keywords: pheochromocytoma, paraganglioma, metastasis, splicing dysregulation, splicing machinery. This work was supported by MICINN (PID2019-105201RB-I00), Beca GETNE 2019, Fundación Eugenio Rodríguez Pascual, ISCIII (CD19/00255).

DOI: 10.1530/endoabs.81.P128

P129

The impact of pregnancy on disease outcome in patients with persistent differentiated thyroid carcinoma

Noemi Giancola[1], Carla Colombo[1,2], Simone De Leo[1], Matteo Trevisan[1], Luca Persani[1,3] & Laura Fugazzola[1,2]
[1]Division of Endocrine and Metabolic Diseases, Istituto Auxologico Italiano IRCCS, Milan, Italy; [2], Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy; [3], Department of Medical Biotechnology and Translational Medicine, University of Milan, Milan, Italy

Background
Pregnancy does not cause differentiated thyroid cancer (DTC) recurrence in patients without structural or biochemical evidence of disease at the time of conception. However, data regarding pregnancy's impact in patients with persistent DTC before conception are still controversial.
Aim
The aim of the study was to determine whether pregnancy could significantly influence the outcome in DTC patients in persistence before pregnancy, but with a biochemical and structural stable disease.
Methods
This was a retrospective evaluation of all women followed for DTC at a tertiary Italian thyroid cancer center who had a pregnancy after initial treatments between 2003 and 2020. Subjects included were required to have biochemical and/or structural persistence within 12 months before pregnancy.
Results
we enrolled 8 patients with papillary thyroid carcinoma (PTC) with a mean age at diagnosis of 27.6 years and a mean time between PTC diagnosis and pregnancy of 60 months. Among the 7 patients with structural disease, five patients had lung metastases, two lymph node metastases and one patient biochemical persistence. Patients were treated with total thyroidectomy, lymphadenectomy and radioactive iodine ablation (RAI). According to 8 th edition of the American Joint Commission on Cancer (AJCC) and 2015 American Thyroid Association (ATA) 2015 guidelines, 75% of women had AJCC stage I and intermediate

risk of recurrence and 25% had AJCC stage II and high risk of recurrence. Evaluation of Dynamic Risk Stratification (DRS) during the 24 months of follow-up showed 88% patients with structural incomplete response and 12% with a biochemical incomplete response. During a mean follow-up of 153 months, none of the patients showed biochemical and radiological progression of disease during pregnancy or within 6 months of delivery and no further treatments were required. One patient with lung metastases had an increase of thyroglobulin during pregnancy, which returned to the pre-pregnancy levels after delivery.
Conclusions
Our data demonstrate that pregnancy is not associated with significant progression in patients with stable persistent DTC before conception. However, further studies are needed to verify the effect of pregnancy on the outcome of patients with persistent and progressive disease.

DOI: 10.1530/endoabs.81.P129

P130

Origins of progesterone in male mice

Hannah Colldén[1], Malin Hagberg Thulin[1], Andreas Landin[2], Anna-Karin Norlén[3], Henrik Ryberg[3], Jianyao Wu[1], Karin L Gustafsson[1], Louise Grahnemo[1], Karin Nilsson[1], Klara Sjögren[1], Matti Poutanen[1], Liesbeth Vandenput[1] & Claes Ohlsson[1]
[1]Gothenburg University, Sahlgrenska Academy, Insitute of Medicine, Gothenburg, Sweden; [2]Sahlgrenska University Hospital, Clinical Pharmacology, Gothenburg, Sweden; [3]Sahlgrenska University Hospital, Clinical Chemistry, Gothenburg, Sweden

The role of progesterone in male physiology is mainly unknown. We recently observed that progesterone was the most abundant sex hormone in orchiectomized (ORX) mice with most of it stored in white adipose tissue (WAT) (1). The aim of the present study was to use a sensitive and validated gas chromatography/tandem mass spectroscopy method to determine the origins of progesterone in male mice. Tissue levels of progesterone were high in adrenals of male mice, indicating that male progesterone may be predominantly adrenal-derived. To determine if progesterone only originates from the adrenals in males, we compared WAT levels of progesterone in ORX + adrenalectomized (ADX) and intact mice. Surprisingly, combined orchiectomy and adrenalectomy did not reduce progesterone levels in WAT (mean ± SEM, 1.638 ± 239 pg/g vs. 1.871 ± 124 pg/g, non-significant). In both groups, we also observed high levels of progesterone along the gastrointestinal tract including the gastric contents. To evaluate food as a potential progesterone source, we analyzed progesterone levels in 20 types of mouse chow and found varying but substantial levels in all tested types (2.319-17.702 pg/g). To identify main sources of food-derived progesterone, we analyzed progesterone levels in several food items, reveling no/low levels in non-animal-derived food items, medium levels in meat and very high levels in dairy products such as cream (123.162 ± 1.282 pg/g). To functionally test if orally ingested progesterone could contribute to tissue levels, we administered isotope-labeled progesterone or vehicle by oral gavage for 10 days to adult ORX + ADX male mice, and data indicated some uptake of labeled progesterone into the WAT. Interestingly, a recent metagenomic study showed an association between gut microbiota (GM) functional traits and circulating progesterone levels in humans (2). Accordingly, we determined the impact of the GM for progesterone levels in WAT and found that germ-free male mice, completely lacking GM, had substantially increased progesterone levels in WAT compared with conventionally raised mice (+ 132% ± 25%; $P<0.001$). In conclusion, in the absence of adrenal-derived progesterone in male mice progesterone levels are maintained by an alternative progesterone source. We propose that food-derived progesterone may be taken up and maintain close to normal progesterone levels in ORX + ADX male mice. Furthermore, GM composition may regulate this uptake of progesterone.
References
1. Colldén *et al*. Endocrinology. 2022; doi: 10.1210/endocr/bqac001.
2. Liu *et al*. Nat Genet. 2022;54(1):52-61.

DOI: 10.1530/endoabs.81.P130

P131

Neuropeptide Y (NPY) and Human cocaine- and amphetamine-regulated transcript (CART) in patients with adrenal pheochromocytoma

Piotr Glinicki, Magdalena Ostrowska, Lucyna Papierska, Alicja Szatko & Wojciech Zgliczyński
Centre of Postgraduate Medical Education, Department of Endocrinology, Warsaw, Poland

Introduction
Pheochromocytoma is a rare tumor that develops from chromaffin cells of the adrenal medulla. In about 90% of cases, it is a benign tumor. Along with catecholamines, neuroendocrine cells of the adrenal medulla have the ability to produce various proteins and neuropeptides and secrete them into the blood. Among the known biologically active substances are: neuropeptide Y and human cocaine- and amphetamine-regulated transcript (CART).
Purpose
The aim of the study was to assess the usefulness of the determination of levels of neuropeptides: neuropeptide Y and CART in the diagnosis of patients with adrenal pheochromocytoma.
Material and methods
Patients were divided into 4 groups:
1. Patients with pheochromocytoma ($n=51$),
2. Patients with adrenal incidentaloma ($n=23$),
3. Patients with primary arterial hypertension ($n=20$),
4. Control group – healthy volunteers ($n=52$).
The following biochemical determinations were performed in all patients: plasma levels of metanephrine and normetanephrine, concentration of chromogranin A (CgA), neuropeptide Y (NPY) and human cocaine- and amphetamine-regulated transcript (CART). Biochemical determinations were made using the LC-MS/MS technique and immunochemical techniques (IRMA, ELISA) were used.
Results
Concentrations of the analyzed biomarkers: CgA, NPY and CART were significantly higher ($P<0.001$) compared to control groups (adenoma, primary hypertension and healthy subjects). Sensitivity, specificity and AUC indices of the analyzed biomarkers: CgA, NPY and CART were compared in the group of patients with pheochromocytoma vs. control groups: adenoma, primary hypertension and healthy subjects. Pheochromocytoma vs. adenoma: CgA: 84% sensitivity and 96% specificity (AUC 0.932); NPY: 80% sensitivity and 78% specificity (AUC 0.808) and CART: 43% sensitivity and 100% specificity (AUC 0.768). Pheochromocytoma vs. primary hypertension: CgA: 78% sensitivity and 100% specificity (AUC 0.945); NPY: 47% sensitivity and 100 specificity (AUC 0.615) and CART: 72% sensitivity and 85% specificity (AUC 0.797). Pheochromocytoma vs. healthy subjects (blood donors): CgA: 84% sensitivity and 98% specificity (AUC 0.923); NPY: 90% sensitivity and 86% specificity (AUC 0.897) and CART: 60% sensitivity and 49% specificity (AUC 0.403).
Conclsion
Among the analyzed biomarkers, CgA concentration determination presented the highest discriminant value between patients with pheochromocytoma and other study groups. Neuropeptide Y showed a high specificity between the analyzed groups, especially in the differential diagnosis of patients with adenoma and patients with essential hypertension.

DOI: 10.1530/endoabs.81.P131

P132

Somatostatin receptor splicing variant SST5TMD4 overexpression in glioblastoma is associated to poor survival, increased aggressiveness features and somatostatin analogs resistance

Jesus Perez Gomez[1,2,3,4], Antonio C. Fuentes-Fayos[1,2,3,4], Miguel E. G-Garcia[1,2,3,4], Annabel Peel[5], Cristóbal Blanco Acevedo[1,2,6], Juan Solivera Vela[1,2,6], Alejandro Ibáñez Costa[1,2,3,4], Manuel David Gahete Ortiz[1,2,3,4], Justo P. Castaño[1,2,3,4] & Raúl M. Luque[1,2,3,4]
[1]Maimónides Biomedical Research Institute of Córdoba (IMIBIC), Córdoba, Spain; [2]University of Cordoba, Department of Cell Biology, Physiology, and Immunology, University of Cordoba, Córdoba, Spain; [3]Reina Sofia University Hospital (HURS), Córdoba, Spain; [4]CIBER Physiopathology of Obesity and Nutrition (CIBERobn), Córdoba, Spain; [5]Cardiff University, School of Biosciences, Cardiff, United Kingdom; [6]Reina Sofia University Hospital, Department of Neurosurgery, Córdoba, Spain

Glioblastoma (GBM; grade IV astrocytoma) is the one of the most malignant and lethal endocrine-related cancers worldwide. Current standard treatment consists of surgery followed by radiotherapy and/or chemotherapy; however, this is only a palliative approach with a mean post-operative survival of scarcely ~12-15 months. Therefore, the identification of novel therapeutic targets to treat this devastating pathology is urgently needed. In this context, the truncated splicing-variant of the somatostatin receptor subtype 5 (SST_5TMD4), which is produced

by aberrant alternative splicing, has been demonstrated to be overexpressed and associated with increased aggressiveness features in several endocrine-related cancers/tumors. However, the presence, functional role, and associated molecular mechanisms of SST_5TMD4 in GBM have not been yet explored. Therefore, we performed herein a comprehensive analysis to characterize the expression and pathophysiological role of SST_5TMD4 in human GBM. We demonstrated that SST_5TMD4 was significantly overexpressed (at mRNA and protein levels) in human GBM tissues ($n=47$) compared to non-tumor brain tissues (control; $n=15$) and grade III-astrocytoma patients ($n=9$). Remarkably, SST_5TMD4 expression was significantly associated with poor overall survival and recurrent tumors in GBM patients. Moreover, *in vitro* SST_5TMD4 overexpression (by specific plasmid) increased, whereas SST_5TMD4 silencing (by specific siRNA) decreased, key malignant features (i.e., proliferation and migration capacity) of GBM cells (U-87 MG/U-118 MG models). Furthermore, SST_5TMD4 overexpression in GBM cells altered the activity of multiple key signaling-pathways associated with tumor aggressiveness and progression (AKT, JAK-STAT, NF-κB and TGFβ routes), and its silencing sensitized GBM cells to the antitumor effect of pasireotide (a somatostatin analog). Altogether, these results demonstrated that SST_5TMD4 is overexpressed and associated with enhanced malignancy features in human GBMs and revealed its potential utility as a novel and useful diagnostic and prognostic biomarker and as a potential target in the future development of therapeutic approaches in patients with this devastating endocrine-related cancer, offering a clinically relevant opportunity that should be tested for use in humans.

Fundings
Spanish Ministry of Science, Innovation and Universities (PID2019-105564RB-I00, FPU16-05059, FPU20-03954, FPU18-06009), Junta de Andalucía (P20_00442, PEER-0048-2020, BIO-0139) and CIBERobn.

DOI: 10.1530/endoabs.81.P132

P133

Rapidly progressive cases of ectopic adrenocorticotropic hormone syndrome

Lucía González Gracia, Gema López Gallardo, Bothayna Oulad Ahmed, Elena Dios Fuentes, Luis Beltrán Romero & Alfonso Soto-Moreno
Virgen del Rocío University Hospital, Sevilla, Spain

Introduction
Adrenocorticotropic hormone (ACTH)-dependent Cushing's syndrome (CS) secondary to an ectopic source is an uncommon condition, accounting for 4-5% of all cases of CS and between 9-18% of cases of ACTH-dependent CS. Although numerous malignancies have been associated with ectopic ACTH syndrome (EAS), lung neuroendocrine tumours (NETs) are the most common. Refractory hypokalemia can be the presenting feature in EAS and is seen in up to 80% of cases. We present two cases which first presented with hypokalemia, refractory to treatment with potassium supplementation and spironolactone.
Cases reports

Table 1

Gender:	Male	Female
Age: (years)	62	56
Clinical presentation	- Hypertension - Newly diagnosed hyperglycaemia - Hyperpigmentation - Peripheral edema	- Constitutional syndrome - Newly diagnosed hypertension and hyperglycaemia - Proximal myopathy - Peripheral edema
Biochemical parameters	Glucose 187 mg/dl K^+ 2.5 mEq/l (3.5 – 5)	Glucose 150 mg/dl K^+ 2.2 mEq/l (3.5 – 5) pH 7.56; $HCO3^-$ 49.1 mEq/l
Hormone parameters	UFC 14219.7 mg/24 h (35 – 135) ACTH > 1500 pg/ml (3.6 – 60.5)	UFC 1268 mg/24 h (35 – 135) ACTH 276.9 pg/ml (3.6 – 60.5)
Tumor localization	Ileum	Lung
Tumour size	32 mm	17 mm
Histopathology	Large-cell neuroendocrine carcinoma	Small-cell neuroendocrine carcinoma
Immunohistochemistry	Chromogranin and synaptophysin positive. ACTH negative	Chromogranin, synaptophysin, CD56 and TTF1 positive. ACTH negative
Ki-67	70-80%	90%
Metastasis	+	+
Treatment of hypercortisolism	Ketoconazole + somatostatin analogs	Ketoconazole
Outcome	Deceased	Deceased
Survival from time of diagnosis	19 days	12 days

UFC: 24 h-urinary free cortisol; Chromogranin, synaptophysin and CD 56: markers of neuroendocrine differentiation. TTF-1: primary site marker (lung and thyroid)

Conclusions
We present two cases of ectopic ACTH syndrome similar in their clinical presentation (newly diagnosed hyperglycaemia and hypertension and severe hypokalemia), tumour aggressiveness and rapidly fatal outcome. Furthermore, we present a case of EAS produced by a NET from the ileum tract. To our knowledge this is extremely rare and only described in isolated case reports

DOI: 10.1530/endoabs.81.P133

P378

Serial liquid biopsies - the NETest - in gastroenteropancreatic NET surveillance

Mark van Treijen[1,2], Tiny Korse[2,3], Wieke Verbeek[2,4], Margot Tesselaar[2,5] & Gerlof D. Valk[1,2]
[1]UMC Utrecht, Endocrine Oncology, Utrecht, Netherlands; [2]AVL/UMC Utrecht Enets Center of Excellence; [3]The Netherlands Cancer Institute, Clinical Chemistry, Amsterdam, Netherlands; [4]The Netherlands Cancer Institute, Gastroenterology, Amsterdam, Netherlands; [5]The Netherlands Cancer Institute, Medical Oncology, Amsterdam, Netherlands

Introduction
The variable tumor behavior in patients with gastro-entero-pancreatic neuro-endocrine tumors (GEPNETs) is challenging. Current general biomarkers are insufficient to predict the disease course. An emerging biomarker is the NETest, a blood-based gene signature that can predict disease status based on the expression of genes involved in tumor biology. While promising, the accuracy and reproducibility of results in daily practice during years of follow up has never been assessed. Evaluation of serial NETest measurements in an individual is needed to determine its place in the clinical armamentarium.
Aims
To evaluate if serial NETest measurements can predict treatment response and reflect disease evolution during years of follow up.
Methods
Serial NETest scores were compared with RECIST1.1 defined disease status in 132 GEP-NET patients over 46 (6-71) months of follow-up. A median of 4 samples was collected in patients on a watch-and-wait strategy or undergoing systemic treatment. Pre- and post-treatment scores (<6 months) were compared with progression-free survival (PFS).
Results
Fluctuating scores [0-100%] were seen in patients with no evidence of disease (NED) and stable disease (SD). None of the 30 patients with NED and 1 of the 28 (4%) patients with SD had all outcomes within the low range. In patients with progressive disease (PD) and not receiving any treatment ($n=16$), ongoing tumor progression was confirmed in consecutive samples in 82%. Patients responding to treatment (PFS > 12 months) had higher pre-treatment NETest scores (76.5; $n=22$) compared to non-responders (33; $n=12$;$P=0.001$). Patients with low pre-treatment scores had a 21 months shorter PFS after treatment (10 vs 31

months;$P=0.008$). The accuracy for treatment response prediction was 0.73 ($P=0.009$). Post-treatment scores had no discriminative value.
Conclusion
Low NETest scores are associated with an indolent tumor behavior in the follow up of individuals, but scores fluctuate over time in patients with NED and SD. Elevated NETest scores in patients on watch-and-wait strategy had limited predictive value while elevated scores – measured before treatment initiation – predicted treatment response and might therefore be used for individualizing decisions on starting systemic therapy.

DOI: 10.1530/endoabs.81.P378

P379

First case report of a natural killer T (NK/T) extranodal nasal lymphoma presenting as a diabetes insipidus

Karol Almendra Alvarado Rosas, Valeria Gonzalez Sacoto, Leticia Serrano Urzaiz, Macarena Lacarta Benítez, Cristina Contreras Pascual, Maria Elena Lopez Alaminos, Pablo Trincado, Patricia De Diego Garcia & Javier Acha Perez
Hospital Universitario Miguel Servet, Endocrinología y Nutrición, Zaragoza, Spain

A 52-year-old male patient with no past medical history of interest was admitted to our Endocrinology Unit with a clinical course developed in the last month of sudden polyuria, nocturia and polydipsia (8 liters/day) associated with bilateral low back and leg pain, a right-side nasal congestion with eye swelling and paresthesia. Physical examination revealed a doubtful thickening of the nasal mucosa and several two-cm- scattered erythematous disseminated skin lesions. Blood samples showed basal sodium levels between 146-148 mEq/dl. A Miller test confirmed the diagnosis of Central Diabetes Insipidus (CDI) with a urine osmolality of 444 mOsm/kg that raised to 720 mOsm/kg after desmopressin. Anterior pituitary hormone levels were within normal range. A pituitary MRI showed a focal 10x7x10 mm posterior lesion with extension towards to the pituitary stalk, along with bilateral mucous thickening in ethmoid cells and occupation of nostrils, especially in the right side. During admission, the patient presented worsening of nasal symptoms, solid and liquid dysphagia and advance of skin lesions, which were biopsied. Oral desmopressin was started at a dose of 90 mg/day and subsequently moved on to 240 mgc/day due to persistent polyuria. Infectious processes, germinoma, autoimmune and associated granulomatous disease were ruled out. Due to symptomatology and imaging tests, a diagnostic lumbar puncture was performed, showing infiltration of 66% NK cells by flow cytometry in CSF. Similar findings were observed in skin biopsy with cutaneous infiltration by T cells with CD3 epsilon, CD 7, CD56, granzyme and perforin positive immunophenotype, positive ISH EBER and ki-67 $>$ 90 %. An 18-FDG-glucose- PET-TC showed extensive supra and infradiaphragmatic nodal invasion with splenic, pituitary, nasosinusal, spinal cord and lumbosacral root cord and probable hepatic, adrenal, cutaneous and bone involvement. According to Pink Scale a diagnosis of high score extranodal T/NK lymphoma, nasal type stage IV with cutaneous and central nervous involvement was stated. The patient started a chemotherapy treatment (SMILE protocol) that included dexamethasone, methotrexate, ifosfamide, l.asparaginase and etoposide with clinical improvement and radiological resolution of brain lesions three months afte the diagnosis.
Conclusion
The diagnosis of central DI always makes it necessary to rule out infectious, autoimmune, infiltrative and hematological diseases. Extranodal NK/T lymphoma (nasal type) is a rare neoplasm with an aggressive behavior, first reported here in presenting with CDI, in which early diagnosis and treatment is essential.

DOI: 10.1530/endoabs.81.P379

P380

Hormonal therapy in breast cancer patients and malignancy risk of thyroid nodules

Alexandra Abegão Matias, Bruno Bouça, Teresa Sabino, Paula Bogalho & José Silva-Nunes
Hospital de Curry Cabral, Department of Endocrinology, Diabetes and Metabolism, Lisbon, Portugal

Introduction
The bidirectional relationship of risk between breast cancer (BC) and thyroid cancer (TC) has been debated. Estrogens are proposed as agents implicated in the risk of developing TC promoting thyroid tumorigenesis. Therapies that reduce the effect of estrogens on their receptors in cancer cells are widely used.
Objective
To correlate the use of hormonal therapy in BC with the prevalence of TC.
Material and Methods
We performed a retrospective analysis of female patients with nodular thyroid pathology and BC followed in our consultation from January 2016 to January 2021. The variables were analyzed using the SPSS software; they are expressed as mean and standard deviation (with a 95% confidence interval).
Results
A total of 3253 patients with nodular thyroid disease were identified. In 4.1% of patients ($n=132$) BC was described in the medical records. Twenty-eight patients were excluded due to lack of data. Regarding the patients included ($n=104$), the mean age at diagnosis of BC was 56 ± 12 years. Patients underwent radiotherapy in 75.9% of cases ($n=79$), hormonal therapy in 72.1% ($n=75$) and chemotherapy in 52.9% ($n=55$). Considering the largest thyroid nodule, the mean diameter in thyroid ultrasound was 22.8 ± 8.5 mm. Fine needle aspiration cytology (FNAC) was performed in 88.5% of patients ($n=92$) and was repeated in 23.9% ($n=22$), mostly due to an initial non-diagnostic result. Considering both procedures, the result was benign in 82.6% ($n=76$), non-diagnostic in 9.8% ($n=9$), follicular lesion of undetermined significance in 2.2% ($n=2$), suspected of malignancy in 2.2% ($n=2$), Hürthle cell tumor in 1.1% ($n=1$) and follicular tumor in 2.2% ($n=2$). Thyroid surgery was performed in 18.3% of patients ($n=19$) with a prevalence of thyroid malignancy of 8.7% ($n=9$). Papillary thyroid carcinoma was diagnosed in eight patients and follicular thyroid carcinoma in one patient. Compared with patients who did not undergo hormonal therapy, patients undergoing hormonal therapy did not show a decrease in cytological (OR = 0.88 [0.16-4.88];$P=0.88$)) or histological (OR = 0.28 [0.07-1.15];$P=0.08$)) risk of TC.
Conclusion
An increased risk of thyroid cancer has been reported in breast cancer survivors. Despite the published evidence on the role of estrogens in the association of BC and TC, in our studied sample there was no relationship between the use of hormonal therapy and the prevalence of TC. Further studies with a larger sample size should be encouraged.

DOI: 10.1530/endoabs.81.P380

P381

A metastatic ACC mouse model: Combined inactivation of Znrf3 & Tp53 results in consistent adrenocortical carcinoma formation

James Wilmouth[1], Julie Olabe[2], Laly Pucheu[2], Roucher Florence[3], Cecily Lucas Rodrigues[2], Christelle Soubeyrand-Damon[2], Kroiss Matthias[4,5], Laura-Sophie Landwehr[4], Martin Fassnacht[4], Anne-Marie Lefrancois-Martinez[2], Antoine Martinez[2] & Pierre Val[2]
[1]iGReD UMR CNRS 6293, INSERM U1103, Clermont-Ferrand, France; [1] iGReD UMR CNRS 6293, INSERM U1103, Clermont-Ferrand, France; [3]Hospices Civils de Lyon, Biochimie Biologie Moléculaire Grand Est - UM Pathologies Endocriniennes Rénales Musculaires et Mucoviscidose, Lyon, France; [4]Division of Endocrinology and Diabetes, University Hospital, University of Würzburg, Department of Internal Medicine I, Würzburg, Germany; [5]LMU Klinikum, Department of Internal Medicine IV, Munich, Germany

Adrenocortical carcinoma (ACC) is an infrequent and aggressive cancer that originates from steroidogenic cells within the adrenal cortex. Half of patients present with metastatic spread at initial diagnosis, and to date, there is no curative therapy for advanced disease. Recent genomic analysis has established that the most aggressive subgroup of ACC patients have overlapping alterations in the WNT/B-catenin pathway and the p53/RB pathway. We therefore set out to develop a metastatic ACC mouse model based on patient genomic alterations. Using Cre loxP technology, we inactivated both Znrf3, a negative regulator of the WNT/beta-catenin pathway, & p53, a potent tumor suppressor, in steroidogenic cells. By 6 months of age, mice with individual inactivation of p53 (PKO) or Znrf3 (ZKO) did not show tumor formation, while the combined inactivation of p53 & Znrf3 (DKO) resulted in aggressive carcinomas that metastasize at a rate of 36.8%. Using the ROSA26^{mTmG} reporter, we identified metastatic deposits in the lymph nodes, peritoneal cavity, lungs and liver of DKO mice. Importantly, metastatic DKOs show a significant increase in adrenal weight and Ki67 index, while having a significant decrease in overall survival. Furthermore, these tumors

are hormonally inactive, representing a subtype of ACC that has not been previously established in available mouse models. Taken together, these results establish that combined inactivation of Znrf3 & p53 in steroidogenic cells provides a habitable environment for the development of metastatic ACC. The timeline and consistent rate of metastasis in this mouse model highlights its importance for the study of metastatic ACC dissemination, immune-tumor interactions, and potential anti-cancer therapies.

DOI: 10.1530/endoabs.81.P381

P382

Effect of metformin on the activity of the mTORC1 complex in patients with type 2 diabetes

Tamara Vatseba[1], Liubov Sokolova[2], Volodymyr Pushkarev[2], Viktor Pushkarev[2], Olena Kovzun[2] & Mykola Tronko[2]
[1]Ivano-Frankivsk National Medical University, Endocrinology, Ivano-Frankivsk, Ukraine; [2]V.P. Komisarenko Institute of Endocrinology and Metabolism of the National Academy of Medical Sciences of Ukraine, Kyiv, Ukraine

Introduction
The increased risk of cancer in patients with diabetes mellitus (DM) creates an interest in finding mechanisms of the possible association of antidiabetic drugs and carcinogenesis. Metformin has the most documented evidence of pleiotropic oncoprotective effects, including increased stabilization of tumour suppressor p53, inhibition of NF-κB activation, slowing of the cell cycle and inhibition of mitosis due to decreased expression of cyclin D and cyclin E, as well as the positive effect on intestinal microbiota. The study of the drug's ability to affect the activation of insulin signalling PI3K/Akt/mTOR, which is involved in the regulation of carcinogenesis and metabolism, continues. The aim of the study was to compare the activity of PI3K/Akt/mTOR in patients with type 2 diabetes on metformin monotherapy and other antidiabetic regimens.
Methods
To assess the activation of the PI3K/Akt/mTOR pathway in patients with type 2 diabetes by enzyme-linked immunosorbent assay in peripheral blood mononuclear cells, the content of natural inhibitor of mTORC1 - phosphorylated PRAS40 and the content of phosphorylated protein kinase p70S6K1 were determined. The amounts of phospho-PRAS40 (*P*-Thr246) and phospho-p70S6K1 (*P*-Thr389) were determined using a microplate reader of "Bio-tek Instruments" company (USA) at a wavelength of 450 nm with the diagnostic ELISA kits (KHO0421, 85-86053 respectively (Invitrogen, USA)).
Results
Significantly lower phospho-PRAS40 levels in patients with type 2 DM on metformin monotherapy compared with patients on combination therapy with sulfonylurea derivatives (SUD) and metformin ($t=2.34$;$P<0.05$); lower levels of phospho-p70S6K in patients on monotherapy with metformin in comparison to patients on combination therapy with SUD and metformin ($t=4.13$;$P<0.05$), combination therapy with SUD and insulin ($t=3.76$;$P<0.05$), combined therapy with SUD, metformin and DPP-4 inhibitors ($t=4.0$;$P<0.05$), on insulin monotherapy ($t=3.85$; $P<0.05$) were found. The decrease in the content of phospho-PRAS40 on metformin monotherapy can be explained by the ability of the drug to increase the interaction of PRAS40 with Raptor in the mTORC1 complex, which influences the phosphorylation activity of PRAS40. Decrease in the content of phospho-p70S6K (depending on the activity of the mTORC1 complex) may be explained by the ability of metformin to increase the level of AMPK, the negative regulator of mTORC1.
Conclsion
The obtained results confirm the property of metformin to inhibit the activity of the mTORC1 complex.
Key words
metformin, type 2 diabetes mellitus, PI3K/Akt/mTOR, phospho-PRAS40, phospho-p70S6K.

DOI: 10.1530/endoabs.81.P382

P383

Circulating cell-free tumour DNA (ctDNA) utilisation in diagnosis and monitoring of thyroid cancer response to treatment - systematic review

Ali Al Jumaah[1,2], Miles J Levy[2], Narendra Reddy[2], Ragini Bhake[2] & Shailesh Gohil[2]
[1]University of Leicester, Leicester, United Kingdom; [2]University Hospitals of Leicester NHS Trust, Department of Endocrinology, Leicester, United Kingdom

Thyroid cancer is the most common endocrine malignancy accounting for 1% of new cancer cases each year. Even after treatment, one in five patients develop recurrence eventually. Therefore, close follow up is crucial after treatment. Current tumour biomarkers are not perfect, and there is a need for a more sensitive and specific way of detecting early recurrence. Liquid biopsies have emerged as a novel marker in tumour surveillance and monitoring response to treatment. In particular, Circulating cell-free Tumour DNA (ctDNA) have been investigated. Here, we review the available evidence regarding the use of ctDNA as a liquid biopsy in the diagnosis and monitoring of thyroid cancer response to treatment.
Methodology
Online database search of PubMed (Medline) was performed using keywords; Circulating Tum* DNA, ctDNA, cfDNA, liquid biopsy, thyroid cancer, thyroid neoplasm*, thyroid carcinoma, papillary, medullary, follicular, anaplastic. Reference lists were reviewed for relevant literature. Modified PRISMA model was adopted for article extraction. Due to significant heterogeneity in trial population characteristics, methodology and outcomes, meta-analysis was not feasible.
Results
After filtering our search to human only trials, some articles were excluded after title reading and screening the text. 11 relevant articles were identified from the online database. 8 more articles were identified from reference lists of relevant reviews raising the total number of articles to 19. Trials included a total of 1163 patients. Of the different tumour types, papillary thyroid cancer (PTC) was the most common type in 71% of patients followed by medullary (MTC) then anaplastic thyroid cancer (ATC) in 14.4% and 10.3% of patients respectively. $BRAF^{V600E}$ was the most commonly sought after ctDNA variant amongst others which included RET and TP53. Tissue mutant DNA detection was performed using digital droplet PCR (ddPCR) and real-time PCR (qPCR) in most trials. Few trials used targeted Next Generation Sequencing technique limited to previously reported mutational hotspot. Concordance rate of tissue-to-peripheral blood mutant DNA detection rate varied from 0% to 86% in trials of diagnosis and surveillance for disease recurrence. The main pitfall was that seeking mutations commonly reported in the literature in both tissue and blood risks missing ctDNA containing less common/unique mutations thereby reducing ctDNA analysis sensitivity.
Conclusion
cT-DNA offers a novel and minimally invasive tool for surveillance and monitoring of thyroid cancer. Research utilizing wider or individualised gene mutation panels is warranted to improve test sensitivity.

DOI: 10.1530/endoabs.81.P383

P384

Appendiceal neuroendocrine neoplasms diagnosed during pregnancy-case series and review of the literature

Orit Twito[1,2], Akirov Amit[2,3], Rosenblum Rachel Chava[1,2], Dana Herzberg[1,2], Kira Oleinikov[4], Rotman-Pikielny Pnina[2,5] & Simona Glasberg[4]
[1]Edith Wolfson Medical Center, Endocrinology, Holon,; [2]Tel-Aviv University, Sackler Faculty of Medicine, Tel-Aviv, Israel; [3]Rabin Medical Center - Beilinson Hospital, Endocrinology, Israel; [4]Hadassah Medical Organization and Faculty of Medicine, the Hebrew University, Neuroendocrine Tumor Unit, Jerusalem, Israel; [5]Meir Medical Center, Endocrinology, Netanya, Israel

Introduction
Although appendicitis occurs in approximately 1:1000 pregnancies, appendiceal neuroendocrine neoplasm (ANEN) diagnosis during pregnancy is very rare. Data on presentation, treatment and prognosis is scarce.
Aim
To describe ANEN cases diagnosed during pregnancy.
Materials and Methods
A retrospective appraisal of 7 consecutive ANEN patients diagnosed during pregnancy from four Israeli tertiary medical centers and comparison with 17 cases described in the literature from 1965-2021.
Results
Age at ANEN diagnosis was 26.4 ± 3.5 years (range 21-33). Patients were diagnosed between gestational weeks 6-40, most frequently in the third trimester (53%). The most common presenting symptom was abdominal pain. Tumor size

was 14.3±8.9 mm (range 3-45 mm). In patients from our series appendiceal base involvement was reported in 2/7; mesoappendiceal invasion in 5/7; lympho-vascular invasion in 2/7. KI-67 staining was reported in 6/7 cases and ranged from 1-10%. Pathology details were lacking in most of the previously published cases. All 7 pregnancies in our series resulted in term delivery with no complications, whereas in historical cases there were one first trimester abortion, one ectopic pregnancy, and one stillbirth. Right hemicolectomy was performed in 5/7 patients in our series and reported in 2/17 historical cases. All hemicolectomies were performed after delivery, 3-16 months after appendectomy. Local metastases were reported in two cases. Follow-up duration was 7-98 months in our patients and 3-48 months in 5 previous cases. No disease recurrence, distant metastases or mortality were noted.

Conclusions

ANEN diagnosis during pregnancy is extremely rare. Pregnancy outcomes were usually favorable and long-term prognosis was excellent.

DOI: 10.1530/endoabs.81.P384

P385

PD-1 and PD-L1 immune checkpoint expression - the prognostic impact on adrenocortical carcinoma

Laura-Sophie Landwehr[1], Iuliu Sbiera[1], Barbara Altieri[1], Hanna Remde[1], Stefan Kircher[2], Silviu Sbiera[1,3], Matthias Kroiss[1,3,4] & Martin Fassnacht[1,3,5]

[1]University Hospital Würzburg, Department of Internal Medicine I, Division of Endocrinology and Diabetes,; [2]University Würzburg, Institute of Pathology; [3]University of Würzburg, Comprehensive Cancer Center Mainfranken; [4]LMU Klinikum München, Medizinische Klinik und Poliklinik IV; [5]University Hospital Würzburg, Clinical Chemistry and Laboratory Medicine

Adrenocortical carcinoma (ACC) is a very severe endocrine malignancy with poor prognosis. While cancer immunotherapies have revolutionized the treatment of several cancer entities, the results of initial studies of different immune checkpoint inhibitors in ACC were heterogeneous and clinically substantial responses were observed only in a subset of patients. Expression of immune checkpoint molecules - programmed cell death 1 (PD-1) and its ligand PD-L1 - has been shown to predict response in different, but not all cancer entities. Using immunohistochemistry, a cohort of 129 ACCs was examined for PD-1 and PD-L1 expression. PD-1 and PD-L1 were present (threshold of $\geq$1% of cells) in 17.4% and 24.4% of samples, respectively, but expression was heterogeneous and in general rather low (median 3.9% (range 1-15) and 19.7% (range 1-90)). Interestingly, PD-1 expression was significantly associated with beneficial progression-free (HR: 0.30, 95% CI 0.13-0.72) and overall survival (HR: 0.21, 95% CI 0.53-0.84) independently of established prognostic factors, including ENSAT tumor stage, resection status, Ki67 proliferation index and glucocorticoid excess. In contrast, its ligand PD-L1 was not associated with clinical outcome in this ACC cohort. In addition, we analyzed the correlation of PD-1 and PD-L1 with tumor-infiltrating lymphocytes. Whereas PD-L1 correlated significantly with the number of $CD3^+$ -, $CD8^+$-, and $FoxP3^+$ T cells ($P=0.0003$, < 0.0001 and < 0.0001, respectively), PD-1 correlated only with $FoxP3^+$ T cells ($P=0.020$). When including both PD-1 and different T cell subtypes in the above-mentioned multivariate Cox regression, the presence of $PD1^+$ cells was the strongest predictor of favorable clinical outcome. In conclusion, this study provides several potential explanations for the heterogeneous results of the immune checkpoint therapy in advanced ACC. In addition, PD-1 expression serves as a strong prognostic biomarker that can easily be applied in routine clinical care as part of histo-pathological assessment.

DOI: 10.1530/endoabs.81.P385

P386

Urinary steroid metabolomics for adrenocortical cancer diagnosis. Comparison of gas chromatography mass spectrometry to liquid chromatography mass spectrometry

Angela Taylor[1], Irina Bancos[2,3], Lorna Gilligan[1], Rick van Veen[4], Vasileios Chortis[1], Fozia Shaheen[1], Carl Jenkinson[1], Donna M O'Neil[1], Beverly Hughes[1], James M Hawley[1,5], Brian Keevil[5], Cedric H L Shackelton[6], Jonathan Deeks[7], Alice J Sitch[7], Michael Biehl[4] & Wiebke Arlt[1]

[1]Institute of Metabolism and Systems Research, Medical School, University of Birmingham, birmingham, United Kingdom; [2]Division of Endocrinology, Diabetes, Metabolism and Nutrition, Mayo Clinic, Rochester, United States; [3]Mayo Clinic, Division of Endocrinology, Metabolism, Diabetes and Nutrition, Department of Internal Medicine, United States; [4]Bernoulli Institute for Mathematics, Computer Science and Artificial Intelligence, University of Groningen, Groningen, Netherlands; [5]Wythenshawe Hospital, Biochemistry Department, Manchester, United Kingdom; [6]UCSF, Beniott Children's Hospital, Oakland, United States; [7]Institute of Applied Health Research, University of Birmingham, Birmingham, United Kingdom

Introduction

Gas chromatography mass spectrometry (GC-MS) is the gold standard method for urinary steroid profiling. However, GC-MS requires chemical derivatisation, long run times, is labour intensive, expensive, and unsuitable for rapid multi-sample analysis, limiting its use in routine clinical practice. GC-MS urinary steroid metabolomics, the combination of steroid profiling and machine learning (Generalized Matrix Learning Vector Quantization) was shown to have superior specificity and sensitivity for adrenocortical carcinoma (ACC) diagnosis compared to imaging technologies (1). The method has subsequently been transferred to liquid chromatography tandem mass spectrometry (LC-MS/MS), selecting 15 diagnostically relevant steroids, decreasing the complexity and the cost of the assay. This method was applied to the EURINE-ACT cohort, 2017 prospectively recruited adrenal tumours patients through an ENS@T collaboration (2). Here we compare GC-MS to LC-MS/MS to evaluate the differences in quantitation and ACC diagnostic ability.

Experimental and Results

After deconjugation the steroid extract was either derivatised for GC-MS analysis (Agilent MSD 5975 with a DB1 column) or run directly via LC-MS/MS (Waters-Xevo with Acquity uPLC, HSS T3 column). Correlation between the two technologies was investigated by comparing steroid quantitation in 481 urines from a range of endocrine conditions, including a healthy control cohort 129 urines (75/54 female/male, 20-81 years). Correlation plots and Bland-Altman plots were used to assess method agreement. To compare diagnostic ability urines from 40 patients with adrenal carcinoma (17/23 female/male, 22-79 years, tumour size 50-230 mm) and 99 patients with non-cancerous adrenal tumours (61/38 female/male, 29-83 years, tumour size 9-55 mm) were assessed. Diagnostic ability was determined via calculation of the area under receiver operated characteristic curve (AUROC). There were statistically significant correlations between the methods for all steroids. The diagnostic ability, AUROC for 31 steroids by GC-MS was 0.969, (SD=0.044), and for 15 steroids by LC-MS/MS, was 0.954 (0.067). The highest estimated sensitivity=specificity was LC-MS/MS for 15 steroids (0.901), followed by GC-MS 31 steroids (0.890).

Conclusions

Despite differences in sample preparation and mass spectrometer design GC-MS and LC-MS/MS showed significantly similar quantitation for all steroids. Reduction of the number of analytes from 31 by GC-MS to 15 by LC-MS/MS does not impact the diagnostic ability for ACC diagnosis. LC-MS/MS should now be introduced into clinical biochemistry laboratories as a routine test for the diagnostic work up for patients with adrenal tumours.

1. Arlt W, *et al*. J Clin Endocrinol Metab. 2011 96(12):3775-84.
2. Bancos I Taylor AE, *et al*. Lancet Diabetes Endocrinol. 2020 8(9):773-781.

DOI: 10.1530/endoabs.81.P386

P387

Prognostic role of targeted methylation analysis in formalin-fixed paraffin-embedded samples of adrenocortical carcinoma

Juliane Lippert[1], Barbara Altieri[1], Breanna Morrison[2], Sonja Steinhauer[1], Gabrielle Smith[3], Antonia Lorey[1], Urlaub Hanna[1], Stefan Kircher[4], Alice J Sitch[2], Martin Fassnacht[1] & Cristina Ronchi[1,3]

[1]Division of Endocrinology and Diabetes, University Hospital of Wuerzburg, Germany; [2]Institute of Applied Health Research, University of Birmingham, United Kingdom; [3]Institute of Metabolism and System Research, University of Birmingham, United Kingdom; [4]Institute of Pathology, University of Wuerzburg, Germany

Adrenocortical carcinoma (ACC) is a rare and aggressive endocrine neoplasia with heterogeneous molecular background and clinical outcome. Previous studies identified hypermethylation in specific genes to be associated with poor

prognosis. Here, we aimed to investigate the role of methylation pattern for prognostic stratification of patients with ACC as compared to clinical parameters, using methods easily applicable in clinical routine. We investigated a total of 237 ACCs (96 M/141F); data were obtained from a previously published retrospective cohort ($n=107$, Lippert *et al* 2018) with updated follow up data (median overall survival (OS)=65 months) and a novel independent cohort ($n=130$, median OS=53 months). Tumour-DNA was isolated from formalin-fixed paraffin-embedded specimens. Leukocyte-DNA was used as reference. Targeted pyrosequencing or Deep Bisulfite Sequencing was used to detect methylation in the promoter region of 5 selected genes (*G0S2, GSTP1, PAX5, PAX6,* and *PYCARD*). Genes were considered "hypermethylated" if percentage values were >25%. Clinical and histological parameters were collected for S-GRAS score calculation as previously published (Elhassan *et al* 2021). Survival analysis was performed for progression-free survival (PFS) and OS. A Cox survival model was applied to test the prognostic impact of hypermethylation in each gene and S-GRAS score, separately and combined. Analyses were also adjusted for cohorts. A total of 25%, 14%, 28%, 49% and 49% cases showed hypermethylation in *G0S2, GSTP1, PAX5, PAX6,* and *PYCARD,* respectively. Hypermethylation in all individual genes – except *GSTP1* - was significantly associated with both PFS and OS with Hazard Ratios (HR) between 1.4 and 2.3. However, overall the models did not perform well. In the model combining methylation of all genes and S-GRAS score, hypermethylation of *PAX5* was the only molecular parameter significantly and independently related to OS (HR=1.9, 95%CI 1.2-3.2). As a comparison, the best HRs for OS were obtained for S-GRAS score group 2 and 3 were 4.5 and 6.8, respectively, when compared to an S-GRAS score group 0.
In conclusion, this study confirms that hypermethylation in preselected genes is significantly associated with worst PFS and OS in ACC. However, only hypermethylation in *PAX5* was related to OS when accounting for S-GRAS score. Assessing targeted methylation is straightforward and feasible in the clinical setting. Therefore, the addition of methylation status of *PAX5* in the baseline evaluation of ACC patients could help to improve accuracy of prognostic classification and enable the direction of personalized management.

DOI: 10.1530/endoabs.81.P387

P388

Endocrine-metabolic disorders in patients with gastroenteropancreatic and lung neuroendocrine tumors

Virginia Zamponi[1], Rossella Mazzilli[1], Flaminia Russo[1], Nevena Mikovic[1], Maria Rinzivillo[2], Ludovica Magi[2], Beatrice Trabalza Marinucci[2], Alessandra Siciliani[2], Francesco Panzuto[2] & Antongiulio Faggiano[1]
[1]Sant'Andrea University Hospital, Department of Clinical and Molecular Medicine, Rome, Italy; [2]Sant'Andrea University Hospital, Department of Medical-Surgical Sciences and Translational Medicine, Rome, Italy

Background
Neuroendocrine tumors (NETs) are characterized by long survival and slow progression. In the clinical practice adifferent types of endocrine-metabolic disorders can occur. Such disorders are either comorbidities related to the neoplasm or side effects of specific oncological treatments. The aim of this study is to evaluate type and prevalence of the endocrine-metabolic disorders in patients with gastroenteropancreatic (GEP) and lung NETs.
Materials and Methods
This single-center study evaluated 58 consecutive patients with sporadic NEN, referring to the ENETS Center in Rome (Sant'Andrea Hospital) from November 2020 to December 2021. Of them 31(53.4%) were affected by GEP NET and 27 (46.6%) by bronchial carcinoid. Twenty patients underwent surgical resection, 12 medical therapy and 26 combined therapies. All patients underwent clinical and biochemical screening for endocrine-metabolic disorders at the baseline and during the follow-up.
Results
Fifty-six over 58 patients (96.6%) were affected by at least one metabolic endocrine disorder. Thyroid dysfunctions were detected in 19 patients (33.9%), including primary hypothyroidism in 16 patients and central hypothyroidism in 1 patient. Six of them occurred after NET diagnosis: 1 after somatostatin analogues (SSA); 2 after targeted therapy and 3 after surgery. Subclinical hyperthyroidism occurred in 2 patients after SSA therapy. Impaired fasting glucose occurred in 23 subjects (41%) and was detected after NET diagnosis in 20 patients (5 after SSA, 4 after surgery, 1 after targeted therapy and 10 after combined therapy). Diabetes occurred in 12 subjects (21.4%) and was detected after NET diagnosis in 8 patients (3 after surgery, 1 after SSA, 1 after targeted therapy and 3 after combined therapy). Dyslipidemia occurred in 23 subjects (41%) and was detected after NET diagnosis in 9 patients (2 after surgery, 1 after targeted therapy and 5 after combined therapy). Hypovitaminosis D occurred in 36 subjects (64.3%) and was detected after NET diagnosis in 19 patients (5 after surgery, 5 after SSA and 9 after combined therapy). Primary hypogonadism occurred in 2 patients and central hypogonadism in 1 patient. Primary adrenal insufficiency occurred in 2 patients after surgery and after SSA respectively, 1 patient was affected by Cushing Syndrome detected after combined therapy.
Conclusions
NET patients represent a high-risk population for the development of endocrine-metabolic disorders. The most frequent alterations are hypovitaminosis D, dyslipidemia and glucose impairment, mainly occurring after medical therapy and/or surgery. In all patients with NET a screening of endocrine-metabolic disorders at diagnosis and during the follow-up is strongly recommended.

DOI: 10.1530/endoabs.81.P388

P389

Znrf3 inactivation leads to a sexually dimorphic immune microenvironment in adrenocortical tumorigenesis

Julie Olabe[1], Wilmouth James[2], Basham Kaitlin[3], Lucas Cecily[4], Roucher-Boulez Florence[4], Tauveron Igor[1], Lefrancois-Martinez Anne-Marie[2], Landwehr Laura-Sophie[5], Kroiss Matthias[5], Fassnacht Martin[5], Hammer Gary[6], Martinez Antoine[2] & Val Pierre[2]
[1]Institut Génétique Reproduction et Développement Inserm UMR6293 - Centre Hospitalier Universitaire, Clermont-Ferrand, France; [2]Institut Génétique Reproduction et Développement Inserm UMR6293, Clermont-Ferrand, France; [3]University of Utah Hospital, Salt Lake City, United States; [4]Hospices Civils de Lyon - Biochimie Biologie Moléculaire Grand Est - UM Pathologies Endocriniennes Rénales Musculaires et Mucoviscidose, Lyon, France; [5]University Hospital, Würzburg, Germany; [6]Departments of Internal Medicine (Metabolism, Endocrinology & Diabetes), Cell & Developmental Biology, and Molecular & Integrative Physiology - University of Michigan, Michigan, United States

Adrenocortical carcinoma (ACC) is a rare and aggressive cancer that originates from steroidogenic cells within the adrenal cortex. The most common alteration in ACC patients is inactivation of the transmembrane E3 ubiquitin-ligase Zinc and Ring Finger 3 (ZNRF3), which is responsible for inhibiting the canonical WNT/Beta-catenin pathway. Using Cre/loxP strategy, we showed that inactivation of *Znrf3* in the adrenal cortex resulted in an initial hyperplasia by 6-weeks, after which sexually dimorphic phenotypes arose. We observed a senescent phenotype and a recruitment of macrophages with a higher phagocytic function in males, leading to regression of neoplastic cells and the absence of aggressive tumors in males. Moreover, androgen treatment of females inactivated for *Znrf3* led to a reverse phenotype with regression. Interestingly, in patients, the incidence of ACC is higher in women. The analysis of histologic and genomic data of ACC patients reinforced the idea of a sexually dimorphic phenotype associated with phagocytic function and macrophages infiltration. Our current aim is to use this mouse model and patient data to highlight the role of macrophages in immunosurveillance and tumor inhibition within the adrenal cortex.

DOI: 10.1530/endoabs.81.P389

P390

Uncovering the immune profile in well-differentiated gastroenteropancreatic neuroendocrine tumors

Franz Sesti[1], Giulia Puliani[1,2], Francesca Sciarra[1], Tiziana Feola[1,3], Roberta Centello[1], Valentina Di Vito[1], Carla Pandozzi[1], Andrea Lenzi[1], Andrea Isidori[1], Mary Anna Venneri[1], Antongiulio Faggiano[4] & Elisa Giannetta[1]
[1]Sapienza University of Rome, Department of Experimental Medicine, Roma, Italy; [2]IRCCS Regina Elena National Cancer Institute, Oncological Endocrinology Unit, Roma, Italy; [3]IRCCS Neuromed Mediterranean Neurological Institute, Neuroendocrinology, Pozzilli, Italy; [4]Sapienza University of Rome, Department of Clinical and Molecular Medicine, Italy

Introduction
Immune tumor microenvironment plays a key role in tumors' growth and metastatic spread, while its role in the heterogeneous field of neuroendocrine

neoplasms (NENs) remains unclear. There is evidence that tumor progression in NENs is promoted by an immunosuppressed microenvironment created by a plethora of infiltrating immune cells. Changes in circulating leukocyte and peripheral blood mononuclear cell (PBMC) subpopulations can mirror the local alteration of the microenvironment, as demonstrated in different kinds of tumors but data in NENs are lacking.
Methods
A prospective controlled observational study was performed recruiting 15 consecutive patients naïve to treatment with histologically proven gastroenteropancreatic (GEP) neuroendocrine tumors (NETs) and 15 healthy controls (Ctrl), matched for age and sex. The primary aim was the quantification of PBMC subpopulations (profiled via flow cytometry).
Results
The mean age of the patients was 60.3 ± 9.7 years (73.3% males). G1 NETs were 46.7%, G2 were 53.3%. Locally advanced or metastatic disease represented the 80%. Immune cell profiling revealed a lower CD3-CD56+ natural killer (NK) cell count in patients with NET than in Ctrl (median [interquartile range], 124 [90-572 *vs* 402 [265-530] cells/μl; $p=0.04$). NK subset analysis showed a reduced percentage of CD56+CD16+ NK cells (81.8% [76.8-89.7%] *vs* 91.7 [88.9-97.6%]; $p=0.004$), a reduced absolute count of CD56+CD16+ NK cells (114 [73-468] *vs* 340 [247-480] cells/μl; $p=0.026$), and a reduced absolute count of CD56dim NK cells (105 [66-544] *vs* 362 [237-461] cells/μl; $p=0.04$) in patients than in Ctrl. Total monocytes count was not significantly different between the study groups. However, patients with NET had a higher percentage of CD14+ CD16++ non-classical monocytes (3.3% [2.1-9.1%] *vs* 1.7% [1.1-2.5%]; $p=0.01$), a higher absolute count of CD14+CD16++ non-classical monocytes (14 [6-23] *vs* 6 [3-10] cells/μl; $P=0.019$), and a lower percentage of CD14+CD16+ intermediate monocytes (5% [2.6-9.2%] *vs* 8.8% [6.1-11.6%]; $p=0.04$). Total CD3+ T lymphocyte count was not significantly different between the study groups. However, a decrease in percentage (mean ± standard deviation, 55.4 ± 8.1% *vs* 63.9 ± 6.6%; $p=0.004$) and in absolute count (554 ± 307 cells/μl *vs* 820 ± 285 cells/μl; $p=0.02$) of CD4+ T helper lymphocytes were found in NETs patients.
Conclusions
The study shows that patients with GEP-NETs have an immune alteration characterized by a low count of cytotoxic NK cells and a high count of anti-inflammatory non-classical monocytes, suggesting a deregulation of CD16 expressing cells. Moreover, a low count of T helper lymphocytes was found. This unfavorable and immunosuppressed immune profile could contribute to tumor growth and progression.

DOI: 10.1530/endoabs.81.P390

P391

Effect of mitotane on male gonadal function

Federica Innocenti[1], Sara Di Persio[2], Marilena Taggi[2], Roberta Maggio[3], Pina Lardo[4], Maria Elena Aloini[4], Rita Canipari[2] & Antonio Stigliano[3]
[1]Unit of Histology and Medical Embryology, Sapienza University of Rome, Italy; [2]Unit of Histology and Medical Embryology, Sapienza University of Rome; [3]Endocrinology - Sant'Andrea Hospital, Sapienza University of Rome, Clinical and Molecular Medicine, Rome, Italy; [4]Endocrinology - Sant'Andrea Hospital, Sapienza University of Rome

Mitotane (MTT) currently represents the treatment of choice for adrenocortical carcinoma (ACC). Clinical evidence shows the occurrence of hypogonadism following treatment with this drug, observed more frequently in male patients. The aim of the study, therefore, was to evaluate the impact of MTT treatment on male gonadal function on adult CD1 mice. At the end of the 45 days of treatment, testes were collected for morphological examination, and a blood sample of each animal was retrieved to evaluate serum hormone levels. Serum testosterone was significantly lower in MTT-treated animals than the control siblings. The testis of the MTT-exposed group showed several degrees of damage: disorganization of the germinal epithelium, a pronounced alteration of the spermatogenic process with a reduction of spermatozoa in the lumen, absence of lumen and a less compact interstitial space and a thickness of the albuginea. Molecular analysis on the interstitial compartment revealed the expected significant decline in mRNA expression of *3βHsd* and *Insl3* in MTT-treated mice, confirming an impairment of androgens production. The expression of mRNA of *Fsh-R* was only slightly down modulated by treatment with MTT, but was not statistically different, proving that Sertoli cells are not the main target of the drug and the alteration of spermatogenesis is not related to Sertoli cell damage. Moreover, the evaluation of the specific gene expression for different stages of germ cell differentiation, stimulated by Retinoic Acid 8 (Stra8), expressed in differentiating spermatogonia and Heat shock protein A 2 (HspA2), a marker of meiotic cells, showed no alteration in the expression of Stra8 and a decrease of HspA2 mRNA in the testes of MTT-treated mice, demonstrating that differentiating spermatogonia are not affected by the drug treatment while impairment of the meiotic progression of germ cells was observed. Finally, the concentration of sperm collected from epididymis cauda was significantly lower in MTT treated animals than in the control group. Moreover, the administration of MTT caused a significant increase in the percentage of spermatozoa with abnormal chromatin structure defined by the DNA fragmentation index (%DFI) compared to the untreated animals. The testosterone replacement therapy only restored some of these parameters.
In conclusion, we demonstrate the negative effects of the MTT treatment on the male reproductive system, including changes in the morphology of testicular tissue and reduction of sperm concentration and sperm quality.

DOI: 10.1530/endoabs.81.P391

P636

Struma ovarii with NIFTP tumor: case report

Ana Sofia Osório[1], Ricardo Fonseca[2], Catarina Roque[2], Gabriela Gasparinho[3] & Sara Abrantes[4]
[1]Hospital Prof. Dr. Fernando Fonseca, Endocrinology, Amadora, Portugal; [2]Hospital Prof. Dr. Fernando Fonseca, Endocrinology, Amadora, Portugal; [3]Hospital Prof. Dr. Fernando Fonseca, Anatomopathology, Amadora, Portugal; [4]Hospital Prof. Dr. Fernando Fonseca, Gynaecology, Amadora, Portugal

Struma ovarii is a form of mature teratoma, a rare germ cell tumor, containing more than 50% thyroid tissue. Malignancy is uncommon. Non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP) inside struma ovarii was never described. A 32 y.o. female with previous history of ovarian cysts was admitted in the emergency room with painfull acute abdominal distention. The MRI revealed a right adnexal mass, predominantly cystic with 82x66x80 mm and surrounding oedema. Suspecting of right ovarian torsion, exploratory laparotomy was performed. The torsion was confirmed and the adnexal mass removed. Histopathologic examination showed mature thyroid follicles with abundant colloid in more than 50% of the tissue - consistent with struma ovarii - and a 1 cm area of NIFTP tumor. Thyroid ultrasound was normal and laboratory exams (thyroid function and thyroglobulin levels) within reference range. Malignant struma ovarii is a rare clinical entity that poses a therapeutic challenge, as there is no 'gold standard' of care. NIFTP is an encapsulated or clearly delimitated, noninvasive neoplasm with follicular growth pattern and nuclear features of papillary thyroid carcinoma, that has an excellent prognosis in thyroid gland, but with yet unknown/uncharacterized behavior as struma ovarii. Of our knowledge, this is the first reported NIFTP in a struma ovarii. The patient is being kept under surveillance by the mutidisciplinary team.

DOI: 10.1530/endoabs.81.P636

P637

Sporadic and Von Hippel-Lindau disease-related pancreatic neuroendocrine tumors definitions are not consistent between the various classification criteria

Reut Halperin[1,2], Yehudit Eden-Friedman[1,2], Liat Arnon[1,2] & Amit Tirosh[1,2]
[1]Sheba Medical Center, Division of Endocrinology, Diabetes and Metabolism, Tel Hashomer, Israel; [2]Tel Aviv University, Department of Medicine, Tel Aviv, Israel

Background
von Hipple-Lindau (VHL) disease comprises hemangioblastomas, renal cell carcinomas (RCC), pheochromocytomas, and pancreatic neuroendocrine tumors (PNET). Diagnosis is based International (two hemangioblastomas, one hemangioblastoma and one visceral lesion, or VHL family history and hemangioblastoma or visceral lesion) or Danish criteria (any two clinical manifestations, one clinical manifestation and family background of VHL or self-genetic diagnosis). The nature of PNET in VHL appears to be distinct from sporadic PNET, as most VHL-related PNET are non-functioning, are lower grade and have a lower rate of metastases, yet head-to-head comparisons are scarce.

Aim
In the current study we wished to compare the characteristics of VHL-related and sporadic PNET. We also tested the hypothesis that diagnosis of VHL according to the International and Danish criteria may comprise two distinct patient populations.
Methods
Patients with a diagnosis of PNET were identified using the MD Clone platform and data including demographic and tumor specific characteristics were gathered. In addition, the presence of any clinical feature of VHL and presence of a family or genetic diagnoses was noted for each patient. Patients were grouped according to a diagnosis of VHL (following either International or Danish criteria) or sporadic PNET.
Results
Twenty-nine patients with VHL, 17 (58%) with PNET and 65 patients with sporadic PNET were identified. Patients with VHL were younger at PNET diagnosis compared with sporadic PNET (50.1±4.7 vs. 62.8±1.5 years, $P<0.001$). There was no significant difference between VHL-related or sporadic PNET in stage and grade, nor in progression or survival. Sporadic PNET were more often located in the body and tail of pancreas. In the subgroup comparison of International vs Danish criteria -based VHL diagnosis, age at diagnosis of PNET, RCC and VHL was younger in the International group. Hemangioblastomas were diagnosed in 90% of patients in the International compared with none in the Danish group. First manifestation of VHL was hemangioblastomas (47%) followed by pheochromocytomas (31%) in the International group compared with RCC (62%) and PNET (37%) in the Danish group. Finally, 50% in the International and none in the Danish group had a family or genetic VHL background.
Conclusions
Patients with PNET diagnosed with VHL according to the International and Danish criteria seem to form two distinct clinical groups, with a greater similarity of the Danish group to patients with sporadic PNET. Further comparisons in other cohorts are warranted, as this may call for different clinical management.

DOI: 10.1530/endoabs.81.P637

P638

TKI related adverse events in patients with progressive and metastatic thyroid carcinoma: a retrospective analysis of our experience with cabozantinib during EXAM and EXAMINER clinical trial

Virginia Cappagli, Valeria Bottici, David Viola, Laura Agate, Eleonora Molinaro & Rossella Elisei
Department of Clinical and Experimental Medicine, Endocrine Unit, University of Pisa, Pisa, Italy

Background
Vandetanib and Cabozantinib are the only two multitarget tyrosine kinase inhibitors approved for the management of metastatic and progressive medullary thyroid cancer. (MTC) Despite their efficacy in terms of progression free survival prolongation and overall response rate, the drug-related toxicity is still a clinical problem, impairing patient's quality of life and the compliance to the treatment. We retrospectively evaluate the adverse events (AEs) occurred during cabozantinib treatment in patient enrolled in the EXAM and EXAMINER clinical trial.
Matherials and Methods
We retrospectively analyzed data from 23 patients with metastatic MTC, follow-up at our department and enrolled in clinical trials with cabozantinib for radiological documented progression of disease. During follow-up a periodically clinical assessment and of tumoral markers (calcitonin and CEA) and hormonal-hematochemical parameters were performed every month, while a radiological assessment with total body CT scan with iodine contrast medium injection every 12 weeks. The clinical evaluation of AEs was performed according to the CTCAE (National Cancer Institute's Common Terminology Criteria for Adverse Events) dictionary.
Results
All patients experienced AEs during treatment, which were classified in laboratoristic (endocrine and not) and clinical ones. The most frequent endocrine AEs observed were hypothyroidism (78.3%), hypocalcemia (47.8%), high levels of ACTH (34.8%) and FSH/lH. The most frequent not endocrine laboratoristic AEs occurred were AST/ALT high levels (82.6%), increasing in amylase and lipase enzyme (39.1%), renal impairment (21.7%), electrolyte n (43.5%), hematological (60.9%) and coagulation (21.7%) alterations. None of endocrine and not endocrine AEs caused drug stopped or dose reduction since they were well managed with supporting therapies. The most frequent clinical AEs observed were gastrointestinal as mucositis (82.6%), diarrhea (73.9%), nausea/vomiting (34.8%), dysgeusia (30.4%), epigastralgy (26.1%), dysphagia (21.7%); thereafter, constitutional AEs as anorexia (21.7%) and weight loss (47.8%) and cutaneous AEs (47.8%). These AEs occurred early after the drug initiation and, despite preventing and supporting therapies, they were the main cause of drug withdrawal and dose reduction. The analysis of which AE could be a predicting factor of response in still ongoing.
Conclusions
Cabozantinib is an effective treatment for MTC patients. However, AEs occur in all patients during follow-up, but while the laboratoristic ones appear later and are well manageable, the clinical ones occur early and are the main responsible for dose reduction and discontinuation, impair patient's quality of life and disease control. The knowledge, prevention and early treatment of these AEs are fundamental for patients' compliance.

DOI: 10.1530/endoabs.81.P638

P639

Does the length of a polyalanine tract in the FOXE1 gene impact the course of familial non-medullary thyroid cancer?

Bartosz Domagała[1], Michał Koziara[1], Malgorzata Trofimiuk-Muldner[2], Anna Skalniak[2] & Alicja Hubalewska-Dydejczyk[2]
[1]University Hospital in Krakow, Department of Endocrinology, Endocrine Oncology and Nuclear Medicine, Krakow, Poland; [2]Jagiellonian University Medical College, Chair and Department of Endocrinology, Krakow, Poland

Familial non-medullary thyroid cancer (FNMTC) constitutes about 3–9% of all thyroid cancers. One of the genes believed to predispose to non-syndromic FNMTC is *FOXE1*. It contains a polyalanine tract (polyAla) with a variable number (11 – 22) of alanine residues. This length polymorphism could lead to changes in the *FOXE1*-encoded protein (*FOXE1* transcription factor) structure and predispose to papillary thyroid cancer (PTC). The aim of the study was to investigate the relationship between the length of the polyAla tract and the stage of PTC at diagnosis (according to AJCC 8th edition) in patients with FNMTC. The study included 27 patients with familial PTC (at least two family members were diagnosed with the disease). The length of the polyAla tract of the *FOXE1* gene was analyzed. The following numbers of polyAla variants were detected: 11-Ala – 2, 12-Ala – 1, 14-Ala – 23, 16-Ala – 28 alleles. The staging at diagnosis was compared in two groups: less than 16-Ala and at least 16-Ala. The stages of pT1a and pT1a (m) were found in 20 alleles in the less than 16-Ala group, whereas in 16 alleles of the at least 16-Ala group, pT1b-pT2(m) was the most common ($P=0.039$). Lymph node metastases were found more frequently in the less than 16-Ala group than in the at least 16-Ala group but this difference was not statistically significant (10 vs. 3 respectively; $P=0.680$).
Conclusions
The analysis of the length of the polyAla tract may be a useful diagnostic tool in predicting the course of PTC in patients with a positive family history.

DOI: 10.1530/endoabs.81.P639

P640

Short fasting test as reliable and effective tool to diagnose insulinoma

Nevena Mikovic, Virginia Zamponi, Rossella Mazzilli, Flaminia Russo, beatrice fazzalari & Antongiulio Faggiano
Sant'Andrea Hospital, "Sapienza" University, Unit of Endocrinology, Department of Clinical and Molecular Medicine, ENETS Center of Excellence, Rome, Italy

Introduction
Insulinomas are rare pancreatic NETs presenting with chronic hypoglycaemia. Current guidelines for diagnosis require a prolonged fasting test (72 h), which implies hospitalization and is difficult to perform, delaying prompt diagnosis and treatment. It has been reported that 65 to 85% of insulinomas could be diagnosed after less of a 24h fasting period and 94 to 95.7% within 48h, although a shorter test for diagnosis has not yet been standardized.
Objective
To predict weather a shorter outpatient fasting test initiated overnight and portrayed up until 24h could be a sensitive method for diagnosing insulinoma.
Materials & Methods
we conducted a retrospective monocentric study to evaluate the diagnostic performance of the short fasting test to achieve the diagnosis of insulinoma. All subjects admitted from 2019 to 2021 at the Unit of Endocrinology of the Sant'Andrea Hospital with clinical suspicion for insulinoma (documented

hypoglycaemia in absence of other known causes or intake of hypoglycaemic drugs) underwent the short fasting test ($n=9$). A comparison study was performed with subjects who underwent the standard prolonged fasting test from 2003 to 2018 ($n=22$). The short fasting test is initiated by the patient overnight at home and proceeds the following day in outpatient setting (Day Hospital). As in the standard protocol, symptoms and capillary blood glucose (CBG) are strictly monitored. Venous blood is drawn for glycaemia, insulin and C-Peptide at admission, in case of symptoms of hypoglycaemia or if CBG ≤ 45 mg/dl. Diagnostic values for insulinoma consist of glucose $<$ 55 mg/dl with insulin $\geq$ 3μU/ml and C-Peptide $\geq$ 0.6 ng/ml. In case of a negative result and a remaining high suspicion for insulinoma, the prolonged test would be performed subsequently.
Results
The final sample consisted of 31 patients, with mean age $\pm$ Standard Deviation (SD) of 44.5 $\pm$ 12.6 years (17-74). Diagnostic values for insulinoma were found in a total of 10 patients: in 6/22 who underwent the prolonged test and in 4/9 who underwent the short fasting test. Time counting from the last meal until diagnosis ranged from 4h to 30h, with average $\pm$ SD of 11 $\pm$ 7.3 h; however, only one patient showed diagnostic values at $>$24h (30h).
Conclusion
In our series, 9/10 (90%) patients with insulinoma were diagnosed within 14 h from the beginning of the fast. A short fasting test could be a valid, sensitive and reliable first-line workup in diagnosing insulinoma, without hospitalization.

DOI: 10.1530/endoabs.81.P640

P641

Management and long term follow up of hyperparathyroidism in multiple endocrine neoplasia type 1: single center experience

Maria Yavropoulou[1], Sofia Vlachou[1], Marina Tsoli[1], Florentia Fostira[2], Gregory Kaltsas[1] & Eva Kassi[1]
[1]Medical School, National and Kapodistrian University of Athens, Greece, Endocrinology Unit, First Department of Propaedeutic and Internal Medicine, Athens, Greece; [2]Molecular Diagnostics Laboratory, INRaSTES, National Center for Scientific Research "Demokritos", Athens, Greece

Background and objective
Multiple Endocrine Neoplasia type 1 (MEN 1) is an autosomal dominant disease characterized by a broad clinical spectrum. Previous multi-center studies, that analyzed large groups of patients with MEN 1 have been reported before but long term follow up data of these patients focusing exclusively on primary hyperparathyroidism (PHPT) are scarce.
Patients and Methods
In this retrospective cohort study we include all patients with PHPT in the context of MEN1 that were under regular follow up in our institution.
Results
Our cohort consisted of 68 patients (39 males and 29 females), with a mean age at MEN1 diagnosis of 39 $\pm$ 13.06 years. Obvious family history of MEN1 was present in 76.7% of the patients. Besides PHPT, pancreatic neuroendocrine tumors were the most commonly neoplasm encountered in 80% of patients (62% non-functioning), followed by pituitary adenomas in 66% (micro 73%, non-functioning 49%). The mean age at PHPT diagnosis was 35.2 $\pm$ 14.0 years. Fifteen patients developed osteoporosis (22%), 22 (64.7%) nephrolithiasis and one nephrocalcinosis. Parathyroidectomy was performed in 57 patients (82.3%). At the initial parathyroid surgery the majority of patients had subtotal parathyroidectomy (61.4%, $n=35$). Long term remission of PHPT was reported in 32 patients (56%), persistence in 7 (12.2%), and recurrent disease in 18 patients (31.5%) at a median follow-up of 4 years (1 to 21 years). Reoperation for recurrent disease was performed in 11 of the 18 patients (61%), and permanent hypoparathyroidism occurred in 11 patients (19.2%%). A total of 23 patients (33.8%) were treated with a calcimimetic agent with favorable results on serum calcium levels, including both first-line and second-line treatment in unoperated patients and persistent or recurrent disease, respectively. Gene analysis was performed in 44 patients (63%) and a variant known to cause MEN1 was identified in 34 patients (77.2%) while 5 (11.3%) had a variant of uncertain significance. No genotype – phenotype associations were reported, albeit the number of patients was small ($n=34$).
Conclsions
PHPT in the context of MEN1 involves a multiglandular disease and remains a therapeutic challenge over long term for treating physicians, as recurrent disease can develop even after 20 years of follow up. Collection of clinical, biochemical, and genetic characteristics of MEN1 in referral centers at a national level is critical for the optimal management of these patients.

DOI: 10.1530/endoabs.81.P641

P642

Abstract withdrawn

DOI: 10.1530/endoabs.81.P6142

P643

Thyroid cancer and thalassemia major: new hypotheses from an old clinical scenario

Maurizio Poggi[1], Irene Samperi[2], Salvatore Monti[1], cecilia motta[1] & Giuseppe Pugliese[1]
[1]Sant'Andrea University Hospital, Endocrinology Unit, ROMA, Italy; [2]Azienda Sanitaria Locale ASL NO, Diabetological Unit, Novara, Italy

Thyroid cancer (TC) is one of the most frequent neoplasia diagnosed in general population with an estimated incidence of 6.6 cases per 100.000 and mortality of 0.43 cases per 100.000. Differentiated thyroid cancer (DTC), which includes papillary (PTC) and follicular cancer (FTC), comprises the large majority (up to 90%) of all thyroid cancer cases. At the moment etiology of TC is not completely understood, with multiple genetic and epigenetic factor that are thought to be important. We report our recent experience, as a dedicated tertiary care unit in the cure of thalassemia major (TM), that could be useful in the knowledge about induction and progression of carcinogenetic process. TM is a clinical disorder characterized by abnormalities in hemoglobin's synthesis with main treatment that is characterized by regularly blood transfusion. This therapy usually esitate in iron overload and tissue damage and could be cause of serological viruses transmission (like hepatitis B and C virus or human immunodeficiency virus). In a group of 126 patients affected by TM and studied by neck ultrasound we found thyroid nodules in 36 out of 126 with a prevalence of about 28.5%. Regarding patients affected by thyroid nodules we found 10 cases of TC with a prevalence of nearly 27% of neoplastic lesion that is higher than one reported in general population. Most of TC patients were female, with a median age at diagnosis of 37 years and with an histological picture of papillary in 9 out of 10. Interestingly most of all were affected by relevant endocrine tissue damage (more than 3 endocrinopathy in nearly 80% of cases) giving us the chanche to consider iron overload as a main actor in pathogenesis. Moreover 80% of patients affected by TC showed Hepatitis C virus (HCV) positivity raising the suspicion that HCV infection could perform a relevant role in induction and progression of disease, as previously reported. In conclusion our work would give a key to consider newer pathogenetic aspects in TC induction and progression. These considerations could be relevant especially in some clinical scenario and could be useful in innovative strategy in prevention, diagnosis and treatment.

DOI: 10.1530/endoabs.81.P643

P644

Sublethal hyperthermia decreases cellular proliferation and transiently disrupts steroidogenesis in adrenal cells

Nathan Mullen[1], Padraig Donlon[1], Katen Duffy[1], Sarah Feely[1], Kate M Warde[1,2], Anna Sorushanova[1], Punit Prakash[3], Martin O'Halloran[4] & Michael Conall Dennedy[1]
[1]National University of Ireland, Galway, Discipline of Pharmacology and Therapeutics, School of Medicine, Galway, Ireland; [2]Huntsman Cancer

Institute, Department of Oncological Sciences, University of Utah, School of Medicine, Utah, United States; [3]Kansas State University, Department of Electrical and Computer Engineering, Manhattan, KS, United States; [4]National University of Ireland Galway, Translational Medical Device Lab, Galway, Ireland

Introduction
Primary Aldosteronism is the most common cause of secondary hypertension. First-line treatment; adrenalectomy resects adrenal nodules and adjacent normal tissue, limiting suitability to those who present with unilateral disease. Use of thermal ablation represents an emerging approach as a possible minimally invasive therapy for unilateral and bilateral disease, to target and disrupt hypersecreting aldosterone producing adenomas, while preserving adjacent normal adrenal cortex. Ablation involves heating tissue >50°C to induce cellular necrosis. Outside the core ablation zone, the transitional zone is an area exposed to variable temperatures between 37°C – 50°C. To understand the feasibility of precision ablation in the adrenal gland, we examined the effect of applying these temperatures to adrenocortical cells to identify i) the required temperature to effectively ablate adrenal cells ii) the extent of damage that may occur to surrounding healthy adrenal cells with exposure to transitional zone temperatures.
Methods
Steroidogenic adrenocortical cell lines, H295R and HAC15, were treated with hyperthermia (high precision water bath) at temperatures of 37, 42, 45, 48 and 50°C. Steroidogenesis was subsequently stimulated using forskolin (10μM) and angiotensin II (10 nM), or cells were treated with Thapsigargin (10uM). Cell death (Propidium iodide staining by flow cytometry), proliferation (xCELLigence real-time cell analysis), protein expression (Western blot/qRT-PCR), steroid secretion (HPLC-Mass spectrometry) and intracellular calcium release (Fluo-4 AM flow cytometry/confocal live imaging) were analysed immediately and 7-days post-treatment.
Results
Cell death occurred at 48°C and 50°C ($P<0.05$ vs 37°C control), but not 45°C, or 42°C. Sublethal hyperthermia (45°C for 30 minutes) induced a heat shock response (upregulated HSP70 and HSP90), alongside a decrease in aldosterone and cortisol secretion ($P<0.05$), reduced expression of steroidogenic enzymes (CYP11B1, CYP11A1)($P<0.05$), and decreased intracellular calcium release 18-h post treatment. At 7-days post sublethal hyperthermia, steroid secretion and steroidogenic enzymatic expression returned to baseline levels.
Conclusion
Hyperthermia at 48°C and 50°C for 15 minutes is required for sustained cell death at 7-days post treatment. Sublethal hyperthermia, equivalent to that produced in the transitional zone during thermal ablation, produces a short-lived unsustained inhibition of steroidogenesis that recovers 7-days post treatment. Therefore, segmental adrenal sparing ablation is possible with recovery of transitional zone following ablation. This underlines the potential for precision technology development for bilateral adrenal ablation as definitive measure to treat PA caused by APA or Micronodular disease.

DOI: 10.1530/endoabs.81.P644

P645

Abstract withdrawn

DOI: 10.1530/endoabs.81.P645

P646

Methodology of the SORENTO clinical trial: assessing the efficacy and safety of high exposure octreotide subcutaneous depot in patients with GEP-NETs

Diego Ferone[1], Jaume Capdevilla[2], Jennifer Ang Chan[3], Wouter W de Herder[4], Daniel Halperin[5], Josh Mailman[6], Simron Singh[7], Mozhgan Dorkhan[8], Lisa Hellström[8], Agneta Svedberg[8] & Fredrik Tiberg[8]

[1]IRCCS Ospedale Policlinico San Martino, Endocrinology, Department of Internal Medicine & Medical Specialties, University of Genova, Genova, Italy; [2]Hospital Universitari Vall d'Hebron, Barcelona, Spain; [3]Dana-Farber Cancer Institute, Boston, United States; [4]Erasmus MC, Rotterdam, Netherlands; [5]The University of Texas MD Anderson Cancer Center, Houston, United States; [6]NorCal CarciNet Community, United States; [7]Sunnybrook Health Sciences Centre, Toronto, Canada; [8]Camurus AB, Sweden

Background
Somatostatin receptor ligands (SRLs) are first-line standard-of-care therapies for gastroenteropancreatic neuroendocrine tumours (GEP-NETs), showing efficacy in tumour and symptom control with an established safety profile. However, disease progression may occur despite standard-dose SRL treatment, requiring more aggressive and toxic treatments. Retrospective/non-randomized data suggest higher-dose SRLs may benefit patients with GEP-NETs who do not respond to standard-dose treatment and provide improved disease control. Octreotide depot (CAM2029) is a novel high-exposure, subcutaneous (SC) formulation. Clinical trials showed ~500% higher CAM2029 bioavailability vs octreotide long-acting release (LAR) (Tiberg *et al*. 2015), and maintenance/reduction of NET symptoms (Pavel *et al*. 2019). Prospective, randomised trial data are needed to confirm the efficacy/safety of higher-dose SRLs such as CAM2029, vs standard-dose SRLs (including octreotide LAR and lanreotide Autogel [ATG]).
Methods
SORENTO is a randomised, multi-centre, open-label, active-controlled Phase 3 trial, aiming to enrol 302 adults with GEP-NETs. Key eligibility criteria: advanced, well-differentiated NET of GEP/presumed GEP origin; ≥ 1 measurable and somatostatin receptor-positive (by nuclear imaging) lesion according to RECIST 1.1; no or <6 months consecutive treatment with long-acting SRLs. Notably, patients with well-differentiated Grade 3 GEP-NETs (excluded by CLARINET and PROMID trials) are eligible. Patients will be randomised 1:1 to CAM2029 20 mg every two weeks (Q2W), or active comparator (octreotide LAR 30 mg intramuscular or lanreotide ATG 120 mg SC, every four weeks). CAM2029 self-/carer-administration is permitted after ≥ 3 supervised/successful administrations. Randomisation stratified by: histological grade, tumour origin and intended comparator. Primary outcome: progression-free survival (PFS; time from date of randomisation to date of first documented disease progression [RECIST 1.1] or death), assessed by a Blinded Independent Review Committee. The study is powered to detect a hazard ratio of 0.65. Key secondary outcomes: overall survival; RECIST 1.1-defined response rate; rescue medication use; patient satisfaction; adverse events. After primary PFS analysis, patients will be followed for up to 2 years for overall survival (if CAM2029 displays superiority in the primary analysis, the comparator group may switch to CAM2029 20 mg Q2W). Patients (in either treatment group) who experience progressive disease in the randomised part of the study may proceed to an open-label extension with intensified CAM2029 treatment, to investigate effects of higher frequency dosing. First patient randomised in Nov-2021; read-out (achieved after 194 events) expected by end of 2024. This novel head-to-head superiority trial is anticipated to demonstrate the potential benefits of CAM2029 as first-line therapy in patients with well-differentiated GEP-NETs. ClinicalTrials.gov identifier: NCT05050942.

DOI: 10.1530/endoabs.81.P646

P647

Ectopic cushing's syndrome due to thymic neuroendocrine tumour - a case report

Lukasz Dzialach[1], Agnieszka Wojciechowska-Luzniak[1], Anna Migda[1], Maria Maksymowicz[2] & Przemysław Witek[1]

[1]Medical University of Warsaw, Department of Internal Medicine, Endocrinology and Diabetes, Warsaw, Poland; [2]Maria Sklodowska-Curie National Research Institute of Oncology, Department of Pathology and Laboratory Diagnostics, Poland

Introduction
Ectopic Cushing's syndrome (ECS) is a rare endocrine condition caused by corticotrophin (ACTH) hypersecretion of nonpituitary neoplasms. Thymic neuroendocrine tumours (NETs) account for about 5-10% of ECS cases, typically with aggressive clinical course.
Case Report
A 31-year-old previously healthy female presented to the emergency department with a 3-week history of fatigue, muscle weakness, headaches and generalized swelling. Physical examination revealed peripheral oedema, high blood pressure (170/100 mmHg) and tachycardia (170 beats/min). Laboratory tests showed

leukocytosis (13.95 x10^9/l), hyperglycemia (478 mg/dl) and metabolic alkalosis with profound hypokalaemia (2.5 mmol/l). She was started on insulin therapy along with aggressive hypokalemia repletion and antihypertensive treatment. Given the overall clinical presentation and resistance to initiated treatment, aggressive CS was suspected. Hormonal tests were as follows: midnight serum cortisol 69.17 mg/dl, urinary free cortisol 11587.5 µg/24h, ACTH 963.7 pg/ml. Chromogranin A (CgA) level was notably elevated (1385.0 ng/ml). Negative HDDDST and CRH tests, negative pituitary imaging with short duration and rapid progression of symptoms were highly suggestive of ECS. To control hypercortisolemia, continuous etomidate infusion was started with significant improvement in the patient's general condition, oedema reduction and normalization of blood pressure, glycemia and potassium level. Computed tomography (CT) revealed a left adrenal mass measuring 80x56x39 mm infiltrating the diaphragm. Whole-body 18F-FDG-PET/CT showed a metabolically active lesion of the left adrenal gland and multiple active bone lesions suggestive of metastatic malignancy. The patient underwent laparoscopic left adrenalectomy with a postoperative significant decline in cortisol level (4.08 mg/dl) and required hydrocortisone replacement. However, histopathology showed adrenal adenoma with extensive necrosis. A follow-up (8 weeks) whole-body PET/CT finally revealed 18F-FDG-avid (SUVmax 9.3) 42x33 mm lesion in the anterior mediastinum. Due to the local invasion, only a partial resection was performed. Histopathology revealed a thymic large cell neuroendocrine carcinoma with atypical thymic carcinoid component [ACTH(+), CgA(+), synaptophysin(+), CD56(+), MGMT:70%, Ki-67:30%, p53: <1%]. Thymectomy was followed by mediastinal radiotherapy and chemotherapy with the ADOC regimen. The patient has been under endocrine and oncological follow-up for almost 3 years, however, due to the progression of the disease, the prognosis is poor.

Conclusions

The diagnosis and management of ECS remain challenging. ACTH-secreting thymic NETs often behave aggressively and lead to the rapid development of severe hypercortisolism causing uncontrolled hypertension and hyperglycemia with hypokalaemic alkalosis requiring prompt intervention. Due to the rarity and complexity of the disease, management of ECS caused by malignant thymic NETs needs a personalized and multidisciplinary approach.

DOI: 10.1530/endoabs.81.P647

P648

Spliceosomic landscape across the histological subtypes of lung neuroendocrine neoplasms: a new layer to disentangle tumor Heterogeneity

Ricardo Blázquez-Encinas[1,2,3], Víctor García Vioque[1,2,3], Alexandra Sexton-Oates[4], María Trinidad Moreno Montilla[1,2,3], Emilia Alors-Pérez[1,2,3], Federica Mangili[1,2,3,5], Nicolas Alcala[4], Matthieu Foll[4], Alejandro Ibañez Costa[1,2,3], Lynnette Fernández Cuesta[4] & Justo P. Castaño[1,2,3,6]

[1]Maimonides Institute for Biomedical Research of Cordoba (IMIBIC), Córdoba, Spain; [2]Reina Sofía University Hospital, Córdoba, Spain; [3]University of Córdoba, Cell Biology, Physiology and Immunology, Córdoba, Spain; [4]International Agency for Research on Cancer, Rare Cancers Genomics, Lyon, France; [5]University of Milan, Clinical Sciences and Community Health, Milan, Italy; [6]CIBER Physiopathology of Obesity and Nutrition, Spain

Lung neuroendocrine neoplasms (LungNENs) are highly heterogeneous tumors, which are classified by the WHO according to their histological grade into low grade: Typical Carcinoids (TC) and intermediate grade Atypical Carcinoids (AC), and high-grade: Large Cell Neuroendocrine Carcinoma (LCNEC) and Small Cell Lung Cancer (SCLC). Recently, a number of studies have tried to untangle the molecular features that define each subtype by applying different approaches, including genomic, transcriptomic and epigenomic analyses, which have provided useful information to better classify and understand LungNENs. However, an emerging layer of complexity tightly linked to every hallmark of cancer remains to be explored in detail in LungNENs: the spliceosomic landscape. Indeed, the status of the alternative splicing pattern and its underlying machinery (spliceosome components and splicing factors) is heavily altered in many tumors, where it relates to cancer development and progression. Thus, here we aimed to analyze the expression of the splicing machinery and the alternative splicing patterns in LungNENs, compare them among the different subtypes, and explore their relationship with their pathophysiological phenotype. To achieve this aim, RNA-seq data of 284 LungNENs samples were analyzed, comprising: 164 TC and AC, 69 LCNEC and 51 SCLC. Specifically, gene expression was calculated with DESeq-2 and alternative splicing events and isoforms were quantified using SUPPA2. We used Principal Component Analysis and Uniform Manifold Approximation and Projection to cluster the samples according to their spliceosomic landscape. Geneset Enrichment Analysis was used to study molecular pathways involved in groups of genes. Results revealed the splicing machinery has clearly distinct expression patterns among the four subgroups of LungNENs, which enable to precisely discriminate them. Moreover, each subgroup displayed a specific profile of alternative splicing events, where certain genes were enriched in relevant biological pathways. Our analyses represent the first comparative study of the spliceosomic landscape of the different histological subgroups of LungNENs and provide new tools and original information to gain further insight to understand LungNEN heterogeneity.

DOI: 10.1530/endoabs.81.P648

Environmental Endocrinology

P134

Autoimmune polyglandular syndromes in childhood: casuistic of a pediatric unit

Bruno Bouça[1], Andreia Nogueira[2], Joana Caetano[3], Rita Cardoso[3], Isabel Dinis[3] & Alice Mirante[3]

[1]Centro Hospitalar Universitário de Lisboa Central, Department of Endocrinology, Diabetes and Metabolism, Lisbon, Portugal; [2]Centro Hospitalar Universitário de Coimbra, Pediatric Department, Coimbra, Portugal; [3]Centro Hospitalar Universitário de Coimbra, Department of Pediatric Endocrinology, Diabetes and Growth, Coimbra, Portugal

Introduction

Polyglandular Autoimmune Syndromes (PAS) are a group of diseases characterized by the association of different endocrine and non-endocrine autoimmune pathologies. Although the diagnosis of PAS is more frequent in adulthood, it can occur in pediatric age, with PAS type 3 being the most frequent.

Objective

To study the prevalence and characteristics of PAS in the pediatric population of a tertiary center.

Methods

Retrospective analysis of the clinical files of patients with type 1 diabetes mellitus, autoimmune thyroid disease (ATD), Celiac Disease (CD) and Addison's disease (AD) followed in a Pediatric Endocrinology consultation from 1 January 2010 to 31st December 2020.

Results and Conclusions

Of the 879 cases consulted, 35 patients with PAS were identified, 27 female, with a mean age at diagnosis of 7.8 ± 4.9 years, mean time elapsed between the 1st and 2 nd manifestation of 50.2 ± 44.3 months and 37.1% had a family history of autoimmune disease. Regarding classification, 3 patients had PAS type 2, 9 patients PAD type 3A, 14 patients PAS type 3C and 9 patients PAS type 4. In the group of PAS type 2 patients (2 males), all had ATD (2 Hashimoto's thyroiditis and 1 Graves' disease). Among patients with PAS type 3 (22 females), 24 had ATD, 9 DM1, 9 CD, 3 Vitiligo, 1 Autoimmune Hepatitis and 1 Systemic Lupus Erythematosus. CD was the first manifestation in 9 patients, DM1 in 6, DAT in 5, Vitiligo in 2 and Autoimmune Hepatitis in 1.Regarding PAS type 4 (5 females), all patients had DM1 and CD, the former representing the first diagnosis in 88.9% of cases.

Conclusion

PAS are rare among the pediatric population. In this sample, all patients were diagnosed with PAS type 2, type 3 or type 4, with the majority being female. The variable clinical presentation is consistent with what is described in the literature, as well as the high prevalence of a family history of autoimmune diseases. Frequently, the time interval until the diagnosis of a second endocrinopathy can be long (decades), which demonstrates the importance of active surveillance of patients with autoimmune diseases.

DOI: 10.1530/endoabs.81.P134

P135

Effects of decamethylcyclopentasiloxane by maternal exposure on the offspring mice behaviors

Eui-Bae Jeung, Donglin Yi, KangMin Kim, Minsu Lee, Jimin Lee & YongIn Kim

Laboratory of Veterinary Biochemistry and Molecular Biology, College of Veterinary Medicine, Chungbuk National University, Cheongju-si, Chungcheongbuk-do, Rep. of South Korea

Decamethylcyclopentasiloxane (D5) is one of the most common chemical ingredients for daily necessities that can be absorbed through the skin, aerosol, or even orally. People are exposed to D5 daily, but the risk of prenatal exposure to D5 is not completely understood. In this study, the effects of prenatal exposure to D5 on neural development were assessed through behavioral tests on offspring mice. First, the developmental neurotoxicity test (DNT) was performed to determine if D5 is a neurotoxicant. From the DNT, D5 was classified as a developmental neurotoxicant because their score of the discriminant function (SDF) was -1.55603, which is less than the standard score 0 of DNT. The estimated daily exposure of D5 to humans has been reported to be around 0.6 mg/kg. In this study, the pregnant mice were treated with 3, 6, and 12 mg/kg of D5 with corn oil per day from embryonic day 10 (E10) through postnatal day 7 through oral administration. All behavior tests were performed after the pups reached six weeks of age. As a result, the administration of 12 mg/kg of D5 (high dose group) increased the repetitive activity in both the grooming and marble burying tests and even a depression in tail suspension and forced swimming test compared to the vehicle group. In addition, high dose group showed a decrease in social behavior and cognitive ability in the three-chamber test. In the novel object recognition test, impairment of memory and exploring ability was found on the high dose group. The expression level of the four genes, brain-derived neurotrophic factor (BDNF), tyrosine hydroxylase (TH), acetylcholinesterase (AChE), and GABA type A receptor associated protein like 1 (GABARAPL1) related to neural development, were measured in the whole brain. The administration of high dose of D5 decreased the transcription level of BDNF and increased AChE and TH compared to the vehicle. On the other hand, there is no meaningful difference in GABARAPL1. These results show that the maternal exposure to D5 impairs the social and memory ability of mouse offspring and alters gene expression in the brain. In conclusion, maternal exposure to D5 can cause behavioral disorders in their offspring. Therefore, it is necessary to discuss the excessive usage of D5.

DOI: 10.1530/endoabs.81.P135

P136

Orbital inflammatory disease following mrna sars-cov-2 vaccine: a case report

Grunenwald Solange[1], Gabriel Lethellier[2], Philippe Imbert[1], Céline Dekeister[3] & Philippe Caron[4]
[1]CHU Larrey, Service d'Endocrinologie, Toulouse, France; [2]CH Intercommunal Castres-Mazamet, Service d'Ophtalmologie, Castres, France; [3]Hôpital Pierre-Paul Riquet, Chirurgie Maxillo-Faciale, Toulouse, France; [1] CHU Larrey, Service d'Endocrinologie, Toulouse, France

SARS-CoV-2 vaccination campaigns document a satisfactory high profile of protection against Covid-19 infection, but auto-immune/inflammatory diseases have been reported following Covid-19 vaccines. A 65-year-old woman reported two days following her first dose of the BNT162b2 mRNA vaccine tearing, eye irritation, conjunctival redness, peri-orbital swelling, spontaneous hematoma of the right lower eyelid, right greater than left proptosis, with a spontaneous improvement of symptoms during the following two weeks. She received the second dose of BNT162b2 vaccine after 6 weeks and noted an aggravation of the right proptosis. An ophthalmic examination noted high intraocular pressure on the right eye (30 mmHg) and brinzolamide, timolol and latanoprost eye drops were progressively introduced. After 3 months, Hertel values were 25 and 19 mm and palpebral fissures 12 and 11 mm for right and left eyes, respectively. The clinical activity score (CAS) was 4/7, but visual acuity, ocular motility and color vision test were normal. TSH concentration was 0.83 mU/l, and anti-thyroid antibodies were negative. CT and MRI scans confirm an asymmetric proptosis with a diffuse infiltration of the orbital fat and hypertrophy of extra-ocular muscles in the right orbit. At 4th month, she reported a visual acuity loss of the right eye (20/30) but fundus examination and optical coherence tomography were normal. She had intravenous 500 mg methylprednisolone infusion every two days and she reported transitory improvement of symptoms. Then she received iv 500 mg methylprednisolone once weekly for 4 weeks. She noted a transient improvement of pain and eyelid edema after each infusion, without reduction of proptosis and CAS after the first 6 intravenous infusions. Then the patient had intravenous 250 mg methylprednisolone infusion once weekly for 4 weeks until an orbital bone-wall decompression of the right orbit was performed. One month after surgery, ophthalmic evaluation reported Hertel value (23 mm), intraocular pressure (17 mmHg) and CAS (2/7) for right eye. To our best knowledge, there is the first report of an orbital inflammatory disease following mRNA SARS-CoV-2 vaccination. The temporal relationship between Covid-19 vaccination and onset of orbital symptoms suggest that SARS-CoV-2 mRNA vaccine can probably be associated with this orbital inflammatory disease. The mechanisms of occurrence of this orbital inflammatory side effect are a manner of debate (molecular mimicry, bystander activation, autoimmune/inflammatory syndrome induced by adjuvants). There is no treatment consensus when patients do not respond to first-line glucocorticoids (immunomodulatory therapy, orbital radiation, decompressive surgery).

DOI: 10.1530/endoabs.81.P136

P137

Di-butyl phthalate exposure in a human adrenocortical cell line impairs steroid hormone synthesis

Liselott Källsten, Paula Pierozan, Jonathan W Martin & Oskar Karlsson
Stockholm University, Science for Life Laboratory, Department of Environmental Science, Stockholm, Sweden

Phthalates are man-made chemicals that are used in many different types of products. The main use is as plasticizers, but they can also be added to, for example, cosmetics, drug coatings, and perfumes. One of the most commonly used phthalates is di-butyl phthalate (DBP), which has been detected in both food and drinking water globally. Once ingested, DBP is rapidly metabolized to its main metabolite, mono-butyl phthalate (MBP), which is frequently detected in human plasma and urine. Studies suggest that DBP has anti-androgenic potential and that it can induce reproductive and developmental effects. However, the molecular mechanisms behind these effects are unknown. We used the human adrenocortical cell line H295R to investigate how DBP and MBP may affect steroid hormone synthesis. After 48-h exposure, samples were collected and the supernatant analyzed by mass spectrometry and cell pellet by western blot to measure the levels of several steroid hormones and key steroidogenic enzymes, respectively. The results demonstrated that DBP induced a dose-dependent decrease in testosterone levels, and a similar decrease was detected for the precursor androstenedione. The corticosterone level also decreased after DBP-exposure, while cortisol increased. MBP induced similar effects as DBP, but with a lower effect size. However, MBP-exposure caused a decrease in cortisol, thereby indicating that there are differences in the mechanism of action between the two compounds. In addition, it was discovered that the decreases in steroid hormone levels are potentiated when the cells are co-treated with dibuturyl-cyclicAMP, which mimics endogenous stimulation of adrenal cells by adrenocorticotropic hormone to increase production of steroid hormones. The results also revealed that the levels of several steroidogenic enzymes were altered, with similar differences between MBP and DBP exposure as for the hormone concentrations. To conclude, these findings suggest that MBP is less potent than its parent compound, that the effects of phthalate exposure on the steroidogenesis are more profound during stimulation, and that both compounds affect steroid hormone production by alterations to the steroidogenic enzymes.

DOI: 10.1530/endoabs.81.P137

P392

A cell-based platform to screen chemical mixtures for endocrine disruptive effects

Denise Strand[1], Erik Nylander[1], Bo Lundgren[2], Jonathan W Martin[1] & Oskar Karlsson[1]
[1]Stockholm University, Department of Environmental Science, Stockholm, Sweden; [2]Stockholm University, Department of Biochemistry and Biophysics, Stockholm, Sweden

Chemical contaminants from human activity are omnipresent in the environment. A great number of common industrial compounds are detected in human blood and urine. Common chemicals such as bisphenols, phthalates and parabens that can interfere with endocrine signaling are classified as endocrine disruptive compounds (EDCs). The sex steroid hormonal signaling pathway is complex and sensitive to interference, as circulating concentrations of these hormones are low. Even miniscule amounts of an active chemical could therefore result in endocrine

disruption and cause adverse effects on development, brain function, and the reproductive- and immune systems. Industrial chemical production require risk assessments that balance societal benefits to potential negative effects on human- and environmental health. These risk assessments are based on observations in short term single-chemical exposure studies, which is not reflective of real-life scenarios where exposure to different chemicals and classes from many sources occurs simultaneously. Additive or synergistic effects are a concern, since the toxicity of different compounds in the biological system could interact and produce an unexpected and exaggerated toxicological response. The single compound approach therefore run the risk to potentially underestimate the biological impact of mixture effects. We have set up a small chemical library of environmental contaminants and employ liquid handling dispensing to reproduce real-world mixtures for screening of toxic effects. The endocrine disruptive potential of these mixtures is investigated by using OECD-validated *in vitro* cell-based methods that assess effects on steroidogenesis and androgen- and estrogen receptor interactions. Our aim is to establish medium or high throughput (MTS/HTS) micro plate-based screening methods for toxicological investigation of the complex chemical mixtures. This set-up will later be applied to investigate the effects of reconstructed individual exposomes based on chemical profiles detected by advanced mass spectrometry analysis of serum collected from a Swedish cohort. This will aid in the development of highly relevant risk assessments for chemical mixtures, in order to protect the general population from endocrine disruptive mixture toxicity.

DOI: 10.1530/endoabs.81.P392

P393

Dioxin-like polychlorinated biphenyl (pcbs) congeners induce inflammatory responses and reduce thyroid-specific genes expression in human thyrocytes via ahr pathways

Rosaria Ruggeri[1,2], Aurelio Minuti[2,3], Federica Aliquò[2,3], Fiorenza Gianì[4], Roberta Masto[4], Davide Romano[3], Angela Avenoso[3], Maria Teresa Cristani[5], Francesco Trimarchi[1], Alfredo Campennì[3], Angela D'Ascola[1] & Salvatore Cannavò[2,6]
[1]University of Messina, Dept Clinical and Experimental Medicine, Messina, Italy; [2]Endocrine Unit, University Hospital G. Martino, Messina, Italy; [3]Dept Biomedical and Dental Sciences, and Morpho-Functional Images, University of Messina, Messina, Italy; [4]University of Catania, Dept Clinical and Experimental Medicine, Catania, Italy; [5]University of Messina, Chemical, Biological, Pharmaceutical and Environmental Sciences, Messina, Italy; [6]University of Messina, Department of Human Pathology of Adulthood and Childhood DETEV, Messina, Italy

Background
PCBs are persistent organic pollutants, able to affect thyroid function (endocrine disruptors) and promote inflammation through multiple mechanisms. The aryl hydrocarbon receptor (AhR), a ligand-activated transcription factor able to bind dioxins and dioxin-like pollutants including PCBs, play a key role in xenobiotic response, by up-regulating specific responsive genes, the so-called "AhR gene battery", including cytochrome P450 1A1 (CYP1A1) and Nuclear factor-2 erythroid related factor-2 (Nrf2), a master regulator of the redox homeostasis with simultaneous anti-inflammatory activity. Aim of the present study was to investigate the influences of the AhR agonist PCBs congeners on thyrocytes *in vitro*.
Methods
Cultured primary thyrocytes were exposed for 24 h to increasing concentrations (5 and 10 μM) of 2.3',4.4',5-pentachlorobiphenyl (PCB 118) and 3.3',4',4',5 Pentachlorobiphenyl (PCB 126). mRNA and proteins expression for IL-1β IL-6, NIS, TG, AHR, CYP1A1 and Nrf2 were evaluated by real-time PCR and Western Blot and ELISA, respectively. Protein quantification was assessed by densitometry analysis
Results
In cultured thyrocytes, exposure to PCB 126 and PCB 118 at 5 and 10 μM concentrations significantly induced the increase of both mRNA and protein levels of the inflammatory cytokines IL-1beta and IL-6 ($P<0.01$ and $P<0.001$, at 5 and 10 μM respectively for mRNA expression; $P<0.05$ and $P<0.01$ at 5 and 10 μM for protein levels). Additionally, both mRNA and protein levels of the AhR and the downstream molecules CYP1A1 and NRF2 were increased in PCBs-treated thyrocytes (for AhR and Nrf2 $P<0.05$ at highest concentration; for CYP1A1 $P<0.05$ and $P<0.01$ at 5 and 10 μM respectively), suggesting activation of AhR pathways and oxidative stress sensitive markers (CYP1A1and NRF2) induction in response to PCBs exposure. On the contrary, the levels of Tg and NIS mRNA and related protein decreased after PCBs treatments at 5 and 10 μM concentrations ($P<0.05$ and $P<0.01$, for mRNA expression at 5 and 10 μM respectively; $P<0.05$ at 10 μM for protein levels), indicating down-regulation of these thyroid-specific genes in PCBs-induced inflammation.
Conclsion
PCB 118 and PCB 126 may promote inflammatory responses, leading to alteration in Tg and NIS genes expression in thyrocytes. Such effects can be partially attributed to the activation of the AhR that, in turn, induces CYP1A1 and NRF2, causing changes in the cellular redox status. These data may contribute to explain the mechanisms underlying thyroid toxicity of dioxin-like PCBs and highlight the potential role of these environmental pollutants in contributing to autoimmune thyroid inflammation and damage.

DOI: 10.1530/endoabs.81.P393

P394

Synergism between bisphenol a exposure and overweight/obesity in increasing the malignancy risk in a cohort of patients with thyroid nodules

Vincenzo Marotta[1], Lucia Grumetto[2], Ilaria Neri[2], Giacomo Russo[3], Anna Tortora[1], Giulia Izzo[4], Domenico Rocco[4] & Mario Vitale[4]
[1]UOC Clinica Endocrinologica e Diabetologica, AOU San Giovanni e Ruggi d'Aragona, Salerno, Italy; [2]Pharm-Analysis & Bio-Pharm Laboratory, Department of Pharmacy, School of Medicine and Surgery, University of Naples Federico II, Napoli, Italy; [3]School of Applied Sciences, Sighthill Campus, Edinburgh Napier University, Edinburgh, United Kingdom; [4]Dipartimento di Medicina, Chirurgia e Odontoiatria, Università di Salerno, Salerno, Italy

Introduction
The plasticizer Bisphenol A (BPA) is an endocrine disruptor with thyroid interfering activity. Obesity is a recognized risk factor for thyroid cancer. A recent study showed that subjects with BMI $\geq$ 25 are more prone to BPA-related thyroid disruption. To date, few and controversial experimental and epidemiological data provide weak evidence about a correlation between BPA exposure and thyroid cancer development. Aim of the present study was to assess a possible link between BPA, body fat excess, and thyroid cancer risk.
Patients and Methods
Multicentre, cross-sectional study including consecutive patients subjected to cytology for diagnostic definition of thyroid nodules. Blood samples were obtained for all enrolled patients. Serum BPA determination was performed by means of high performance liquid chromatography coupled in tandem with fluorescence and ultraviolet detection. Inclusion criteria: a) age $\geq$ 18 years; b) clinical management performed in one of the involved centres. Exclusion criteria: a) inconclusive cytology (TIR -3A, -3B, -1 categories); b) clinical and/or cytological and/or histological features of autoimmune thyroiditis; c) clinical and/or cytological and/or histological features of medullary thyroid cancer; d) modifications in lifestyle and anthropometric variables occurred within the previous 5 years. BPA exposure was assessed by means of a qualitative approach, categorizing the subjects in exposed (detectable serum BPA levels) and not-exposed (undetectable BPA levels).
Results
Statistical analysis included 94 patients: 30 males and 64 females (median age 52 years); 54 benign nodules, 40 thyroid cancers; 28 normal weight patients (BMI $<$ 25), 66 overweight/obese patients (BMI $\geq$ 25 $<$ 30 in 30 cases; BMI $\geq$ 30 in 36 cases). Detectable BPA was found in 78 cases. In the overall study group and in the BMI$<$25 group exposure to BPA was not significantly related to the risk of malignancy ($P=0.119$; OR 1.84 with 95% CI 0.76-4.45 and$P=0.755$; OR 0.83 with 95% CI 0.28-2.47, respectively). By contrast, in the BMI$\geq$25 group, BPA-exposed subjects showed significantly higher risk of malignancy ($P=0.046$; OR 2.88 with 95% CI 0.79-10.54).
Conclusions
In our series, BPA exposure conferred higher risk of thyroid cancer only in case of concomitant overweight/obesity, therefore suggesting a synergistic action between BPA and the excess of adipose tissue in promoting thyroid carcinogenesis.

DOI: 10.1530/endoabs.81.P394

P395

The endocrine disruptor cadmium affects both ERα+ and ERα- breast cancer cell lines

Viviana Maria Bimonte[1], Claudia Sabato[2], Sofia Trocchianesi[3], Zein Mersini Beşharat[2], Agnese Po[3], giuseppina catanzaro[2], Italia Falcone[4], Alessandra Fabi[5], Roberto Bei[6], Michele Milella[7], Alessandra Vacca[2], Elisabetta Ferretti[2] & Silvia Migliaccio[1]
[1]Foro Italico University Rome, Dept of Movement, Human & Health Sciences, Rome, Italy; [2]Sapienza University Rome, Dept of Experimental Medicine, Rome, Italy; [3]Sapienza University Rome, Dept of Molecular Medicine, Rome, Italy; [4]IRCCS-Regina Elena National Cancer Institute Rome, Medical Oncology 1, Rome, Italy; [5]Fondazione Policlinico Universitario A. Gemelli Rome, Precision Medicine in Breast Cancer Unit, Rome, Italy; [6]Tor Vergata University Rome, Dept of Clinical Sciences and Translational Medicine, Rome, Italy; [7]University of Verona, Section of Oncology, Verona, Italy

The highly toxic heavy metal Cadmium (Cd) is widely spread in the environment and could exert estrogen-like activity in tissues including breast. Previous studies demonstrated that Cd binds to estrogen receptor α positive (ERα+) breast cancer (BC) cells. In this new study, we evaluated effects of Cd on both ERα+ and ERα negative (ERα-) BC models with the aim to further characterize the mechanisms involved in Cd-related BC carcinogenesis. Specifically, the effect of Cd exposure was evaluated on BC cell lines MCF7 (ERα+, PR+, HER-), T47D (ERα+, PR+, HER+), and MDA-MB-231(ERα-, PR-, HER-). First of all, the effects of Cd on cell proliferation and death were evaluated. Cells treated with increasing concentrations (0.5-10 μM) of Cd showed a significant decrease in cell viability from the dosage of 5 μM after 24h in MCF7, after 48h in MDA-MB-231 and after 72h in T47D cells. The levels of steroid receptors expressed by the cells before and after Cd were also evaluated. In detail, ERα, estrogen receptor α (ERα), androgen receptor (AR), and progesterone receptor (PR) were evaluated after Cd exposure. ERα decreased in ERα+ cells while ERα expression increased in all cells. PR levels were reduced or not modulated in all cells. AR levels were increased in both ERα+ and ERα- cell models. We evaluated the ratio of AR/ERα and AR/ERα and we found that Cd induced a significant increase in the two ratios in both ERα+ and ERα- cell models. Furthermore, activation of cellular signaling pathways were evaluated. Cd induced activation of p38 MAPK in all cell lines, activation of PhAKTser473 in T47D and activation of ERK1/2 in MDA-MB-231 cells. Finally, Cd exposure induced a significant increase in the pro-inflammatory cytokines IL-6 and IL-8. In conclusion, our study demonstrates that Cd has a role in regulating cell viability, steroid receptors phenotype, cellular signaling pathways and pro-inflammatory cytokines in both ERα+ and ERα- cell models.

DOI: 10.1530/endoabs.81.P395

P649

Neonatal thyroid stimulating hormone as indicator of Iodine status in Lithuania

Lina Zabuliene[1], Marius Miglinas[1,2], Deimante Brazdziunaite[2,3], Marija Smirnova[2,4], Jurgita Songailiene[2,3], Nomeda Bratcikoviene[3,4], Valdas Banys[3], Ernesta Macioniene[1,2] & Algirdas Utkus[2,3]
[1]Faculty of Medicine, Vilnius University, Institute of Clinical Medicine, Vilnius, Lithuania; [2]Vilnius University Hospital "Santaros Klinikos", Vilnius, Lithuania; [3]Faculty of Medicine, Vilnius University, Institute of Biomedical Sciences, Vilnius, Lithuania; [4]Vilnius Tech, Faculty of Fundamental Sciences, Vilnius, Lithuania

Background
World Health Organization (WHO), United Nations International Children's Emergency Fund (UNICEF), and the International Council for Control of Iodine Deficiency Disorders included neonatal thyroid stimulating hormone (nTSH) as one of the indicators for assessing iodine deficiency at a population level and as a monitoring tool in programs of iodine supplementation. A prevalence of nTSH concentrations in dry blood spots (DBS) above 5 mIU/l below 3% has been proposed as the threshold indicating iodine sufficiency. Since 1994 WHO and UNICEF reached an agreement to recommend Universal Salt Iodization as a key strategy for prevention and elimination of Iodine Deficiency Disorders worldwide. In Lithuania mandatory universal salt iodization program was implemented in 2005. The aim of this study was to evaluate nTSH data to assess the current status of iodine nutrition in Lithuania.
Methods
The study was conducted as a part of nationwide program NATRIJOD aimed to evaluate sodium and iodine status in Lithuania (the country with 2 784 279 inhabitants in 2021). We retrospectively analyzed the results of nTSH tests from the National Newborn Screening Program for congenital hypothyroidism database between 2002 and 2018. According to screening methodology, heel-prick blood samples of newborns were collected on filter paper cards. Results of samples collected >48 h after birth were analyzed. The nTSH concentration was measured in DBS using fluorometric enzyme immunoassay (Labsystems). Anonymized results of nTSH tests from 492143 cards were retrieved, congenital hypothyroidism cases and inadequately sampled DBS were excluded, frequency of results at the cut-off of nTSH above 5 mIU/l was calculated.
Results
The prevalence of nTSH above 5 mU/l varied between 1.21 % (in 2013) and 5.43 % (in 2004). Since 2011 overall prevalence of nTSH above 5 mU/l was less than 3% and only one region has had frequency above 3% for several years. In 2018 increase in the prevalence of nTSH above 5 mU/l was noted in three regions of the country, indicating possible mild iodine deficiency in these regions.
Conclusions
Despite that children, pregnant women and adult in Lithuania are mildly iodine deficient, based on median urinary iodine concentrations data, the prevalence of nTSH above 5 mU/l was low, suggesting a need to re-evaluate universal cut-off of nTSH and investigate other potential factors impacting nTSH results in order to detect early mild iodine deficiency in population and achieve sustainable elimination of iodine deficiency.

DOI: 10.1530/endoabs.81.P649

P650

Potential synergic and antagonistic effects of EDC mixtures on human prostate cells

Aldo Mileo[1], Lorenzo Riccio[1], Michele Francesco Di Tolla[2], Vittoria D'Esposito[2], Teresa Chianese[1], Vincenza Laforgia[1], Pietro Formisano[2] & Maria De Falco[1]
[1]Department of Biology, Naples, Italy; [2]Department of Medical and Translational Scieces, Naples, Italy

Endocrine Disrupting Chemicals (EDCs) are a heterogeneous class of compounds so called for their ability to interfere with the endocrine system. These environmental pollutants are detected in different environmental matrices; they can bioaccumulate in adipose tissue and biomagnificate in food chain due to their high hydrophobicity and low water solubility[1]. Two EDCs usually used in the manufacture of domestic, industrial, and agricultural products are Dibutylphtalate (DBP) and Nonylphenol (NP). They are found in personal-care products, children's toys, and food products, so human population appears to be predominantly exposed to them, through ingestion or skin contact. It has been demonstrated that both are able to damage male reproductive system[2-4]. Due to the important role of prostate gland in male reproduction and fertility, in the present work, we evaluated the effects of DBP and NP, used alone or in different mixtures with or without endogenous sexual hormones as 17-α-estradiol and testosterone on human prostate cell line PNT1A. The first data showed that all EDCs, alone or in mixtures affected cell proliferation. Specifically, we observed a hyperproliferative estrogen-like behaviour of NP that in mixtures seemed to hide the antiandrogenic effect of DBP. We have also shown that DBP and NP activated estrogen receptor pathways, mainly interacting with ERα. Moreover, we investigated EDC ability to induce inflammation that is a first step to prostate gland hyperplasia. We observed that cytokines and chemokines levels, such as IL-9 PDGF, TNFα, MIP-1α, MIP-1α, IL-1α were altered after all the treatments, suggesting NP and DBP involvement in the onset of inflammation processes. In conclusion, we have pointed attention on dangerousness of the mixtures able to induce a strong imbalance of prostate cell physiology.
References
1. De Falco M and Laforgia V. Int J Environ Res Public Health. 2021 18(18): 9772. doi: 10.3390/ijerph18189772
2. Di Lorenzo M, *et al*. Ecotoxicol Environment Saf 2018; 147:565-73. https://doi.org/10.1016/j.ecoenv.2017.09.030
3. Forte M, *et al*. Toxicology 2016; 357-358, 21-32. https://doi.org/10.1016/j.-tox.2016.05.024
4. Forte M, *et al*. Ecotoxicol Environment Saf 2019; 180:412-9. https://doi.org/10.1016/j.ecoenv.2019.05.035

DOI: 10.1530/endoabs.81.P650

P651

Di-(2-ethylhexyl) phthalate decreases forskolin-stimulated progesterone synthesis in human granulosa cells

Dragana Samardzija Nenadov, Biljana Tesic, Nebojsa Andric & Kristina Pogrmic-Majkic
University of Novi Sad, Faculty of Sciences, Department of Biology and Ecology, Novi Sad, Serbia

Di-(2-ethylhexyl) phthalate (DEHP) is an endocrine disruptor that belongs to the group of phthalates. Human exposure to DEHP is ubiquitous, considering its use in plastics and other common consumer products. *In vivo* and *in vitro* studies demonstrate its harmful effects on female reproductive system. The aim of this study was to investigate the effects of short term exposure to DEHP on progesterone synthesis in human granulosa cells. The human nonluteinized granulosa cells (HGrC1) were exposed for 48 h to 25 μM DEHP alone or in the presence of 25 μM forskolin (FOR), stimulator of progesterone synthesis. The results showed that exposure to DEHP did not affect the viability of HGrC1 cells. DEHP did not affect basal but decreased FOR-stimulated progesterone production in HGrC1 after 48 h. To clarify the potential mechanism of DEHP-induced decrease in progesterone production in FOR-stimulated HGrC1, we have analyzed the expression of key genes involved in progesterone synthesis. The results showed that DEHP decreased FOR-stimulated mRNA and protein expression of steroidogenic acute regulatory protein, which regulates rate limiting step in progesterone synthesis. Furthermore, the mRNA expression of 3-beta-hydroxysteroid dehydrogenase, an enzyme that converts pregnenolone to progesterone, was downregulated in FOR-stimulated cells after DEHP exposure. These results indicate that short-term exposure to DEHP decreases progesterone production in human granulosa cells, which could have negative impact on ovarian function and fertility. Funding: Science Fund of the Republic of Serbia, program PROMIS, project DETOX, grant number 6062573.

DOI: 10.1530/endoabs.81.P651

Pituitary and Neuroendocrinology

P138

Takayasu's artheritis presenting as a large sellar mass with neurological and hypopituitarism manifestations

Elena Galazzi[1], Noemi Giancola[1], Valeria Citterio[1], Mirella Moro[1], Laura Addobbati[2], Sabrina Avignone[3,4], Franco Capsoni[5,6] & Luca Persani[1,7]
[1]Istituto Auxologico Italiano, Endocrine and Metabolic Diseases Unit, Milano, Italy; [2]Istituto Auxologico Italiano, Division of Neurology and Stroke Unit, Milano, Italy; [3]University of Milan, Italy; [4]Fondazione IRCCS Ca' Granda OspedaleMaggiore Policlinico, Neuroradiology Unit, Milano, Italy; [5]Department of Biomedical Sciences for Health (BIOMETRA), Milano, Italy; [6]istituto auxologico Italiano, Allergology, Clinical Immunology & Rheumatology Unit, Milano, Italy; [7]University of Milan, Department of Medical Biotechnology and Traslational Medicine (BIOMETRA), Italy

Introduction
Only one case of hypophysitis secondary to Takayasu's artheritis (TKA) has been described so far. We report the second case of a TKA presenting with a massive sellar and cerebrovascular infiltration.
Clinical case
A 52 years-old female was referred to endocrine outpatient clinics after a brain MRI performed for a 2-year history of headaches, dizziness and general discomfort. Past medical history included hypertension and aspecific sympthoms (fatigue, nausea, loss of libido). Pituitary MRI found a 13 mm sellar tumor-like lesion extending to the optic chiasm with homogenous gadolinium uptake, pituitary stalk thickening and ectopic neurohypophysis; parasellar T2 dark sign was suggestive for an infiltrating process of the cavernous sinus. Brain angio-RMN revealed sub-occlusion of the intracranial and extracranial trait of the left carotid artery with compensation circles and a stenotic intracranial trait of the right carotid artery. Visual field examination resulted in bitemporal hemianopsias. Endocrine work-up revealed panhypopituitarism with mild hyperpolactinemia, probably secondary to deafferentation. Diabetes insipidus was inferred by low urine osmolarity (290 Osm/kg), but requiring revaluation after glucocorticoids replacement. Adrenal and thyroid function were promptly replaced with sudden recovery of fatigue and nausea. Even in the absence of systemic inflammatory symptoms nor increased inflammatory reactants, screening for possible causes of secondary hypophysitis was undertaken. Serum IgG4 levels, serum and liquor angiotensing converting enzyme levels, serum quantiferon testing and liquor culture, ANCA antibodies were all negative. Doppler ultrasound of carotid arteries revealed possible signs of left carotid dissection but no signs of temporal arteries involvement. Hence, evidence of mild stenosis of coeliac and upper mesenteric artery and left common femoral artery on angio-CT together with a mild uptake in the thoracic and abdominal aorta on 18-FDG PET led to the diagnosis of TKA. Immunosuppressive therapy with high doses of methylprednisolone (1 g bolus e.v. for 3 consecutive days) followed by a down-tapering scheme from 50 mg/day prednisone p.o. was undertaken, then shifted to cortone acetate at replacement doses over one year. Follow-up radiological investigations at 6-12 months showed a marked reduction of pituitary infiltrate and up-take of thoracic/abdominal aorta but an unchanged intracranial artery stenosis. Concomitantly, endocrine follow-up revealed a normalization of prolactin levels and gonadotrope/thyrotrope axis, which allowed the discontinuation of levothyroxine replacement therapy.
Conclusion
Pituitary gland and hypothalamus are very unusual yet possible sites of TKA infiltration. Massive sellar infiltration allowed diagnosis of systemic vasculitis even without inflammatory manifestations, reasonably reducing diagnostic delay and fatal consequences.

DOI: 10.1530/endoabs.81.P138

P139

Pituitary apoplexy in the aftermath of a SARS-CoV-2 infection: a case series from Amiens University Hospital

Joe Balmain[1], Abdallah Al-Salameh[1,2] & Rachel Desailloud[1,2]
[1]Amiens University Hospital, Department of Endocrinology, Diabetes Mellitus and Nutrition, Amiens, France; [2]University of Picardie Jules Verne, PeriTox=UMR_I 01, Amiens, France

Introduction
Since the outbreak of the COVID-19 pandemic, several cases of pituitary apoplexy following a SARS-CoV-2 infection have been described in several countries. Here, we describe a case series of pituitary apoplexy occurring in the aftermath of a SARS-CoV-2 infection to alert physicians about possible neuroendocrinological damage caused by the virus that can lead to visual sequelae and hypopituitarism.
Methods
We retrospectively identified all the adult patients treated at Amiens University Hospital between March 2020 and May 2021 for pituitary apoplexy confirmed by cerebral imaging and following an RT-PCR-confirmed SARS-CoV-2 infection.
Results
Eight cases (6 women, 2 men) occurred between March 2020 and May 2021 and were reviewed in this study. The mean age at diagnosis was 67.5 ± 9.8 years. Only one patient had a 'known' non-functional pituitary macroadenoma. Pituitary apoplexy occurred within 0-16 weeks after COVID-19. The most common symptom of pituitary apoplexy was a sudden headache. Visual disturbances and/or ocular palsies occurred in six patients while seven patients presented with corticotropic and thyrotropic insufficiencies. There was no diabetes insipidus. Brain imaging was typical in all cases. Only two patients required decompression surgery, whereas the others were managed conservatively. The clinical outcome was favorable for all patients but without recovery of their pituitary deficiencies. No death occurred in our series.
Conclusion
Being the largest case series in the literature, our study provides support for the hypothesis that SARS-CoV-2 may be a new precipitating factor for pituitary apoplexy. The ruling out of various known precipitating factors of pituitary apoplexy reinforces the plausibility, strength, consistency, and coherence of the causal association between SARS-CoV-2 infection and pituitary apoplexy. The main hypothesis to explain the neurotropism of SARS-CoV-2 involves direct infection by the virus, with the olfactory bulb constituting a gateway in the early phase of infection via neuronal pathways, notably via nasal cells during aerosolization. Although angiotensin converting enzyme 2 (ACE2), the cellular receptor for SARS-CoV-2, is not expressed in olfactory neurons, it is expressed in sustentacular and perivascular cells which have structural and protective roles on olfactory neurons. The other putative gateway is via hypothalamic tanycytes glial cells which have been shown to express ACE2 and type 2 transmembrane protease serine (TMPRSS2), both of them are implicated in virus entry. It is essential that practitioners be alerted about possible pituitary disease due to the virus so that such patients are recognized and appropriately managed, hence improving their prognosis.

DOI: 10.1530/endoabs.81.P139

P140

Efficacy of lanreotide 120 mg primary therapy on tumor shrinkage and ophthalmologic symptoms in acromegaly after one month

Hamza Benderradji[1], Vernotte Elise[1], Soto Ares Gustave[2], Woillez Jean Philippe[3], Perbet Romain[4], Karnoub Mélodie-Anne[5], Soudan Benoît[6], Jannin Arnaud[7], Richard Assaker[5], Buée Luc[8], Vincent Prevot[9], Maurage Claude-Alain[4], Pigny Pascal[6], Vantyghem Marie-Christine[1], Merlen Emilie[1] & Christine Cortet Rudelli[1]

[1]Department of Endocrinology, Diabetology, and Metabolism, Lille University Hospital, Lille, France; [2]Department of Radiology, Lille University Hospital, Lille, France; [3]Department of Ophthalmology, Lille University Hospital, Lille, France; [4]Department of Pathology, Lille University Hospital, Lille, France; [5]Department of Neurosurgery, Lille University Hospital, Lille, France; [6]Department of Biochemistry & Hormonology, Lille University Hospital, Lille, France; [7]Department of Endocrinology, Diabetology, and Metabolism, Lille University Hospital, Nord, Lille, France; [8]University of Lille, Inserm, CHU Lille, Lille Neuroscience & Cognition, UMR-S1172, Lille, France; [9]University of Lille, Inserm, CHU Lille, Lille Neuroscience & Cognition, UMR-S1172, Lille, France

Introduction
Few studies to date have attempted to evaluate the early efficacy of first-generation somatostatin analogs in somatotroph macroadenomas.
Objective
To investigate the short-term efficacy of primary therapy with lanreotide 120 mg on tumor shrinkage and ophthalmologic symptoms in newly diagnosed patients with acromegaly.
Design and patients
This single-center retrospective study included 21 patients who were newly diagnosed with acromegaly resulting from pituitary macroadenoma and were receiving a primary monthly treatment with lanreotide 120 mg. Clinical, hormonal, ophthalmologic and MRI scan evaluations were conducted after the first and the third months of treatment.
Results
Tumor volume reduction was more pronounced at one month [mean volume change -31.4 $\pm$ 19.5%, $P<0.0001$] than between the first and third month of treatment [mean volume reduction -20.6 $\pm$ 13.4%, $P=0.0009$]. The mean volume change between baseline and the third month was -46.4 $\pm$ 21.6, ($P<0.0001$). A significant volume reduction ($\geq$ 25%) was observed in 61.9% of individuals (13/21) at the first month and in 82.3% (14/17) after three months of treatment. Among 14 individuals with optic chiasm compression and visual field defects, visual field normalization was observed in 3 cases (21.4%) and improvement in 7 cases (50%) at one month. The decrease in GH and IGF-1 serum values was significant at one month.
Conclusions
Primary treatment with lanreotide 120 mg in patients with somatotroph macroadenomas provides early significant tumor shrinkage with rapid improvement of visual symptoms at the end of the first month.

DOI: 10.1530/endoabs.81.P140

P141

Bartter syndrome type I: a rare cause of polyuria-polydipsia syndrome with failure to thrive in a child

Ioana-Cristina Barbacariu[1], ilona-beatrice blesneac[1], Andreea Rosu[1], Madalina Protop[1], Mihaela Munteanu[2,3], Eusebiu-Vlad Gorduza[3,4] & Cristina Preda[1,3]

[1]"Sf. Spiridon" Clinical Emergency County Hospital, Endocrinology, Iasi, Romania; [2]"Sf. Maria" Clinical Emergency Children's Hospital, Pediatric Nephrology, Iasi, Romania; [3]"Grigore T. Popa" University of Medicine and Pharmacy, Iasi, Romania; [4]"Cuza Vodă" Clinical Obstetrics and Gynecology Hospital, Maternal-Fetal Medicine, Iasi, Romania

Introduction
Bartter syndrome (BS) is a rare autosomal recessive disorder, with an estimated prevalence of 1 in 1.000.000. It is characterized by a primary defect in sodium chloride reabsorption in the medullary thick ascending limb of Henle's loop. Severe hypokalemia, metabolic alkalosis, hyponatremia, hypochloremia, hyperaldosteronism, and increased urinary loss of sodium, potassium, and chloride can raise the suspicion of BS, but genetic testing is required for a definitive diagnosis. Correct diagnosis and early treatment prevent the impairment of renal function, the development of complications and improve the prognosis.
Case report
We present the case of a 3 years and 7 months-old boy, admitted to our Pediatric Endocrinology Department for short stature (H = 87 cm, -3.32 SD), underweight (W = 9.5 kg) and massive polyuria-polydipsia syndrome (ingestion volume = 5000-7000 ml/day and urine volume = 4000-5000 ml/day) with normal blood pressure. He is the first child of non-consanguineous parents, born prematurely by cesarian section at 32 weeks gestation, appropriate for gestational age, with perinatal asphyxia requiring intensive care. Severe unexplained polyhydramnios was diagnosed in the second trimester and required 3 amnioreductions. During his first 3 years of life, he had multiple hospitalizations in the Pediatric Gastroenterology department where celiac disease, mucoviscidosis and intestinal parasitosis were excluded. In our department, the laboratory tests revealed metabolic alkalosis, hypokalemia, hyponatremia, a high urinary calcium/creatinine ratio and a high urinary potassium/creatinine ratio. Hormonal evaluation identified normal for age thyroid, adrenal and gonadal function, with a possible growth hormone (GH) deficiency (low baseline GH and IGF-1), as well as an elevated copeptin value. The abdominal ultrasound showed bilateral medullary nephrocalcinosis and the brain MRI was normal. As the clinical diagnosis of BS was established, he was started on potassium chloride supplementation and was referred to the Pediatric Nephrology Department where indomethacin was added. The genetic testing detected 3 pathogenic variants in the SLC12A1 gene, confirming BS type I. At the six months follow-up, we noted a reduction of polyuria (=3500 ml/day) and polydipsia (=4000 ml/day), with improved weight gain, while plasma potassium and bicarbonate levels normalized.
Conclusions
Despite being rare in clinical practice, the diagnosis of BS should be considered in any premature neonate with unexplained polyhydramnios and in any child with growth failure, hypokalemia, polydipsia and polyuria. Correct diagnosis and early treatment improve the quality of life of these children, allowing them to reach their full growth potential. Genetic testing helps to establish a specific diagnosis and provides the basis of genetic counseling for family members.

DOI: 10.1530/endoabs.81.P141

P142

Chondrosarcoma of the cavernous sinus treated with postoperative proton radiation therapy: case report and endocrinological follow up after 36 months

Davide Masi[1], renata risi[1], angela balena[1], alessandra caputi[1], maria elena spoltore[1], rebecca rossetti[1], mikiko watanabe[1], Rossella Tozzi[2], Elena Gangitano[1], stefania mariani[1], Andrea Lenzi[1], lucio gnessi[1] & carla lubrano[1]

[1]Sapienza University of Rome, Department of Experimental Medicine, Section of Medical Pathophysiology, Food Science and Endocrinology, Roma, Italy; [2]Sapienza University of Rome, Department of Molecular Medicine, Roma, Italy

Case Summary
In May 2018, a 22-year-old man was admitted to the Emergency Room of Polyclinic Umberto I Hospital of Rome, because of progressive headaches and binocular diplopia. Brain MRI revealed a heterogeneous T1WI-hypointense and T2WI-hyperintense mass of 40x28x25 mm (CC, LL, AP) including calcification areas in the left paramedian region of the clivus invading the homolateral cavernous sinus. The patient underwent partial tumour resection via infratemporal approach and a diagnosis of intermediate grade myxoid chondrosarcoma was confirmed on histopathology. The patient was discharged with no neurological deficit. Two months later, the patient presented with newly onset of hypoesthesia of the face, ophthalmoplegia, and dizziness. A new MRI showed a heterogeneous calcified mass of 36x25x25 mm (CC, LL, AP) arising from the left cavernous sinus, expanding into the left sphenoid wing and impinging the pituitary gland, which was attributable to relapse of chondrosarcoma. Therefore, a second surgical resection was performed and after three months the patient was treated with high-dose (70 Gy/35 fractions) intensity-modulated proton therapy (IMPT). The patient was discharged without replacement therapy. The treatment resulted in a marked volumetric reduction of the pathological tissue which was stably maintained in the following three years of follow-up. Pituitary function evaluation tested normal except for mild hyperprolactinemia likely due to deviation of the pituitary stalk (Table 1).
Conclusion
The treatment of intracranial chondrosarcomas still remains a major challenge, as brain surgery and IMPT can have a detrimental effect on healthy cerebral areas located proximally to the lesion. This case confirms that IMPT can prevent tumour enlargement while preserving normal pituitary function.

Table 1

Patient's characteristics		36-months follow-up	
Age (years)	22	ACTH	17.60 pg/ml [5.00 - 60.00]
Gender	Male	Cortisol	10.90 mg/dl [3.70 - 19.40]
Symptoms	headache, diplopia, cranial nerve injury	PRL	**34.03 ng/ml** [3.46 - 19.4]
Tumor site	Skull base	TSH	2.00 μUI/ml [0.35 - 4.94]
Histology	Myxoid Chondrosarcoma	FT4	0.99 ng/dl [0.70 - 1.48]
Differentiation	G2	FT3	2.89 pg/ml [1.71 - 3.71]
KPS scores	100	FSH	5.53 mUI/ml [0.95 - 11.95]
Brainstem compression	No	LH	2.16 mIU/ml [0.57 - 12.07]
Optic apparatus compression	No	Estradiol	28.00 pg/ml [11-44]
Recurrent disease	Yes	Total Testosterone	389.04 ng/dl [240.24 -870.68]
Radiotherapy (IMPT)	70Gy/35 fractions	GH	0.31 ng/ml
Metastases	No	IGF1	124.00 ng/ml [98.70 - 289.00]
Any compression	Cavernous sinus, pituitary gland, temporo-mesial parenchyma	Serum sodium	136 mEq/l [136 - 145]
		Serum potassium	4.10 mEq/l [3.50 - 5.10]

DOI: 10.1530/endoabs.81.P142

P143

Efficacy and safety of long-term high doses of cabergoline in prolactin secreting tumor

Chiara Bona[1], Nunzia Prencipe[2], Enrico Mazza[3], Alessandro Maria Berton[1], Fabio Bioletto[1], Emanuele Varaldo[1], Daniela Cuboni[1], Cristina Gottero[3], Valentina Gasco[2], Ezio Ghigo[1] & Silvia Grottoli[1]

[1]University of Turin, Department of medical sciences, Division of Endocrinology, Diabetology and Metabolism, Turin, Italy; [2]A.O.U. Città della Salute e della Scienza, Department of medical sciences, Division of Endocrinology, Diabetology and Metabolism, Turin, Italy; [3]ASL Città di Torino, Maria Vittoria Hospital, Division of Endocrinology and Metabolic Diseases, Turin, Italy

Purpose
The aim of this study was to identify any predictive factors for need of high doses of cabergoline (CAB) in prolactinomas and to study any relationship between adverse events onset and CAB cumulative dose.
Methods
Forty-two patients harboring resistant prolactinomas (High Dose group-HD; cabergoline dose $\geq$ 3.5 mg/week) were matched by gender, age and pituitary tumor diameter at diagnosis with subjects under standard doses (Standard Dose group - SD). All 84 patients were evaluated in terms of response to treatment and for adverse events onset.
Results
Except for higher PRL levels at diagnosis, no significant differences were documented between HD and SD, nor at diagnosis neither at last follow-up. In HD overall treatment duration was significantly longer (P 0.041) and CAB cumulative dose significantly higher (P 0.0001), with lower response rate, both in biochemical (P 0.0007) and morphological (P 0.03) terms. In particular, PRL levels were significantly lower in SD both at diagnosis and after 3, 6, 12 month of CAB and at nadir (respectively p 0.016, P0.0009, $P<$ 0.0001, P0.0001 and P0.003), this last occurring with a CAB dose lower in SD ($P<0.0001$). Adenoma diameter was smaller in SD (P 0.021) after 12 months of CAB. ROC curves highlighted a threshold PRL value of 1081 ng/ml al diagnosis (sensitivity 62% and specificity 71%, AUC 0.67; P0.007) as predictive for high doses necessity, of 75 ng/ml after 3 months of therapy (sensitivity 81% and specificity 60%, AUC 0.74; P0.0001), of 58 ng/ml after 6 months (sensitivity 76% and specificity 81%; AUC 0.80; $P<$ 0.0001) and of 10 ng/ml after 12 months (sensitivity 97% and specificity 48%; AUC 0.77; $P<0.0001$). All ten patients (over 45 studied, 22.2%) who developed valvular fibrosis were in HD (P 0.019) and underwent a higher cumulative dose of CAB (P 0.003). Five patients (5.9%) developed impulse control disorder, equally distributed among two groups (P 0.67), without significant difference (P 0.40) in CAB cumulative dose.
Conclusion
A PRL value higher than 58 ng/ml after 6 months resulted as the best predictive factor for high doses necessity. No additional risk of impulse control disease was detected in HD, but a higher prevalence of heart valvular fibrosis was recorded. Even though this finding may be partly due to echocardiographic test mainly being performed in such patients, this data should not be underestimated.

DOI: 10.1530/endoabs.81.P143

P144

Gene expression profiling of subcutaneous adipose tissue reveals new biomarkers in active acromegaly

Camilla Maria Falch[1,2,3], Mai C. Arlien-Søborg[4,5], Jakob Dal[4,5], Arvind Sundaram[6], Annika E. Michelsen[3], Thor Ueland[3], Linn G. Olsen[1,3], Ansgar Heck[1,2], Jens Bollerslev[1,2], Jens Otto Jorgensen[4,5] & Cristina Olarescu[1,2,3]

[1]Oslo University Hospital, Section of Specialized Endocrinology, Department of Endocrinology, Oslo, Norway; [2]University of Oslo, Institute for Clinical Medicine, Faculty of Medicine, Oslo, Norway; [3]Oslo University Hospital, Research Institute for Internal Medicine, Oslo, Norway; [4]Aarhus University Hospital, Department of Endocrinology and Internal Medicine, Aarhus, Denmark; [5]Aarhus University Hospital, Medical Research Laboratory, Department of Clinical Medicine, Aarhus, Denmark; [6]Oslo University Hospital, Department of Medical Genetics, University of Oslo., Oslo, Norway

Objective
Patients with acromegaly present increased insulin resistance despite reduced adipose tissue (AT) mass. Growth hormone (GH) stimulates lipolysis, but the role of AT as a metabolic factor in patients with acromegaly is still uncertain. Moreover, there is a need for better biomarkers of disease activity in acromegaly.
Methods
RNA-sequencing was performed on paired subcutaneous AT (SAT) biopsies from patients ($n=6$) with active acromegaly and after disease control obtained by surgery. Clustering and pathway analyses were investigated. HTRA1, METRNL, S100A8, S100A9, PDGFD, PTX3, MMP9, TEK, ANGPT1, GRN and FLT1 and corresponding proteins were selected for further analyses. In a lager patient cohort ($n=23$), serum proteins were measured by immunoassay. Correlations between GH, insulin like growth factor-I (IGF-I), and visceral AT (VAT), SAT, total AT and serum proteins were analyzed. The *in vitro* effects of GH and IGF-I stimulation on the gene expression of HTRA1, METRNL, S100A8, S100A9 and PDGFD in human subcutaneous adipocytes, endothelial cells (HUVEC) and monocytes (THP-1) were investigated.
Results
743 genes were significantly differentially expressed (470 genes downregulated, 273 upregulated after disease control, p-adjusted <0.05). The patients clustered according to disease activity. Pathways related to growth hormone activity, extracellular matrix deposition/adhesion/collagen, and inflammation/vascularization were among the differentially expressed signaling pathways. Of notice, several collagen genes were upregulated in active disease. Serum levels of HTRA1, METRNL, S100A8, S100A9, and PDGFD significantly decreased after disease control ($P<0.05$). HTRA1, S100A8 and S100A9 correlated with VAT ($0.725<R<0.551$, $P<0.05$). *In vitro* GH and IGF-I stimulation of subcutaneous adipocytes and HUVEC did not change gene expression of HTRA1, METRNL, S100A8, S100A9 and PDGFD. METRNL was increased by IGF-I in THP-1 monocytes.
Conclusion
Disease activity has a stronger impact on the mRNA signature of SAT that overplays the inter-individual differences. Novel candidate genes upregulated in SAT of active acromegaly were identified. Among them, HTRA1, METRNL, S100A8, S100A9 and PDGFD can represent potential biomarkers for disease activity and metabolic risk factors in acromegaly.

DOI: 10.1530/endoabs.81.P144

P145

The role of advanced glycation end products on vertebral fractures in patients with acromegaly

Meliha Melin Uygur, Dilek Dereli Yazıcı & Dilek Gogas Yavuz
Marmara University, School of Medicine, Division of Endocrinology and Metabolism, Istanbul, Turkey

Introduction
Acromegalic osteopathy is an emerging complication characterized by high risk for vertebral fractures (VFS), whereas bone mineral density (BMD) may not be useful to predict the risk. Recent studies have reported that increased advenced glycation end products (AGEs) are associated with bone fragility. We aimed to evaluate the relationship between AGEs and VFs in patients with acromegaly.
Study design
Cross-sectional
Patients & Methods
We enrolled 70 subjects from the Department of Endocrinology and Metabolism Disease, Marmara University Medical School in acromegaly group (AG) and compared with 70 healthy controls (HC) without any risk factors for secondary osteoporosis and pituitary disorder. We performed vertebral morphometric evaluation of the lateral thoracic and lumbar spine X-ray images, and collected demographic, biochemical, clinical data. AGEs were measured by the auto-fluorescence (AF) reader.
Results
The prevalence of VFs was significantly higher despite elevated BMD in AG than HC (32.9% vs. 8.6%; $P<0.001$). Controlled/cured acromegaly had higher VFs prevalence than active acromegaly (12.5% vs. 38.9%, $P=0.06$). AG had significantly higher levels of AGEs, HbA1c and CTx than HC ($P=0.04$, $P=0.01$, $P=0.001$; respectively). There was a negative correlation between AGEs and CTx in AG ($r=$-0.371, $P=0.001$). In multivariate logistic regression analysis (Table-1), disease duration, IGF-1 levels were negatively correlated with VFs, whereas AF was positively related to the VFs ($R^2=19.23$, $P=0.02$) in the AG.
Conclusion
VFs might occur independently from the disease activity and duration and be an early complication of the acromegaly. AGEs may be useful for assessing the risk of prevalent VFs in this clinical setting.
References
1. Mazziotti G *et al*. Bone turnover, bone mineral density, and fracture risk in acromegaly: a meta-analysis. The Journal of Clinical Endocrinology & Metabolism. 2015;100(2):384-94.
2. Yamamoto. "Serum Pentosidine Levels Are Positively Associated with the Presence of Vertebral Fractures in Postmenopausal Women with Type 2 Diabetes." *The journal of clinical endocrinology & metabolism.* 93.3 (2008): 1013–1019
3. Yamamoto. "Low Serum Level of the Endogenous Secretory Receptor for Advanced Glycation End Products (esRAGE) Is a Risk Factor for Prevalent Vertebral Fractures Independent of Bone Mineral Density in Patients with Type 2 Diabetes." *Diabetes care.* 32.12 (2009): 2263–2268.

Table 1

	OR	95% CL	*P* value
Age	0.995	0.943-1.1051	0.86
Disease duration	0.790	0.664-0.940	0.008
Insulin-Like Growth Factor-1	0.991	0.985-0.998	0.012
Fasting Plasma Glucose	1.036	0.958-1.119	0.37
İnsulin	1.217	0.610-2.430	0.57
HOMA-IR	0.502	0.034-7.395	0.61
Auto-Fluor-escence	15.535	1.442-167.329	0.024
B-Cross Laps	5.609	0.339-92.944	0.22
Osteocalcin	0.993	0.930-1.059	0.82

DOI: 10.1530/endoabs.81.P145

P146

Central Diabetes Insipidus, family report, molecular study, and its importance

Luis Filipe Sá[1], Rafaela Sousa[1], Darine Villela[2], Thereza Cavalcanti[2], Michele Migliavacca[2], Rosita Fontes[3], Marilia Guimarães[4], Micheline Souza[4], Paula Coelho[1,3], Mariana Botelho[1], João Nascimento[1], Mirna Carvallo[1], Pedro Viveiros[1], Delmar Lourenço Jr[5], Erika Naliato[6] & Alice Violante[4]
[1]Federal University of Rio de Janeiro (UFRJ), Hospital Universitario Clementino Fraga Filho, Rio de Janeiro, Brazil; [2]Diagnósticos da America S.A. (DASA), GeneOne, São Paulo, Brazil; [3]Diagnósticos da América S.A. (DASA), Diagnósticos da América S.A. (DASA), Duque de Caxias, Brazil; [4]Federal University of Rio de Janeiro (UFRJ), Endocrinology, Rio de Janeiro, Brazil; [5]University of São Paulo (USP), Hospital das Clínicas da USP, São Paulo, Brazil; [6]Ricardo A T Castilho Center of Studies, Teresopolis Medical Association, teresopolis, Brazil

Introduction
Central diabetes insipidus (CDI) occurs due to deficient secretion of arginine vasopressin (AVP) or antidiuretic hormone (ADH) by the posterior pituitary. It is a rare disease with an estimated prevalence of 1:25000. CDI can be acquired or congenital, secondary to malformation or genetics. Familial CDI (genetic inheritance) is mainly autosomal dominant. More than 80 mutations in the AVP gene have been described. In hereditary CDI, the age of onset is variable. Symptoms arise mostly in childhood but, very often, later. Clinical features include polyuria and polydipsia of variable severity, dehydration, in the absence of volume replacement, and hypernatremia. Partial deficit of oxytocin and carrier protein, estrogen-stimulated neurophysin (ESN), and anterior pituitary hormone deficiency may coexist. The aim of this study is to describe the clinical cases and genetic study of a father and his male firstborn with familial CDI diagnosed with a rare variant c.329G>A;p.p.(Cys110Tyr), in heterozygosity in the AVP gene.
Case Reports
Patient 1 presented polydipsia and low body weight at two years of age. Diagnosis of CDI was confirmed with a water deprivation test. Magnetic resonance imaging (MRI) of skull and sella showed only absence of the neuropituitary signal. Treatment was instituted with intramuscular synthetic vasopressin, and posteriorly modified to nasal desmopressin acetate (DDAVP) spray. He remains without signs and symptoms to date, at 41 years of age, on regular use of DDAVP. Patient 2 is the firstborn of patient 1 and first presented polydipsia and nocturia at age of four. Diagnosis was established at 11 years of age with a water deprivation test. MRI of skull and sella showed only absence of the neuropituitary signal. Treatment was instituted with DDAVP nasal spray and maintained until the present time; at 17 years of age, he remains asymptomatic. Genetic study was performed by exome sequencing, which described the c.329G>A;p.(Cys110Tyr) variant, identified in heterozygosity in the *AVP* gene. This very rare variant results in the substitution of amino acid in the protein encoded and is classified as likely pathogenic. The absence of any other manifestation, unlike other genetic causes of CDI, is highlighted.
Conclusion
We emphasize the possibility that rare diseases, such as CDI, may be familial, and the need for a clinical investigation of family members with similar manifestations and molecular testing and genetic counseling if possible.

DOI: 10.1530/endoabs.81.P146

P147

Are pre-operative intratumoral haemorrhages and post-operative bleeds sentinel indicators of ''silent'' corticotroph adenomas?

Mohummad Shaan Goonoo[1], Andreea Bojoga[2], Saurabh Sinha[3] & Miguel Debono[4]
[1]Sheffield Teaching Hospitals NHS Foundation Trust, Endocrinology and Metabolic Medicine, Sheffield, United Kingdom; [2]C.I. Parhon National Institute of Endocrinology, Endocrinology and Metabolic Medicine, Bucure||ti, Romania; [3]Sheffield Teaching Hospitals NHS Foundation Trust, Neurosurgery, United Kingdom; [1] Sheffield Teaching Hospitals NHS Foundation Trust, Endocrinology and Metabolic Medicine, Sheffield, United Kingdom

Background
Silent corticotroph adenomas (SCAs) are considered to be clinically silent and non-secreting but exhibit positive adrenocorticotropic hormone (ACTH) immunostaining. Whether, SCAs behave more aggressively than other non-functioning adenomas, remains controversial. We characterized our tertiary centre cohort of SCA patients, compared them to gonadotroph adenomas (GAs) and assessed for features predictive of recurrence.
Objective
To compare characteristics and outcomes of SCAs with GAs at a major tertiary centre.

Methods
We reviewed cases of SCAs operated by one neurosurgeon between January 2010 and January 2019 and matched them by age and sex to the GAs operated on by the same neurosurgeon in a 1:2 ratio.
Results
Our retrospective cohorts included SCAs ($n=13$) followed for median 57 months (range, 13-163 months) and GAs ($n=26$) followed for 72 months (range, 12-132 months). Compared to GAs, SCAs were of similar diameter (2.6 vs 2.0 cm, $P=0.149$) but had an increase in residual tumour size on radiological reporting in 38.5% cases compared to 19.2% among GAs. Intratumoral haemorrhage on *pre-operative* magnetic resonance imaging was reported in 53.8% of the SCAs and 11.5% of GAs ($P=0.008$). Higher mean pre-operative ACTH levels (44.7 vs. 23.0 ng/l, $P=0.024$) and lower mean post-operative prolactin (170.3 vs 305.6 mUI/l, $P=0.032$) were observed in the SCAs group. There was no perioperative mortality in either group. However, in the SCAs group 4/13 patients had significant immediate post-operative haemorrhage (two patients had acute subarachnoid haemorrhage predominantly in the suprasellar region, another had a large acute haematoma around suprasellar cistern requiring craniotomy; the last patient had significant sellar bleeding but good recovery postoperatively) whereas among the GAs, there was no post-operative haemorrhage. At one-year post-operative follow-up, 5/13 patients of SCAs had new onset secondary adrenal insufficiency compared to 1/26 in the GA cohort. During follow-up, all-cause mortality (non-pituitary surgery related) was higher among SCAs compared to GAs (30.8% and 19.2% respectively). Sex, tumour size, Ki67% indices and immediate post-operative cortisol measurement were not statistically found to be influencing the predictability of recurrence.
Conclusion
Our study shows that in the SCAs group, intratumoral haemorrhage was significantly higher and accompanied with greater risk of post-operative complications especially bleeding. A higher rate of deaths was observed in the SCA group but this needs to be confirmed in larger studies.

DOI: 10.1530/endoabs.81.P147

P148

AZP-3813, a bicyclic 16-amino acid peptide antagonist of the human growth hormone receptor as a potential new treatment for acromegaly

Stéphane Milano[1], Haruaki Kurasaki[2], Tatsuya Tomiyama[2], Patrick Reid[2], Aart Jan Van der Lely[3] & Michael D. Culler[4]
[1]Amolyt Pharma, Ecully, France; [2]PeptiDream, Inc., Kawasaki-Shi, Kanagawa, Japan; [3]Erasmus University Medical Center, Rotterdam, Netherlands; [4]Amolyt Pharma, Cambridge, Massachusetts, United States

Medical treatment of acromegaly is based on either suppressing pituitary GH secretion or inhibiting GH action by preventing interaction with its receptor in order to suppress the elevated levels of IGF1. AZP-3813 is a 16-amino acid, bicyclic peptide antagonist of the GH receptor (GHR) derived from peptide sequences discovered using a unique, cell-free in vitro transcription-translation system screened against the human GHR, and that was optimized by rational design to increase binding affinity, solubility and half-life. The K_D of AZP-3813 for the human GHR is 1.9 nM, and 18.5 nM for the rat GHR. The circulating half-life of AZP-3813 in the rat is 11.2 h. To examine the ability of AZP-3813 to antagonize the interaction between GH and its receptor *in vivo* and thereby reduce IGF1 levels, we injected normal, 5-week old (~150g), male Sprague Dawley rats subcutaneously either with vehicle or with AZP-3813 at doses of 0.3, 1, 3, 10 or 30 mg/kg BID or with 10 or 30 mg/kg QD ($n=8$/group). Blood samples were collected immediately prior to AZP-3813 injection and at 24, 48 and 72 h after injection, and were assayed for total IGF1 content by radioimmunoassay. Twenty-four hours after injection, IGF1 levels were suppressed in a dose-related manner, with maximal and similar degrees of suppression achieved with 30 mg/kg AZP-3813 administered either QD or BID (38.4 + 3.8% and 39.2 + 3.7% decrease from vehicle-treated controls, respectively). By 48 h post-injection, IGF1 levels had returned to the level observed in vehicle-treated control rats. In a follow-up experiment, AZP-3813 was administered subcutaneously daily for 4 days at a dose of 30 mg/kg, either QD or BID. As a comparator, the commercially available GH antagonist, pegvisomant, was also administered subcutaneously for 4 days at a dose of 100 mg/kg QD. Blood samples to be assayed for IGF1 were collected immediately prior to compound injection on all days, and at 24, 48 and 72 h after the last injection. IGF1 was maximally suppressed by AZP-3813 within 24 h after the first injection (47.2 + 2.6% decrease vs vehicle-treated controls), and, with continued treatment, the suppression was maintained through 24 h after the last injection. In contrast, pegvisomant treatment gradually lowered IGF1, reaching a maximal suppression of 32.5 + 3.6% 24 h after the third injection. These results demonstrate that the potent GHR antagonist activity exhibited by AZP-3813 translates to *in vivo* suppression of IGF1 levels, and support its development as a potential therapy for acromegaly.

DOI: 10.1530/endoabs.81.P148

P149

Clinical aspects of pituitary tumors in patients with Multiple Endocrine Neoplasia Type 1: results from the preliminary study

Stanislaw Zgliczynski[1,2], Magdalena Kochman[3], Wojciech Zgliczynski[3] & Tomasz Bednarczuk[4]
[1]Medical University of Warsaw, Department of Internal Medicine and Endocrinology, Warsaw, Poland; [2]Medical University of Warsaw, Doctoral School of the Medical University of Warsaw, Warsaw, Poland; [3]Centre of Postgraduate Medical Education, Department of Endocrinology, Warsaw, Poland; [1] Medical University of Warsaw, Department of Internal Medicine and Endocrinology, Warsaw, Poland

Introduction
Multiple Endocrine Neoplasia Type 1 (MEN1) is a rare disease inherited in an autosomal dominant pattern, caused by mutations in the MEN1 gene. The cardinal components of this syndrome are: primary hyperparathyroidism (PHPT), gastroenteropancreatic neuroendocrine tumors (NETs) and pituitary tumors.
Aim
The aim of the study was to evaluate clinical features of MEN1 patients under care of two teritiary centers in Warsaw, Poland with special focus on pituitary lesions.
Material and methods
We have used an authorial pre-prepared form in order to gain detailed data on the clinical course of the disease. Until the submission of this abstract (January 2022), study group consisted of 73 participants with diagnosed MEN1 syndrome, aged from 18 to 76 years old (mean 43 $\pm$14 years) and followed-up from 2014 to 2022. As many as 47 of patients were women, 26 were men.
Results
In our group nearly 42% of subjects suffered from all three main components of MEN1 syndrome. Among them: 93% developed PHPT, 78% NETs, 60% pituitary tumors. In 77% of patients we have found other benign neoplasms of which the most common were adrenal adenomas (38%). What is more, 12% of subjects developed other malignant tumors. Out of 44 patients with pituitary tumors, in 26 imaging tests showed pituitary microadenomas, yet macroadenomas were present in next 18 cases. Most common type of tumor was prolactinoma (52%), with a predominance of microadenomas (32% of all pituitary tumors). Moreover, acromegaly was diagnosed in 6 patients what accounted for 14% of pituitary gland lesions cases. At least one pituitary surgery was performed in 11 subjects, 9 of them had hormonally active adenomas (4 prolactinomas, 3 cases of acromegaly, 2 non-functioning pituitary adenomas, 1 thyrotropinoma and 1 corticotropinoma). In two cases more than one operation was required. Dopamine agonists were administered to 18 patients. After PHPT, pituitary tumor was second most frequent first diagnosed component of MEN1 (26% of the group). In nearly 10% of all patients it manifested itself as menstrual disorders or decreased libido. Only in 9% patients NETs were diagnosed as the first component.
Conclusions
Despite the fact that pituitary tumors are the third most frequent tumors in MEN1, they are more likely to cause clinical manifestations than NETs. In our group there was relatively high prevalence of acromegaly. What is more, we observed frequent occurrence of other malignant tumors and noted a large number of adrenal gland adenomas.

DOI: 10.1530/endoabs.81.P149

P150

Glucagon-stimulated copeptin measurements in the differential diagnosis of diabetes insipidus: a double-blind randomized placebo-controlled study

Cihan Atila[1], Odile Gaisl[1], Deborah Vogt[2], Laura Werlen[2], Gabor Szinnai[3] & Mirjam Christ-Crain[1]
[1]University Hospital Basel, Department of Endocrinology, Diabetology and Metabolism, Basel, Switzerland; [2]University Hospital Basel, Department of Clinical Research, Basel, Switzerland; [3]University Children's Hospital Basel, Department of Paediatric Endocrinology and Diabetology, Basel, Switzerland

Background
The differential diagnosis between central diabetes insipidus and primary polydipsia is challenging. To date, the most reliable approaches are copeptin measurement after hypertonic saline infusion or arginine, which is a known growth hormone secretagogue but has recently been shown also to stimulate the neurohypophysis. Similar to arginine, glucagon is also known to stimulate growth hormone release, but its effect on the neurohypophysis and in the differential diagnosis of diabetes insipidus is unknown.
Methods
In this double-blind, randomized, placebo-controlled trial, we enrolled 22 healthy participants, 10 patients with central diabetes insipidus, and 10 patients with primary polydipsia at the University Hospital Basel. Each participant underwent the glucagon test, i.e., subcutaneous injection of 1 mg glucagon, and placebo test, i.e., subcutaneous injection of 1 ml 0.9% sodium. Plasma copeptin levels were measured at baseline and 30, 60, 90, 120, 150, 180 minutes after injection. The primary objective was to determine whether glucagon stimulates copeptin and to explore whether the copeptin response differentiates between central diabetes insipidus and primary polydipsia.
Results
All 42 participants underwent both tests. The median (IQR) age of all participants was 27 years (23; 32), 59% were female. In healthy participants, glucagon injection stimulated copeptin with a median (IQR) increase of 7.56 (2.38; 28.03) pmol/l, while placebo had no effect (0.10 pmol/l (-0.70; 0.68); treatment difference: 7.67 (1.98, 27.09) pmol/l, $P < 0.001$). In patients with central diabetes insipidus, copeptin showed no relevant increase after glucagon injection, with an increase of 0.55 pmol/l (0.21; 1.65), whereas copeptin was stimulated in patients with primary polydipsia with an increase of 15.70 (5.99; 24.39) pmol/l. Using a copeptin cutoff level of $>$ 4.6 pmol/l had a 100% sensitivity (95%CI 100-100) and 90% specificity (95%CI 70-100) to discriminate between diabetes insipidus and primary polydipsia. The test was safe and well tolerated with a median (IQR) test burden according to VAS of 1.5 (1; 4) in healthy participants, 3 (1.5; 4.5) in central diabetes insipidus, and 3 (2; 4.5) in primary polydipsia.
Conclusion
In conclusion, glucagon stimulates the neurohypophysis, and glucagon-stimulated plasma copeptin has the potential to be used for a safe, novel, and precise test in the differential diagnosis of polyuria-polydipsia syndrome.

DOI: 10.1530/endoabs.81.P150

P151

Sexual brain processing is enhanced by melanocortin-4 receptor agonism

Layla Thurston[1], Tia Hunjan[1], Edouard Mills[1], Matt B Wall[1,2], Natalie Ertl[1,2], Maria Phylactou[1], Beatrice Muzi[1], Bijal Patel[1], Emma Alexander[1], Sofiya Suladze[1], Manish Modi[1], Pei Eng[1], Paul Bassett[3], Ali Abbara[1], David Goldmeier[4], Alexander Comninos[1,5] & Waljit Dhillo[1,5]
[1]Imperial College London, Endocrinology and Investigative Medicine, London, United Kingdom; [2]Invicro, London, United Kingdom; [3]Statsconsultancy Ltd, Amersham, United Kingdom; [4]Imperial College Healthcare NHS Trust, Sexual Medicine, London, United Kingdom; [5]Imperial College Healthcare NHS Trust, Endocrinology, London, United Kingdom

Introduction
Hypoactive sexual desire disorder (HSDD) is characterized by a persistent deficiency of sexual fantasies and desire for sexual activity, causing marked distress or interpersonal difficulty. It is the most prevalent female sexual health problem worldwide, affecting approximately 1 in 10 women, but has limited treatment options despite its substantial health, social, and economic burden. Melanocortin-4 receptor (MC4R) agonists have emerged as a promising therapy for women with HSDD, although, to date, their mechanism of action is unknown. This study aims to use functional MRI to uncover the reproductive neuroendocrine pathways involved and elucidate how MC4R agonists treat HSDD in women.
Methods
We conducted a randomized, double-blinded, placebo-controlled, crossover clinical study in 31 premenopausal women with HSDD. A combination of psychometric, functional neuroimaging and hormonal analyses were used to investigate the effect of MC4R agonism on sexual brain processing. Participants attended twice, receiving either a subcutaneous injection of an MC4R agonist (Bremelanotide 1.75 mg) or placebo at each study visit, thereby acting as their own controls.
Results
MC4R agonism significantly increased self-reported sexual desire for up to 24-h post administration, compared to placebo ($P = 0.007$). During functional MRI, MC4R agonism enhanced cerebellar and supplementary motor area activity, as well as deactivating the secondary somatosensory cortex, specifically in response to visual erotic videos, compared to placebo ($Z = 2.3$, $P < 0.05$). In addition, MC4R agonism enhanced functional connectivity between the amygdala-insula and amygdala-thalamus during prolonged visual erotic stimuli, compared to placebo ($P = 0.025$). MC4R agonism resulted in a mean increase in LH of 1.1 iU/l (F [1.58] = 13.38, $P = 0.0005$), and FSH of 0.35 iU/l (F [1.60] = 10.97, $P = 0.0016$) across the 300-minute duration of the study, with no effect observed on circulating estradiol or progesterone levels.
Discussion
We demonstrate that MC4R agonism deactivates the secondary somatosensory cortex which can reduce the detrimental self-monitoring process often observed in HSDD, thereby increasing sexual desire. Furthermore, cerebellar and supplementary motor area activation by MC4R agonism are associated with increased sexual arousal and sexual motor imagery respectively. Finally, MC4R agonism enhanced functional connectivity between key limbic structures which can be disrupted in HSDD. In conclusion, these data identify the previously undescribed neural substrates and connections through which MC4R agonism modulates sexual brain processing to increase sexual desire. These findings provide mechanistic insight for the action of MC4R agonism in sexual behaviour and are relevant to ongoing therapeutic development for HSDD and for MC4R agonist development more widely.

DOI: 10.1530/endoabs.81.P151

P152

Up to one third of the children with attention deficit with hyperactivity disorder (ADHD) may have an isolated and increased free-T3 level

Hervé Caci[1] & Philippe Caron[2]
[1]Hôpitaux Pédiatriques de Nice, CHU Lenval, Nice, France; [2]CHU Larrey, Endocrinology, Toulouse, France

Introduction
Thyroid hormones are involved in the development of the fœtus and the child, and abnormal thyroid function is expected to play a role in neurodevelopmental disorders such as Attention Deficit with Hyperactivity Disorder (ADHD). The high prevalence of ADHD in patients with resistance to thyroid hormone syndrome is well documented but, surprisingly, the reported literature showed ambiguous results mostly suggesting that the thyroid function tests are normal in the majority of patients with ADHD. However, it is possible to pinpoint a number of methodological and analytical limits in the thyroid evaluation of patients in the studies. Here we report on the prevalence of isolated and increased free-T3 level in the presence of normal free-T4 and TSH levels in children with ADHD.
Methods
Serum free-T3, free-T4 and TSH levels were measured in children referred to the first author (HC) in the last two decades and diagnosed with ADHD. No control was possible on the analytic methods as thyroid function tests were performed in town laboratories.
Results
Out of 1.967 patients, 701 children with ADHD (boys $n = 562$, girls $n = 139$) between 6 and 18 years old had complete thyroid function tests (free-T3, free-T4 and TSH levels). According to the reference intervals noted in laboratory reports, a TSH level was abnormal in 16 patients (2.28%): 2 decreased TSH level with normal free-T3 and free-T4 level, 14 increased TSH level with either normal or elevated free-T3 and/or free-T4. Out of the 685 normal-TSH remaining patients, 435 (63.50%) had a normal thyroid profile, and 217 (31.68%): 180 boys (32.67%) and 37 girls (27.61%) showed an isolated and increased free-T3 level. There was no effect of gender: χ^2 (1) = 0.677 ($P > .4$).
Discussion
In children with ADHD, an isolated and increased free-T3 level is frequent and unrelated with gender. This result should be further confirmed and documented. If so, this abnormal thyroid profile may constitute an endophenotype for a significant proportion of children with ADHD, and yield to new pathophysiological hypotheses in the neurodevelopment disorders.
Conclusion
Abnormal thyroid function tests are not rare in children with ADHD, more specifically we highlighted an isolated and increased free-T3 level with normal free-T4 and TSH levels in up to one third of children with ADHD. These results warrant confirmation; this is the main objective of the on-going prospective "ThyrADHD" study (NCT05080491).

DOI: 10.1530/endoabs.81.P152

P153

Subtype-specific pattern of white blood cell differential in endogenous Cushing's syndrome

Mario Detomas[1], Barbara Altieri[1], Irina Chifu[1], Hanna Remde[1], Laura-Sophie Landwehr[1], Silviu Sbiera[1], Matthias Kroiss[1,2], Martin Fassnacht[1] & Timo Deutschbein[1,3]
[1]University Hospital Würzburg, Würzburg, Germany; [2]Klinikum der Universität München, München, Germany; [3]Medicover Oldenburg MVZ, Oldenburg, Germany

Objective
Glucocorticoid excess impairs immune function, thereby predisposing patients with endogenous Cushing's syndrome (CS) to infections. However, it is still not clear whether there is a CS-subtype specific pattern in white blood cell (WBC) and WBC differential (WBCD) count.
Methods
Retrospective monocentric cohort study in patients with either overt endogenous CS or adrenal adenomas with autonomous cortisol secretion (ACS), with WBC and WBCD analysis at initial diagnosis and after remission.
Results
270 patients (Cushing's disease (CD), $n=88$; ectopic CS (ECS), $n=31$, cortisol-producing adrenal adenoma (CPA), $n=39$; ACS, $n=63$; adrenocortical carcinoma (ACC), $n=49$; were analyzed. Total leukocytes and neutrophils correlated positively with serum cortisol after 1-mg dexamethasone (1 mg-DST) ($r=0.346$ and $r=0.471$, respectively, $P<0.0001$), while a negative correlation was observed for lymphocytes and eosinophils ($r=$-0.399 and $r=$-0.519, each $P<0.0001$). Correlations were confirmed with the 24h-urinary free cortisol (24h-UFC). CD and ECS differed in numbers of neutrophils and lymphocytes ($P<0.0001$). A cut-off of 6.1 for the neutrophil/lymphocyte ratio (NLR) allowed reliable differentiation between CD and ECS (sensitivity 90.0%, specificity 89.4%, AUC 0.918). NLR allowed a better differentiation between CD and ECS than 1 mg-DST and 24h-UFC (AUC respectively 0.83 and 0.74). Regarding CPA and ACC, a difference in platelet/lymphocyte ratio (PLR) was observed (sensitivity 59.6%, specificity 80.6%, and AUC 0.713 with a cut-off of 187.9). Already 3 months after biochemical remission, neutrophils decreased (delta change -47.0%, -29.7%, and -26.2%) and lymphocytes increased (+123.2%, +78.1%, and +17.7%) substantially (always ECS, CPA, and CD).
Conclsion
Most immune cells correlate with the degree of hypercortisolism but differ also among CS subtypes. WBCD and NLR could allow a first differentiation of ACTH-dependent CS. Normalization of WBCD is observed already after 3 months from CS remission.

DOI: 10.1530/endoabs.81.P153

P154

Role of apparent strong ion difference in the differential diagnosis of thiazide associated hyponatremia

Laura Potasso[1,2], Julie Refardt[1], Sophie Monnerat[1,2], Bettina Winzeler[1] & Mirjam Christ-Crain[1,2]
[1]University Hospital of Basel, Endocrinology, Diabetology and Metabolism, Basel, Switzerland; [2]University of Basel, Basel, Switzerland

Background
Differential diagnosis of hyponatremia is challenging, particularly for thiazide associated hyponatremia (TAH), as patients might have either volume depletion in need for fluid substitution or syndrome of inappropriate antidiuresis (SIAD)-like presentation requiring fluid restriction. Urine indices are of little utility, because they are influenced by thiazide therapy. Apparent strong ion difference (aSID) describes the relation between sodium, potassium and chloride in serum and is used in evaluation of acid-base disorders according to Stewart model. aSID could help in the differential diagnosis of TAH because a value >40 identifies patients with contraction alkalosis due to relative hypochloremia, and hypochloremic alkalosis is a well-known possible adverse effect of thiazide diuretics.
Material and Methods
This was a post-hoc analysis of prospectively collected data of hospitalized patients with hypotonic hyponatremia <125 mmol/l. TAH patients were divided according to treatment response in patients needing intravenous fluid substitution or fluid restriction. Treatment response was defined as a sodium increase of at least 4 mmol/l/die or >130 mmol/l based on chart review. aSID at baseline was calculated with the formula serum sodium plus potassium minus chloride and a value >40 was used to identify volume-depleted TAH patients. Descriptive analysis was carried out to find differences between volume-depleted and SIAD-like TAH patients, and patients with SIAD without thiazide use. Logistic regression and ROC curves were computed to investigate the role of aSID >40 for differential diagnosis of hyponatremia in TAH patients, in addition to known factors for identifying SIAD patients as body mass index (BMI) and fractioned uric acid excretion (FUA) with the previous described cut-off of 12%.
Results
Out of 303 hyponatremia patients, 131 (43.2%) had a TAH and 75 (24.8%) SIAD without thiazide use. Among TAH patients, 81 (61.8%) were successfully treated with fluid substitution and 31 (23.7%) with fluid restriction. 19 patients (14.5%) were excluded as they received no treatment, or needed to switch treatment during hospitalization. No differences in baseline characteristics were seen between patients with SIAD and SIAD-like TAH patients, except for BMI, lower in SIAD patients (mean(SD) 23.5(5.1) vs 27.0(5.7) kg/m2, $P=0.003$). A higher BMI and a FUA <12% had a sensitivity of 84% with a specificity of 60% in identifying volume-depleted TAH patients. Adding aSID >40 improved the specificity to 74% maintaining a sensitivity to 82%.
Conclusion
In hospitalized patients with TAH, calculation of aSID may help differentiating patients with volume depletion in need of fluid substitution from SIAD-like manifestation requiring fluid restriction.

DOI: 10.1530/endoabs.81.P154

P155

Genetic subtype differences in relation to health problems among adults with Prader-Willi syndrome

Anna Rosenberg[1], Karlijn Pellikaan[1], Charlotte Wellink[1], Juan Tellez Garcia[1], Denise van Abswoude[1], Laura van Zutven[2], Hennie Brüggenwirth[2], James Resnick[3], Aart Jan Van der Lely[1] & Laura De Graaff[1]
[1]Erasmus MC, University Medical Center Rotterdam, Division of Endocrinology, Rotterdam, Netherlands; [2]Erasmus MC, University Medical Center Rotterdam, Department of Clinical Genetics, Rotterdam, Netherlands; [3]College of Medicine, University of Florida, Department of Molecular Genetics and Microbiology, Gainesville, United States

Background
Prader-Willi syndrome (PWS) is a complex rare genetic disorder associated with hypothalamic dysfunction, pituitary hormone deficiencies, hyperphagia and (morbid) obesity. PWS is caused by loss of expression of paternally expressed genes on chromosome 15q11.2-q13. The most common genetic mechanisms leading to PWS are paternal deletion (DEL) and maternal uniparental disomy (mUPD). DELs can be subdivided in type 1 and (smaller) type 2 deletions (DEL-1, DEL-2). Most research has focused on behavioral, cognitive and psychological differences between patients with a DEL-1, DEL-2 or mUPD. However, little is known about the genetic subtype differences in relation to physical health problems.
Methods
We reviewed the medical files of all adults with genetically confirmed PWS who visited the outpatient clinic of the Center for Adults with Complex Rare Genetic Syndromes at the Erasmus University Medical Center, Rotterdam, the Netherlands, between January 2015 and June 2021. All patients underwent a systematic health screening, including a structured interview, a medical questionnaire, a complete physical examination, biochemical measurements, and a review of the medical records. Health problems, physical complaints, symptoms of disease and behavioral challenges were compared between adults with an mUPD and DEL and between adults with a DEL-1 and DEL-2.
Results
Twenty-eight adults had an mUPD and 65 a DEL (13 DEL-1, 27 DEL-2, 25 unspecified). Gender, age and BMI did not differ between the genetic subgroups. Although psychiatric problems (psychotic episodes) were significantly more often present in adults with an mUPD ($P<0.001$) and scoliosis was more prevalent among patients with DEL ($P=0.04$), there was only a slight difference in prevalence of other medical problems like hypertension, cold intolerance, edema, hyperphagia, skin picking, abdominal pain and fatigue. There were no significant differences between DEL-1 and DEL-2. However, fatigue, cold intolerance, edema and hyperphagia were slightly more prevalent among adults with a DEL-1, whereas osteopenia, constipation and skin picking were more prevalent among adults with a DEL-2.
Conclusion
The differences in health problems between PWS adults with DEL-1, DEL-2 and mUPD are mostly present in the psychological domain. Especially psychotic episodes were more frequent in adults with an mUPD. Apart from scoliosis, there were no significant differences in physical health outcomes between the genetic subtypes.

DOI: 10.1530/endoabs.81.P155

P156

Prevalence of comorbidities in a US adult population with growth hormone deficiency

Alden Smith[1], Janna Manjelievskaia[2], Allison Komirenko[3] & Cynthia Morrow[2]
[1]Ascendis Pharma Inc, Health Economic Outcomes Research, Palo Alto, United States; [2]IBM Watson Health, Cambridge, United States; [3]Ascendis Pharma Inc, Clinical Development, Palo Alto, United States

Background
Adults with growth hormone deficiency (GHD) have increased central fat deposits, hypertriglyceridemia, and hyperglycaemia, with an increased risk of developing metabolic syndrome and cardiovascular disease, conditions that can lead to a diminished quality of life. This study analyzed comorbidities among adults with GHD in the US who had Medicaid or commercial health insurance.
Methods
In this retrospective cohort study using IBM Marketscan Medicaid and Commercial Research Database data, adults (aged $\geq$18 years) diagnosed with GHD between Jan. 1, 2008, and Dec. 31, 2017, were matched (1:3) to controls without GHD (or other short stature-related disorders) on age, gender, plan type (commercial vs Medicaid), region, and race (Medicaid only). Baseline comorbidities and medications were measured during the 12 months pre-index. All-cause and GHD-related healthcare utilization and somatropin use were measured during the variable follow-up period.
Results
A total of 24.373 commercial and 2.579 Medicaid patients with GHD met the study inclusion criteria and were matched to 73.119 commercial and 7.728 Medicaid controls, respectively. Demographic makeup of patients with and without GHD was similar, demonstrating effective matching. About half the patients were male. Median age at index was 48 years for commercial patients and 37 years for Medicaid patients. Mean follow-up time was 35 and 37 months for commercial patients and controls, and 41 and 31 months for Medicaid patients and controls, respectively. GHD patients were disproportionately affected by comorbidities compared to controls: endocrine conditions ($>$68% in GHD cases vs. $\leq$10% in controls), metabolic conditions ($>$93% in GHD cases vs. $\leq$39% in controls), hepatic and renal function conditions (18-23% in GHD cases vs. $<$10% in controls), and cardiovascular disease (41-53% in GHD cases vs. $<$29% in controls), and were disproportionately treated with concomitant medications.
Conclusions
Adults with GHD experience a substantial comorbidity burden compared to non-GHD controls.

DOI: 10.1530/endoabs.81.P156

P157

Inverse relationship between il-6 and sodium levels in patients with COVID-19 and other respiratory tract infections

Sophie Monnerat[1], Cihan Atila[1], Roland Bingisser[2], Martin Siegemund[3], Maurin Lampart[4,4], Marco Rüegg[2], Núria Zellweger[3], Stefan Osswald[4], Katharina Rentsch[5], Mirjam Christ-Crain[1] & Raphael Twerenbold[4,6]
[1]Department of Endocrinology, Diabetology and Metabolism, University Hospital Basel, Basel, Switzerland; [2]Emergency Department, University Hospital Basel, Basel, Switzerland; [3]Department of Intensive Care, University Hospital Basel, Basel, Switzerland; [4]Department of Cardiology and Cardiovascular Research Institute Basel (CRIB), University Hospital Basel, University of Basel, Basel, Switzerland; [5]Department of Laboratory Medicine, University Hospital Basel, Basel, Switzerland; [6]University Center of Cardiovascular Science & Department of Cardiology, University Heart and Vascular Center Hamburg, Hamburg, Germany

Background
Hyponatremia is highly prevalent in patients with COVID-19. One of the most common causes of hyponatremia in these patients is the syndrome of inadequate antidiuresis (SIAD). Interleukin 6 (IL-6) is a key mediator of inflammation in COVID-19. We hypothesized that hyponatremia in COVID-19 is due to IL-6 mediated non-osmotic arginine vasopressin (AVP) secretion, and that the inverse association between IL-6 and plasma sodium concentration is stronger in COVID-19 compared to other respiratory infections.
Methods
This is a secondary analysis of a prospective, observational, cohort study including patients with COVID-19 suspicion admitted to the Emergency Department, University Hospital of Basel, Switzerland, between March and July 2020. We included patients with PCR-confirmed COVID-19 and patients without COVID-19 but similar symptoms, further subclassified in bacterial and other viral respiratory infections. The primary objective was to investigate the association between plasma sodium levels and IL-6 levels.
Results
500 patients were included, of whom 184 (37%) with COVID-19, 92 (18%) with bacterial respiratory infections, 224 (45%) with other viral respiratory infections. Hyponatremia prevalence was higher in patients with COVID-19 compared to patients with other viral respiratory infections (28% vs 12%, $P<0.01$), and similar to patients with bacterial respiratory infections (28% vs 30%, $P<0.41$). In all three groups, median [IQR] IL-6 levels were significantly higher in hyponatremic compared to normonatremic patients (COVID-19: 43.4 [28.4, 59.8] vs 9.2 [2.8, 32.7] pg/ml, $P<0.0001$; bacterial: 122.1 [63.0, 282.0] vs 67.1 [24.9, 252.0] pg/ml, $P<0.05$; viral: 14.1 [6.9, 84.7] vs 4.3 [2.1, 14.4] pg/ml, $P<0.05$). IL-6 levels were negatively correlated with plasma sodium levels in COVID-19, whereas the correlation in bacterial and other viral infections was weaker (COVID-19: $\rho=-0.52$, $P<0.001$; bacterial: $\rho=-0.24$, $P=0.056$, viral: $\rho=-0.24$, $P<0.001$).
Conclusion
IL-6 levels were inversely correlated with plasma sodium levels, with a stronger correlation in patients with COVID-19 compared to patients with bacterial and other viral infections. IL-6 might stimulate AVP secretion and lead to higher rates of hyponatremia due to the syndrome of inadequate antidiuresis in these patients.

DOI: 10.1530/endoabs.81.P157

P158

Effect of growth hormone deficiency on serum high-sensitivity C-reactive protein levels in adult patients with non-functioning pituitary tumors

Yasufumi Seki, Noriyoshi Takano, Kaoru Yamashita, Kanako Bokuda, Nobukazu Sasaki, Toru Ishikawa, Miwa Kimura, Satoshi Watanabe, Daisuke Watanabe, Satoshi Morimoto & Atsuhiro Ichihara
Tokyo Women's Medical University, Department of Endocrinology and Hypertension, Tokyo, Japan

Background
Growth hormone (GH) deficiency causes visceral obesity and fatty liver and increases cardiovascular event risks. Because serum high-sensitivity C-reactive protein (hs-CRP) levels, which has been used to estimate those risks, was reported to be decreased by GH supplementation therapy in GH deficient patients, it has been suggested that inflammatory processes might be activated in GH deficient state. However, the clinical factors associated with increased hs-CRP levels in patients with GH deficiency have been still unknown.
Patients and Methods
We retrospectively reviewed charts of 134 patients with non-functioning pituitary adenoma (NFPA) and Rathke's cysts who underwent preoperative GH-releasing peptide-2 (GHRP-2) tests and investigated the association between GH secretion and background characteristics. Patients who had a history of pituitary surgery, severe renal insufficiency or active inflammatory diseases or received GH supplementation therapy were excluded. GH secretion was determined by GHRP-2 tests.
Results
Among 134 patients (94 NFPAs and 40 Rathke's cysts), 46 (34%) presented severe GH deficiency, as diagnosed using GHRP-2 tests. Serum hs-CRP levels were significantly higher in the patients with severe GH deficiency than in those without severe GH deficiency (723 [299-1285] vs 278 [124-561] ng/ml, $P<0.001$). Serum hs-CRP levels were significantly higher in men ($P=0.003$) and in patients with diabetes mellitus ($P=0.040$) and were significantly correlated with age ($r_s=0.19$, $P=0.039$), body mass index ($r_s=0.37$, $P<0.001$), serum levels of gamma-glutamyl transpeptidase ($r_s=0.28$, $P=0.001$), creatinine ($r_s=0.30$, $P<0.001$), low-density lipoprotein cholesterol ($r_s=0.21$, $P=0.013$), triglyceride ($r_s=0.38$, $P<0.001$) and free thyroxine ($r_s=-0.30$, $P=0.001$), blood hemoglobin A1c levels ($r_s=0.20$, $P=0.018$), peak GH response to GHRP-2 ($r_s=-0.47$, $P<0.001$) and IGF-1 SD score ($r_s=-0.18$, $P=0.040$). In the multiple regression analysis, peak GH response to GHRP-2 was a significant variable for determining serum hs-CRP levels ($\alpha=-0.340$, $P=0.003$) after adjustment with age, sex, BMI, smoking, alcohol consumption, hypertension, diabetes mellitus, serum levels of gamma-glutamyl transpeptidase, creatinine, triglyceride and free thyroxine and adrenal function.
Conclusion
GH deficiency was significantly associated with increased serum hs-CRP levels independent to obesity and liver dysfunction in adult patients with non-functioning pituitary tumors. GH deficient state might cause inflammation independent to development of visceral obesity and fatty liver.

DOI: 10.1530/endoabs.81.P158

P159

What is the relevance of he systematic use of gadolinium (Gd) during the MRI follow-up of non-functioning pituitary adenomas (NFPAs)?

Axel Villemaire[1], Celine Mouly[2], Grunenwald Solange[3], Gilles Adam[4], Jean Darcourt[5], Sofia Patsoura[5], Margaux Roques[5], Isabelle Catalaa[5], Helio Fayolle[6], Christophe Cognard[5], Jean-Christophe Sol[7], Philippe Caron[8] & Bonneville Fabrice[9]

[1]CHU Purpan, Neuroradiology, Toulouse, France; [2]CHU Larrey, Endocrinology, Toulouse, France; [2]CHU Larrey, Endocrinology, Toulouse, France; [4]CHU Purpan, Neuroradiology, Toulouse, France; [4]CHU Purpan, Neuroradiology, Toulouse, France; [6]CHU Purpan, Nuclear médecine, Toulouse, France; [7]CHU Purpan, Neurosurgery, Toulouse, France; [2]CHU Larrey, Endocrinology, Toulouse, France; [9]CHU Purpan, Neuroradiology, Topulouse, France

Objective
To compare the performances of the coronal contrast-enhanced T1-weighted (ceT1-w) and T2-weighted (T2-w) sequences, for the diagnosis of progression during the MRI follow-up of NFPAs.
Materials and methods
106 patients who had at least two MRIs for the follow-up of NFPA were retrospectively included. The largest diameter of the adenomas was measured on coronal ceT1-w and separately on T2-w sequences for all the MRIs of the follow-up, and by 2 independent neuroradiologists on a sample of 100 examinations to assess interobserver variability. Progression was defined by an increase $\geq$ 2 mm of this diameter between 2 MRIs. Progress thresholds of 3 and 4 mm were also tested. The concordance was analyzed between the results of ceT1-w and T2-w sequences.
Results
On 580 follow-up MRIs, there was 93.1% concordance between ceT1-w and T2-w coronal sequences. In case of a possible progression, there was 64.4% concordance for a threshold of 2 mm, 87.7% for 3 mm and 97.1% for 4 mm. The discordance was mainly observed on the first postoperative MRI and in case of multiple recurrences. Kappa was better for the diagnosis of progression on T2-w than on ceT1-w sequences (0.67 vs 0.54). Of note, an agreement of 100% was noted between the 2 sequences on the 82 follow-up MRIs of patients with complete surgical resection.
Conclusion
The coronal ceT1-w and T2-w sequences were concordant in 93.1% during the MRI follow-up of NFPAs, meaning that the systematic injection of Gadolinium should be questioned. If first-line examination without gadolinium injection could be proposed, our results indicate that ceT1-w sequences should be kept for the first postoperative MRI and for the follow-up of aggressive and recurrent NFPAs.

DOI: 10.1530/endoabs.81.P159

P160

Differences in pituitary apoplexy

Betina Biagetti[1], Silvana Isabel Sarria Estrada[2], Cordero-Asanza Esteban[3], Anas Chaachou-Charradi[4], Karelis Ng-Won[2], Marta Cicuendez Lopez Ocana[3], Irene Hernández-Hernández[1], Alba Rojano Toimil[1], M Pilar Costa Forner[1], Martinez-Saez Elena[4], Anna Casteras[1] & Rafael Simo Canonge[1]

[1]Hospital Vall d'Hebron, Endocrinology, Barcelona, Spain; [2]Hospital Vall d'Hebron, Neuroradiology Section, Radiology Department, Barcelona, Spain; [3]Hospital Vall d'Hebron, Neurosurgery and Neurotraumatology, Barcelona,; [4]Hospital Vall d'Hebron, Pathology Department, Barcelona, Spain

Objective
Pituitary apoplexy (PA) is a rare, sometimes life-threatening clinical syndrome. However, some cases are subclinical (SPA), just revealed by MR performed during the follow-up of known pituitary adenomas or due to other conditions. Our aims were to describe the clinical characteristics and evolution of the patients with SPA compared with patients with acute PA (APA). We also compare the results of surgery vs conservative management in the APA group.
Design
Retrospective longitudinal study.
Methods
We retrospectively analysed a database of a tertiary reference centre searching for patients diagnosed with pituitary apoplexy between January 2010 and August 2021. We analysed the risk factors that differentiate SPA to APA and compared the clinical course between patients who received conservative vs surgical treatment. Statistical analysis was done using Fisher's exact, Mann–Whitney test or Kruskal-Wallis with Bonferroni correction if required.
Results
Thirty-seven patients were identified (17 men, 20 women; age range 18.3–80.8 years, median age 47.7 years). Out of 37 patients, 29 (78.4%) had APA [of which 17 underwent surgery and 12 were conservatively managed] and 8 (21.6%) had SPA. T2DM (11 vs 0; $P < 0.05$), dyslipidemia (10 vs 0$P = 0.05$) and bigger tumours (5589 $\pm$ 8562 mm vs 650 $\pm$ 879 mm; $P < 0.05$) with chiasmatic compression and sinus invasion were more frequent in APA vs SPA and in patients requiring surgery. During follow-up (23.0 $\pm$ 42.0 months), 13/37 (35.1%) patients developed hypopituitarism without differences between groups. Pituitary adenomas' volumes shrunk spontaneously in 13/20 (65%) of non-surgical patients with a median of volume reduction at 1 year MRI of (40.0% vs 23.7%) in conservatively APA vs SPA group respectively. 2 patients had a new apoplexy episode and 4 patients died, 1 related to PA.
Conclusions
These data suggest that bigger tumours in T2DM patients have higher risk of APA and could require surgery. In non-surgical group, the pituitary tumor shrinkage is clinically relevant after one year of PA. Hypopituitarism is quite frequent independently of PA type even in patients with SPA.

DOI: 10.1530/endoabs.81.P160

P161

The prevalence of metabolic syndrome in patients with hyperprolactinemia

Eunheui Kim, Myungsoo Im, Soree Ryang, Wook Yi & Injoo Kim
Pusan National University Hospital, Busan, Rep. of South Korea

Objective
Hyperprolactinemia might be related to weight gain, metabolic syndrome, and insulin resistance. The aim of this study was to evaluate that patients with hyperprolactinemia were higher prevalence of metabolic syndrome than civilian population.
Methods
From 1st Jan. 1998 to 17th Nov. 2017, 950 patients newly diagnosed hyperprolactinemia in Pusan National University Hospital, Pusan, South Korea, were selected to enroll in a study conducted on hyperprolactinemia and metabolic syndrome. We analyzed the metabolic components measured value within 3 months of the highest plasma prolactin value recorded. Information of waist circumference, serum triglyceride, serum HDL cholesterol, blood pressure, fasting plasma glucose, and medication for dyslipidemia or hypertension or diabetes mellitus were collected. Moreover, we also collected the measured value of BMI, LDL cholesterol, total cholesterol. We compare the metabolic component value of our hyperprolactinemia patients with KNHANES 2010-2015 data.
Results
In 20s~50s fasting blood glucose and in 20s and 30s LDL cholesterol of hyperprolactinemia patients were higher than Korean population, but there was no significance. In 20s total cholesterol ($P = 0.008$) and in 30s systolic blood pressure ($P = 0.00$) of hyperprolactinemia patients was significantly higher than Korean population. The prevalence of metabolic components were higher in patients with hyperprolactinemia than Korean population at triglyceride and blood pressure in 20s, 30s, but there was no significance. But, at fasting blood glucose in 20s, the prevalence of metabolic components were significantly higher in patients with hyperprolactinemia than Korean population ($P = 0.006$). Incidence of obesity of patients with hyperprolactinemia was higher than Korean population over 30s, but there was no significance.
Conclusion
This study suggests the necessity of evaluation of metabolic syndrome for patients with hyperprolactinemia. In the future, larger epidemiological studies on prevalence of metabolic syndrome in patients with hyperprolactinemia should be performed.

DOI: 10.1530/endoabs.81.P161

P162

Pituitary apoplexy: a retrospective study in a pituitary reference unit

Giselle Giron[1], Rosa Camara-Gómez[1], Lorena Hernandez[1], Regina Lopez[1], Elena Vera[1] & Juan Francisco Merino Torres[1,2]

[1]La Fe University and Polytechnic Hospital, València, Spain; [2]University of Valencia, València, Spain

Pituitary apoplexy (PA) is a rare syndrome that requires urgent assistance. It is due to ischemia or hemorrhage of pituitary tissue, almost always inside a pituitary tumor. PA may be the first manifestation of a neuroendocrine tumor or occur during follow up.
Objective
To describe the characteristics of patients with PA treated in the Department of Endocrinology and Nutrition in the last 10 years and study the presence of possible risk factors for it.
Patients and method
Descriptive, single-center, retrospective study. We selected from electronic records 48 patients with the diagnosis of PA treated in the Endocrinology and Nutrition Department from 2010 to 2020. Demographic, clinical, biochemical, radiological and anatomopathological data were collected. The results are expressed as mean and standard deviation (SD) in the case of quantitative variables or percentage in the case of qualitative variables (SPSS 25.0).
Results
67% of the patients were men with a median age at diagnosis of 58.5 years (SD 13.9). As vascular risk factors they presented: hypertension (50%), diabetes (9.5%), and dyslipidemia (42.9%). Other coexisting clinical situations were: pregnancy (1), rheumatoid arthritis (1), Wegener's disease (1) and postoperative coronary bypass (1). The diagnosis was established with an average of 3 days from the onset of symptoms. The most frequent symptoms were: headache (79.1%), visual alterations (69.8%), nausea/vomiting (51.2%) and fluid and electrolyte disorders (20.9%), especially hyponatremia (50%). 40.5% of the patients had a known pituitary neuroendocrine tumor: pituitary macroadenomas (82%), pituitary macroadenomas with invasion of the cavernous sinus (45.2%), non-functioning tumors (52.9%) and prolactinoma treated with cabergoline (17.9%). Most patients (90.4%) presented some hormonal deficit: LH/FSH (76.3%), TSH (50%), GH (44.7%), ACTH (42.8%), ADH (2.3%). Panhypopituitarism was present in 26.2%. No patient passed away in the acute moment. 71.4% of the cases were treated with endoscopic transsphenoidal surgery for persistent headache and/or visual alterations. 76.2% of the patients continued with hormonal replacement treatment after surgery, of which 7 patients (21.9%) recovered total pituitary function, with an average of 4.6 months (SD 2.6) after the event.
Conclsions
- Pituitary apoplexy is more frequent in males and in pituitary neuroendocrine tumors bigger than 1 cm especially in cases with cavernous sinus invasion.
- Hypertension and dyslipidemia are very prevalent in patients with pituitary apoplexy.
- Despite being a condition that requires urgent assistance, the diagnosis is delayed for days from the onset of symptoms even with patients with known pituitary tumors.

DOI: 10.1530/endoabs.81.P162

P163

Clinical applicability of using SAGIT instrument and AcroQol in the management of patients with acromegaly

Rok Herman[1], Katja Goricar[2], Andrej Janez[1] & Mojca Jensterle[1]
[1]University Medical Center Ljubljana, Department of Endocrinology, Diabetes and Metabolic Diseases, Ljubljana, Slovenia; [2]Pharmacogenetics Laboratory, Institute of Biochemistry and Molecular Genetics, Faculty of Medicine, University of Ljubljana, Ljubljana, Slovenia

Objective
We aimed to evaluate the ability of SAGIT Instrument and AcroQoL questionnaire to discriminate acromegaly control status and to correlate SAGIT scores to AcroQoL results in a cohort of the national referral centre.
Methods
Cross-sectional study included 72 patients followed between 2000 and 2020. We retrospectively determined SAGIT score at the diagnosis. Based on the data from the most recent follow up and additional telephone interviews, we determined the patients' current SAGIT score and assess quality of life by AcroQoL.
Results
At follow up (median duration of 8 (5-12) years), 55 (76.4%) patients were classified as cured or controlled on pharmacotherapy based on biochemical criteria (median IGF-1 0.97 times ULN), while17 patients (23.6%) had uncontrolled disease (median IGF-1 2.65 times ULN). All 5 SAGIT categories significantly lowered from baseline to follow up, with the global score decreasing from 14 (12-15) to 4 (3-6) ($P<0.001$). The duration of diagnostic delay significantly correlated with subscores S, A, G and global score at diagnosis. SAGIT at baseline did not discriminate the current disease status, whereas the follow up global score and its G and I components discriminated between the current disease activity status, with the global score 4 (3-5) in cured/controlled group vs 6 (4.5-8) in uncontrolled group ($P=0.007$). At follow up, the median global AcroQoL score for our cohort was 69.3% (50-84.1), with the highest median score in the Personal relationship subscale and the most affected Physical Performance subscale. AcroQoL was not able to discriminate disease activity status. From the examined variables (BMI, IGF-1 levels, time to remission, disease duration, diagnostic delay, age, gender, adenoma size, and the presence of diabetes mellitus and hypopituitarism), only BMI had significant negative correlations with the global AcroQoL score. At baseline and follow up, there were statistically significant negative correlations between SAGIT subscores S and A and all AcroQoL subscales. The presence of swelling at baseline had a significant effect on the global AcroQoL score ($P=0.035$). At follow up, the significant elements that correlated with the global AcroQol score were joint symptoms ($P=0.002$), headaches ($P<0.001$), sleep apnea ($P=0.006$) and hypertension ($P=0.002$).
Conclusions
Our results emphasise the complementary nature of Patient- and Clinician-reported outcome tools in assessing acromegaly control status. The data identifies the critical role of signs, symptoms, and associated comorbidities as important patient-oriented treatment targets, beyond SAGIT sub-scores G, I and T, by which clinicians could further increase the impaired QoL in this population.

DOI: 10.1530/endoabs.81.P163

P164

Links between posterior pituitary activity, other endocrine abnormalities and psychometric profile in anorexia nervosa: a multimodal evaluation

Bogdan Galusca[1,2], Doua Singoh Sandra Emmanuelle[1,2], Natacha Germain[1,2], Merabet Mannel[1,2,3], Redouté Jérôme[1,3], Claire Boutet[1,4] & Massoubre Catherine[1,5]
[1]TAPE Reaserch Unit, EA 7423, Jean Monnet University, Saint Etienne, France, Saint-Étienne, France; [2]CHU Nord Saint-Étienne, Saint-Priest-en-Jarez, France; [3]Cermep - Imagery Du Vivant, Bron, France; [4]CHU Nord Saint-Étienne, Radiology, Saint-Priest-en-Jarez, France; [5]Psychiatry Department, CHU Saint Etienne Saint Etienne, France, France

Introduction
Opioid system activity was found disturbed in several reward circuit areas in restrictive anorexia nervosa (AN) patients but also surprisingly at the pituitary level. However, the potential role of this specific abnormality of pituitary in AN physiopathology remains unclear or unknown.
Objectives
The first aim was to find the exact pituitary location (posterior and/or anterior) of this disturbed opioid activity and then to study the link between this disturbed opioid activity and pituitary hormone activity.
Methods
In vivo [^{11} C] diprenorphin cerebral non-displaceable binding potential (BP_{ND}) was assessed by PET imaging. Volumes and intensities were also extracted from MRI scans and processed for each pituitary region and compared in three groups of young women: 12 undernourished (AN), 11 recovered AN patients (ANrec), and 12 Controls (C). A lower BP_{ND} may account for an increased opioid tone and vice versa. Plasma hormones from anterior pituitary and neurohypophysis (NH) twelve points circadian profile including copeptin and oxytocin, endogenous opioids levels and psychological scores eating-related, were evaluated in these subjects as well as in 13 bulimic (BN) patients.
Results
[^{11} C] diprenorphin pituitary binding was found to be fully localized in NH. Only AN patients' NH present lower [^{11} C] diprenorphin BP_{ND} than Controls, interpreted as a higher opioid tone. AN had lower anterior pituitary volume than controls and ANrec while ANrec still had a smaller anterior pituitary volume than controls. Concerning posterior pituitary volume, only AN had significant lower volume than controls. NH [^{11} C] diprenorphin BP_{ND} correlated directly with the anterior pituitary volume. Both AN and ANrec show lower copeptin/24h than in Controls but no difference in oxytocin. BN patients showed an increase in copeptin and a decrease in oxytocin levels compared to Control group. In AN patients copeptin inversely correlate with Restrained Eating while oxytocin correlate with the External Eating score. NH [^{11} C] diprenorphin BP_{ND} correlated among others things with leptin, BMI, pituitary BP, hypothalamus BP, Amygdal IBP, but not with copeptin or oxytocin.
Conclusion
The disruption of opioid activity observed in the previous study appears to be mainly localized in the neurohypophysis. Neurohypopysis opioid tone in AN seem not to impact the vasopressin or oxytocin release but still may interfere in gonadal axis regulation. Copeptin seems to be a good indicator of hydration state and may be a good tool to detect hidden restrictive or purging behaviors. Specific

correlations with the psychological characteristics of anorexia nervosa still suggest a pathophysiological involvement.

DOI: 10.1530/endoabs.81.P164

P165

Effects of the SGLT2-inhibitor empagliflozin in patients with chronic syndrome of inadequate antidiuresis (SIAD) - results of a double-blind, randomized, placebo-controlled, crossover trial

Julie Refardt[1], Cornelia Imber[2], Rianne Nobbenhuis[3], Sailer Clara Odilia[3], Aaron Haslbauer[3], Deborah Vogt[3], Manfred Berres[4], Bettina Winzeler[3], Stephanie Bridenbaugh[3] & Christ-Crain Mirjam[3]
[1]University Hospital Basel, Endocrinology, Switzerland; [2]University Hospital Basel, Switzerland; [3]University Hospital Basel; [4]University Koblenz

Introduction
Hyponatremia is the most common electrolyte disorder and the syndrome of inappropriate antidiuresis (SIAD) is one of its main causes. However, treatment options for chronic SIAD-induced hyponatremia are inadequate. This is problematic because hyponatremia has been associated with neurocognitive deficits, although there is little data on its reversibility. We previously showed that the sodium-glucose cotransporter 2 (SGLT2) inhibitor empagliflozin is a promising short-term treatment option for hospitalized patients with SIAD-induced hyponatremia, promoting osmotic diuresis via urinary glucose excretion. However, there are no data on long-term treatment in outpatients nor its effect on neurocognitive function.
Material and Methods
In this double-blind, randomized, placebo-controlled, crossover trial we compared 4-week treatment with empagliflozin 25 mg/day to placebo in addition to fluid restriction of $\leq$1.5L/24h in outpatients with chronic SIAD-induced hyponatremia (serum sodium $<$135 mmol/l). At baseline and after both treatment cycles, patients underwent neurocognitive testing (Montreal Cognitive Assessment (MoCA) test). There was a 2-week wash-out period between the two treatment cycles, and a follow-up visit was scheduled 30 days after completion of the treatment phase. The primary endpoint was the difference in serum sodium levels (mmol/l) after 4 weeks of treatment with empagliflozin or placebo, calculated using a linear mixed-effects model.
Results
14 patients, 50% female, with a median (IQR) age of 72 years (65-77) completed the trial. Median (IQR) serum sodium level at baseline was 131 mmol/l (130-132). Under treatment with empagliflozin, median (IQR) serum sodium level increased to 134 mmol/l (132-136), while no notable change was seen under placebo (130 mmol/l (128-132)). This resulted in a 4.1 mmol/l (95% CI 1.7-6.5) higher serum sodium level after 4 weeks of empagliflozin treatment compared to placebo ($P=0.004$). This effect was independent of severity of SIAD. In addition, treatment with empagliflozin led to improved neurocognitive function, as shown by an increase of 1.2 points (SE 0.5) in the MoCA test ($P=0.042$). Treatment with empagliflozin was generally well tolerated, no serious adverse events occurred during the observation period.
Conclsion
This trial shows that the SGLT-2 inhibitor empagliflozin is a promising new treatment option for outpatients with chronic SIAD-induced hyponatremia. Furthermore, hyponatremia treatment led to an improvement of neurocognitive function.

DOI: 10.1530/endoabs.81.P165

P166

Pasireotide imaging study: magnetic resonance imaging as a predictor of therapeutic response in acromegaly

Sabina Ruiz[1], Eva Venegas Moreno[2], Joan Gil[1], ROSA CAMARA[3], Betina Biagetti[4], Maria Angeles Galvez Moreno[5], Silvia Maraver[6], Inmaculada Gonzalez-Molero[7], Antonio Picó-Alfonso[8], Pablo Abellán Galiana[9], pablo trincado[10], Maria Teresa Herrera Arranz[11], Pilar Olvera[11], Gemma Xifra Villarroya[12], Ignacio Bernabeu[13], Sharona Azriel Mira[14], Lourdes García-GarcíA-Doncel[15], Mireia Jorda[1], Elena Valassi[1] & Manel Puig-Domingo[1]
[1]Germans Trias i Pujol Hospital, Badalona, Spain; [2]Virgen del Rocío University Hospital, Sevilla, Spain; [3]La Fe University and Polytechnic Hospital, València, Spain; [4]La Vall d'Hebron, Barcelona, Spain; [5]Hospital Universitario Reina Sofia, Córdoba, Spain; [6]Hospital Universitario Virgen de la Victoria, Málaga, Spain; [7]Hospital Regional Universitario de Málaga, Málaga, Spain; [8]General University Hospital of Alicantet, Alacant, Spain; [9]Hospital General Universitari de Castelló, Castelló de la Plana, Spain; [10]Miguel Servet Hospital Outpatients, Zaragoza, Spain; [11]Our Lady of Candelaria University Hospital, Santa Cruz de Tenerife, Spain; [12]Hospital Universitari de Girona Doctor Josep Trueta, Girona, Spain; [13]Santiago Clinic Hospital CHUS, Santiago de Compostela, Spain; [14]Infanta Sofia University Hospital, San Sebastián de los Reyes, Spain; [15]Hospital Universitario De Jerez, Jerez de la Frontera, Spain

Background
T2-weighted magnetic resonance imaging (MRI) signal has been recently linked with a better tumor response to pasireotide treatment in patients with acromegaly (ACRO). Our aim was to evaluate the prevalence of this radiological feature and its association to therapeutic outcomes in a large cohort of ACRO patients treated with pasireotide.
Methods
A retrospective multicentre study was performed in 15 Spanish tertiary university hospitals including patients with active ACRO who have been taking pasireotide as a second-line treatment according to current clinical guidelines. Pituitary tumor T2-weighted MRI signal was classified as "iso-hyperintense" or "hypointense" by local neuro-radiologists. Insulin-like growth factor 1 (IGF-1) levels and tumor volume reduction ($\geq$25% from baseline) were assessed after 6 and 12 months of pasireotide treatment and results analysed according to MRI pre-treatment signal. Response to pasireotide was defined as "complete" when normalization of IGF-I levels was achieved or "partial" when a decreased of $\geq$50% in IGF-I was obtained. "No response" was defined as $<$50% decrease in IGF-I from baseline.
Results
Sixty-nine patients were included (50.7% females, age 48.3$\pm$13.3), of whom 55 (79.7%) had previously undergone surgery and 63 (92.6%) treatment with first-generation somatostatin analogues, remaining with active disease before initiation of pasireotide. MRI signal was hypointense in 20 (29%) and hyperintense in 49 (71%) of the patients. Hyperintense group showed larger initial tumor compared to hypointense (7900$\pm$2000 mm^3 vs 679$\pm$1500 mm^3 $P=0.001$). Complete response to pasireotide treatment at 6 months was observed in 40 (58.8%), partial response in 1 (1.5%), and no response in 27 (39.7%) patients, while at 12 months, 40 (69%), 1 (1.7%) and 17 (29.3%) were under the aforementioned control categories, respectively, and it was not related to MRI signal category. A $\geq$25% reduction from basal tumor volume was observed in 18 (43.9%) patients after 12 months of pasireotide treatment, in the hyperintense signal group (15 out of 49 patients) (mean reduction -2064$\pm$2638 mm^3 $P=0.04$) while in the hypointense signal group in only 3 patients a decrease $\geq$25% was observed, while in the rest the tumor volume did not changed or increased. There was no correlation of volume decrease and normalization of IGF-1.
Conclusion
Almost 70% of acromegaly patients who had not responded to first-generation somatostatin analogues showed a complete hormonal response to pasireotide, regardless of the T2-weighted MRI signal, at one year of follow-up. Compared to hypointense, hyperintense T2-weighted MRI signal is associated to a better tumor shrinkage response over time.

DOI: 10.1530/endoabs.81.P166

P167

Patient-reported outcomes (PRO) in adult growth hormone deficiency (aghd) for an improved patients' management: results from the management of AGHD(MAGHD) study

Maria Laura Monzani[1,2], Simone Pederzoli[1,2], Alessio Bellelli[1,2], Elisa Magnani[3], Chiara Diazzi[1], Caterina Golinelli[2], Marco Pacchioni[4], Mirko Orsini[4] & Vincenzo Rochira[1,2]
[1]Unit of Endocrinology, Department of Medical Specialties, Azienda Ospedaliero-Universitaria of Modena, Modena, Italy; [2]Unit of Endocrinology, Department of Biomedical, Metabolic and Neural Sciences, University of Modena and Reggio Emilia, Modena, Italy; [3]Endocrinology Unit, AUSL-IRCCS of Reggio Emilia, Reggio Emilia, Italy; [4]DataRiver Srl, Modena, Italy

Background
AGHD is a recognized clinical entity, but symptoms are quite nonspecific; the lack of objective tools able to measure patients' health status remains the main barrier in clinical monitoring and treatment.
Aim
The MAGHD Study aims improving AGHD patients' management through a Smartphone app (MAGHDApp) and a fit-watch integrated with a software

framework able to merge daily data of patients' well-being and physical activity with clinical data collected in institutional databases, giving feedbacks to both patients and clinicians.
Methods
Eighty-three AGHD patients (31 Females, 52 Males, mean age 56.27 + 14.68 years) referring to a single endocrinological center entered the 24-months study. During the first year, AGHD patients performed biannual clinical visits with clinical, biochemical and multidimensional assessment through validated questionnaires (QoL-AGHDA, QLS-H, IIEF-15, FSFI, WEMWBS, IPAQ, PSQI). In parallel, MAGHDApp was developed to daily collect patient reported outcomes (PRO) derived from answers to questionnaires; moreover, a web-platform was exploited to collect data from fit-watch (number of steps, calories burned and hours of sleep). During the second year, patients were invited to use MAGHD technologies recording data, independently from patients' biannual visits. Up-to-now, only data from MAGHDApp have been analyzed.
Results
Fifty-eight patients (70%, mean age 59.9 ± 13.3) entered the second phase using MAGHD technology (MAGHDGroup), the other 25 (30%, mean age 64.4 ± 14.8) were monitored in the second phase as well as in the first. Patients of MAGHDGroup were younger than the others ($P < 0.05$), with no differences in gender distribution between the two groups ($P = 0.09$). During the second year, each questionnaire was sent to patients 6 times and MAGHDplatform collected about 12.000 PRO. Globally, the mean response rate was 60%, no differences were registered according to the type of questionnaire addressed (QoL-AGHDA = 62%, QLS-H = 62%, IIEF-15 = 58%, FSFI = 60%, WEMWBS = 61%, IPAQ = 58% and PSQI = 57%). 66% of questions were answered within 3 h from sending.
Conclusions
This real-life study suggests innovative and technological solutions for management of AGHD patients. These preliminary data document the feasibility of this kind of monitoring, especially in young AGHD patients, and a fair patients' adherence. PRO from MAGHDApp seems to guarantee a reliable, daily monitoring of patients' well-being. This information, coupled with physical activity data, could make patients directly involved in the healthcare process and help clinicians in AGHD management and follow-up.
Acknowledgment
This clinical study is conducted thanks to the competitive assignment of an Independent Grant for Learning & Change, Dissemination & Implementation by Pfizer Inc.

DOI: 10.1530/endoabs.81.P167

P168

Impact of USP8 mutations on corticotroph tumor cells responsiveness to pasireotide

Erika Peverelli[1], Giusy Marra[1], Donatella Treppiedi[1], Genesio Di Muro[1,2], Emanuela Esposito[1], Anna Maria Barbieri[1], Rosa Catalano[1], Federica Mangili[1], Marco Locatelli[3,4], Andrea Lania[5,6], Emanuele Ferrante[7], Rita Indirli[1,7], Anna Spada[1], Maura Arosio[1,7] & Giovanna Mantovani[1,7]
[1]University of Milan, Department of Clinical Sciences and Community Health, Milano, Italy; [2]University Sapienza of Rome, PhD Program in Endocrinological Sciences, Roma, Italy; [3]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Neurosurgery Unit, Milan, Italy; [4]University of Milan, Department of Pathophysiology and Transplantation, Milan, Italy; [5]Humanitas Clinical and Research Center, IRCCS, Endocrinology, Diabetology and Medical Andrology Unit, Rozzano, Italy; [6]Humanitas University, Department of Biomedical Sciences, Milan, Italy; [7]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Endocrinology Unit, Milan, Italy

Somatic mutations in the ubiquitin specific peptidase 8 (USP8) gene have been associated with higher levels of somatostatin (SS) receptor subtype 5 (SSTR5) in adrenocorticotroph hormone (ACTH)-secreting pituitary neuroendocrine tumors (PitNETs). However, a correlation between the USP8 mutational status and favorable responses to pasireotide, the somatostatin multi-receptor ligand acting especially on SSTR5, has not been investigated yet. Here, we studied the impact of USP8 mutations on pasireotide responsiveness in human and murine corticotroph tumor cells. SSTR5 upregulation was observed in USP8-mutated tumors and in USP8 wild-type primary tumor cells transfected with S718del USP8 mutant. However, cell transfection with S718del USP8 and C40-USP8 mutants in *in vitro* sensitive cultures from USP8 wild-type tumors abolished their ability to respond to pasireotide and did not confer pasireotide responsiveness to the *in vitro* resistant culture. Pasireotide failed to reduce ACTH secretion in primary cells from one S718P USP8-mutated tumor but exerted a strong antisecretory effect in primary cells from one P720R USP8-mutated tumor. In agreement, AtT-20 cells transfection with USP8 mutants led to SSTR5 expression increase but pasireotide could reduce ACTH production and cyclin E expression in P720R USP8 overexpressing cells, only. *In situ* Proximity Ligation Assay and immunoflurescence experiments revealed that P720R USP8 mutant is still able to bind 14-3-3 proteins in AtT-20 cells without affecting SSTR5 localization. In conclusion, P720R USP8 mutation might be considered as a molecular predictor of favorable response to pasireotide in corticotroph tumor cells.

DOI: 10.1530/endoabs.81.P168

P169

Identification of a novel SSTR3 full agonist and its activity in non-functioning pituitary adenoma model

Daniela Modena[1], Maria Luisa Moras[1], Giovanni Sandrone[1], Andrea Stevenazzi[1], Barbara Vergani[1], Pooja Dasgupta[2], Andrea Kliewer[2], Sebastian Gulde[3,4], Mathias Schillmaier[5,6], Raul M. Luque[7,8], Stefan Schulz[2], Natalia Pellegata[4,9,10] & Christian Steinkuhler[1]
[1]Italfarmaco Group, Preclinical R&D, Cinisello Balsamo (MI), Italy; [2]Institut für Pharmakologie und Toxikologie am Universitätsklinikum Jena, Jena, Germany; [3]Institute for Diabetes and Cancer, Helmholtz Zentrum München, Neuherberg, Germany; [4]Joint Heidelberg-IDC Translational Diabetes Program, Heidelberg University Hospital, Heidelberg, Germany; [5]Department of Nuclear Medicine, Klinikum rechts der Isar, School of Medicine, Technical University of Munich, Munich, Germany; [6]Department of Diagnostic and Interventional Radiology, Klinikum rechts der Isar, School of Medicine, Technical University of Munich, Munich, Germany; [7]Maimonides Institute for Biomedical Research of Córdoba (IMIBIC), Department of Cell Biology, Physiology, and Immunology, University of Córdoba and Hospital Universitario Reina Sofía, Cordoba, Spain; [8]Centro de Investigación Biomédica en Red de Fisiopatología de la Obesidad y Nutrición, (CIBERobn), Cordoba, Spain; [9]Institute for Diabetes and Cancer, Helmholtz Zentrum München, Neuherberg, Germany; [10]University of Pavia, Department of Biology and Biotechnology "L. Spallanzani", Pavia, Italy

Non-functioning pituitary adenomas (NFPAs), mainly gonadotroph pituitary adenomas (GPAs), are the second most common type of PAs. Given the lack of symptoms secondary to hormone hypersecretion, NFPAs are often diagnosed when they cause mass effects. At this stage they are invasive (50% of cases), they cannot be completely resected and often recur. Despite their frequency, no standard of care drug treatment currently exists for these tumors. SSAs (somatostatin agonists) like octreotide and lanreotide, binding to somatostatin receptor (SSTR) 2 and to a lesser extent to SSTR5 and SSTR3, are poorly efficacious in NFPAs. Similarly, the pan-agonist pasireotide, binding to SSTR 1,2,3,5, showed only modest efficacy in a recent phase II clinical trial of NFPA patients. SSTR3 was found to be frequently and strongly expressed in NFPAs, while SSTR2 only in few patients and SSTR5 only exceptionally. We here report the characterization of ITF2984, a novel cyclic hexapeptide pan-SSTR agonist with high SSTR3 specificity. While structurally analogous to other pan-agonists, ITF2984 shows higher affinity for SSTR3 vs known molecules. Molecular modeling revealed that higher α-II' turn probability in ITF2984 correlated with higher SSTR3 affinity, thus providing a rationale for its unique selectivity. ITF2984 inhibited GH release from GHRH-stimulated rat anterior pituitary primary cells similarly to pasireotide. To functionally characterize ITF2984 mode of action, the following assays were performed:

- Receptor internalization in HEK293 and U2OS cell lines overexpressing human SSTRs.
- SSA-mediated activation of human SSTRs by western blotting using phosphosite-specific antibodies.
- Agonist-mediated G protein-signaling of SSTR3 (GIRK activation) in SSTR3 overexpressing HEK293 and AtT20 cells.

Unlike pasireotide and octreotide, ITF2984 induced SSTR3 internalization and phosphorylation, as well as GIRK activation in a pharmacologically relevant concentration range. Thus, ITF2984 behaved as a full SSTR3 agonist. The *in vivo* activity of ITF2984 was tested in the MENX NFPA rat model. Adenomas developing in this model have a gender-specific SSTR3 expression pattern, with higher expression levels in females. Consistent with its receptor affinity profile and the in vitro data, ITF2984 showed selective antitumor activity in female rats, accompanied by a decrease in proliferation (KI67 positivity). In addition, ITF2984 selectively induced SSTR3 mRNA expression in female rat tumors, suggesting a compensatory gene upregulation. These data are in line with an *in*

vivo engagement of SSTR3 and a predominantly SSTR3-driven antitumor activity of ITF2984 and provide an *in vivo* proof-of-concept for the potential clinical use of ITF2984 in NFPAs and other SSTR3-driven diseases.

DOI: 10.1530/endoabs.81.P169

P170

Safety comparison of 40- vs 60- mg/day doses of oral octreotide capsules for treatment of acromegaly in the chiasma optimal trial

Susan L. Samson[1], Lisa B. Nachtigall[2], Maria Fleseriu[3], Mark E. Molitch[4], Andrea Giustina[5], Asi Haviv[6], Nienke Biermasz[7], Laurence Kennedy[8], Mojca Jensterle[9], Patrick Manning[10], Atanaska Elenkova[11], Shlomo Melmed[12] & Christian J. Strasburger[13]
[1]Mayo Clinic, Department of Medicine and Neurological Surgery, Jacksonville, United States; [2]Massachusetts General Hospital and Department of Medicine, Harvard Medical School, Neuroendocrine Unit, Boston, United States; [3]Oregon Health & Science University, Pituitary Center, Portland, United States; [4]Northwestern University Feinberg School of Medicine, Chicago, United States; [5]San Raffaele Vita-Salute University, Institute of Endocrine and Metabolic Sciences, Milan, Italy; [6]Amryt Pharmaceuticals DAC, Dublin, Ireland; [7]Leiden University Medical Center (LUMC), Leiden, Netherlands; [8]Cleveland Clinic Foundation, Cleveland, United States; [9]University Medical Center Ljubljana, Department of Endocrinology, Diabetes and Metabolic Diseases, Slovenia; [10]Dunedin Hospital, Dunedin, New Zealand; [11]Medical University Sofia, USHATE "Acad. Ivan Penchev", Department of Endocrinology, Sofia, Bulgaria; [12]Cedars-Sinai Medical Center, Los Angeles, United States; [13]Charite-Universitätsmedizin, Campus Mitte, Department of Clinical Endocrinology, Berlin, Germany

Background
Oral octreotide capsules (OOC) are a treatment option for patients with acromegaly in the United States who have previously responded to injectable somatostatin receptor ligands (iSRLs, octreotide or lanreotide). In previous phase 3 studies, the safety of OOC was shown to be consistent with iSRLs, without dose-dependent adverse reactions. In the double-blind, placebo-controlled period (DPC) of the CHIASMA OPTIMAL trial (NCT03252353), patients were randomized to twice-daily OOC at 40- mg/day, with the option for up-titration to 80- mg/day. In contrast, patients entered the open-label extension (OLE) at a 60- mg/day dose.
Objective
Examine the safety of 40- mg/day vs 60- mg/day OOC doses.
Methods
Eligible patients had the option to enroll in the OLE following the core trial. All patients received OOC 60- mg/day upon entering the OLE regardless of prior treatment in the DPC, including patients who received placebo in the DPC. OOC doses were up- or down-titrated based on insulin-like growth factor I (IGF-I) level and/or acromegaly signs or symptoms. The current analysis compared the incidence of treatment-emergent adverse events (TEAEs), serious adverse events (SAEs), TEAE-related study drug discontinuation, and acromegaly-related TEAEs (defined as new or worsening signs or symptoms of acromegaly).
Results
Twenty-eight patients randomized to OOC in the DPC (40- mg/day dose) and 19 who were originally randomized to placebo and continued into the OLE (60- mg/day dose) were included in the analysis. Biochemical control was similar in both groups as demonstrated by mean IGF-I levels over the respective periods. Ninety-six percent of patients on 40- mg/day and 57.9% on 60- mg/day experienced $\geq$1 TEAEs. Two patients on 60- mg/day reported a total of 2 SAEs, both deemed unrelated to study drug. Two patients on 40- mg/day experienced TEAEs leading to study drug discontinuation (headache and gastrointestinal symptoms). The incidence of acromegaly-related TEAEs was generally lower in those on 60- mg/day vs 40- mg/day.
Conclsions
This is the first analysis exploring differences in OOC doses. The nature and incidence of TEAEs occurring with a starting OOC dose of 60- mg/day vs 40- mg/day were similar, though this analysis was limited by differences in TEAE reporting across sequential phases of a lengthy trial. A trend was observed for decreased incidence of acromegaly-related TEAEs with the 60- mg/day dose. This finding is in line with previous analyses showing no dose-related TEAEs with OOC.

DOI: 10.1530/endoabs.81.P170

P171

Efficacy of pasireotide LAR for acromegaly: a long-term real-world monocentric study

Benedetta Zampetti[1], Emanuela Isabella Carioni[1], Paolo Dalino Ciaramella[1], Erika Grossrubatscher[1], Daniela Dallabonzana[1], Roberto Attanasio[2] & Renato Cozzi[1]
[1]Grande Ospedale Metropolitano Niguarda, Endocrine Unit, Milano, Italy; [2]Scientific Committee Associazione Medici Endocrinologi, International Chapter of Clinical Endocrinology, Italy

Patients
Nineteen acromegalic patients (8 females, 21-69 years-old, with macroadenoma, microadenoma or no evidence of pituitary tumor in 15, 2, 2, respectively) resistant to first generation somatostatin analogs (FG-SA) at high doses and/or intolerant to pegvisomant were switched to pasireotide LAR (PasLAR). Eleven had persistent disease after neurosurgery and two had also undergone radiosurgery (12 and 24 months before starting PasLAR). Six complained of acromegalic headache (symptomatic score was 3/3 in 5 and 2/3 in the other). On FG-SA IGF-1, GH and HbA1c were (mean, range) 193% upper limit normal age-matched range (ULNR) (120-303), 5.2 ng/ml (0.6-25), and 40.6 mmol/mol (29-54), respectively. No patient was taking antidiabetic drugs.
Protocol
PasLAR was injected every 28 days, starting with 40 mg for 3 months, uptitrated to 60 mg if IGF-1 persisted pathologic or downtitrated to 20 mg if IGF-1 was $<$ 50% ULNR. GH, IGF-1, HbA1c were assessed at 28, 84 and 168 days after starting protocol. Treatment was withdrawn if IGF-1 remained pathologic after 3 months on 60 mg q 28 days.
Results
PasLAR normalized **IGF-1** in 10/19 patients after the first injection and was withdrawn in 5 unresponsive patients at 6 months. After 12 months, IGF-1 was 74% ULNR (29-133, normal in 9/14) and GH 1.2 ng/ml (0.2-3.9). At the last follow-up (mean 26 months, range 6-60, ongoing dose 20 mg in 3, 40 mg in 7 patients, and 60 mg in 4) IGF-1 was 74% ULNR (22-195, normal in 11/14) and GH 0.7 ng/ml (0.1-2.5). **Headache** quite disappeared in all patients (in 5/6 after the first injection) and reappeared with pathologic IGF levels after PasLAR withdrawal in one irradiated patient. **Tumor shrinkage** (20-35% of basal volume) was observed in 6/7 evaluated patients without previous irradiation at 6-36 months after the start of PasLAR. **HbA1c** was 43.9 mmol/mol (32-66) at 12 months and 43.3 mmol/mol (29-66) at the last follow-up. Glucose metabolism derangement was observed in 6 patients (until DKA in one). Metformin was started in 4 patients and GLP-1 RA in two (in one coupled with insulin). In two patients PasLAR was withdrawn at 36 and 60 months due to poor compliance in the first and QTc lengthening in the second, who had started amiodarone treatment.
Conclusion
Pas-LAR should be considered a second option in patients resistant to FG-SA for its high efficacy and safety. Its quick action allows early identification of responsive patients. Efficacy on severe headache is outstanding.

DOI: 10.1530/endoabs.81.P171

P172

Towards a pituitary apoplexy classification based on clinical presentation and patient journey

Mathijs Guijt[1], Amir Zamanipoor Najafabadi[1], Irene Notting[2], Alberto M Pereira[1], Marco Verstegen[3], Nienke Biermasz[1], Wouter van Furth[3] & Kim Claessen[1]
[1]Leiden University Medical Center (LUMC), Department. of Medicine, Division of Endocrinology, and Centre for Endocrine Tumors Leiden, Leiden, Netherlands; [2]Leiden University Medical Center (LUMC), Department. of Ophthalmology, Leiden, Netherlands; [3]Leiden University Medical Center (LUMC), University Neurosurgical Center Holland, Leiden, Netherlands

Purpose
The condition of pituitary apoplexy contains the clinical spectre from life-threatening emergency to a condition with chronic symptoms and self-limiting course, which partly determines diagnostic delay and management. Outcome evaluation of course and management of pituitary apoplexy is hampered by the diverse presentation of this condition and requires appraisal. This study aimed to describe the patient journey, clinical presentation and management of various types of pituitary apoplexy in a new classification to facilitate future outcome evaluation and identify unmet needs in the current care process.

Methods
A single-center retrospective patient chart study was conducted between 2005-2021 ($n=98$). Outcome measures were clinical symptoms at first presentation in hospital, being headache, consciousness, visual acuity, visual field defects (VFD), ophthalmoplegia, nausea, vomiting, fever and hypopituitarism and care process characteristics. We described their patient journey and identified three different types, differing in clinical presentation, in-hospital route and final treatment.
Results
Mean age was 47.6 ± 16.6 years, and 51.0% was male. Most patients belonged to the acute apoplexy subtype (type A, 52%), followed by the subacute (type B, 22.5%) and non-acute subtype (type C, 25.5%). Type A generally presents with acute onset headaches, VFD or ophthalmoplegia emergency setting, with lowest mean visual acuity of both eyes and frequent hypocortisolism. Type B presents both with acute onset and chronic headaches, with VFD or ophthalmoplegia that sometimes require acute surgery. Type C usually presents with chronic headaches without acute onset and no urgent ophthalmologic complaints that require acute surgery. Next to differences in clinical presentation at hospital entry, we also showed that patients of different apoplexy subtypes go through a different type of care process with different initial working diagnosis, different attending medical specialties, and eventually different treatments.
Conclusion
Pituitary apoplexy can be approached as a spectrum of disease with 3 main subtypes, being acute, subacute and non-acute, with a different initial presentation, different in-hospital route resulting in different management. The most important unmet needs in the care process of pituitary apoplexy patients are: 1) delay in referral to a Pituitary Tumors Center of Excellence (PTCOE), 2) underdiagnosis of apoplexy subtypes B and C, since subacute and non-acute complaints are not recognized as pituitary apoplexy; 3) lack of long-term outcome evaluation of different treatment modalities within subtypes. Acknowledging subtypes will serve improvements in patient care, and outcome evaluations.

DOI: 10.1530/endoabs.81.P172

P173

The immune microenvironment landscape in pituitary tumors, genes and cells

Sandra Vela Patiño[1,2], Ma. Isabel Salazar[2], Ilan Remba-Shapiroa[1], Eduardo Peña-Martínez[1], Gloria Silva-Roman[1,2], Sergio Andoneui-Elguera[1], Keiko Taniguchi-Ponciano[1], Laura Bonifaz[3], Cristina Aguilar-Flores[3], Moises Mercado[1] & Daniel Marrero-Rodríguez[1]
[1]Hospital de Especialidades, Centro Medico Nacional Siglo XXI, Instituto Mexicano del Seguro Social, Unidad de Investigación Medica en Enfermedades Endocrinas, Mexico; [2]Escuela Nacional de Ciencias Biologicas, Laboratorio de virología e inmunovirología, Departamento de Microbiología, Mexico; [3]Hospital de Especialidades, Centro Medico Nacional Siglo XXI, Instituto Mexicano del Seguro Social, Unidad de Investigación Medica en Inmunoquimica, Mexico

The tumor immune microenvironment is essential, it could influence a favorable or negative response against the tumor cells, and it has been related to therapy response and prognostic factors. Tumor infiltrating lymphocytes (TILs) plays an important role in the development, progression, and tumor control, thus presence of TILs could be related to disease-specific traits. The aim of the present work is to evaluate the expression of immune-related genes in forty-two pituitary adenomas (PA) distributed in the three major lineages, NR5A1- (Clinically non-functioning PA), TBX19- (ACTH adenoma) and POU1F1- (GH, TSH, PRL adenoma) through whole transcriptome analysis and RT-qPCR, and to identify the microenvironment immune cells infiltrating the tumor through transcriptome deconvolution and immunofluorescence. We found characteristic expression profiles of immune-related genes including interleukins and chemokines for each tumor lineage. Genes such as IL4I1, IL36A, TIRAP, IL17REL and CCL5 were upregulated in all PA whereas IL-34, IL20RA and IL2RB characterize the NR5A1-, TBX19- and POU1F1-derived tumors, respectively. Transcriptome deconvolution showed that macrophages, CD4+ T cells, CD8+ T cells, NK cells, and neutrophils could be infiltrating the PA. CD4+ and CD8+ T cells and NK cells infiltration predicted was corroborated by immunofluorescence in pituitary adenomas. In conclusion, we found characteristic immune response gene expression profiles for each pituitary tumor lineage, that explain partially, the immune response CD8+, CD4+ T cells, NK cells and macrophages infiltration. Our results suggest a crosstalk between the tumor cells and its microenvironment.

DOI: 10.1530/endoabs.81.P173

P174

The positive feedback exerted by mtor inhibitor everolimus in pituitary neuroendocrine tumoral cells is reverted by cabergoline co-treatment

Federica Mangili[1], Emanuela Esposito[1], Donatella Treppiedi[1], Rosa Catalano[1], Giusy Marra[1], Genesio Di Muro[1], Anna Maria Barbieri[1], Marco Locatelli[2], Andrea Gerardo Lania[3], Anna Spada[1], Maura Arosio[4], Giovanna Mantovani[4] & Erika Peverelli[1]
[1]University of Milan, Department of Clinical Sciences and Community Health, Milan, Italy; [2]Neurosurgery Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy; [3]Endocrine Unit, IRCCS Humanitas Clinical Institute, Humanitas University, Rozzano, Rozzano, Italy; [4]Endocrinology Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Department of Clinical Sciences and Community Health, University of Milan, Milan, Italy

The mTOR inhibitor everolimus has been shown to display antimitotic effects on diverse neoplasms, including pituitary neuroendocrine tumors (PitNETs); however, its effect is reduced by an escape mechanism that increases AKT phosphorylation (*P*-AKT) leading to survival pathway activation. Dopamine receptor type 2 (DRD2) reduces p-AKT in some non-functioning PitNETs (NF-PitNETs) and in lactotrophs MMQ cells, through a α-arrestin 2-dependent mechanism. This study aims to analyze the efficacy of everolimus combined with DRD2 agonist cabergoline in reducing proliferation in primary cultured NF-PitNETs and MMQ cells, to analyze AKT phosphorylation and α-arrestin 2 activity. We found that 9 out of 14 NF-PitNETs were resistant to everolimus 1 nM, but the combined treatment with cabergoline inhibited cell proliferation in 7 out of 9 tumors (-31.4 ± 9.9%, $P<0.001$ vs basal), accordingly increased p27 and reduced cyclin D3 expression. In everolimus unresponsive NF-PitNETs group, 3 h everolimus treatment determined a significant increase of p-AKT/total-AKT ratio (2.1-fold, $P<0.01$, vs basal), and this effect was significantly reverted by cabergoline cotreatment. To investigate the molecular mechanism involved, we used MMQ cells as a model of everolimus escape mechanism. Indeed, 1 nM everolimus did not affect MMQ cells proliferation and increased p-AKT/total-AKT ratio (+1.53 ± 0.24-fold, $P<0.001$ vs basal), whereas cabergoline significantly reduced cell proliferation (-22.8 ± 6.8%, $P<0.001$ vs basal) and AKT activity. The combined treatment of everolimus and cabergoline induced a significant reduction of both cell proliferation (-34.8 ± 18%, $P<0.001$ vs basal and $P<0.05$ vs cabergoline alone) and p-AKT/total-AKT ratio (-34.5 ± 14%, $P<0.001$ vs basal and $P<0.05$ vs cabergoline alone). Moreover, to test a possible involvement of α-arrestin 2, silencing experiments were performed in MMQ cells. Our data showed that the lack of α-arrestin 2 prevented everolimus and cabergoline co-treatment inhibitory effects on both AKT activation and cells proliferation. These results unveiled that cabergoline overcomes the everolimus escape mechanism in primary NF-PitNETs cultured and MMQ cells inhibiting AKT phosphorylation, paving the way for a potential role of β-arrestin 2 as a biomarker predicting PitNETs responsiveness to combined therapy with dopamine agonists.

DOI: 10.1530/endoabs.81.P174

P175

Low post-operative cortisol after TSS for pituitary surgery predicts short term but not long term remission

Vanitha Karunakaran[1], Mohamed Okasha[2], Nick W Thomas[2], Sinan Barazi[2], Eleni Maratos[2], Benjamin C Whitelaw[1], Jackie Gilbert[1], Paul V Carroll[3], Jonathan Shapey[2] & Simon J B Aylwin[1]
[1]King's College Hospital, Department of Endocrinology, London, United Kingdom; [2]King's College Hospital, Department of Neurosurgery, London,

United Kingdom; [3]Guy's and St Thomas' NHS Foundation Trust, Department of Endocrinology, London, United Kingdom

Background
It is generally accepted that a post-operative cortisol of <50 nmol/l is a good predictor of long-term remission following trans-sphenoidal surgery (TSS).
Aim
We wished to determine the rate of late recurrence and need for consequent intervention in patients who had initial biochemical remission after TSS for pituitary dependent Cushing's.
Methods
We performed a retrospective analysis of our patients who underwent TSS for pituitary Cushing's between 2004 and 2019. Remission was defined as post-operative 0900 cortisol of <50 nmol/l within 3 months following TSS including patients who had surgical re-exploration during the initial admission due to a high day 2 post-operative cortisol. Those with post-operative basal cortisol greater than or equal to 50 nmol/l were considered to have 'persistent disease'. Late recurrence was defined as the emergence of biochemical cortisol excess during the follow-up period (non-suppressible cortisol, and/or elevated urine free cortisol). Kaplan-Meier curves were plotted to determine the rates of recurrence and need for second intervention in patients initially in remission and re-intervention rates were compared to those with persistent disease.
Results
86 patients (mean age 47years; 65 females, 21 males) underwent TSS for pituitary Cushing's; 28/86 had macro- and 58/86 micro-adenomas. Median follow-up time was 9 years (range 1-16). 52/86 (60%) patients were in remission (39% of macro- and 71% of microadenoma) after TSS including 5/9 patients who had immediate re-exploration. 12/52 (23%) relapsed during follow-up. Using a Kaplan Meier analysis, the 5 year remission rate was 68% and 10 year remission rate was 53% in those with immediate post-op cortisol <50 nmol/L. In total, of the 52 patients in remission post-operatively, 23% relapsed and all had a further intervention (2^{nd} TSS $n=6$; radiotherapy $n=6$). Early relapse requiring intervention was uncommon in the remission group; only 1/52 patients had a second intervention within 1 year and 3/52 within 3 years. In contrast, 30/86 patients had persistent cortisol excess and of these 83% (25/30) had a repeat intervention in the first year after surgery.
Conclsions
Our data demonstrate a significant recurrence rate (32% at 5yrs) in patients considered by the most stringent criteria to be in remission following TSS leading to further intervention. Our data also demonstrate that those with persistent disease are likely to require a second intervention shortly after initial surgery. A post-operative cortisol of <50 nmol/l is a predictor of short-term remission but is not necessarily a confident long-term predictor of remission.

DOI: 10.1530/endoabs.81.P175

P176

Antagonist of growth hormone-releasing hormone (GHRH) inhibits SARS-CoV-2 Spike protein-induced inflammation in macrophages and PBMCs

Giuseppina Granato[1], Iacopo Gesmundo[1], Tatiana Lopatina[1], Maria Felice Brizzi[1], Andrew Victor Schally[2] & Riccarda Granata[1]
[1]Division of Endocrinology, Diabetes and Metabolism, Department of Medical Science, University of Turin, Turin, Italy; [2]Department of Medicine, Miller School of Medicine, University of Miami, Miami, United States

Macrophages play essential roles in the immune defence and their hyperactivation has been implicated in epithelial damage in acute respiratory distress syndrome (ARDS), commonly observed in severe COVID-19 patients. In these cells, SARS-CoV-2 spike (S) protein triggers aberrant production of pro-inflammatory cytokines like interleukin-1 beta (IL-1β), interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α), as well as reactive oxygen species (ROS) and matrix metalloproteinases (MMPs), which contribute to viral pathogenesis. Thus, one of the therapeutic strategies to reduce acute lung injury and multi-organ dysfunction in COVID-19 would be to blunt macrophage-mediated inflammatory response. Interestingly, it has been recently shown that the interaction between S protein and lipopolysaccharide (LPS) leads to aggravated inflammation in monocytes and peripheral blood mononuclear cells (PBMCs). The hypothalamic hormone growth hormone-releasing hormone (GHRH), in addition to promoting pituitary GH release, exerts many peripheral functions, including the regulation of inflammatory responses. GHRH antagonists, in turn, display potent anticancer and antinflammatory activities, also on in vitro and *in vivo* models of LPS-induced inflammation and lung diseases. However, the role of GHRH antagonists in models of COVID-19 remains to be explored. Thus, we aimed to assess the potential antinflammatory role of GHRH antagonist MIA-602 in human THP-1 macrophages and PBMCs stimulated with LPS, either alone or in combination with S protein. Human monocytic THP-1 cells were differentiated into macrophages with phytohemagglutinin (PMA); PBMCs were obtained from buffy coats of healthy donors by density-gradient separation. Both THP-1 cells and PBMCs were pretreated for 2 h with LPS, then incubated for 24 h with MIA-602, alone or in combination with S protein. The mRNA and protein levels of cytokines were analyzed by real-time PCR and ELISA, respectively. We found that the combination of S protein and LPS potently enhanced the levels of inflammatory cytokines, when compared with each compound alone. Importantly, MIA-602 completely blocked the inflammatory response to LPS + S protein and reduced by over 50% the increase in both gene expression and secretion of TNF-α, IL-1β and IL-6. Moreover, in support of its antinflammatory role, MIA-602 reduced ROS and MMP-9 levels, by 10% and over 30% respectively, as assessed by Muse cell analyzer and gelatin zymography. Overall, these results suggest that GHRH antagonists may be potential therapeutic candidates for attenuating the inflammatory cascade in patients with COVID19.

DOI: 10.1530/endoabs.81.P176

P177

Use of corrected SUVmax as a prognostic indicator of response to PRRT

Marta Opalinska[1], Anna Sowa-Staszczak[2], Adrian Kania-Kuc[1], Ibraheem Al Maraih[1], Aleksandra Gilis-Januszewska[2] & Alicja Hubalewska-Dydejczyk[2]
[1]University Hospital in Kraków, Nuclear Medicine Unit, Department of Endocrinology, Oncological Endocrinology and Nuclear Medicine, Krakow, Poland; [2]Jagiellonian University Medical College, Chair and Department of Endocrinology, Krakow, Poland

Background
PRRT is an effective treatment option (especially for controlling disease progression)for disseminated neuroendocrine tumors (NETs), with good expression of the somatostatin receptors. Despite significant progress in NET personalized management, searching for novel predictive and prognostic factors of response to PRRT is crucial for more effective follow-up, better treatment choices leading to more favorable final outcome. Some recent studies indicate that the response to PRRT assessed on the basis of imaging of somatostatin receptors may be a potentially useful tool for prediction of overall PRRT effect.
Methods
10 patients with disseminated NET lesions who underwent [68Ga]Ga-DOTA-TATE-PET/CTs before and after PRRT were eligible to the analysis. 5 patients received 177Lu-DOTA-TATE whereas 5 tandem (mix 1:1 of 177Lu- and 90Y-DOTA-TATE)therapy. PET/CTs examinations were performed on average 3.2 months before and 4.6 months after treatment. For all measurable metastatic lesions in both PET/CTs(before and after PRRT) the corrected SUVmax was calculated as the ratio of SUVmax of lesion to SUVmax of normal liver tissue. The next step was to evaluate the change of corrected SUVmax between PET/CTs done before and after PRRT, compared to the first PET/CT. Finally, those results were complied with the result of PRRT assessed after mean follow-up time 20.3 months as: 1. Partial response (PR) 2. Stabilization(SD) 3. Progression(PD) of the disease.
Aim
Assessment if corrected SUVs change in 68Ga-somatostatin analogue PET/CT in response to PRRT may have a predictive value in patients with NET and if it differ in between PRRT with 177Lu-DOTA-TATE alone or tandem therapy.
Results
During follow-up the PR was confirmed in 1 patient, 4 had stabilization and 5 progression of the disease. Among the whole group of lesions there was a mean 27.3% reduction in corrected SUVmax in comparison between PET/CTs done before and after PRRT, and 27.4% and 27.2% reduction in Lu-177 group and tandem group, respectively. The decrease of lesion's corrected SUVmax for patient with PR was 56.4%for tandem therapy, in none of patients treated with 177Lu-DOTA-TATE regression was observed. In the SD group the average decrease od SUVmax was 42.9%for Lu-177 and 8.7%for a tandem PRRT. In patients with PD the increase in corrected SUVmax was observed, 3.6%for Lu-177 and 14.6%for tandem therapy.

Conclsion
A decrease of the mean value of corrected SUVmax in metastatic NET lesions after PRRT may have a predictive value in estimation of progression risk. There were no statistically significant differences in SUVmax changes between 177Lu-DOTA-TATE and tandem therapy.

DOI: 10.1530/endoabs.81.P177

P178

Metastatic pheochromocythoma and paragangliomas: clinical and follow-up characteristics in a reference unit

Giselle Giron[1], Maria Isabel Del Olmo Garcia[1], Angel Segura[1], Stephan Prado[1], Pilar Bello[1], Rosana Palasi[1], Jose Luis Ponce[1], Susana Lopez Agullo[1], Lidia Gómez-Elegido Tenés[2] & Juan Francisco Merino Torres[1,2]
[1]La Fe University and Polytechnic Hospital, València, Spain; [2]University of Valencia, València, Spain

Introduction
Pheochromocytomas(PCC) and paragangliomas(PGGLs) are rare neuroendocrine tumors. Management is very complex, this is why physicians involved in the management of these patients need to take into account not only clinical aspects but also genetics of these tumors. We present a group of patients diagnosed of metastatic PGG or PCC, their characteristics and long term follow-up.
Methods and design
Descriptive and unicentric study that includes 23 patients diagnosed with metastatic PCC/PGGLs, assessed at *Hospital Universitari i Politècnic La Fe* in Valencia, Spain between 2011 and 2022. Demographic, surgical, anatomopathological, clinical, imaging tests and treatments variables are included. Results are expressed as mean and standard deviation (SD) in the case of quantitative variables or percentage in the case of qualitative variables (SPSS 25.0).
Results
55% of the patients were women. Mean age at diagnosis of the primary tumor was 39 years, and at diagnosis of the first metastasis was 45 years (SD 19). 86% where carriers of a mutation, 54.5% germinal mutation: SDHB 66.7%, SDHD 16.7%, AF2 8.3%, SDHA 8.3%. The 28% remaining had somatic line mutations: CSDE1 29%, NF1, EPAS1, FH, HRAS and VHL in 14.3% each. All of the cases underwent surgery. On the pathological study of the primary tumor all of the patients had at least one value of bad prognosis, with high risk of malignization potential in 8 cases (PASS and GAP scores more than 3 points). For follow up and treatment decision we utilized different imaging techniques: 68GalioPET-CT (100%) with positive uptake in 72.2% of cases, 123-MIBG (77.3%), 18FDG PET-CT (86.4%). The mean of treatment lines used in each patient was 2.7. Regarding systemic treatment: Somatostatin analogues were the most used (72.7%), followed by QT CVD (45.5%), Lu-DOTA-TATE (30%), MIBG (22%). Treatment with Lu-DOTA-TATE manages to stabilize the disease in more than 50% of cases (57.1%) with an average PFS of 21 months, with a partial response on hormonal secretion (PR) in more than 50%. Chemotherapy with CVD: 50% have a PR, 10% a CR in 10% of cases continues an ED. 50% of the metastatic PCC/PGGs treated with CVD were carriers of the SDHB mutation.
Conclsion
- Germline and somatic genetic studies are essential to guide the management of these patients.
- Treatment with Lu-DOTA-TATE seems effective in patients with positive uptake in Ga68-PET-CT with considerable PFS.
- Patients should be assessed within a multidisciplinary committee and framed in Reference Units, given their therapeutic complexity.

DOI: 10.1530/endoabs.81.P178

P179

Role of beta arrestins and G proteins in mediating DRD2 signaling in pituitary tumors

Emanuela Esposito[1], Federica Mangili[1], Genesio Di Muro[1], Anna Maria Barbieri[1], Donatella Treppiedi[1], federico arlati[1], Rosa Catalano[1], Giusy Marra[1], emma nozza[1], Maura Arosio[1,2], Giovanna Mantovani[1,2] & Erika Peverelli[1]
[1]University of Milan, Department of Clinical Sciences and Community Health, Milan, Italy; [2]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Endocrinology Unit, Milan, Italy

Dopamine receptor type 2 (DRD2) agonists (DA) are the first-choice treatment for prolactin (PRL)-secreting pituitary tumors, but poorly effective in non-functioning (NF)-PitNETs. Along with G protein-dependent signaling, DRD2 also mediates non-canonical beta-arrestin-dependent pathways, where reduction of AKT phosphorylation plays a leading role for the antiproliferative effect of DRD2 in pituitary tumors. Through UNC9994 and MLS1547, a beta-arrestin 2-biased and a G protein-biased agonist, respectively, the present study aimed to clarify the role of G proteins and beta-arrestin 2 in mediating DRD2 signaling in rat tumoral lactotroph cells MMQ and in human primary cultured NF-PitNET cells. In MMQ cells, treatment with UNC9994 reduced cell proliferation (-41.4 ± 20% at 100 nM, $P<0.01$ *vs* bas) with a greater efficacy compared to cabergoline (-22.2 at 100 nM ± 10.9%, $P<0.01$ *vs* bas), while MLS1547 treatment resulted into a slight lowering of cell proliferation (-10.8 ± 7.4% at 100 nM, $P<0.05$ *vs* bas). Accordingly, UNC9994 was more efficient in reducing AKT phosphorylation (-45.5 ± 16%, $P<0.01$ *vs* bas) than cabergoline, whereas an increased AKT phosphorylation was detected after MLS1547 treatment. Consistently, cabergoline and UNC9994 treatments determined a significant reduction of cyclin D3 (-14.7 ± 5.8%, $P<0.01$ *vs* bas and -18.8 ± 9%, $P<0.05$ *vs* bas, respectively), together with an upregulation of p27/Kip1 (+35 ± 20%, $P<0.05$ *vs* bas and +41.6 ± 20.5%, $P<0.05$ *vs* bas, respectively). Beta-arrestin 2 silencing reverted either UNC9994 and cabergoline anti-proliferative effects, as well as their effects on AKT phosphorylation. Pretreatment with pertussis toxin (PTX) maintained the antiproliferative effects of cabergoline (-16.6 ± 3.6%, $P<0.001$ *vs* bas) and UNC9994 (-31 ± 1.9%, $P<0.001$ *vs* bas), while it abolished the ability of MLS1547 in reducing cell proliferation. After 6 h treatment with MLS1547, cell migration showed a considerable reduction (-44 ± 10% at 1μM, $P<0.001$ *vs* bas), to a greater extent than cells treated with UNC9994 (-31 ± 19% at 1μM, $P<0.01$ *vs* bas). 5 out of 8 human primary cultured NF-PitNET cells *in vitro* responsive to cabergoline antiproliferative effects (-31 ± 9.4%, $P<0.001$ *vs* bas) showed a significant reduction of cell proliferation after UNC9994 and MLS1457 treatments (-27.4 ± 7.5%, $P<0.001$ *vs* bas, and -21.7 ± 9.3%, $P<0.01$ *vs* bas, respectively). On the other hand, 3 out of 8 NF-PitNETs that did not respond to cabergoline appeared to be unresponsive also to UNC9994 and MLS1547. In conclusion, our data demonstrated a relevant role for the beta-arrestin 2-dependent pathway in regulating DRD2 inhibitory effects on tumoral growth, whereas the canonical G protein-mediated signaling seemed to be key in controlling cell migration.

DOI: 10.1530/endoabs.81.P179

P396

Precision medicine: new perspectives for the treatment of GH-secreting tumors - the miss study

Alessandro Maria Berton[1], Nunzia Prencipe[2], Luca Bertero[3], Marina Corsico[4], Daniela Cuboni[1], Marco Baldi[1], Chiara Bima[5], Antonio Bianchi[5], Giovanna Mantovani[6], Francesco Ferraù[7], PAOLA SARTORATO[8], Irene Gagliardi[9] & Silvia Grottoli[1]
[1]University of Turin, Division of Endocrinology Diabetology and Metabolism, Department of Medical Sciences, Turin, Italy; [2]"AOU Città della Salute e della Scienza di Torino" University Hospital, Division of Endocrinology Diabetology and Metabolism, Department of Medical Sciences, Turin, Italy; [3]University of Turin, Pathology Division 2U, Department of Medical Sciences, Turin, Italy; [4]"AOU Città della Salute e della Scienza di Torino" University Hospital, Division of Neuroradiology, Department of Diagnostic and Interventional Radiology, Turin, Italy; [5]Università Cattolica del Sacro Cuore, Fondazione Policlinico Universitario A. Gemelli, IRCCS, Endocrinology and Diabetology Unit, Department of Translational Medicine and Surgery, Rome, Italy; [6]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, University of Milan, Endocrinology Unit, Department of Clinical Sciences and Community Health, Milan, Italy; [7]University Hospital G. Martino, University of Messina, Endocrine Unit, Department of Human Pathology of Adulthood and Childhood G. Barresi, Messina, Italy; [8]General Hospital, Montebelluna, Department of Internal

Medicine, Treviso, Italy; [9]University of Ferrara, Section of Endocrinology and Internal Medicine, Department of Medical Sciences, Ferrara, Italy

Introduction
First-generation SRL (fg-SRL) represent the treatment of choice in acromegaly patients with post-neurosurgical adenomatous remnant and GH-hypersecretion. Anyway, approximately 60% of patients do not achieve adequate disease control. The main predictors of resistance include male sex, young age, invasiveness of the lesion and its hyperintensity on T2-weighted MRI scans; but also, SSTR2 expression, the cytokeratin pattern, Ki-67 and the presence of AIP gene mutation.
Aim
To identify the most relevant predictors of fg-SRL resistance among the most used clinical and histological parameters, specific to the Italian acromegaly population.
Methods
The MISS was an Italian multicenter, retrospective, case-control study, involving the Centers of Turin, Rome, Milan, Messina, Treviso and Ferrara (study duration 5/2018-12/2020). Non-response was defined after six months of full-dose fg-SRL treatment by the presence of both uncontrolled age-adjusted IGF-I, random GH levels and a tumor shrinkage $<20\%$. Controls were collected in a ratio of 1 to 2 compared to resistant cases.
Results
Ninety-six patients were enrolled (63 resistant cases and 33 controls). Age at diagnosis was associated with the condition of fg-SRL resistance, even when corrected for IGF-I values (coefficient -0.04, OR 0.96, AUC 0.62, $P=0.035$). An iso/hyperintense signal in T2-weighted MRI scans resulted the strongest radiological predictor (coefficient 1.19, OR 3.3, AUC 0.64, $P=0.027$), even if corrected for the maximal tumor diameter at diagnosis. Both a low grade SSTR2 expression and a sparsely granulated (SG)/intermediate cytokeratin pattern proved to be predictors of the resistant condition (coefficient 1.52, OR 4.58, AUC 0.7, $P=0.013$; coefficient 0.97, OR 2.65, $P=0.047$, respectively); the latter resulting also to be superior to the T2-wheighted intensity on MRI (coefficient 1.71, OR 5.56, AUC 0.76, $P=0.003$). Among those patients undergone neurosurgery without any neoadjuvant treatment, the absence of an appreciable tumor remnant led to a negligible probability of non-response to medical treatment, even considering random GH at three months after surgery for the inclusion in the model (coefficient -3.09, OR 0.04, AUC 0.82, $P=0.003$).
Conclusions
A T2-iso/hyperintense MRI pattern was associated with a 3.3-fold greater probability of resistance to fg-SRL. Moreover, both a SG/intermediate granulation pattern and a low grade SSTR2 expression led to a 5 times greater probability of being resistant. Finally, the absence of an appreciable post-surgical remnant suggested a better response to fg-SRL. These factors deserve to be evaluated before setting up medical treatment with fg-SRL. Future guidelines should take this emerging evidence into account when making recommendations on therapeutic choice.

DOI: 10.1530/endoabs.81.P396

P397

The cut-off limits of GH response to GHRH + arginine test related to body mass index for the diagnosis of adult GH deficiency: do we need to review our diagnostic criteria?

Daniela Cuboni, Emanuele Varaldo, Fabio Bioletto, Alessandro Maria Berton, Chiara Bona, Nunzia Prencipe, Ezio Ghigo, Mauro Maccario, Silvia Grottoli & Valentina Gasco
University of Turin, Department of Medical Science, Division of Endocrinology, Diabetes and Metabolism, Turin, Italy

Introduction
The diagnosis of GH deficiency (GHD) in adults is based on a reduced GH response to provocative tests. The proportion of patients with low GH response to provocative tests increases with the number of other pituitary hormone deficiencies and several studies involving panhypopituitary patients have shown that under certain circumstances GH stimulation tests may be unnecessary to diagnose GHD.
Objective
Aim of this study was to re-evaluate the diagnostic cut-offs of GH response to GHRH + arginine (ARG) test in function of BMI. To this aim the patients' pituitary function was considered as the gold standard for the diagnosis or exclusion of GHD; in particular GHD was defined by the presence of at least 3 others pituitary deficits, while a preserved somatotropic function was defined by the lack of others pituitary deficits.
Methods
The GH responses to GHRH + ARG were studied in 349 patients with history of hypothalamic-pituitary disease [age (mean ± SD): 43.8 ± 16.5 years; BMI: 27.4 ± 9.2 kg/m^2]. Patients were divided into lean (143), overweight (107) and obese (99) subjects according to BMI. The best GH cut-off to GHRH + ARG, defined as the one with the best sensitivity (SE) and specificity (SP), was identified using the receiver-operating characteristic curve (ROC) analysis.
Results
The best GH cut-off to GHRH + ARG was 5.5 μg/l in lean subjects (SE 89.2%, SP 79.7%), 4.2 μg/l in overweight subjects (SE 94.0%, SP 62.5%) and 2.8 μg/l in obese subjects (SE 85.7%, SP 83.3%). The diagnostic accuracy was 85.3, 82.2 and 84.8% respectively.
Conclusions
To our knowledge this is the first study that evaluate the diagnostic cut-offs of GH response to GHRH + ARG in function of BMI using a clinical definition of GHD as gold standard. Our results suggest that with this new approach, the GHRH + ARG cut-offs should be revised.

DOI: 10.1530/endoabs.81.P397

P398

SARS-CoV-2 infection in acromegaly patients: case series

Stefana Bilha, Anca Matei, Andra Cristiana Istrate, Letitia Leustean, Maria Christina Ungureanu, Dumitru D. Branisteanu & Cristina Preda
"Grigore T. Popa" University of Medicine and Pharmacy Iasi, Endocrinology, Iasi, Romania

Introduction
SARS-Cov-2 infection challenged the appropriate management of acromegaly, because of delayed or limited admissions and treatment. Despite lack of data regarding SARS-Cov-2 infection in acromegalic patients (only one case reported to date), increased susceptibility to infection and poor prognosis might be triggered by the associated metabolic, cardiovascular and respiratory comorbidities. We report a series of acromegaly patients with a positive PCR test at their admission in our Endocrinology Department and their COVID-19 disease evolution.
Methods
All inpatient admissions in our unit undergo RT-PCT testing for SARS-CoV-2 infection from the debut of the pandemic according to the local protocol. Inpatient admisssions for acromegaly diagnosis and monitoring during the first 4 waves of the COVID-19 pandemic (March 1st 2020 to November 30th 2021 – 21 months) were reviewed and compared to the acromegaly inpatient admissions during the same period of time before the pandemic (June 1st 2018 to February 29th 2020).
Results
The number of inhospital admission for acromegaly dropped by aproximately 50% during the first 4 waves of the pandemic compared to the same length of time prior to the pandemic (155 vs 359 inpatient admissions for acromegaly). Among the 86 patients admitted for acromegaly diagnosis or monitoring during the pandemic (approximately 2 admission per patient), 4 patients (aged between 39 and 61 years(y) old) had a positive RT-PCR test for SARS-CoV-2 infection. All were overweight or obese (BMI range 28-34 kg/m^2) and 3 out of 4 had ongoing active disease and were under lanreotide treatament (IGF1 serum concentrations: 180 to 334 ng/ml (<2 ULN); basal GH: 1.59 to 3.19 ng/ml); SAGIT overall score between 2 and 8. Two out of 4 patients had a mild case of COVID-19 (First: 61 y old, active disease, heart failure, severe sleep apnea, restrictive respiratory dysfunction, vaccinated against SARS-CoV-2; second: 39 y old, active disease, type 2 diabetes mellitus, unvaccinated), while the other 2 were completely asymptomatic (Third: 46 y old, active disease, unvaccinated; Fourth: 61 y old, biochemical control, unvaccinated). Patients were managed according to local protocol for SARS-CoV-2 infection.
Conclusions
Although SARS-CoV-2 infection occurs is thought to have a worse prognosis in acromegaly patients due to the coexistence of cardiometabolic complications and

impaired respiratory function, all patients in our series developed only mild or asymptomatic COVID-19 cases, despite being rather obese and having biochemically active disease with one exception.
Keywords: active acromegaly, SARS-CoV-2, COVID-19

DOI: 10.1530/endoabs.81.P398

P399

Familial neurohypophyseal diabetes insipidus: an extremely rare report of a family with a nonsense mutation in the arginine vasopressin gene

Diogo Ramalho[1], Joana Serra-Caetano[2], Rita Cardoso[2], Patrícia Rosinha[3], Bárbara Filipa Araújo[4], Inês Rua[5], Orlando Rodrigues[6], Isabel Dinis[2] & Alice Mirante[2]
[1]Centro Hospitalar de Vila Nova de Gaia/Espinho, Endocrinology, Vila Nova de Gaia, Portugal; [2]Hospital Pediátrico, Centro Hospitalar e Universitário de Coimbra, Pediatric Endocrinology, Coimbra, Portugal; [3]Centro Hospitalar do Baixo Vouga, Endocrinology, Aveiro, Portugal; [4]Centro Hospitalar e Universitário de Coimbra, Endocrinology, Coimbra, Portugal; [5]Hospital Pediátrico, Centro Hospitalar e Universitário de Coimbra, Pediatrics, Coimbra, Portugal; [6]Hospital Pediátrico, Centro Hospitalar e Universitário de Coimbra, Medical Genetics, Coimbra, Portugal

Introduction
Familial neurohypophyseal diabetes insipidus (FNDI) is a rare form of central diabetes insipidus (CDI) characterized by childhood-onset progressive polydipsia and polyuria due to mutations in the *arginine vasopressin-neurophysin II* (*AVP-NPII*) gene.
Case description
Two male siblings were referred at 1 month of age to exclude CDI owing to a family history of CDI in the father and paternal grandfather. The proband was the father diagnosed at 3 months old. The grandparent was diagnosed later, in his early twenties, when diuresis was about 15 L daily. His symptoms had apparently not been recognised since childhood. At 6 months of age, the older sibling (1) drank 500 ml of water/night and 1.5 L of water/daily and the younger sibling (2), at 11 months old, drank 800 ml of water/night and had 2 diaper changes/night, in a total of 2500 ml water intake and 8 diaper changes/day. No growth deceleration was observed in both. Physical examination and past medical history were unremarkable. Random urine specific gravity was lower than 1.005. Glycemia, thyroid function, serum osmolality, 8 am. cortisol, creatinine, sodium, potassium and calcium were within normal range. The sibling 1 was admitted for elective water deprivation test that confirmed CDI (basal serum and urinary osmolality: 278 mOsm/Kg and 292 mOsm/kg; serum and urinary osmolality at the end: 289 mOsm/kg and 281 mOsm/kg; urinary osmolality after 10 mg of desmopressin [DDAVP]: urinary osmolality of 574 mOsm/kg [increased by 102%]). He promptly initiated DDAVP (0.025 mg, twice daily) with clinical improvement. Pituitary magnetic resonance imaging confirmed a small and hypointense neurohypophysis. CDI was presumptively assumed in the sibling 2, and symptoms improved under DDAVP (0.025 mg, twice daily). Sequencing analysis of the *AVP-NPII* gene revealed the same mutation in the four family members, a heterozygous nonsense mutation in the NPII coding region (c.343G>T, p.Glu115Ter) of the *AVP-NPII* gene. Currently, the four patients are asymptomatic under DDAVP.
Discussion and conclusions
To our knowledge, there is only another family with this autosomal dominant mutation described worldwide. Genetic counselling should be offered to ensure an early and adequate diagnosis and treatment. It should also provide the family with accurate information on preimplantation genetic testing (PGT) in order to obtain genetically healthy descendants. In Portugal, FNDI requires prior authorization from the "National Council for Medically Assisted Procreation" for couples who intend to perform a PGT cycle.

DOI: 10.1530/endoabs.81.P399

P400

European Registries for Rare Endocrine Conditions (EuRRECa): results from the core registry on hypothalamic and pituitary conditions

Ana Luisa Priego Zurita[1], Natasha Appelman-Dijkstra[1], Nienke Biermasz[1], Jillian Bryce[2], Pia Burman[3], Luis Castaño[4], Mehul Dattani[5], Olaf M. Dekkers[1], Benedetta Fibbi[6], Hoong-Wei Gan[7], Sonia Gaztambide[4], Gabriele Haeusler[8], Florentina Haufler[8], Harshini Katugampola[5,7], Lasolle Hélène[9], Hermann L Müller[10], Gerald Raverot[9], Itxaso Rica[4], Charlotte van Beuzekom[1], Zdenek Sumnik[11], Friso de Vries[1], Amir Zamanipoor Najafabadi[12], Faisal Ahmed[1,2,13] & Alberto M Pereira[1]
[1]Leiden University Medical Centre, Department of Medicine, Division of Endocrinology, Leiden, Netherlands; [2]University of Glasgow, Office for Rare conditions, Glasgow, United Kingdom; [3]Skane University Hospital Malmö, University of Lund, Department of Endocrinology, Lund, Sweden; [4]Hospital Universitario Cruces, UPV/EHU, Biocruces Bizkaia, CIBER-DEM/CIBERER, Bilbao, Spain; [5]University College London Great Ormond Street Institute of Child Health, Genetics & Genomic Medicine Programme, London, United Kingdom; [6]Careggi University Hospital, Endocrinology Unit, Florence, Italy; [7]Great Ormond Street Hospital for Children, Department of Paediatric Endocrinology, London, United Kingdom; [8]Medical University of Vienna, Department of Pediatrics and Adolescent Medicine, Vienna Bone and Growth Center, Vienna, Austria; [9]Reference Center for Rare Pituitary Diseases HYPO, Groupement Hospitalier Est, Hospices Civils de Lyon, Endocrinology Department, Bron, France; [10]University Children's Hospital, Klinikum Oldenburg AöR, Department of Pediatrics and Pediatric Hematology/Oncology, Oldenburg, Germany; [11]Charles University 2 nd Faculty of Medicine and University Hospital Motol, Department of Pediatrics, Prague, Czech Republic; [12]Leiden University Medical Centre, University Neurosurgical Center Holland, Leiden, Netherlands; [13]University of Glasgow, Developmental Endocrinology Research Group, Royal Hospital For Children, GLASGOW, United Kingdom

Introduction
The European Registries for Rare Endocrine Conditions (EuRRECa) was created in collaboration with the European Reference Network on Rare Endocrine Conditions (Endo-ERN), the European Society for Paediatric Endocrinology and the European Society of Endocrinology to support the needs of the endocrine community. The Core Registry, one of its platforms, enables the collection of longitudinal patient and clinician reported outcomes. A module collecting aspects of the care and outcomes of the patients with pituitary tumours has been active since November 2021.
Aim
To describe the population registered in the EuRRECa Core Registry between June 2019 and December 2021 in the Hypothalamic and Pituitary group of conditions.
Methods
Core Registry clinical contributors are invited to register new and existing cases of endocrine conditions seen in their centres. Diseases are mapped according to the Orphanet nomenclature. A core data set and a condition-specific data set collect information regarding demographics, diagnosis and outcomes.
Results
A total of 159 cases have been registered by 5 centres from 4 countries. Of 159 cases, 5(3%) were between 0-9 years of age, 6(4%) between 10-17 years and 148 (93%) over 18 years. In the latter, the commonly reported conditions include pituitary adenoma 91/148 (62%) and acquired hypopituitarism 45/148 (30%) followed by suprasellar tumours 6/148 (4%) and other sellar and parasellar tumours 3/148 (2%). Of 91, 38(41%) were non-functioning pituitary adenoma, 20 were prolactinoma (22%), 16 (18%) were unspecified functioning pituitary adenoma, 12(13%) were unspecified pituitary adenoma, 3 (3%) were somatomammotropinomas and 2 (2%) were corticotroph adenomas. Diagnosis was reported by the combination of clinical assessment, biochemistry and MRI in 84/159 cases (53%), histology was added in 10 cases (6%) and genetic testing in 3(2%). Of 159 cases, 154(97%) were under active follow-up. Participation in a different detailed disease registry was reported in 15/159 cases. Biobank samples were available in 12/159 (8%). Twenty-one patients (13%) had expressed an interest in using the patient platform, 16(76%) had been sent an invitation to join and of these, 4(25%) activated their account. Of 159, 67 cases have been entered into the pituitary tumour module.
Conclusion
Pituitary adenoma is the most reported condition in the Hypothalamic and Pituitary group with most patients being over 18 years. These results support the creation of a pituitary adenoma detailed module which provides clinicians the opportunity of sharing aspects of the condition and care of their patients with health care professionals and the research community.

DOI: 10.1530/endoabs.81.P400

P401

Prevalence, type and evolution of autoimmune diseases with respect to hormone control in patients with cortisol, GH and prolactin hypersecretion

Federica Guaraldi[1], Matteo Zoli[1,2], Emanuela Arvat[3], Martina De Martin[4], Francesca Pecori Giraldi[4], Scaroni Carla[5], Davide Gori[2], Roberta GIORDANO[3], Silvia Grottoli[3], Ezio Ghigo[3], Sofia Asioli[2] & Diego Mazzatenta[1,2]
[1]IRCCS Istituto delle Scienze Neurologiche di Bologna, Pituitary Unit, Bologna, Italy; [2]Alma Mater Studiorum - Bologna University, Department of Biomedical and Neuromotor Sciences (DIBINEM), Bologna, Italy; [3]University of Turin, Department of Medical Sciences, Turin, Italy; [4]Istituto Auxologico Italiano, Department of Clinical Sciences and Community Health, Milan, Italy; [5]Azienda Ospedaliero Universitaria of Padua, Department of Medicine DIMED, Padua, Italy

Background
In vitro and animal experiments have clearly demonstrated that excessive cortisol, GH and prolactin secretion, as well as dopamine agonists (D2As) and somatostatin analogs (SSAs), often prescribed for their treatment, affect the immune response and the onset/evolution of autoimmune diseases (AIDs) through direct and indirect complex mechanisms. Data from clinical studies are very scanty.
Study aim
To assess the 1) distribution of AIDs according to patient age and gender, adenoma and AID type; and 2) evolution of AID(s) with respect to hormonal activity and eventual DA/SSA treatment, in patients with Cushing's disease (CD), acromegaly and prolactinoma with respect to patients with non-functioning adenoma (NFPA; controls).
Patients and methods
Clinical data of interest were collected retrospectively and prospectively from patient records and a purposely designed questionnaire.
Results
715 patients. 144 with CD (118 F; previous treatment:144 endoscopic surgery (ES), 12 radiation therapy (RT), 18 adrenalectomy, 42 medical therapy (MT); 120 under remission, 24 active disease under treatment); 124 with acromegaly (75 F; previous treatment: 100 ES, 25 RT, 60 medical therapy; 81 remission, 43 active disease under treatment); 260 with prolactinoma (162 F; previous treatment: 29 ES, 4 RT, 251 medical therapy; 177 remission, 83 active disease under treatment) and 187 NFPA (101 F; previous treatment: 170 ES and 17 RT). Age at evaluation was similar among groups. Patients with AID were 39 (27.1%) in CD, 23 (18.5%) in acromegaly, 52 (21%) in prolactinoma, and 17 (9%) in NFPA group. CD was associated with the highest risk of developing AIDs ($\chi2=8.42$, $P<0.0001$); prevalence in acromegaly and prolactinoma was similar and higher than in NFPAs ($P<0.0001$). In all groups, females were typically affected ($P=0.001$). AID type, gender and age distribution were similar to the general population. Almost all patients presented a single AID. Hashimoto's thyroiditis was the most common ($P<0.001$), followed by psoriasis and rheumatoid arthritis. AIDs diagnosed before CD ($n=24$) typically improved during overt hypercortisolism and recurred after CD remission, except for Hashimoto's thyroiditis (independent evolution). New onset/recrudescence of AIDs ($n=13$) occurred from some weeks to some years after CD remission (median 1 year). AIDs similarly occurred before and after prolactinoma diagnosis; in acromegaly they mainly occurred during active disease ($P>0.01$); for both groups AID evolution was independent from hormone control and SSA/D2A treatment.
Conclusions
Patients with pituitary adenomas, especially females with CD, deserve careful and repeated evaluation of AIP during follow-up, independently from adenoma size and treatment.

DOI: 10.1530/endoabs.81.P401

P402

Central pontine myelinolysis: Case report

Paloma González Lázaro[1], Cristina Contreras Pascual[2], Cristina Montalban Méndez[1], Antonio Moreno Tirado[1], Maria Zhao Montero Benítez[1] & Pedro Jimenez Torrecilla[1]
[1]Hospital General La Mancha Centro, Alcázar de San Juan, Spain; [2]Hospital Santa Barbara, Soria, Spain

Introduction
Central pontine myelinolysis (CPM) is a rare and potentially life-threatening complication of a sudden rise in serum osmolality. Along with extrapontine myelinolysis, it is part of the osmotic demyelination syndrome (ODS). Known risk factors include severe hyponatremia, alcoholism, thiazide use, hypokalemia, and malnourishment.
Case report
We report the case of a 31-year-old-male with history of alcohol and cannabis dependence, who had attended a private clinic two weeks earlier for gastric balloon placement, he was admitted to the emergency-department reporting nausea and vomiting with oral intolerance, nervousness, and agitation. He was initially detected to have hypo-osmolar hyponatremia (osmolality: 261 mmol/l, sodium: 114 mmol/l), and hypokalemia. His urine analysis revealed a urine osmolality of 279 mmol/l with a sodium level of 13 mmol/l supposedly because of hypovolemia due to inadequate fluid intake. The patient received intravenous potassium and was to be given 2000 ml of NaCl 0.9% in the first 24 h; Also, thiamine was prophylactically started to prevent Wernicke encephalopathy. Approximately 16 h after admission, the sodium levels increased to 123 mmol/l. The patient received glucose 5% infusion when sodium levels increased to 125 mmol/l within the first 24 h. In the following week the sodium levels normalized with a daily increase of 1-3 mmol/l. The potassium levels normalized quickly as well. During this period, the patient developed ataxia and resting tremors. Vitamin doses were switched to therapeutic because Wernicke encephalopathy was suspected. In the following days the patient's neurological status deteriorated leading to a 'locked in' state when he was only able to open and move his eyes. An MRI of the brain showed a hyperintense signal in the central pontine region. Following the diagnosis of CPM, he was rehabilitated with occupational and physiotherapy.
Discussion
Our case, a patient with history of alcohol and cannabis dependence syndrome, complicated by central pontine myelinolysis probably due to an overly rapid correction of plasma osmolality. Given the fact that our patient had multiple risk factors and severe hyponatremia (<120 mmol/l) he would have benefited from a more intensively controlled rise in serum sodium levels or more aggressive lowering of sodium levels when overcorrection became apparent.
Conclusion
CPM is a rare complication of a rapid correction of serum osmolality, and we should always be aware of this complication. In patients with multiple risk factors, CPM might be prevented by frequent control of electrolytes and osmolality in combination with volume status and urinary output.

DOI: 10.1530/endoabs.81.P402

P403

GH/IGF-I impact hepatic lipid accumulation in non-acromegalic individuals with and without non-alcoholic fatty liver disease

Paul Fellinger[1], Hannes Beiglboeck[1], Lorenz Pfleger[1], Sabina Smajis[1], Martin Gajdosik[1], Rodrig Marculescu[2], Greisa Vila[1], Yvonne Winhofer[1], Alexandra Kautzky-Willer[3], Michael Krebs[1], Martin Krssak[1] & Peter Wolf[1]
[1]Division of Endocrinology and Metabolism, Internal Medicine III, Vienna, Austria; [2]Medical University of Vienna, Wien, Austria; [3]Medical University of Vienna, Department of Medicine III, Division of Endocrinology & Metabolism, Vienna, Austria

Background
Growth hormone (GH) plays an important role in modifying body composition. In acromegaly, a state of chronic GH/IGF-I excess, visceral and ectopic fat mass, especially in the liver, are significantly reduced. The aim of this study was to investigate the impact of GH/IGF-I on hepatocellular lipid content (HCL) and energy metabolism in a non-acromegalic cohort of patients with and without non-alcoholic fatty liver disease (NAFLD).
Methods
We performed a cross-sectional study in 76 non-acromegalic individuals (36 females). Concentrations of glucose, insulin, c-peptide and GH were measured every 30 minutes during a standardized 2-h-75g oral glucose tolerance test (OGTT). Insulin sensitivity was estimated by the oral glucose insulin sensitivity index (OGIS). IGF-I was measured prior to the OGTT and was given as the percentage of the sex-, age-, and assay specific upper limit of normal (IGF-I ULN). Liver parameters, like HCL and ATP synthesis rate (*k*ATP), as well as high energy phosphorous metabolites were analysed using 1H- as well as 31P-magnetic resonance spectroscopy (MRS) at 7 Tesla. NAFLD was defined as HCL $>5.5\%$.
Results
In the whole cohort (age: 43.4+-15.3y; BMI: 25.7+-4.3 kg/m^2; IGFI-ULN: 65.7+-17.2% [IQR 33.6-102.6%]) the median HCL was 2.79% [IQR 1.35-9.5%] with 27 patients presenting with a HCL higher than 5.5% indicating NAFLD. Fasting GH (0.21 [0.1; 0.6] ng/ml vs 0.67 [0.2; 2.5] ng/ml;$P=0.0055$), as well as dynamic GH levels during OGTT (AUC_{GH}: 15.30 [7.2; 25.6] ng/ml/min vs 48.8 [25.7; 143.2] ng/ml/min;$P=0.0002$). IGF1-ULN correlated significantly with

high-energy phosphorous metabolites but did not correlate with *k*ATP in the whole cohort. In the multiple logistic regression analysis IGF1-ULN as well as fasting glucose were next to BMI and OGIS a significant, independent predictor for NAFLD.

Conclsion

In summary, here we show that increased HCL is associated with lower fasting and post-glucose-load GH concentrations in otherwise healthy individuals with or without NAFLD, while both GH and IGF-I independently relate to the presence of NAFLD. The relationship between GH/IGF-I metabolism and HCL could be further investigated as a potential therapeutical target in patients with NAFLD.

DOI: 10.1530/endoabs.81.P403

P404

Change in androgens and adrenal hormones during long-term osilodrostat treatment in patients with Cushing's disease: Results from the Phase III, prospective LINC 3 study

Rosario Pivonello[1], Beverly M.K. Biller[2], Shimatsu Akira[3], John Newell-Price[4], Antoine Tabarin[5], Greisa Vila[6], Andrea Piacentini[7], Alberto Pedroncelli[8] & Maria Fleseriu[9]

[1]Università Federico II di Napoli, Dipartimento di Medicina Clinica e Chirurgia, Sezione di Endocrinologia, Naples, Italy; [2]Massachusetts General Hospital, Neuroendocrine and Pituitary Tumor Clinical Center, Boston, MA, United States; [3]Omi Medical Center, Kusatsu, Japan; [4]The Medical School, University of Sheffield, Department of Oncology and Metabolism, Sheffield, United Kingdom; [5]CHU de Bordeaux, Bordeaux, France; [6]Medical University of Vienna, Division of Endocrinology and Metabolism, Department of Internal Medicine III, Vienna, Austria; [7]Recordati SpA, Milan, Italy; [8]Recordati AG, Basel, Switzerland; [9]Oregon Health & Science University, Pituitary Center, Departments of Medicine and Neurological Surgery, Portland, OR, United States

Introduction

Osilodrostat decreases cortisol production by inhibiting 11β-hydroxylase, increasing adrenal hormones above the blockade. Here, we describe these effects of osilodrostat and associated adverse events (AEs). The efficacy and safety of osilodrostat in patients with Cushing's disease (CD) were confirmed in the published Phase III, prospective LINC 3 study (NCT02180217).

Methods

137 patients with CD (mUFC >1.5x upper limit of normal) were enrolled in a 48-week (W) core phase including an 8W double-blind, randomised-withdrawal period for eligible patients. 106/113 patients who completed W48 entered an optional extension, ending when all ongoing patients completed $\geq$72W of treatment or discontinued. Testosterone, 11-deoxycortisol, 11-deoxycorticosterone and aldosterone were assessed centrally at baseline and regular intervals by liquid chromatography-tandem mass spectrometry, and dehydroepiandrosterone sulfate (DHEAS) by chemiluminescence immunoassay. Hirsutism (females; rated on a semi-quantitative scale: 0=absent; 1=mild; 2=moderate; 3=severe), blood pressure, oedema and serum potassium were assessed regularly.

Results

Median osilodrostat exposure was 130W (range 1–245); median osilodrostat dose was 7.4 mg/day (range 0.8–46.6). Following an increase during the core phase, mean testosterone levels stabilised in males and decreased towards baseline levels in females during long-term treatment. Of females with baseline, W48 (n=76) and W72 (n=64) assessments, hirsutism score improved from baseline in 26 and 22 patients at W48 and W72, respectively, and remained unchanged in 37 and 33 patients. Mean (SD) DHEAS levels decreased during the core phase to within the normal range, then stabilised during the extension (W48 and W72; females: 1.6 [1.6] and 1.0 [0.9] μmol/l; males: 3.4 [3.3] and 3.0 [3.1] μmol/l). Aldosterone levels also decreased and then stabilised during long-term treatment. Overall, mean potassium levels remained stable throughout the study. AEs related to accumulation of adrenal hormone precursors were reported in 58.4% (n=80/137) of patients, regardless of study drug relationship, and managed with additional therapy in 36.5% (n=50/137) of patients. The most common AEs were hypertension (n=24), peripheral oedema (n=22) and hypokalaemia (n=18), managed with concomitant medication in 17, 6 and 4 patients, respectively. They mostly occurred during the first 26W of treatment (females: 35.5%; males: 49.1%) at different osilodrostat doses (1–60 mg), with no discernable dose-related effect. Few patients discontinued treatment because of these AEs (1.5%; n=2/137).

Conclusions

Adrenal hormone levels frequently change when initiating osilodrostat but stabilise during long-term treatment. AEs associated with these changes are manageable without osilodrostat discontinuation; they should be closely monitored and treatment initiated as needed to achieve optimal patient outcomes.

DOI: 10.1530/endoabs.81.P404

P405

Impact of urinary and late-night salivary cortisol levels on clinical signs of hypercortisolism and quality of life in patients with Cushing's disease treated with osilodrostat

John Newell-Price[1], Maria Fleseriu[2], Rosario Pivonello[3], Richard Feelders[4], Andre Lacroix[5], Richard Auchus[6], Andrea Piacentini[7], Alberto Pedroncelli[8] & Beverly M.K. Biller[9]

[1]The Medical School, University of Sheffield, Department of Oncology and Metabolism, Sheffield, United Kingdom; [2]Oregon Health & Science University, Pituitary Center, Departments of Medicine and Neurological Surgery, Portland, OR, United States; [3]Università Federico II di Napoli, Dipartimento di Medicina Clinica e Chirurgia, Sezione di Endocrinologia, Naples, Italy; [4]Erasmus Medical Center, Department of Internal Medicine, Endocrine Section, Rotterdam, Netherlands; [5]Centre hospitalier de l'Université de Montréal, Montreal, Canada; [6]University of Michigan, Ann Arbor, Division of Metabolism, Endocrinology and Diabetes, Departments of Internal Medicine and Pharmacology, Ann Arbor, MI, United States; [7]Recordati SpA, Milan, Italy; [8]Recordati AG, Basel, Switzerland; [9]Massachusetts General Hospital, Neuroendocrine and Pituitary Tumor Clinical Center, Boston, MA, United States

Background

24-h mean urinary free cortisol (mUFC) and late-night salivary cortisol (LNSC) levels are complementary parameters recommended for screening and monitoring treatment response in patients with Cushing's disease (CD). In the published core period of the Phase III LINC 3 study (NCT02180217), therapy with osilodrostat (potent oral 11β-hydroxylase inhibitor) produced rapid, sustained reductions in mUFC and LNSC alongside improvements in clinical signs of hypercortisolism in patients with CD. Here, we explored these improvements by mUFC and/or LNSC control.

Methods

The core LINC 3 study enrolled 137 adults with CD and mUFC >1.5xULN who received open-label osilodrostat over 48 weeks (W; starting dose: 2 mg twice daily; maximum: 30 mg twice daily); eligible patients were randomised in an 8W placebo-controlled, withdrawal period (W26–34). mUFC (three-sample average; normal 11||138 nmol/24h) and LNSC (single sample; normal $\leq$2.5 nmol/l) were assessed centrally by liquid chromatography-tandem mass spectrometry. Cardiovascular/metabolic-related parameters, physical features (rating: 0=absent; 1=mild; 2=moderate; 3=severe), and CushingQoL and Beck Depression Inventory II (BDI-II) scores were also evaluated. Data were recorded at baseline and regularly until W48. Analyses are presented for patients with both mUFC and LNSC assessments, defined as: both mUFC+LNSC controlled, only mUFC controlled, only LNSC controlled, and both mUFC+LNSC uncontrolled. Control was defined as $\leq$ULN.

Results

Of evaluable patients at baseline (n=87), 74 (85.1%) had both mUFC+LNSC uncontrolled. At W48, 38 patients (54.3%) had both mUFC+LNSC controlled, 21 (30.0%) had only mUFC controlled, 3 (4.3%) had only LNSC controlled, and 8 (11.4%) had both mUFC+LNSC uncontrolled. Mean improvements from baseline to W48 in cardiovascular/metabolic-related parameters were generally greater in patients with both mUFC+LNSC controlled than patients with only mUFC or LNSC controlled or both mUFC+LNSC uncontrolled, respectively: weight, ||5.9, ||3.3, ||2.2, –3.8 kg; systolic blood pressure, ||14.4, ||8.0, ||7.4, ||3.0 mmHg; diastolic blood pressure, –8.6, ||4.8, ||8.2, ||4.0 mmHg; fasting plasma glucose, ||0.9, ||0.3, ||0.8, ||0.6 mmol/l. CushingQoL/BDI-II scores improved from baseline to W48 irrespective of mUFC and/or LNSC control. Patients with both mUFC+LNSC controlled or only mUFC controlled had the greatest proportion with improved physical manifestations of hypercortisolism (facial rubor, striae, fat pads, bruising, hirsutism [females], muscle atrophy).

Discussion

After 48W of osilodrostat treatment, most evaluable patients had both mUFC+LNSC controlled or only mUFC controlled. Improvements in clinical signs of hypercortisolism and health-related quality of life occurred irrespective of mUFC and/or LNSC control; however, improvements were greater in patients with both mUFC+LNSC controlled for some clinical outcomes.

DOI: 10.1530/endoabs.81.P405

P406

GLP-1 receptor agonists stimulate growth hormone release

Ingrid Reppo[1], Keiu Heinla[2], Tuuli Sedman[2] & Vallo Volke[1]
[1]Tartu University Hospital, Department of Endocrinology, Tartu, Estonia; [2]University of Tartu, Tartu, Estonia

The secretion of growth hormone (GH) is under the feedback control of numerous nutritional and endocrine factors. The most widely used endocrine dynamic tests used to diagnose GH deficiency, insulin hypoglycemia test, and glucagon test, are time-consuming and cumbersome both for patients and medical personnel. There is an unmet need for easier to conduct, shorter, and safer diagnostic tests. We and other groups have previously demonstrated that acute administration of glucagon-like peptide-1 receptor agonist (GLP-1RA) moderately stimulated the hypothalamic-pituitary-adrenal axis in healthy volunteers. As GLP-1RAs possess multiple metabolic effects, we hypothesized that they may also affect the secretion of GH. We report here the results from 2 clinical trials of GLP-1 RAs on GH secretion. In a pilot single-group, open-label clinical trial the effect of a single subcutaneous injection of 10 μg exenatide was tested on healthy volunteers ($n=10$). Exenatide elicited a robust increase of GH levels compared to pre-treatment values ($P<0.05$) with the peak occurring around 60-90 minutes in most subjects. Oral semaglutide is the first oral GLP-1 RA available. We next conducted a randomized, placebo-controlled, crossover clinical trial to test the effect of oral semaglutide on GH release. The study included 10 adult healthy volunteers (age 26-47, 5 females, and 5 males). All participants were tested on two occasions that were at least 1 month apart and received randomly oral semaglutide (7 mg) or placebo. Participants were asked to avoid strenuous physical activity the day before testing. Basal fasting ($\geq$ 8 h) blood samples were taken in the morning (8-9 am) after at least 15 minutes of rest. Study medication was taken with up to 40 ml of water. Post-treatment blood samples were drawn 60, 90, 120, 150, 180, and 240 minutes thereafter. The intensity of nausea according to the visual analog scale (0- no nausea, 10 – vomiting) was also registered. The primary endpoint of the study was the change in growth hormone concentration. The effect of oral semaglutide on GH was variable but did induce a clinically significant GH increase in some study subjects. We conclude that GLP-1 RAs hold a promise for a GH stimulation test and further studies are warranted.

DOI: 10.1530/endoabs.81.P406

P407

Endoscopic surgery for acromegaly: results and predictors of outcome from a 22-year experience of a referral Pituitary Centre

Federica Guaraldi[1], Matteo Zoli[1,2], Davide Gori[2], Riccardo Cavicchi[3], Ernesto Pasquini[4], Giacomo Sollini[4], Sofia Asioli[2] & Diego Mazzatenta[1,2]
[1]IRCCS Istituto delle Scienze Neurologiche di Bologna, Pituitary Unit, Bologna, Italy; [2]Alma Mater Studiorum - Università di Bologna, Department of Biomedical and Neuromotor Sciences (DIBINEM), Bologna, Italy; [3]Alma Mater Studiorum - Università di Bologna, School of Medicine - Neurosurgery Residency Program, Bologna, Italy; [4]Ospedale Bellaria, ENT Division, Bologna, Italy

Background
Endoscopic surgery (ES) performed in Pituitary Centers of Excellence (PCOE) represents the gold standard treatment for GH-secreting adenomas. However, rate of cure greatly varies according to definition criteria, follow-up duration, various patient and adenoma features, and surgeon ability.
Study aim
To assess short- (3 month) and long-term ($\geq$1 year) outcome and identify predictors of ES, in a large and homogeneous cohort of acromegaly patients.
Subjects and methods
Clinical, radiological, and histological data at enrolment and follow-up of consecutive patients with GH-secreting adenoma, treated by ES at an Italian PCOE, from 1998 to 2020, were retrospectively analyzed.
Results
291 patients (167 females; mean age at surgery 46.2 $\pm$12.4 years) were included. 195 (67%) had a macroadenoma with invasion of surrounding structures (Hardy-Wilson-Knosp classification) in 92.3% of the cases. According to Trouillas grading, 183 (62.9%) were grade 1a, 35 (12%) 1b, 48 (16.5%) 2a, and 25 (8.5%) 2b. 269 patients were treated by ES and 22 by combined ES-craniotomy. 134 were naïve for treatment; 35 had been treated with surgery; 107 with medical therapy and 21 with radiation therapy. Histological examination revealed 250 GH- (150 sparsely and 99 densely granulated) and 41 GH-PRL-secreting adenomas. At 3-month follow-up, 217 (74.6%) patients presented disease remission, 74 (25.4%) had residual adenoma. At last follow-up (mean duration 67.8$\pm$50.4 months; range 12-240.8), 197 patients (67.7%) were cured; 94 (32.3%) had residual adenoma, controlled by medical therapy in 63.8% of the cases. During follow-up, 9 (3%) patients underwent second surgery, 90 (30.9%) received medical therapy and 4 (1.4%) radiation therapy. At last follow-up, 16 (5.4%) suffered from hypopituitarism, 11 (3.7%) from central diabetes insipidus. Surgical complications included cerebrospinal fluid leak ($n=35$; 12%) and epistaxis ($n=2$;0.7%) . According to multivariate regression analysis, GH <1 μg/l at 48h post-surgery and dense granulation were positive predictors; age <30 years, male gender, tumor invasiveness, Trouillas grade 2b and previous surgery were negative predictors ($P<0.0001$) of short- and long-term outcome. The chance of developing invasive highly proliferative adenoma (2b) was inversely related to age ($P<0.02$; OR 6.6 for age <30 vs. >60 years old). Moreover, 2b adenomas increased the risk of complications ($P<0.005$), independently from gender and histological features.
Conclusions
Our study, performed on the largest available cohort of acromegaly patients, supports the indications of ES in PCOE as first and second line treatment, independently from patient and tumor features, for the overall high chance of cure and very low risk profile.

DOI: 10.1530/endoabs.81.P407

P408

Pituitary adenomas in the elderly may be hiding behind age-related comorbidities

Sandra Pekic Djurdjevic[1,2], Marko Stojanovic[1,2], Emilija Manojlovic Gacic[1,3], Mirjana Doknic[1,2], Dragana Miljic[1,2], Toplica Milojevic[4], Mihailo Milicevic[1,4], Aleksandar Stanimirovic[4], Sandra Banjalic[5], Zvezdana Jemuovic[2], Marija Jovanovic[1,5], Marina Nikolic Djurovic[1,2], Danica Grujicic[1,4], Vera Popovic[1] & Milan Petakov[1,2]
[1]Faculty of Medicine, University of Belgrade, Belgrade, Serbia; [2]Clinic for Endocrinology, Diabetes and Diseases of Metabolism, University Clinical Center, Belgrade, Serbia; [3]Institute of Pathology, Belgrade, Serbia; [4]Clinic for Neurosurgery, University Clinical Center, Belgrade, Serbia; [5]Center for Radiology and Magnetic Resonance Imaging, University Clinical Center, Belgrade, Serbia

Background
Extended life expectancy and increase in neuroimaging availability, lead to increase in incidence of pituitary adenomas (PA) diagnosed after the age of 70. Recognition of PA in the elderly may be challenging and delayed due to symptoms overlapping with aging and comorbidities.
Objective
To investigate character and presenting symptoms of PA in patients diagnosed after the age of 70.
Methods
105 patients (7.9%) with PA diagnosed after the age of 70 (58 males, 55.2%) were identified from the PA database ($n=1332$) of the Department of Neuroendocrinology for the past 17 years. Gender, age at diagnosis, tumor size, presenting signs and symptoms, presence of comorbidities and hyponatremia, functional type of PA and treatment modality were analyzed.
Results
Mean age at diagnosis was 74.5$\pm$0.4 years (range: 70-85). Thirteen patients (12.4%) were older than 80 years at diagnosis. Eighty-three patients (79%) had two or more comorbidities. Nonfunctional PA (NFPA) were significantly more prevalent ($n=85$; 81%) than functional PA ($n=20$; 19%; $P<0.01$). Eleven patients (10.5%) had acromegaly, six (5.7%) had prolactinoma, and three patients had corticotropinoma (2.9%). NFPA patients were older than those with functional PA (75.0$\pm$0.5 vs 72.7$\pm$0.6; $P<0.05$). Macroadenomas ($n=97$; 92.4%) were significantly more prevalent than microadenomas ($n=8$; 7.6%; $P<0.01$). Six patients with microadenoma had acromegaly. PA were significantly larger in males (28.6$\pm$1.8 vs 21.8$\pm$1.8 mm, $P<0.01$). Thirteen patients (12.4%) had gigantic adenomas (>4 cm), nine with NFPA. Prolactinomas (35.6$\pm$3.8 mm) were significantly larger than NFPA (25.8$\pm$1.4 mm) and acromegaly (13.1$\pm$2.9 mm), $P<0.01$. Presenting symptoms included: headache ($n=52$, 49.5%), visual impairment (often misinterpreted as cataract) ($n=46$, 43.8%), and cranial nerve palsies ($n=11$, 10.5%). Twelve patients (11.4%) had hyponatremia due to secondary hypocorticism. Dyslipidemia was diagnosed in 58 patients (55.2%). In 60 (57.1%) PA was detected fortuitously by imaging for reasons unrelated to pituitary disease, during investigation for non-specific neurological symptoms (gait, speech impairment, dizziness, falls, memory impairment, dementia, depression, loss of consciousness, deafness), headache, head trauma, cerebrovascular insults or subarachnoid hemorrhage. Hypopituitarism was confirmed as complete in 45 patients (42.9%), and partial in 15 patients (14.3%). Fifty-two patients (49.5%) underwent transphenoidal surgery, with no

severe complications. Six patients (5.7%) with prolactinomas and six patients (5.7%) with acromegaly were medically treated.
Conclusion
The age-incidence for pituitary tumors shows a typical high risk in the elderly. Nonfunctioning macroadenomas are the most prevalent. Age-related comorbidities led to the late diagnosis of pituitary tumors in most elderly patients which accounted for the pituitary tumor size (macroadenomas in most).

DOI: 10.1530/endoabs.81.P408

P409

Differences of clinical characteristics and treatment of sporadic and MEN-1 related insulinomas

Marta Opalinska[1], Aleksandra Gilis-Januszewska[2], Karolina Morawiec-Sławek[2], Ewelina Rzepka[2], Anna Bogusławska[2], Anna Sowa Staszczak[2] & Alicja Hubalewska-Dydejczyk[2]
[1]University Hospital in Krakow, Department of Endocrinology, Oncological Endocrinology and Nuclear Medicine, Kraków, Poland; [2]Jagiellonian University Medical College, Chair and Department of Endocrinology, Kraków, Poland

Background
Although in most cases insulinomas are small and benign tumors, in about 4% they are malignant, mainly in course of inherited syndromes like MEN1, tubular sclerosis or neurofibromatosis type 1. While in case of benign tumors surgery is usually curative, the metastatic form brings difficulties in managing due to dissemination and the risk of recurring, life-threating, severe hypoglycemias. To elucidate the clinical differences between sporadic and MEN-1 linked insulinoma we review clinical characteristics and treatment in cohort of patients treated in our centre since implementation of electronic database.
Material
Data was reviewed from patients diagnosed with insulinoma managed at our centre from 2015 to 2021 year.
Results
There were 19 cases of insulinomas (9 women and 10 men). In 6 (32%) cases the mutation in menin gene were confirmed. The median age at diagnosis in the whole group was 58 years, (range 16-87 years) in case of sporadic and MEN-1 related insulinoma 69 years (range 29-87 years) and 40 years (range 6-79 years) respectively. In case of MEN-1 related insulinoma at diagnosis 5/6 patients had primary hyperparathyroidism (PHP) in one case it was confirmed 11 years after insulinoma diagnosis. None of patients with negative MEN-1 gene mutations had PHP, 2 out of 13(13%) had dissemination of insulinoma at diagnosis. Median of Ki67 in case of sporadic insulinoma was 2% range (1-12%) and in case of MEN-1 related insulinoma 2% range (1-5%). In 3 cases (50%) of MEN-1 related insulinoma there was more than one lesion of neuroendocrine characteristic in pancreas. In 6 out of 19 cases (32%) insulinoma was disseminated at diagnosis, in 23% cases (3 out of 13) of sporadic and in 50% (3 out of 6) cases of MEN-1 related insulinoma. All patients with disease limited to pancreas were treated radically by surgery (in 3cases by tumor enucleation, in 8 cases with partial or total pancreatodudenectomy). One of MEN-1 patient had recurrence of hypoglycemia after surgery due to appearance of new insulinoma lesion. The patients with dissemination were treated, due to symptomatic hypoglycemia, with combination of diazoxide, somatostatin analogues and PRRT. 5 out of 6 patients with insulinoma in course of MEN-1 mutation are still alive), one died because of coexisting pancreatic cancer.
Conclusion
There are clinical differences between the course of sporadic and MEN-1-associated insulinoma. In the case of disseminated disease, there is often a need for multi-drug treatment to delay progression and prevent episodes of severe hypoglycemia.

DOI: 10.1530/endoabs.81.P409

P410

Favorable liver safety profile of the selective glucocorticoid receptor modulator relacorilant in healthy and hepatically impaired adults and in patients with cushing syndrome

Andreas G. Moraitis, Joseph Custodio & Iulia Cristina Tudor
Corcept Therapeutics, Menlo Park, United States

Background
Relacorilant is a highly selective glucocorticoid receptor (GR) modulator in development for the treatment of endogenous Cushing syndrome (CS). Unlike the GR antagonist mifepristone, relacorilant lacks affinity for the progesterone and other receptors. In a phase 2 study in patients with CS (Pivonello *et al*, 2021), relacorilant provided clinically meaningful changes in several cortisol-excess-related comorbidities, including hypertension and hyperglycemia, without undesirable antiprogesterone effects or drug-induced hypokalemia. Four clinical studies of relacorilant in patients with CS are ongoing: GRACE (NCT03697109), a phase 3 trial enrolling patients with endogenous CS of all etiologies; GRADIENT (NCT04308590), a phase 3 trial focusing on hypercortisolism due to adrenal adenomas or hyperplasia; a phase 2/3 long-term extension trial (NCT03604198); and a phase 1b trial in patients with adrenocortical carcinoma and glucocorticoid excess (NCT04373265). Here, we report data from open-label phase 1 and 2 studies of relacorilant in healthy and hepatically impaired adults and in adult patients with CS.
Methods
Data from 3 studies are reported: a study including subjects with hepatic impairment in which 9 subjects with moderate hepatic impairment (Child-Pugh Class B) and 9 matched controls with normal hepatic function received relacorilant (300 mg QD) for 10 days; a phase 1 fixed-sequence drug-drug interaction study (NCT03512548) in which 28 healthy subjects received relacorilant (300 mg QD) for 10 days followed by 10 days of relacorilant (300 mg QD) + itraconazole (200 mg QD); and a phase 2 study in which 35 patients with endogenous CS received relacorilant (100–400 mg QD) for up to 16 weeks (NCT02804750).
Results
While relacorilant is eliminated primarily hepatically, no apparent difference in relacorilant pharmacokinetics in subjects with moderate hepatic impairment vs matched controls was observed, with relacorilant exposures largely overlapping across both groups. Reductions in liver function tests (LFTs) were also observed in this study. In healthy adults receiving relacorilant followed by relacorilant + itraconazole (an agent with reported liver toxicity), a similar trend toward reduced LFTs was seen throughout the study. In the phase 2 study in patients with CS, reductions in LFTs were also observed, including normalization of LFTs in some patients with abnormal values at baseline.
Conclusions
These results suggest that relacorilant has a favorable liver safety profile, including a trend toward improved LFTs in volunteers and patients with normal and abnormal liver function. The hepatic impairment study results support relacorilant use without dose adjustment in patients with moderate hepatic impairment.

DOI: 10.1530/endoabs.81.P410

P411

Independent injection vs healthcare-setting administration of somatostatin analogues: A systematic literature review

Cesar Luiz Boguszewski[1], Marta Korbonits[2], Audrey Artignan[3], Almudena Martín García[4], Aude Houchard[5], Antonio Ribeiro-Oliveira[6] & Wouter W de Herder[7]
[1]Federal University of Parana, Department of Internal Medicine, Curitiba, Brazil; [2]Barts and the London School of Medicine and Dentistry, Department of Endocrinology, London, United Kingdom; [3]Costello Medical, Cambridge, United Kingdom; [4]Patient author; [5]Ipsen, Boulogne-Billancourt, France; [6]Ipsen, Cambridge, United States; [7]Erasmus MC, Department of Internal Medicine, Rotterdam, Netherlands

Background
A systematic literature review (SLR) was conducted to assess the use of independent injections (self/partner/home-administered) as an alternative to healthcare-setting injections for chronic diseases. The primary objective was to identify studies reporting on independent injection of somatostatin analogues (SSAs). Comparative evidence on independent injection of other medications was examined as a secondary objective.
Methods
MEDLINE/Embase/the Cochrane Library were searched for records published between January 2001–September 2021, using terms for independent injection. Congresses (2019–2021) and SLR bibliographies were also hand-searched. Abstracts/full-text publications were reviewed by two independent reviewers. Studies were eligible if they reported on efficacy/effectiveness, adherence, safety, economic or patient-reported outcomes in populations receiving independent injections of SSAs (primary objective) or other monthly subcutaneous treatments (secondary objective). Studies investigated under the secondary objective were required to include a comparator in the healthcare setting.
Results
3.430 unique records were screened, of which 12 studies, comprising
18–3,921 patients, were included, all reporting on SSAs (lanreotide or octreotide).

No studies were identified to support the secondary objective. In four studies reporting comparative efficacy/effectiveness, independent injection was associated with equal/greater disease control in patients with acromegaly and neuroendocrine tumors (NETs) compared with healthcare-setting administration. Treatment adherence, defined as successful injection administration, was shown in 74%–93% of patients with acromegaly receiving independent injections in two studies, both assessing lanreotide. A higher proportion of injection-site reactions was observed in patients self-injecting lanreotide compared with partner injections (19% vs 2%, $P<0.05$). Two studies reported non-serious adverse events, which were rare in both the independent and healthcare-administration settings. Preference for independent injection varied between studies/disease indications, ranging from 4%–100% across five studies, with patients citing increased autonomy and convenience for preference over healthcare-setting administration. Lower anxiety, perceived safety, and the ability to communicate with a healthcare provider (HCP) were factors underlying a preference for healthcare-setting administration. Self- or partner-injection was associated with economic savings compared with the healthcare setting across five studies, including nurse, travel, and administration time.

Conclusions

Independent injection is similar to the healthcare setting regarding efficacy/effectiveness, adherence, and safety outcomes. Patient preferences for administration setting varied and may reflect the need for improved patient education/training, or home care program support for those where independent injection is a preferred/suitable option.

Self- or partner-injection also provided cost savings. Our findings provide a basis to understand outcomes related to independent injection and empower patients to discuss optimal treatment choices with their HCP.

DOI: 10.1530/endoabs.81.P411

P412

Sodium alterations impair the long-term prognosis of hospitalized patients with COVID-19 pneumonia: hospital readmissions and mortality rates after a 18-month follow-up

Marianna Martino, Nairus Aboud, Michele Perrone, Paolo Falcioni, Giulia Giancola, Alessandro Ciarloni, Gianmaria Salvio, Francesca Silvetti, Augusto Taccaliti & Giorgio Arnaldi

Università Politecnica delle Marche, Division of Endocrinology and Metabolic Diseases AOU Ospedali Riuniti Ancona; Department of Clinical and Molecular Sciences (DISCLIMO) UNIVPM, Ancona, Italy

Background

Dysnatremia is common in hospitalized patients, often worsening the prognosis in pneumopathies and critical illnesses, such as COVID-19. Here, hyponatremia is an indicator of pulmonary involvement, while hypernatremia is associated with worse assistance outcomes, particularly when resulting from an overcorrected hyponatremia. Longer hospitalizations, readmissions after discharge and higher short- and long-term mortality rates have been observed in acute patients experiencing sodium abnormalities.

Objective and methods

117 patients hospitalized for COVID-19 between 1st March and 30th April 2020 and participating the "EPISODICO" study [1] were followed-up for 18 ± 4 months. The proportion of emergency room or hospital readmissions (Ancona University Hospital) for all causes, the mortality rate after recovery from COVID-19 and their association with recurrent sodium alterations were assessed.

Results

Of the 97 discharged patients (70 males, 62 ± 12 years), almost 30% were readmitted to the emergency room or any hospital department at least once. At readmission, 10% patients had hyponatremia, 14% had hypernatremia, whereas 7% patients experienced both disorders ("mixed dysnatremia") by the end of follow-up. Gender, age, clinical and biochemical features of their previous hospitalization for COVID-19 were similar between readmitted and non-readmitted patients, the former having overlapping sodium levels in both hospitalizations. Considering the whole "EPISODICO" cohort, mortality rate at the end of follow-up was 25%, since twenty patients died in the "EPISODICO" study and further nine patients died during follow-up: of them, 4 died as outpatients in 1-11 months after discharge, and 5 as inpatients in 3-17 months after the first discharge. Last available sodium levels were significantly lower in dead patients as compared to survivors (137 ± 11 vs 141 ± 3 mmol/l, $P=0.026$). Death occurred in 2/3 patients having hyponatremia at readmission and in 100% patients encountering mixed dysnatremia. When only "EPISODICO" participants with sodium alterations during their COVID-19 hospitalization were selected, readmission rate was 26% and mortality rate at the end of follow-up was 28%.

Conclusions

Similarly to what happens in other acute medical conditions, COVID-19-related sodium alterations are frequently associated with hospital readmissions and long-term mortality. The worst outcomes involve patients whose sodium abnormalities recur after discharge, particularly hyponatremia at the time of hospital readmission and mixed dysnatremia occurring during hospital stay.

References

[1] Martino M *et al*. "Sodium alterations impair the prognosis of hospitalized patients with COVID-19 pneumonia" Endocr Connect. 2021 Oct 15;10(10):1344-1351. doi: 10.1530/EC-21-0411.

DOI: 10.1530/endoabs.81.P412

P413

Osilodrostat provides sustained clinical benefits and improves health-related quality of life in patients with cushing's disease: results from the Phase III LINC 4 study

Richard Feelders[1], Monica Gadelha[2], Marie Bex[3], Przemysław Witek[4], Zhanna Belaya[5], Yerong Yu[6], Adina F. Turcu[7], Anthony Heaney[8], Richard Auchus[9], Andrea Piacentini[10], Alberto Pedroncelli[11] & Peter J. Snyder[12]

[1]Erasmus Medical Center, Department of Internal Medicine, Endocrine Section, Rotterdam, Netherlands; [2]Medical School and Hospital Universitário Clementino Fraga Filho, Universidade Federal do Rio de Janeiro, Neuroendocrinology Research Center, Endocrinology Section, Rio de Janeiro, Brazil; [3]University Hospitals Leuven, Department of Endocrinology, Leuven, Belgium; [4]Medical University of Warsaw, Department of Internal Medicine, Endocrinology and Diabetes, Warsaw, Poland; [5]Endocrinology Research Centre, Department of Neuroendocrinology and Bone Disease, Moscow, Russian Federation; [6]West China Hospital of Sichuan University, Department of Endocrinology and Metabolism, Chengdu, China; [7]University of Michigan, Ann Arbor, Division of Metabolism, Endocrinology and Diabetes, Ann Arbor, MI, United States; [8]University of California, Los Angeles, Division of Endocrinology, Diabetes and Metabolism, Department of Medicine, Los Angeles, CA, United States; [9]University of Michigan, Ann Arbor, Division of Metabolism, Endocrinology and Diabetes, Department of Pharmacology, Ann Arbor, MI, United States; [10]Recordati SpA, Milan, Italy; [11]Recordati AG, Basel, Switzerland; [12]Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, United States

Background

Cushing's disease (CD) is associated with hypercortisolism-induced cardiovascular morbidity and mortality and impaired patient quality of life (QoL). We report long-term effects of osilodrostat (potent 11β-hydroxylase inhibitor) on cardiovascular/metabolic-related risk factors, physical features of hypercortisolism and QoL in CD patients following the core and extension phases of the LINC 4 study (NCT02697734).

Methods

LINC 4 comprised a 12-week (W), randomised, double-blind, placebo-controlled period, 36W of open-label osilodrostat, and an optional extension in adults with CD and (mUFC >1.3x upper normal limit). Dose adjustments were permitted based on efficacy/tolerability (open-label range, 1–30 mg bid). Cardiovascular/metabolic-related parameters, physical features of hypercortisolism (rating: 0 = absent;1 = mild;2 = moderate;3 = severe), and CushingQoL scores were evaluated at core baseline, every 2, 4, 12 or 24W (depending on study phase/parameter) and at extension end-of-treatment (EOT). Change from baseline is provided for patients with assessments at core baseline, W48 and EOT.

Results

Of 65 patients completing W48, 60 entered the extension. Median (range) osilodrostat exposure from core baseline to study end: 87.1 (2–127) W; median (IQR) average dose: 4.6 (3.7–9.2) mg/day. Mean changes (95%CI) in cardiovascular/metabolic-related parameters from core baseline to W48 and EOT, respectively, included decreases in systolic (-9.7 [$-14.9,-4.6$] and -12.4 [$-17.4,-7.4$] mmHg; baseline: 131.5 mmHg) and diastolic (-4.2 [$-7.3,-1.2$] and -5.6 [$-8.9,-2.4$] mmHg; baseline 87.5 mmHg) blood pressure, fasting plasma glucose (-3.1 [$-6.8,0.6$] and -3.5 [$-8.5,1.4$] mg/dl; baseline: 95.3 mg/dl) and cholesterol (-0.5 [$-0.8,-0.2$] and -0.6 [$-0.9,-0.3$] mmol/l; baseline: 5.5 mmol/l). Improvements (mean change [95%CI]) from core baseline to W48 and EOT occurred for weight (||4.3 [||5.9,||2.6] and ||6.8 [||8.8,||4.8] kg; baseline: 78.3 kg) and waist circumference (||4.5 [||6.0,||3.1] and ||7.6 [||9.6,||5.6] cm; baseline: 102.8 cm). Physical features of hypercortisolism improved (severity reduced) or remained stable from core baseline to EOT in most patients (respectively): ecchymosis (21% [$n=10/48$], 79% [$n=38/48$]); striae (26% [$n=12/46$], 72% [$n=33/46$]); hirsutism

(females: 29% [$n=11/38$], 61% [$n=23/38$]); muscle weakness (33% [$n=16/49$], 61% [$n=30/49$]); facial rubor (48% [$n=23/48$], 46% [$n=22/48$]); central obesity (55% [$n=27/49$], 37% [$n=18/49$]); fat pads (dorsal: 58% [$n=28/48$], 31% [$n=15/48$]; supraclavicular: 65% [$n=32/49$], 35% [$n=17/49$]). CushingQoL score improved from core baseline to W48 and EOT (mean change [95%CI]: 12.0 [8.2.15.9] and 17.1 [12.5.21.7]; baseline: 51.8).
Conclusion
Alongside cortisol control, most cardiovascular/metabolic-related parameters continued to improve during long-term osilodrostat treatment. Additionally, most physical features of hypercortisolism, including hirsutism, improved or remained stable, and CushingQoL score improved. Osilodrostat is an effective treatment that may alleviate disease burden for many CD patients.

DOI: 10.1530/endoabs.81.P413

P414

Predictive factors of somatostatin receptor ligand response in acromegaly – a prospective study

Mirela Diana Ilie[1,2], Antoine Tabarin[3], Alexandre Vasiljevic[4], Bonneville Jean-Francois[5], Lucile Moreau-Grangé[6], Franck Schillo[7], Brigitte Delemer[8], Anne Barlier[9], Dominique Figarella-Branger[10], Ségolène Bisot-Locard[11], Alexandre Santos[11], Philippe Chanson[12] & Gerald Raverot[4]
[1]Claude Bernard University Lyon 1, Villeurbanne, France; [2]C.I. Parhon National Institute of Endocrinology, Bucureşti, Romania; [3]Hospital Center University De Bordeaux, Bordeaux, France; [4]Group Hospital Is - Hcl, Bron, France; [5]Hospital Center Universitaire De Liège, Luik, Belgium; [6]Hospital Center University De Rouen, Rouen, France; [7]Centre Hospitalier Régional Universitaire de Besançon, Besançon, France; [8]CHU of Reims - Maison Blanche Hospital, Reims, France; [9]Conception, Marseille, France; [10]CHU Timone, Marseille, France; [11]Novartis Pharma, Rueil-Malmaison, France; [12]Bicetre Hospital, Le Kremlin-Bicêtre, France

Context
Somatostatin receptor ligands (SRLs) are the cornerstone medical treatment of acromegaly, however many patients remain uncontrolled under SRLs. Well-established predictive markers of response are needed.
Objective
We aimed to explore the relationship between responsiveness to SRLs, on one hand, and somatostatin (SST)2A and 5 receptor expression, adenoma granulation, and T2-weighted MRI signal intensity (T2WSI), on the other hand.
Design
Multicentric, prospective, observational cohort study, conducted in France.
Methods
Forty-nine naive patients with active acromegaly following surgery were treated with octreotide (Group 1; $n=47$), or pasireotide if also uncontrolled under first-generation SRL (Group 2; $n=9$). Data was collected at baseline, month 3 and 6. Biochemical measurements, immunohistochemistry studies, and MRI readings were centralized.
Results
In Group 1, IGF-I decrease from baseline to month 6 positively correlated with SST2A immunoreactive score (IRS), $P=0.01$. Densely granulated/intermediate adenomas had greater IGF-I and GH decrease under octreotide than sparsely granulated adenomas ($P=0.02$ and$P=0.006$, respectively), and expressed greater levels of SST2A ($P<0.001$), coupled with lower levels of SST5 ($P=0.004$). T2WSI changed between the preoperative MRI and month 6-MRI in half of the patients. SST5 IRS was higher in hyperintense than in hypointense adenomas (preoperative MRI), $P=0.04$. Most sparsely granulated and most hyperintense adenomas expressed high SST5 levels.
Conclusion
We prospectively confirm that SST2A and adenoma granularity are good predictors of response to octreotide, and that SST5 is not. We propose the IRS for scoring system harmonization. The MRI sequences must be optimized in order to be able to use the T2WSI as a predictor of response to treatment.

DOI: 10.1530/endoabs.81.P414

P415

Effects of somapacitan on glucose metabolism in adults with GH deficiency

Gudmundur Johannsson[1], Beverly MK Biller[2], Hidenori Fukuoka[3], Ken Ho[4], Michael Højby Rasmussen[5], Navid Nedjatian[6], Claus Sværke[5], Kevin CJ Yuen[7] & Yutaka Takahashi[8]
[1]University of Göteborg and Sahlgrenska University Hospital, Göteborg, Sweden; [2]Massachusetts General Hospital and Harvard Medical School, Neuroendocrine Unit, Boston, United States; [3]Kobe University Hospital, Division of Diabetes and Endocrinology, Kobe, Japan; [4]Garvan Institute of Medical Research, Darlinghurst, Australia; [5]Novo Nordisk A/S, Global Development, Søborg, Denmark; [6]Novo Nordisk Health Care AG, Global Medical Affairs - Rare Endocrine Disorders, Zurich, Switzerland; [7]Barrow Neurological Institute and St. Joseph's Hospital and Medical Center, University of Arizona College of Medicine and Creighton School of Medicine, Barrow Pituitary Center, Phoenix, United States; [8]Nara Medical University, Department of Diabetes and Endocrinology, Nara, Japan

Somapacitan is a once-weekly, long-acting growth hormone (GH) derivative approved for the treatment of adult GH deficiency (AGHD). Our objective was to evaluate the effects of somapacitan on glucose metabolism compared with daily GH or placebo in patients with AGHD using data from three previously published phase 3 trials: REAL 1 (NCT02229851), REAL 2 (NCT02382939) and REAL Japan (NCT03075644). REAL 1 was a randomised, placebo-controlled (double-blind) and active-controlled (open-label) trial in GH-naïve patients, who received somapacitan ($n=120$), daily GH ($n=119$) or placebo ($n=61$) for 34 weeks (main phase). In a subsequent 52-week extension (86 weeks of treatment in total), patients receiving somapacitan continued with somapacitan ($n=114$), patients receiving daily GH were re-randomised to receive either somapacitan ($n=51$) or daily GH ($n=52$), and patients receiving placebo were switched to somapacitan ($n=55$; not included in this analysis). REAL 2 and REAL Japan were randomised, open-label, active-controlled trials in patients previously treated with daily GH. In REAL 2, patients received somapacitan ($n=61$) or daily GH ($n=31$) for 26 weeks. In REAL Japan, patients received somapacitan ($n=46$) or daily GH ($n=16$) for 52 weeks. In these *post hoc* analyses, the absolute or relative change from baseline between treatments for HbA1c, fasting plasma glucose (FPG), fasting serum insulin and index of insulin resistance (HOMA-IR) was explored. In treatment-naïve patients (REAL 1), there were no statistically significant ($P<0.05$) differences between somapacitan and placebo for any glucose-related endpoints at week 34 (main phase). No statistically significant differences in HbA1c were observed between somapacitan and daily GH at week 34 or week 86 (main phase plus extension). Transient differences were seen at week 34 between somapacitan and daily GH (with higher values reported for daily GH) for FPG (estimated treatment difference [95% CI]: –0.16 mmol/l [–0.30; –0.03]), fasting serum insulin (estimated treatment ratio [ETR] [95% CI]: 0.85 [0.73; 0.99]) and HOMA-IR (ETR [95% CI]: 0.80 [0.69; 0.94]); these differences were not seen at week 86. In previously treated patients (REAL 2, REAL Japan and REAL 1 patients who received daily GH in the main phase and were re-randomised for the extension), no statistically significant differences were seen between treatments for any glucose-related endpoints. No new cases of diabetes were reported in somapacitan-treated patients in these trials. In conclusion, somapacitan was similar to daily GH and had no clinically relevant adverse effects on glucose metabolism in treatment-naïve or previously treated patients with AGHD in these phase 3 trials.

DOI: 10.1530/endoabs.81.P415

P416

Cabergoline monotherapy in acromegaly – a multicenter, retrospective, cohort study of non-irradiated patients using current criteria for disease control

Sandrine A Urwyler[1,2,3], Irene Samperi[1,2,3], Kirstie Lithgow[1,2,3], Akash Mavilakandy[4], Mike Matheou[5], John Ayuk[1,2,3], Karin Bradley[6], Aparna Pal[5], Narendra Reddy[4] & Niki Karavitaki[1,2,3]
[1]Institute of Metabolism and Systems Research, College of Medical and Dental Sciences, University of Birmingham, Birmingham, United Kingdom; [2]Centre for Endocrinology, Diabetes and Metabolism, Birmingham Health Partners, Birmingham, United Kingdom; [3]Queen Elizabeth Hospital, University Hospitals Birmingham NHS Foundation Trust, Department of Endocrinology, Birmingham, United Kingdom; [4]Department of Diabetes and Endocrinology, University Hospitals of Leicester NHS Trust, Leicester Royal Infirmary, Leicester, United Kingdom; [5]Oxford Centre for Diabetes, Endocrinology and Metabolism, Oxford University Hospitals NHS Foundation Trust, Oxford, United Kingdom; [6]Department of Endocrinology, Bristol Royal Infirmary, University Hospitals Bristol and Weston NHS Foundation Trust, Bristol, United Kingdom

Background
Dopamine agonists (DA) are included in the management algorithm of acromegaly. Studies on cabergoline monotherapy report IGF-1 normalisation in

between 0% and 100% of the patients during treatment periods ranging between 2.6 and 24 months. However, in many of these studies, previous radiotherapy is a confounding factor. Furthermore, real world data applying the current disease control criteria (normal IGF-1 and GH < 1 mg/l) are not available. The aim of this study was to investigate the efficacy and safety profile of cabergoline monotherapy in non-irradiated patients with uncontrolled acromegaly.
Patients and methods
In this multicenter, retrospective cohort study, non-irradiated patients offered cabergoline monotherapy for uncontrolled acromegaly were identified from the registries of four UK Pituitary centers (Birmingham, Bristol, Leicester and Oxford). Clinical, laboratory and imaging data were collected and analyzed.
Results
Sixty-nine patients were included. Median age at diagnosis of acromegaly was 50.5 years (range 28-78), 34.7% of the patients were females and 21.7% of the tumours were prolactin-co-secreting. Prior to starting cabergoline, IGF-1 levels were 2.13 (median) times the upper limit of normal (ULN) (range 1.02-8.54). Median duration of cabergoline treatment was 23 months (3-252). Normal IGF-1 was achieved in 31.8% (22/67) of the patients within a reported median interval of 12.5 months (2-84). Median weekly cabergoline dose at most recent review was 2.5 mg (0.25-4) in the responders, and 3 mg (0.25-7) in the non-responders ($P = 0.39$). On univariate regression analysis, IGF-1 normalisation was significantly related with the presence of a prolactin co-secreting adenoma (B 1.38, $P = 0.030$) and lower pre-cabergoline IGF-1 ULN levels (B -0.73, $P = 0.015$). ROC analysis showed that IGF-1 < 1.55 ULN had sensitivity 50% and specificity 85% in predicting achievement of normal IGF-1; sensitivity and specificity for IGF-1 < 1.97 ULN were 75% and 67.5%, respectively (AUC 0.760). GH < 1 mg/l was found in 25% (14/56) the patients, whereas 16.1% (9/56) had achieved both GH and IGF-1 criteria. Side effects were recorded in 5 patients (nausea $n = 2$, nasal congestion $n = 1$, dizziness/blurred vision/-abdominal pain/weakness $n = 1$, hair loss $n = 1$).
Conclusions
In this large cohort of non-irradiated patients with acromegaly, cabergoline normalised IGF-1 in 32% of the cases and dose did not differ between responders and non-responders; efficacy of treatment was associated with the presence of prolactin co-secreting adenoma and pre-cabergoline IGF-1 ULN levels. Achievement of both optimal GH and IGF-1 levels was seen in only 16% of the patients.

DOI: 10.1530/endoabs.81.P416

P417

Terlipressin induced acute severe hyponatremia

Begoña Pla Peris, Icíar Castro de la Vega, Mayet Roxana Padilla Segura, Esther Serisuelo Meneu, Pablo Abellán Galiana, Javier Maravall, Susana Pérez Naranjo, Margarita González Boillos & Agustín Ángel Merchante Alfaro
Hospital General Universitario de Castellón, Spain

Introduction
Terlipressin is a non-selective vasopressin analogue used in patients with decompensated cirrhosis, gastrointestinal haemorrhage or hepatorenal syndrome. It directly binds to V1 receptors improving circulatory volume by causing splanchnic vasoconstriction and portal hypertension inhibition, and has a full V2 receptor agonism in the collecting duct. In consequence, it increases reabsorption of water and can lead to a decrease in plasma osmolality and hyponatremia. Hyponatremia induced by Terlipressin is uncommon (1/1.000 to <1/100, Summary of Product Characteristics). Maximal plasma levels are reached after 1-2h following iv administration and metabolic elimination takes place within a 4-6 h period.
Case Presentation
We present the case of a 46-year-old man admitted to hospital with cirrhosis needing liver resection for liver metastases from colorectal cancer. Patient was treated with 1 mg of terlipressin intravenously every 6 h and isotonic intravenous maintenance fluids (0.9% NaCl) 1000 ml every 24 h. 36 h later he presented with lethargy, confusion, nausea and vomiting. Laboratory findings showed severe hyponatremia (108 mmol/l [134-145]) with low osmolality (231 mOsm/kg [280-305], and normal blood glucose levels (100 mg/dl). He was euvolemic at physical examination. Natremia levels 36 h before the start of terlipressin treatment were 132 mmol/l. Urinary osmolarity and urinary sodium were not available at this moment, given the priority of correcting the symptomatic severe hyponatremia. Treatment with intravenous infusion of hypertonic saline was started and terlipressin was discontinued, sodium levels returning to normal over 48 h (132 mmol/l [134-145]).
Conclusion
Hyponatremia induced by Terlipressin is uncommon and can develop rapidly. It is reversible with cessation of therapy and requires careful consideration. This case is an illustration of this undesirable effect. As endocrinologists, we must be familiar with terlipressin pharmacokinetic properties. Sodium levels and fluid balance should be monitored intensively and immediately after first terlipressin dose.

DOI: 10.1530/endoabs.81.P417

P418

Is there a difference in clinical skills gained between healthcare professionals of high- and low and middle-income countries with online simulation-based learning?

Anisah Ali[1], Kashish Malhotra[2], Dengyi Zhou[1], Tamzin Ogiliev[3], Carina Synn Cuen Pan[1], Emily Warmington[1], Wentin Chen[1], Harjeet Kaur[1], Jameela Sheikh[1], Pavithra Sakthivel[1], Rachel Nirmal[1], Vina Soran[1], Zakee Abdi[4], Isabel Allison[1], Simran Piya[5], Nia Evans[6], Thia Hanania[1], Dwi Delson[7], Eka Melson[8,9], Meri Davitadze[10], Punith Kempegowda[9,11] & Simba Simulation[9]
[1]University of Birmingham, College of Medical and Dental Sciences, Birmingham, United Kingdom; [2]Dayanand Medical College and Hospital, Punjab, India; [3]Lancaster University Medical School, Lancaster, United Kingdom; [4]Medical University of Plovdiv, Plovdiv, Bulgaria; [5]University of Edinburgh, College of Medicine and Veterinary Medicine, Edinburgh, United Kingdom; [6]Royal Glamorgan Hospital, Cwm Taf Morgannwg University Health Board, Rhondda Cynon Taff, United Kingdom; [7]University of Dundee, School of Medicine, Dundee, United Kingdom; [8]NHS Tayside, Ninewells Hospital, Dundee, United Kingdom; [9]Institute of Metabolism and Systems Research, University of Birmingham, Birmingham, United Kingdom; [10]Georgian-American Family Medicine Clinic, 'Medical House', Tbilisi, United Kingdom; [11]University Hospitals Birmingham NHS Foundation Trust, Queen Elizabeth Hospital, Birmingham, United Kingdom

Background
There is a differential clinical learning opportunity for healthcare professionals in low- and middle-income countries (LMICs) compared to high-income countries (HICs). Barriers to learning include cost, time and accessibility. Simulation via Instant Messaging - Birmingham Advance (SIMBA) is a free virtual simulation-based model aimed at improving clinicians' professional development, without compromising patient safety. The study compared the impact of SIMBA in LMICs and HICs, on participants' professional development and learning.
Methods
Between May 2020 and October 2021, 16 SIMBA sessions were conducted. Participants interacted with moderators over WhatsApp to solve anonymised real-life clinical scenarios. Following simulation, interactive Zoom sessions were led by experts in relevant fields, allowing participants to ask any questions regarding the cases. Participants completed pre- and post-SIMBA surveys as part of their activity on the day of simulation. They were grouped based on their country of residence as HICs and LMICs based on the 2022 World Bank Report to compare their performance, perceptions and improvements in core competencies as defined by the Accreditation Council of Graduate Medical Schools using the Chi-square test. Thematic analysis of open-ended questions was also performed.
Results
In total, 462 participants completed both the pre- and post-SIMBA surveys, of which 29.7% ($n = 137$) were from LMICs. While participants from HICs reported better knowledge on patient management (LMIC: 77.4% vs HIC: 86.5%;$P = 0.01$), those from LMIC reported higher improvement in professionalism (LMIC: 41.6% vs HIC: 31.1%;$P = 0.02$). Both groups reported similar gains in patient care (LMIC: 51.8% vs HIC: 57.2%;$P = 0.28$), systems-based practice (LMIC: 56.9% vs HIC: 47.1%;$P = 0.052$), practice-based learning (LMIC: 72.3% vs HIC: 65.5%;$P = 0.15$), communication skills (LMIC: 31.4% vs HIC: 25.8%;$P = 0.22$), applying simulated topics to their practice ($P = 0.266$), engagement ($P = 0.197$), and overall quality of the teaching session ($P = 0.101$) . In thematic analysis, the major strengths of SIMBA over traditional methods were providing individualised, structured, and engaging sessions.
Conclusion
SIMBA improves healthcare professionals' clinical competencies from both LMICs and HICs demonstrating that SIMBA can provide equivalent teaching experiences irrespective of country of residence. Furthermore, international accessibility due to the virtual nature of SIMBA shows potential for global scalability, especially in LMICs where it can help to provide standardised medical training and steer future global health education policy development.

DOI: 10.1530/endoabs.81.P418

P419

Obstructive sleep apnea syndrome (OSAS) in acromegaly: does the gender matter?

Giacomo Pio[1], Tiziana Feola[2,3], Liliya Rostomyan[4], Giuseppe Vitrani[2], Patrick Petrossians[4], Albert Beckers[4], Andrea Romigi[2] & Marie-Lise Jaffrain-Rea[2,5]
[1]University of L 'Aquila, Department of Biotechnological and Applied Clinical Sciences; [2]Neuromed IRCCS, Pozzilli, Italy; [3]Sapienza University of Rome, Department of Experimental Medicine; [4]Centre Hospitalier Universitaire de Liège, Department of Endocrinology; [5]University of L'Aquila, Department of Biotechnological and Applied Clinical Sciences, L'Aquila, Italy

Obstructive sleep apnea syndrome (OSAS) is a frequent cardiovascular risk factor in acromegaly. We aimed to retrospectively evaluate sex-related differences in OSAS characteristics and indications of non-invasive ventilation.
Patients and Methods
Thirty-nine adult patients (16 F, 23 M) from two European centers were studied by home sleep apnea test (HSAT) or polysomnography (PSG). OSA was defined by an apnea-hypopnea index (AHI) $\geq$5/h and analyzed according to age, gender, disease activity, obesity, diabetes mellitus, hypertension and nocturnal continuous positive airway therapy (CPAP). Categorical variables were considered in all cases, whereas, except for pre/post-ventilation AHI, sleep parameters were used in cases defined according to the last International Classification of Sleep Disorders (ICSD-3, 2014) ($n=33$). Data are expressed as median (range) and statistical analysis based on non-parametric tests.
Results
The median age at diagnosis of acromegaly and at PSG were 48.5 and 52.0 yrs respectively, 25/39 patients (64.1%) had an active disease. OSAS was diagnosed in 36/39 patients (92%) and classified as mild/moderate ($\geq$5 AHI$<$30) in 12/39 (30.8%) and severe (AHI$\geq$30) in 24/39 patients (61.3%). Severe OSAS tended to be more frequent in M (17/23 v*s* 7/16 F, $P=0.057$), who were more frequently advised to start CPAP therapy (21/23 vs 9/15 F, $P=0.037$). Males had a significantly higher BMI (32.6 vs 28.4 kg/m^2 $P=0.017$) and higher prevalence of hypertension (21/23 vs 8/16, $P<0.004$) despite similar age, GH and IGF1 ULN at the time of diagnostic HSAT/PSG. Overall, AHI was significantly correlated with patients age ($\rho=0.36$, $P=0.023$) but not with BMI, and similar in diabetic and non-diabetic patients. By univariate logistic regression, hypertension was the only independent predictor of severe OSAS ($P=0.018$). Nocturnal cardiorespiratory monitoring. Sleep evaluation was also obtained on CPAP therapy in 17 patients (6 F, 11 M), out of which 10 (58.8%) had controlled acromegaly (3 F, 7 M). A significant decrease in AHI (median – 90.4%, $P<0.001$) was observed in all but one patient. OSAS was controlled in 11/17 patients (64.7%; 5/6 F, 6/11 M), including 8/12 with severe OSAS (66.7%), and regardless of hypertension.
Conclusion
OSAS is extremely common in acromegaly, especially using the ICSD-3 criteria, and HSAT may be recommended for routine screening. We found hypertension as a major predictor of severe OSAS, which tended to be more frequent in men. CPAP was found to be effective regardless of OSAS severity and should be encouraged in such patients.

DOI: 10.1530/endoabs.81.P419

P420

A rare posterior pituitary tumor with thyroid transcription factor-1 positivity

Şeyma Aksoy, sebnem burhan, Rukiye Dilara Tekin Uzman & Esra Şüheda Hatipoğlu
Istanbul Başakşehir Çam and Sakura City Hospital, Endocrinology and Metabolism Diseases, Istanbul, Turkey

Introduction
A pituitary adenoma is directly assumed to originate from anterior pituitary. It is expected that pathologies of posterior hypophysis cause diabates insipitus (DI). However recently posterior pituitary tumors (PPTs) are also declared which are not associated with DI in contrast to what is expected. Rather they have a clinical and radiologic presentation akin to anterior pituitary adenomas. Differentiation of two conditions is mainly based on pathologic immunohystochemical staining of posterior pituitary tumors with Thyroid Transcription Factor-1 (TTF-1), which is universally positive in posterior pituitary tumors but negative in anterior ones. PPTs are believed to originate from pituicytes, which are specialized glia of the posterior pituitary. Incidences of these rare tumors are as low as less than 0.5% of sellar tumors (1). Transsphenoidal surgery (TSS) is the treatment of choice for symptomatic PPT.
Case report
A 44-year-old man presented with headache. Magnetic resonance imaging (MRI) indicated a 22x12.7x13 mm pituitary lesion. Anterior pituitary hormones at presentation were within normal levels. Patient underwent TSS. Patologic evaluation showed a nullcell adenoma with Ki-67 (MIB-1) index of % 5-6. A residual 16x15 mm tumor was detected in the pituitary MRI 3 months after the operation. The patient underwent TSS again at the postoperative 11th month. GH, ACTH, TSH, LH, FSH, pit-1, SF-1 staining was negative in patological examination. TTF-1 was positive. Synaptophysin and S-100 protein were weakly positive. GFAP, EMA and chromogranin were negative. Ki-67 (MIB-1) index was % 15. Due to TTF-1 positivity, PPTs and metastatic neuroendocrine tumors were included in the differential diagnosis. Neuroendocrine tumor metastasis was ruled out as chromogranin, insulinoma-associated protein 1 and cytokeratins were negative. FDG-PET also did not show a primary/metastatic malignancy. On follow-up there was no recurrence or residual tumor and no hormonal deficiency.
Discussion
PPTs generally arise in the region of the sella and present similarly to nonfunctional pituitary adenomas, making it difficult to distinguish them from other common pituitary lesions based on hormonal status and imaging alone. TTF-1 positivity is crucial to diagnosis. Because of the high rate of recurrence, TTF-1 positive tumors should be followed up at close intervals. (1) Shibuya M. Welcoming the new WHO classification of pituitary tumors 2017: revolution in TTF-1-positive posterior pituitary tumors. Brain Tumor Pathol. 2018 Apr;35(2): 62-70.

DOI: 10.1530/endoabs.81.P420

P421

Efficacy of methotrexate in the treatment of isolated, steroid-resistant sarcoidosis of the hypothalamic-pituitary system

Pawel Kuca[1], Agnieszka Wojciechowska-Luzniak[1], Lukasz Dzalach[1], Anna Migda[1], Grzegorz Zielinski[2], Maria Maksymowicz[3] & Przemyslaw Witek[1]
[1]Medical University of Warsaw, Department of Internal Medicine, Endocrinology and Diabetics, Warsaw, Poland; [2]Military Institute of Medicine, Department of Neurosurgery, Warsaw, Poland; [3]The Maria Sklodowska-Curie National Research Institute of Oncology, Department of Patomorphology, Warsaw, Poland

Isolated sarcoidosis of the hypothalamic-pituitary system is a very rare form of neurosarcoidosis. It usually leads to secondary damage to endocrine function, resulting in hypopituitarism and diabetes insipidus. A 32-year-old male patient with progressive deterioration of his general condition, weakness, polyuria, dizziness and visual field disturbances was admitted to the Department of Endocrinology for the diagnosis of a tumor in the hypothalamic-pituitary region. MRI showed a tumor (19x16x15 mm) with suprasellar extension, and hormonal evaluation revealed multi-hormonal pituitary insufficiency and diabetes insipidus. The patient was referred for pituitary surgery: the lesion initially described in MR as a tumor was sub totally removed from the fronto-parietal access. The histopathological examination revealed a hypothalamic sarcoidosis. Based on the imaging studies performed, the presence of sarcoid lesions in other typical locations (lungs, lymph nodes, heart, eye, skin) was excluded. Isolated sarcoidosis of the pituitary system was diagnosed. Methylprednisolone treatment was initiated at 500 mg/week for 6 weeks, followed by 250 mg/week for 6 weeks. Additionally, the patient required replacement treatment with l-thyroxine, testosterone and desmopressin. Following 12 weeks of methylprednisolone therapy MRI showed a progression of the infiltrative process: the tumor was enlarged (20x19x17 mm) and two satellite foci appeared. Due to the clinically and radiologically identified steroid resistance of the lesions, immunosuppressive treatment with methotrexate was introduced in the 15 mg sc regimen for 7 days for 4 weeks, and then 25 mg sc every 7 days chronically. Subsequent MRI examinations performed 3, 12 and 24 months after the initiation of methotrexate therapy showed a regression of the infiltrative process in the CNS and decompression of the optic chiasm together with clinical improvement and no signs of sarcoid lesions in other locations. At the same time, no complications of the applied treatment were observed. In the control hormonal tests, the features of multi-hormonal anterior pituitary insufficiency were maintained, which required continuation of substitution treatment. In conclusion, an optimal treatment of isolated neurosarcoidosis of the hypothalamic-pituitary system has not been clearly established. Steroid therapy with high doses of methylprednisolone should be considered first, but the possibility of steroid resistance should also be considered. The use of immunosuppressants, such as methotrexate as a second line therapy, may have a positive effect on reducing the extent of the sarcoid

process. Such a treatment is effective and safe, although the time frame and the dosing schedule of methotrexate are still unknown.

DOI: 10.1530/endoabs.81.P421

P422

Aberrant expression of clock genes in human gastric neuroendocrine tumors type 1

Angeliki Karapanagioti[1,2], Narjes Nasiri-Ansari[1], Kosmas Daskalakis[3], Erasmia Vlachou[4], Georgios Kyriakopoulos[1,5], Harpal Randeva[6,7], Gregory Kaltsas[2] & Eva Kassi[1,2]
[1]National and Kapodistrian University of Athens, Medical School, Department of Biological Chemistry, Athens, Greece; [2]National and Kapodistrian University of Athens, Medical School, 1st Department of Propaedeutic Internal Medicine, Laiko General Hospital, Athens, Greece; [3]Örebro University, Department of Surgery, Faculty of Medicine and Health, Sweden; [4]NIMITS Medical Institution Military Shareholder Fund, Department of Gastroenterology, Athens, Greece; [5]Evangelismos General Hospital, Department of Pathology, Athens, Greece; [6]University Hospital Coventry & Warwickshire, Warwickshire Institute for the Study of Diabetes, Endocrinology and Metabolism (WISDEM), Coventry, United Kingdom; [7]Warwick Medical School, Divisions of Translational and Experimental Medicine-Metabolic and Vascular Health, Coventry, United Kingdom

Introduction
Gastric neuroendocrine tumors (GNET) are rare gastric neoplasms which are developed due to hypergastrinemia and enterochromaffin-like (ECL) cell hyperplasia. Although the effect of the circadian clock system disruption on tumorigenesis has been already studied in various malignancies and autoimmune diseases, the role of the peripheral clock system in the transition from ECL-cell hyperplasia to GNEN1 (Type 1 Gastric Neuroendocrine Neoplasms) remains unexplored.
Aim
We aimed to investigate the expression of clock-related genes in peripheral blood mononuclear cells (PBMCs) and gastric tissues of the same patients with ECL-cell hyperplasia and patients with GNEN1.
Methods
Fresh frozen gastric tissues were collected between (9:00 -11:00 am) from 9 patients diagnosed with GNEN1. The histological reports confirmed the presence of ECL and GNEN1 lesions (in each separate specimen) collected from the same patient. PBMCs were also isolated from the whole blood (8:00-9:00am) of the same patients and 10 patients with confirmed ECL-cell hyperplasia. CLOCK, BMAL1, CRY1, PER2, REV-Erb, ROR-α, GR-α genes expression was evaluated by qPCR in PBMCs, ECL-cell hyperplastic and its paired GNEN1 lesions. Clinical, histological and epidemiological data of patients were also collected.
Results
The mean age of patients was 57.8 ± 12.8 years old. Paired analysis revealed that the expression of BMAL-1 and CLOCK was significantly ($P < 0.01$) increased while the expression of REV-Erb and GR-α was reduced ($P < 0.05$) in GNE1 tissue as compared to adjacent ECL tissue. There was no significant difference in the expression of PER-2 and CRY-1 in GNE1 tissues as compared to adjacent ECL tissues. Interestingly, the expression of CLOCK, PER2 and REV-Erb was significantly increased in PBMCs of GNE1 as compared to patients with ECL-cell hyperplasia.
Conclusion
Our data indicate for the first time that there is aberrant circadian clock gene expression in human gastric neuroendocrine tumors in both gastric lesions and PBMCs. Since CLOCK gene was overexpressed, apart from GNEN1 lesions, in PBMCs of patients with GNEN1 as compared to PBMCs isolated from subject diagnosed with ECL-cell hyperplasia, its potential role as an non-invasive biomarker of transition of ECL-cell hyperplasia to non-invasive GNEN1 could be explored. However, a larger sample size of patients is necessary to evaluate the role of dysregulation of the local circadian clock system in the development and/or evolution of these neoplasms.

DOI: 10.1530/endoabs.81.P422

P423

The diagnosis of vertebral fractures on routine chest radiography of acromegaly patients: a real-life study

Chiara Sardella[1], Claudio Urbani[2], GIULIA MARCONCINI[3], Daniele Cappellani[3], Luca Manetti[3], Annalisa De Liperi[4], Chiara Romei[5], Riccardo Morganti[6], Claudio Marcocci[7] & Fausto Bogazzi[3]
[1]University Of Pisa, Department of Clinical and Experimental Medicine-Section of Endocrinology, Pisa, Italy; [2]University of Pisa, Department of Clinical and Experimental Medicine-Section of Endocrinology, Pisa, Italy; [2]University of Pisa, Department of Clinical and Experimental Medicine-Section of Endocrinology, Pisa, Italy; [4]Pisa University Hospital, Radiology Department-2 nd Radiology Unit, Pisa, Italy; [5]Pisa University Hospital, Radiology Department-2 nd Radiology Unit, Pisa, Italy; [6]University of Pisa, Section of Statistics, Pisa, Italy; [7]Universa of Pisa, Department of Clinical and Experimental Medicine-Section of Endocrinology, Pisa, Italy

Objectives
The primary objective was to study the prevalence and the risk factors of vertebral fractures (VFs) in acromegaly patients either at diagnosis of acromegaly or during the follow-up. The role of routine chest radiography for detecting VFs in acromegaly was also evaluated.
Design and methods
A retrospective cohort study was performed on 60 consecutive acromegaly patients, in a tertiary referral center. The presence of VFs was firstly evaluated in each patient on lateral radiograph of the thoracolumbar spine (X-spine) performed at the last clinical visit during the follow-up. Secondly, routine chest X-rays (X-chest) performed at the time of diagnosis of acromegaly because part of the general evaluation at admission, were retrospectively reviewed for detecting VFs and compared to X-spine. Data were evaluated using binary logistic regression.
Results
Overall, 27 (45%) out of 60 patients had VFs at X-spine. Among those patients 37% had fractured vertebrae at the time of the diagnosis of acromegaly, although undiagnosed. Patients with VFs at baseline had higher IGF-1 index compared to those who had fractures after the diagnosis of acromegaly ($P = 0.043$). The comparison between the X-spine and the X-chest revealed an incidence of new VFs in 40% of patients, after diagnosis of acromegaly. The determinants of VFs were age (HR 1.05, $P = 0.038$) and hypogonadism (HR 6.14, $P = 0.025$). Conversely, therapy for acromegaly or bone mineral density values did not influence the outcome.
Conclusion
Nearly 40% of patients, who suffer from VFs, had fractured vertebrae undiagnosed on chest radiography at time of diagnosis of acromegaly. At baseline, VFs might correlate to the severity of acromegaly. After diagnosis of acromegaly, patients are at high risk of developing new fractures especially when hypogonadism is associated. On routine chest radiography, acromegaly patients should be also evaluated for the presence of VFs.

DOI: 10.1530/endoabs.81.P423

P424

Assessment of quality of life in women with Sheehan syndrome

Salma Salhi, Ibtissem Oueslati, Wafa Grira, Fatma Chaker, Nadia Khessairi, Meriem Yazidi & Melika Chihaoui
La Rabta University Hospital, Department of Endocrinology, Tunis, Tunisia

Introduction
Sheehan syndrome represents a rare cause of hypopituitarism. It results from postpartum ischemic necrosis of the pituitary gland. Data evaluating the quality of life in women with Sheehan syndrome are scarce. The aim of this study was to assess the quality of life in patients with Sheehan syndrome and to determine its associated factors.
Methods
A cross-sectional study including women with Sheehan syndrome was conducted in the department of endocrinology, La Rabta hospital. Clinical and paraclinical data were collected. Quality of life was assessed using the Short Form Survey-36 (SF-36). Predefined thresholds were used to categorize patients' quality of life: SF-36 overall score < 30: poor quality of life, 30-60: average quality of life, and > 60: good quality of life.
Results
Forty-two women with Sheehan syndrome were enrolled in this study. Their mean age was 61.9 ± 9.6 years. The mean duration and the mean delay in diagnosis of Sheehan syndrome were 31.5 ± 10.2 and 11.8 ± 9.3 years, respectively. All participants had corticotroph, thyrotropin, gonadotropin, and prolactin deficiencies. The overall quality of life score was 50.9 ± 15.2. The averages of role limitation due to physical health, vitality, emotional well-being, bodily pain, and general health scores were below 50. The quality of life was good in 11 patients (26%), average in 27 patients (64%), and poor in 4 patients (10%). Role limitation due to physical health score was negatively correlated with age ($r = -0.326$, $P = 0.04$) and the disease duration ($r = -0.423$, $P = 0.006$). General health

score ($r=0.354$, $P=0.027$) and vitality score ($r=0.365$, $P=0.022$) were correlated with the daily dose of hydrocortisone.
Conclusion
The majority of women with Sheehan syndrome had average to poor quality of life. The most affected dimensions were role limitation due to physical health, vitality, emotional well-being, bodily pain, and general health. Age, disease duration, and the daily dose of hydrocortisone may affect the quality of life in women with Sheehan syndrome.

DOI: 10.1530/endoabs.81.P424

P425

In-hospital hyponatremia is associated with loss of independence at discharge among older patients

Tanu Hans[1], Navjot Singh[1] & Jubbin Jagan Jacob[2]
[1]Christian Medical College & Hospital, Department of Medicine, Ludhiana, India; [2]Christian Medical College & Hospital, Department of Endocrinology, Ludhiana, India

Context
Hyponatremia is a hormonal disorder of water metabolism encountered in 2% of community dwelling adults in America and in over 15-20% of hospitalized adults.[1,2] Hyponatremia leads to increase in risk of falls, cognitive deficits, gait disturbances, loss of independence, prolongation of hospital stay and mortality among older patients admitted to hospitals.[3]
Objective
To determine in-hospital mortality among older patients admitted to the hospital with concomitant hyponatremia and to assess length of hospital stay and degree of independence at discharge from hospital
Methods
This was an observational cohort recruited from the medical and allied wards of a tertiary care teaching hospital in India. Older patients ($\geq$60 years) with documented hyponatremia (Serum Sodium $<$ 135 mEq/l) who provided informed consent were included. Patients with suspected pseudohyponatremia and those with functional impairments prior to hospitalization were excluded. A similar number of age and gender matched older patients without hyponatremia during hospital stay were recruited as a control group. Demographic and clinical data was noted from the patients' records. Primary outcome measured was in-hospital mortality. Other outcomes included length of hospital stay (LOHS) and loss of independence recorded on the day of discharge by assessment of Katz index of independence (KII) in daily living.[4] A lower score indicates loss of independence.
Results
Hundred and twenty-five patients with hyponatremia and an equal number of controls were consented. Mean age (68.8$\pm$7.7 vs.68.2$\pm$6.5 years P-value$=$0.8) and male gender (57.6% vs.56.8% P-value$=$0.8) were comparable and mean serum sodium were 127.1$\pm$5.5 vs 137.9$\pm$2.5 mEq/l respectively among cases vs. controls (P-value$<$0.0001). In-hospital mortality was higher among patients with hyponatremia (20(16%) vs. 11(8.8%), P-value$=$0.08) but not statistically significant. LOHS was longer (8.4$\pm$5.7 vs. 5.0$\pm$2.8 days, P-value$<$0.0001) and KII scores were lower (3.9$\pm$1.9 vs. 4.8$\pm$1.5, P-value$=$0.0003) among cases. Severe functional impairment at discharge (KII $<$2) was significantly higher among cases (29.5% vs. 13.1%, P-value$=$0.006). Significant positive correlation was seen between serum sodium and KII scores (correlation coefficient -0.28, P value$=$0.003) suggesting increasing loss of independence at discharge with lower sodium values.
Conclsions
Older patients with hyponatremia during hospitalization were less likely to survive the hospital stay and spend longer time in hospital. Loss of independence was significantly associated with both presence of hyponatremia and co-related with the severity of hyponatremia.
References
1. J Appl Lab Med. 2021;6(1):63-78.
2. Am J Med. 2006;119(7 Suppl 1): S30-S35.
3. QJM. 2009;102(3):175-182.
4. JAGS, 31(12), 721-726

DOI: 10.1530/endoabs.81.P425

P426

3P syndrome: pheochromocytoma, paraganglioma, pituitary adenoma

Barbora Havlinova[1], Filip Gabalec[1], Miroslav Solař[2], Jiri Horacek[1] & Jan Cap[1]
[1]University Hospital Hradec Kralove and Charles University, Faculty of Medicine in Hradec Kralove, 4th Department of Internal Medicine - Hematology, Hradec Králové, Czech Republic; [2]University Hospital Hradec Kralove and Charles University, Faculty of Medicine in Hradec Kralove, 1st Department of Internal Medicine – Cardioangiology, Hradec Králové, Czech Republic

Neuroendocrine tumours, especially pheochromocytomas, paragangliomas and pituitary adenomas, are more common in younger patients in 3rd–5th decade of life. PitNETs are the most common intracranial tumours, while PHEO and PGL are rare. The hormonal activity, signs and symptoms of NET are variable. PGL, PHEO and PitNET in one patient remains an exceptional association. 72 cases of concomitant pituitary adenoma and PGL have been reported to date. The first record of a patient with acromegaly and PHEO dates back to 1952. We present a case of a 39-year-old man with non-specific symptoms including high blood pressure, headache, sweating and specific apparent acromegalic features on the face and hands. Screening CT scan found vascularized expansion (up to 6.5 cm) with cystic necrosis in the area of both adrenal glands. Initial measurement showed high plasma levels of catecholamines and their metabolites, prolactin, growth hormone and IGF-I. Then MRI examination of the brain was indicated and found intrasellar expansion (2 cm x 2.3 cm x 2 cm) prominent into the sphenoid cavity. Genetic analysis was performed due to endocrine syndromic comorbidities in a young patient which revealed a germline mutation in the gene MAX. Treatment included bilateral adrenalectomy of PHEO and neurosurgical intervention. Because acromegaly was not adequately controlled after surgery, somatostatin analogue was introduced. In up to 25 % of cases, especially in younger people, pheochromocytomas may be caused by an inherited mutation of various genes (SDHB, SDHD, SDHC, VHL, MAX, RET). Mutation frequencies in the MAX gene are uncommon. They lead to incorrect regulation of the MYC-MAX-MXD1 path, which is coupled to the mTOR path. So far, the most effective treatment is the surgical removal of the neuroendocrine tumours. Performing genetic analysis is not a routine, but for related individuals, it's a possibility to detect a malignant form of the disease earlier.

DOI: 10.1530/endoabs.81.P426

P427

Long-term Tolvaptan therapy in the treatment of SIAD in Elderly- A case report with challenging cytochrome P 450 drug interactions

Keerthi Madhurya Kethireddi & Sathish Babu Parthasarathy
Princess Royal Hospital, Endocrinology & Diabetes, Haywards Heath, United Kingdom

Background
Chronic SIAD with its disabling impact is challenging to manage in elderly patients as fluid restriction or demeclocycline often has a limited success. Tolvaptan is a novel selective antagonist of vasopressin receptor (V2R) which is safely used in patients with SIAD and other conditions with hypervolemia. We report a case of longest Tolvaptan use with significant challenges amongst our case series which we had previously published
Method
A Case Report of SIAD managed with long term Tolvaptan therapy with significant cytochrome P450 drug interactions. A 78-year-old male presented with recurrent falls and reduced mobility in April 2017. He had multiple falls prior and was being investigated for cavitating lung lesion in Right Upper lobe. He was found to have severe euvolemic hyponatremia (serum sodium of 104 nmol/l) with a paired serum (228 mOsm/kg) and Urine Osmolalities (419 mOsm/kg), a normal Cortisol of 666 nmol/l and a normal Thyroid function test. His prior baseline sodium was around 130 mmol/l. SIAD was confirmed which failed to respond to fluid restriction (19 days) and demeclocycline (10days). A clinical diagnosis of Aspergillosis was made and oral Itraconazole was started. We commenced Tolvaptan 7.5 mg once daily dose (smaller dose) given drug interaction between Itraconazole (CYP3A4 Inhibitor) and Tolvaptan. Hyponatraemia improved back to baseline within 48 h and patient was discharged on Tolvaptan (7.5 mg OD). Trials of stopping Tolvaptan therapy were unsuccessful (2017, 2019). Patient presented with increased fatigue and low basal cortisol (9 nmol/l) in 2018 despite normal serum electrolytes. Diagnosis of Secondary adrenal Insufficiency was made (250 microgram Short Synacthen test - Cortisol 0 Minutes- 73 nmol/l, 30 minutes- 131 nmol/l, Serum ACTH $<$ 3 ng/l). This is due to known interaction of potent CYP3A4 inhibitor (Itraconazole) with Seretide Inhaler therapy (Fluticasone dipropionate) in our patient. Steroid replacement therapy with Hydrocortisone was commenced. Tolvaptan dose frequency was gradually reduced to 7.5 mg twice weekly (since 2020). There were only 15 endocrine clinic

appointments over 246 weeks with no adverse effects and no further admissions since 2017.
Conclsion
We present our experience of longest use of Tolvaptan in an elderly patient with no adverse events. Clinicians must be aware of potential Cytochrome *P*450 drug interactions to avoid complications. Long term Tolvaptan use in chronic refractory SIAD appears to be safe, feasible and cost effective. More prospective studies are needed for guidance in using vasopressin receptor antagonists in chronic disabling SIAD.

DOI: 10.1530/endoabs.81.P427

P428

RNA profiling of human growth hormone-secreting and non-functioning pituitary adenomas reveals novel and differentially expressed immune related genes

Emma Jayne Spiteri[1,2], Robert Formosa[3,4], Jean Paul Ebejer[2], Nikolai Paul Pace[2], Mark Gruppetta[3,5], David Saliba[1,2] & Josanne Vassallo[3,5]
[1]Department of Applied Biomedical Science, Faculty of Health Science, University of Malta, Msida, Malta; [2]Centre for Molecular Medicine and Biobanking, University of Malta, Msida, Malta; [3]Division of Endocrinology, Department of Medicine, Faculty of Medicine and Surgery, Mater Dei Hospital, University of Malta, Msida, Malta; [4]Queen Mary University London, Campus Malta, Victoria, Gozo, Malta; [5]Neuroendocrine Clinic, Department of Medicine, Mater Dei Hospital, Msida, Malta

Pituitary neuroendocrine tumours (PitNETs) are broadly classified as non-functioning pituitary adenomas (NFPAs) and functional pituitary adenomas (FPAs) which include growth hormone secreting adenomas (GHPAs). Since the role of the immune system in PitNET pathogenesis is still poorly understood, we employed RNA-sequencing technology to unravel differentially expressed genes in GHPAs and NFPAs. Here we present an RNA-sequencing workflow of GHPAs ($n=3$) and NFPAs ($n=7$) which revealed a total of 7945 differentially expressed genes. Reactome, Gene Ontology and KEGG pathway analysis further revealed 57 genes involved in immune regulation. These genes fell into functional categories of chemokines, cytokines, interleukins, signal transduction and adhesion molecules. 6 immune genes including *GATA3, CCL3,* and *CXCL9* were selected for further validation by qRT-PCR in 14 additional PitNET samples. A number of possible pathways implicated in PitNET functioning were also highlighted. The most significant were 'T_H1 and T_H2 cell differentiation', 'cytokine-cytokine receptor pathway', and 'chemokine receptors bind chemokines'. Through our findings, we highlight distinct gene expression profiles in NFPAs and GHPAs and suggest that some of these genes could be considered as novel PitNET diagnostic markers for these two subtypes. We are currently validating these novel markers by immunohistochemistry in an array of PitNET subtypes.

DOI: 10.1530/endoabs.81.P428

P429

Time from first symptoms to diagnosis in patients with pituitary adenomas

Cecilia Follin[1], Christina Dahlgren[2], Caroline Alkebro[3], Pia Burman[4], Per Dahlqvist[5], Charlotte Höybye[6], Margareta Lindgren[5], Oskar Ragnarsson[7], Helena Wik[8], Maria Wärn[9], Anna-Karin Åkerman[10], Britt Eden Engström[11], Bertil Ekman[12] & Maria Forsgren[13,14]
[1]Department of Oncology, Skåne University Hospital, Lund, Sweden; [2]Department of Endocrinology, University Hospital, Linköping, Sweden; [3]Department of Medicine, Örebro University Hospital, SE-701 85 Örebro, Sweden; [4]Department of Endocrinology, Skånes University Hospital, University of Lund, SE-205 02 Malmö, Sweden; [5]Department of Public Health and Clinical Medicine, Umeå University, SE-901 87 Umeå, Sweden; [6]Department of Molecular Medicine and Surgery, Karolinska Institute and the Department of Endocrinology, Karolinska University Hospital, SE-171 76 Stockholm, Sweden; [7]Department of Internal Medicine and Clinical Nutrition, Institute of Medicine at Sahlgrenska Academy, University of Gothenburg and The Department of Endocrinology, Sahlgrenska University Hospital, SE-413 45 Gothenburg, Sweden; [8]Department of Endocrinology, Sahlgrenska University Hospital, SE-413 45 Gothenburg, Sweden; [9]Department of Endocrinology, Karolinska University Hospital, SE-171 76 Stockholm, Sweden; [10]Department of Medicine, Örebro University Hospital, SE-701 85 Örebro, Department of Molecular Medicine and Surgery, Karolinska Institutet, Stockholm, Örebro, Sweden; [11]Department of Medical Sciences, Endocrinology and Mineral Metabolism, Uppsala University and Department of Endocrinology and Diabetes, Uppsala University Hospital, SE-751 85, Uppsala, Sweden; [12]Department of Endocrinology in Linköping, Department of Internal Medicine in Norrköping, and Department of Health, Medicine and Caring Sciences, Linköping University, SE581 83, Linköping, Sweden; [13]Department of Endocrinology and Diabetes, Uppsala University Hospital, SE-751 85, Uppsala, Sweden; [14]Regional Cancer Centre Stockholm, Gotland, Stockholm, Sweden

Background
Subtle symptoms such as fatigue, weight gain and depression are commonly present for years in patients with pituitary adenoma (PA) before the diagnosis is made. A delayed diagnosis with risk of increased morbidity and mortality may be due to differences between patient-reported symptoms and symptoms reported in the patient's medical record.
Aim
To estimate diagnostic delay and investigate the concordance between patient-reported symptoms and the medical record documentation in patients with PA.
Method
Patients with PA attending seven University Hospitals in Sweden participated. Age at first symptoms, age at diagnosis, experience of first symptoms, symptoms at diagnosis, and first healthcare contact were collected from the medical records, the Swedish Pituitary Register and patient questionnaires. The concordance between patient reports and medical record documentation was assessed using kappa statistics.
Results
657 patients (322 women) were included (non-functioning PA (NFPA) $n=314$, prolactinoma $n=118$, acromegaly $n=164$, Cushing's Disease (CD) $n=58$. Median age at inclusion was 61 yrs (19-92) for men and 52 yrs (18-91) for women. A significant difference in duration of onset of symptoms to final diagnosis between men and woman was reported; median 1 yr (0-31) for men and 2 yrs (0-44) for women ($P<0.001$). Patients with acromegaly had the longest diagnostic delay; median 4 yrs (0-32), significantly longer than for NFPA; median 1 yr (0-20), ($P<0.001$). Among NFPA the most frequent patient-reported symptoms were headache, visual deficit and tiredness; for prolactinomas menstrual irregularities, headache, tiredness; for acromegaly change in appearance, snoring, headache and for CD weight gain, tiredness and weakness. Substantial agreement between patient report and medical record was found in visual deficit in NFPA and prolactinomas (Cohen's kappa >0.6) and in menstrual irregularities in prolactinomas (Cohen's kappa >0.7). In prolactinomas we found poor agreement for galactorrhea, and in acromegaly for weakness and tiredness. In CD we found no agreement at all in weakness and dizziness. The first healthcare contact was endocrinologists for NFPA and general practitioners for prolactinomas, acromegaly and CD.
Conclusion
We report a substantial and highly variable diagnostic delay in patients with PA, most pronounced in women. Visual deficit and menstrual irregularities showed substantial agreement between the endocrinologists' documentation and patient reported data, whereas weakness, tiredness and dizziness showed poor agreement. The most frequent entry to diagnosis was general practitioners. An increased awareness of symptoms from pituitary adenomas through increased information to the general population and directed education of health professionals may contribute to earlier diagnosis.

DOI: 10.1530/endoabs.81.P429

P430

Psychological impact of Covid-19 national lockdown on patients with Cushing's syndrome in Italy: a case-control study

Nicola Di Paola[1], Mattia Barbot[2], Emanuele Ferrante[3], Francesco Ferraù[4], Federico Gatto[5], Rosa Maria Paragliola[6], Giuseppe Reimondo[7], Giorgio Arnaldi[8], Valentina Guarnotta[9], Rosario Ferrigno[1], Chiara Simeoli[1], Giovanna Mantovani[3,10], Carla Scaroni[2], Felice Iasevoli[11], Annamaria Colao[1,12] & Rosario Pivonello[1,12]
[1]Università "Federico II" di Napoli, Dipartimento di Medicina Clinica e Chirurgia, Sezione di Endocrinologia, Naples, Italy; [2]University-Hospital of Padova, Endocrinology Unit, Department of Medicine, DIMED, Padua, Italy; [3]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Endocrinology Unit, Milan, Italy; [4]University of Messina, Endocrine Unit, University Hospital 'G. Martino', Department of Human Pathology of Adulthood and Childhood 'G. Barresi'DETEV, Messina, Italy; [5]IRCCS Ospedale Policlinico San Martino, Endocrinology Unit, Genoa, Italy;

[6]Università Cattolica del Sacro Cuore, Fondazione Policlinico "Gemelli" IRCCS, Unit of Endocrinology, Department of Translational Medicine and Surgery, Rome, Italy; [7]University of Turin, San Luigi Hospital, Division of Internal Medicine, Turin, Italy; [8]Università Politecnica delle Marche, Ospedali Riuniti di Ancona, Clinica di Endocrinologia e Malattie del Metabolismo, Dipartimento di Scienze Cliniche e Molecolari (DISCLIMO), Ancona, Italy; [9]Università degli studi di Palermo, Dipartimento di Promozione della Salute, Materno-Infantile, di Medicina Interna e Specialistica di Eccellenza "G. D'Alessandro", UOC di Malattie endocrine, del Ricambio e della Nutrizione, Palermo, Italy; [10]University of Milan, Department of Medical Sciences and Community Health, Milan, Italy; [11]University of Naples Federico II, Department of Neuroscience, Naples, Italy; [12]Unesco Chair for Health Education and Sustainable Development, Federico II University, Naples, Italy

During the spring of 2020, a national lockdown was adopted in Italy to prevent COVID-19 pandemic spread. Restrictive measures have been associated with impaired psychological outcome in the general population. As patients with Cushing's Syndrome (CS), including Cushing's disease (CD), adrenal CS (ACS), and ectopic CS (ECS), are reportedly associated with a higher prevalence of anxiety, stress susceptibility, depression, and maniac episodes, during both active disease and remission, a higher psychological vulnerability during lockdowns cannot be excluded. The aim of the current study was to evaluate the presence of psychological impairment in CS patients associated with the Italian national lockdown due to COVID-19 pandemic, as compared with healthy subjects. The study enrolled 156 CS patients (134 CD, 18 ACS, 4 ECS; 118 F, 38 M; age: 21-70 yrs) and 156 age-, sex-, and education level-matched healthy subjects. General Anxiety Disorder-7 (GAD-7), Perceived Stress Scale (PSS) and Patient Health Questionnaire-9 (PHQ-9) were telematically and anonymously administered to study participants during the last three weeks of Italian national lockdown. Higher scores of GAD-7, PSS and PHQ-9 indicated higher anxiety, perceived stress and depression. Demographic, social, and clinical information were also collected for a correlation with the psychological status. Comparing CS patients and healthy subjects, no significant differences were observed neither in the questionnaires scores nor in the prevalence of general anxiety, high perceived stress, and depression. In CS patients, higher GAD-7, PSS, and PHQ9 scores were contemporary observed in females ($P \leq 0.01$), higher GAD-7 and PSS scores were contemporary observed in patients <50 yrs ($P<0.05$), whereas isolated higher PSS scores were observed in patients with lower educational levels ($P \leq 0.02$), currently under glucocorticoid (GC) replacement therapy ($P=0.017$), and going out from home less than once a week during national lockdown ($P \leq 0.03$). Considering CS patients currently treated with medical therapy, isolated higher GAD-7 scores were observed in patients currently treated with pituitary-directed drugs ($P=0.005$ *vs* adrenal-directed drugs). In conclusion, although CS patients did not suffer increased psychological morbidity, namely general anxiety, stress perception and depressive status, compared to healthy subjects during Italian national lockdown, an increased psychological morbidity may be observed in CS patients with some specific clinical characteristics, namely female sex, age $<$ 50 yrs, lower educational levels, with strict adherence to restrictive measures, as well as in CS patients currently under GC replacement treatment or pituitary-directed drugs. Therefore, an empowered, focused psychological follow-up may be required in these CS patients during national lockdowns.

DOI: 10.1530/endoabs.81.P430

P431

Acromegaly and aging: a double hit against quality of life?

Irene Gagliardi[1], Sabrina Chiloiro[2], Maria Vallillo[2], Marta Bondanelli[1], Stefano Volpato[1], Antonella Giampietro[2], Antonio Bianchi[2], Laura De Marinis[2], Maria Chiara Zatelli[1] & Maria Rosaria Ambrosio[1]
[1]Section of Endocrinology, Geriatrics & Internal, Dept of Medical Sciences, University of Ferrara, Italy; [2]UOC Endocrinology and Diabetology, Department of Translational Medicine and Surgery, Fondazione A Gemelli, IRCCS, Universitaà Cattolica del Sacro Cuore, Italy

Introduction
Acromegaly patients (ACRO) show increased morbidity that affects health and quality of life (QoL). Elderly ACRO are going to increase in the next few years, but evidence regarding their management is lacking.
Aim
To evaluate physical, functional and cognitive performances of elderly ACRO and the relationship with QoL.
Methods
Multicenter case-control study conducted on 42 older ACRO ($\geq$ 65 years) compared to an age- and gender-matched control group (CTR). Each patient underwent a multidimensional geriatric evaluation. QoL was tested with SF-36 questionnaire.
Results
Mean age in both groups was 73 $\pm$ 6 years and female gender was most represented (69%). 13 ACRO were in remission and 29 had active disease controlled by medical therapy except for one patient. ACRO showed worse mobility skills, poorer functional status assessment and lower cognitive evaluation scores than CTR ($P<0.05$). Age negatively correlated with mobility skills, instrumental and basic daily activities execution (IADL and BADL) and cognitive performance in ACRO ($P<0.05$). ACRO presented less satisfactory scores in 5 out of 8 SF-36 questionnaire domains as compared to CTR: physical activity (PA), physical pain (PP), general health (GH), vitality (V), social activities (SA) ($P<0.05$). PA, V and SA scores worsened with the increasing number of drugs and comorbidities ($P<0.01$). Increasing BMI positively correlated with better PA scores, but no associations were found between BMI and mobility skills. In ACRO, better mobility, IADL, BADL and cognitive performances correlated with more satisfactory PA, PP, GH, V and SA scores ($P<0.01$). Mobility skills, BADL, IADL and cognitive evaluation strongly correlated with all 8 SF-36 domains in ACRO ($P<0.01$). Conversely, no correlations were found in CTR. All comorbidities were more frequent in ACRO than CTR. Musculoskeletal and bone diseases were more frequent in ACRO than in CTR (52% vs. 12%; 64% vs. 10%; $P<$ 0.05) and independently associated with geriatric outcomes in ACRO.
Conclusions
Elderly ACRO show worse performance in mobility skills, functional and cognitive status as compared to no acromegaly patients, supporting increased frailty worsening with aging. Poorer geriatric outcomes directly affect many aspects of QoL and health self-perception. A major prevalence of comorbidities in ACRO group might explain these discrepancies. Our data support the inclusion of a multidimensional geriatric evaluation in routine clinical practice to improve elderly ACRO management and, consequently, ACRO QoL. Further studies are needed to identify the most appropriate geriatric tools.

DOI: 10.1530/endoabs.81.P431

P432

A systematic literature review to evaluate extended dosing intervals in the pharmacological management of acromegaly

Maria Fleseriu[1], Zhaoyun Zhang[2], Kate Hanman[3], Keval Haria[3], Aude Houchard[4], Sheila Khawaja[5], Antonio Ribeiro-Oliveira[6] & Monica Gadelha[7]
[1]Pituitary Center at Oregon Health & Science University, Portland, United States; [2]Fudan University, Shanghai, China; [3]Costello Medical, London, United Kingdom; [4]Ipsen, Boulogne-Billancourt, France; [5]World Alliance of Pituitary Organizations, Zeeland, Netherlands; [6]Ipsen, Cambridge, United States; [7]Universidade Federal de Rio de Janeiro, Rio de Janeiro, Brazil

Background
Acromegaly is a rare disorder characterized by excess growth hormone (GH) and insulin-like growth factor 1 (IGF-1). Extended dosing intervals (EDIs) of pharmacological treatments may reduce patient burden and costs compared with standard dosing. This systematic literature review (SLR) investigated treatment of acromegaly at EDIs.
Methods
MEDLINE/Embase/the Cochrane Library (2001–June 2021) and key congresses (2018–2021) were searched for relevant literature with a dual reviewer process; identified SLR bibliographies were also reviewed. Included publications reported efficacy/effectiveness, safety, humanistic, and economic outcomes in longitudinal/cross-sectional studies in adult patients with acromegaly. Interventions included EDIs of lanreotide autogel (LAN), octreotide long-acting release (OCT), and pasireotide (all administered less often than every four weeks), oral octreotide (less than twice daily), pegvisomant (PEG; less than once daily), and cabergoline (less than twice weekly), with no comparator required. PROSPERO 2021: CRD42021278922.
Results
In total, 35 publications reported on 27 studies: 14 PEG, 9 LAN, and 4 OCT (monotherapies/combination therapies) at EDIs. No identified studies assessed oral octreotide, pasireotide, or cabergoline EDIs. Baseline characteristics differed across studies. As compared with Baseline, treatment at EDIs resulted in reduced IGF-1 levels in 12/16 studies assessing LAN, OCT, or PEG (7–104 patients treated at EDIs) and GH levels in 5/6 studies (LAN/OCT; 15–32 patients). Normalized IGF-1 and/or GH was achieved/maintained in 70%–100% of patients in 12/13 studies (LAN/OCT/PEG; 15–124 patients). Proportions of patients experiencing adverse events ($n=4$ studies reporting overall events; LAN/OCT/-PEG; 8–96 patients) and discontinuing treatment ($n=9$; LAN/OCT/PEG; 7–124

patients) were similar across EDI and standard regimens. Health-related quality of life (HRQoL) improvement from Baseline was reported in 9/10 studies (LAN/OCT/PEG; 7–109 patients) and did not deteriorate with EDIs vs standard regimens. Patients preferred EDIs (2/2 studies; LAN/OCT; 8–112 patients), and satisfaction with EDIs was high (2/2 studies; LAN/OCT; 13–109 patients). Reduced costs were observed with EDIs vs standard regimens in 3/3 studies (9–23 patients) with LAN (120 mg every 6 vs 4 weeks), OCT (20–30 mg every 6–12 vs 4 weeks), and PEG (40–160 mg weekly vs 15–60 mg daily, both with LAN/OCT).
Conclusion
Clinical, safety, and HRQoL outcomes in patients with acromegaly were similar and costs lower with EDIs vs standard regimens. Satisfaction was high with EDIs. Variation in endpoints and small, heterogenous patient populations precluded conducting meta-analyses. Physicians should consider EDIs where appropriate.
Funding: Ipsen; medical writing support: Costello Medical.

DOI: 10.1530/endoabs.81.P432

P433

Gene therapy of growth hormone resistant dwarfism in the laron mouse model – comparison of two doses

Kian Chuan Sia[1], Shu Uin Gan[1], Siti Humairah Mohd Rodhi[1], John J. Kopchick[2], Michael J. Waters[3] & Kok Onn Lee[1]
[1]National University of Singapore, Singapore, Singapore; [2]Ohio University, United States; [3]The University of Queensland, Australia

Growth hormone receptor (GHR) defective Laron Syndrome (LS) has been treated with daily subcutaneous recombinant insulin-like-growth factor 1 (IGF1) injections lasting many years. We have reported the results of treatment of 4-5 week old Laron dwarf mice (GHR-/-) with a single injection of an adeno-associated virus vector with a murine GHR (AAV-GHR) and a liver specific promoter at a dose of 4×10^{10} vector genome per mouse (Sia *et al*, Gene Therapy 2022).
Methods
In the present study, we report the results of increasing the dose to four times our earlier reported dose: 16 X 10^{10} vector genome per mouse. In both groups of mice, low dose (previous 4 X 10^{10}) and high dose were injected at the same age of 4-5 weeks. Mice injected with the same doses of AAV-Luciferase were used as controls. The mice were monitored for a total of 20 weeks, after which they were euthanized. The organs were harvested and weighed. Serum was obtained for analyses.
Results
The serum growth hormone (GH) levels decreased, and IGF1, IGF binding protein 3 (IGFBP3) and acid labile subunit (ALS) increased compared to the respective controls. There was a significant increase in body weight and length with both doses, but the difference between the two doses was not statistically significant. All the major organs increased in weight and size, but there was no significant difference between the 2 doses.
Conclusion
Surprisingly, increasing the single dose by four times did not result in a significant increase in the response.

DOI: 10.1530/endoabs.81.P433

P434

Recovery of pituitary dysfunction following surgery and radiotherapy in non-functioning pituitary macroadenomas

Ziad Hussein[1,2], Hani J Marcus[3], Joan Grieve[3], Neil Dorward[3], Peirre Bouloux[1] & Stephanie Baldeweg[1,4]
[1]University College London, United Kingdom; [2]Sheffield Teaching Hospitals NHS Foundation Trust, United Kingdom; [3]National Hospital for Neurology and Neurosurgery, United Kingdom; [4]University College London Hospitals Nhs Foundation Trust, United Kingdom

Background
Hypopituitarism is often part of the presenting clinical manifestation for patients with non-functioning pituitary macroadenomas (NFPMs). Rate of recovery of hypothalamic-pituitary endocrine axes following therapy is uncertain with no clear predictive factors.
Aims
The aim of this study was to assess the degree of hypopituitarism recovery following surgery and radiotherapy in patients with NFPMs.
Methods
All patients treated with surgery and radiotherapy for NFPMs between 1987 and 2018 with more than 6 months follow-up were identified. A retrospective case note review was performed.
Results
In total, 383 patients were identified, 256 patients (256/383; 67%) were men. The median age was 57 years (IQR 48-67) with median follow-up of 5 years (IQR 2-9). At diagnosis, growth hormone deficiency occurred in 115 patients (115/273; 31%), hypogonadotropic hypogonadism in 160 patients (160/375; 43%), 132 patients (132/375; 36%) recorded to have adrenal insufficiency and 157 patients (157/375; 42%) developed secondary hypothyroidism. Panhypopituitarism was reported in 100 patients (100/377; 26%). Surgery only was performed in 318 patients (318/383; 83%) while 65 patients (65/383; 17%) needed surgery and radiotherapy to control tumour relapse. The degree of pituitary insufficiency recovery after NFPMs therapy is shown in the table. The combination of surgery and radiotherapy was associated with less likelihood of improvement in the case gonadotropins and TSH deficiencies as well as anterior hypopituitarism to patients who underwent surgery only. Notably, none of TSH deficient patients regained normal thyroid function post irradiation. Younger age was associated with a higher rate of improvement in gonadotroph deficiency ($P=0.004$), secondary hypocortisolism ($P=0.01$) and anterior hypopituitarism ($P=0.006$). Gender and extent of resection of NFPA on postoperative MRI scan was not related to pituitary recovery.

Table 1

	Total	Surgery	Surgery and radiotherapy	*P* value
GH	28/115 (24%)	27/99 (27%)	1/16 (6%)	0.1
FSH/LH	36/160 (23%)	35/137 (26%)	1/23 (4%)	0.02
ACTH	41/132 (31%)	38/113 (33%)	3/19 (21%)	0.2
TSH	20/157 (13%)	20/130 (15%)	0/27 (0%)	0.03
Panhypopituitarism	32/100 (32%)	31/87 (36%)	1/13 (8%)	0.06

Conclsion
Recovery of pituitary hormone deficit may occur post NFPMs therapy. Factors associated with higher probability of reversal of pituitary hypofunction remain not fully understood. Patients should have regular endocrine evaluation post treatment to assess improvement in pituitary hypofunction and the need for long term replacement therapy.

DOI: 10.1530/endoabs.81.P434

P435

Liver steatosis in an *in vivo* model of hyponatremia secondary to SIAD

Giada Marroncini[1], Laura Naldi[1], Cecilia Ancheschi[1], Benedetta Fibbi[2] & Alessandro Peri[1]
[1]University of Florence, Experimental and Clinical Biomedical Sciences "Mario Serio", Firenze, Italy; [2]Careggi University Hospital, Endocrinology, Firenze, Italy

Hyponatremia is the most frequent electrolytic disorder in clinical practice. It is estimated that in about 50% of cases hyponatremia is secondary to the syndrome of inappropriate antidiuresis (SIAD). Hyponatremia is associated with a worse outcome and with increased mortality in several diseases, including cancer. *In vitro* and *in vivo* evidence shows that low [Na^+] is associated with neurological and extra-neurological alterations, which include for instance bone demineralization, leading to osteoporosis. In order to better elucidate tissue alterations associated with reduced [Na^+], we developed and characterized an *in vivo* model of hyponatremia secondary to SIAD, induced in a total of 38 Fox $^{nu/nu}$ mice by subcutaneous infusion of the vasopressin analogue 1-deamino [8-D-arginine] vasopressin (dDAVP) via osmotic minipumps for a total of 14 days. Mice were randomly divided into three experimental groups and sacrificed at different times: two groups were infused with 0.3 and 0.5 ng/h dDAVP, respectively (A and B, $n=11$ for each group) and one control group was infused with isotonic saline solution (0.9% NaCl) (C, $n=16$). After the initiation of dDAVP infusion, mice gained weight, urinary volume was reduced and urine osmolarity increased. Starting from a baseline serum [Na^+] of 151 $\pm$ 1.57 mEq/l (mean + SE), a serum

[Na^+] of 131.01 ± 5.76 mEq/l and 116.7 mEq/l ± 5.19 mEq/l was achieved in group A and B, respectively, at the end of dDAVP administration. The day of sacrifice different organs were collected, fixed and processed for histological analysis. In particular, we focused on liver, because evident morphological alterations were observed in hyponatremic mice. Specifically, peripheric steatosis was observed, with accumulation of lipid droplets into hepatocytes and collagen fibers. Western blot analysis of proteins involved in hepatic lipid metabolism confirmed the increased lipogenic status associated with the progressive reduction of serum [Na^+]. The expression of the heme oxigenase-1 (HMOX1) gene, which we had previously found to be upregulated in low [Na^+], significantly increased both in hepatic stellate cells and in Kupffer cells, as confirmed by serial immunohistochemical analysis for α-Smooth Muscle Actin, F480 and HMOX-1. In view of these original findings, we hypothesize that hyponatremia might be consider a trigger for liver steatosis. This observation has a potential impact on clinical grounds, also because liver steatosis is known to possibly evolve into cirrhosis and ultimately into cancer.

DOI: 10.1530/endoabs.81.P435

P436

Growth hormone-releasing hormone (GHRH) promotes survival and proliferation of neural stem cells and reduces amyloid-β-induced toxicity

Francesca Pedrolli[1], Dana Banfi[1], Iacopo Gesmundo[1], Michela Guglielmotto[2,3], Elena Tamagno[2,3], Andrew V. Schally[4], Ezio Ghigo[1] & Riccarda Granata[1]
[1]Division of Endocrinology, Diabetes and Metabolism, Department of Medical Sciences, University of Turin, Turin, Italy; [2]Department of Neuroscience, University of Turin, Italy; [3]Neuroscience Institute Cavalieri Ottolenghi Foundation (NICO), University of Turin, Italy; [4]Division of Endocrinology, Department of Medicine, University of Miami Miller School of Medicine, Florida, Miami, United States

Neurogenesis, the process by which new neurons are generated from precursors, persists in discrete regions of the adult hippocampus. The hippocampus is critical for learning and memory and is the main target of Alzheimer's Disease (AD), which causes massive neuronal death, reduction in neurogenesis, and impairment in cognitive functions. Therefore, preventing neuronal loss or increasing the production of new neurons may represent a potential therapeutic strategy to reduce the AD-induced cognitive decline. Growth hormone-releasing hormone (GHRH) and its agonistic analogs, apart from promoting growth hormone (GH) secretion from the pituitary, exert many peripheral functions, including stimulation of cell survival, cardioprotection and neuroprotection. Furthermore, expression of GHRH, as well as GHRH-receptor (GHRH-R) and its splice variants (SVs), has been demonstrated in different brain regions, including the cerebral cortex, cerebellum, hippocampus, and brain stem cells. To date, however, the role of GHRH on neurogenesis and neuroprotection is still unknown. Thus, we aimed to investigate the role of GHRH on survival, proliferation, apoptosis, and differentiation of rat hippocampal neural stem cells (NSCs), in stress conditions such as growth factor deprivation and amyloid-β peptide 1-42 ($A\beta_{1-42}$)-induced toxicity, and to define the underlying mechanisms. We found the expression of both mRNA and protein for pituitary GHRH-R in NSCs. GHRH dose-dependently increased cell survival and proliferation, while reducing apoptosis in NSCs cultured under both growth factor deprivation and exposure to $A\beta_{1-42}$. These effects were blocked by the GHRH-R antagonist JV-1-36. The underlying mechanisms involved $G_{\alpha s}$/cAMP/PKA/CREB signaling, as demonstrated using specific inhibitors, and phosphorylation of ERK1/2, PI3K/Akt, and GSK-3β but not mTOR/p70S6K. Furthermore, GHRH counteracted the $A\beta_{1-42}$-induced phosphorylation of Tau protein and the inhibition of GSK-3β phosphorylation. GHRH also blocked the effect of $A\beta_{1-42}$ on elevation of the proapoptotic protein BAX and on inhibition of the antiapoptotic protein Bcl-2. In addition, our preliminary results suggest an antinflammatory role of GHRH, via inhibition in the mRNA levels of inflammatory cytokines (IL-6, TNF-α, INF-γ) and ROS activity. Finally, the role of GHRH was investigated on the differentiation of NSCs into neuronal lineages, such as neurons, astrocytes, and oligodendrocytes. Interestingly, GHRH increased the mRNA and protein levels of the neuronal marker *Tuj1*/NeuN and the astrocytes marker *GFAP* while showing no effect on the oligodendrocyte marker *Ripk1*. Collectively, these results indicate a role for GHRH in preventing neuronal loss and promoting neurogenesis, suggesting therapeutic potential for its agonistic analogs in neurodegenerative diseases, such as AD.

DOI: 10.1530/endoabs.81.P436

P437

The screening and management of diabetes mellitus type 2 in patients with acromegaly- a tertiary centre service evaluation

Harry Gray & Justyna Witczak
Cardiff University, Cardiff, United Kingdom

Introduction
Acromegaly is the result of chronic growth hormone (GH) excess, which leads to decreased insulin sensitivity and increased glucose production, to the extent that the impaired blood glucose regulation (IGR) can be recognised as Type 2 Diabetes Mellitus (T2DM). This project looked to identify whether patients were adequately screened or identified as having T2DM on diagnosis of acromegaly. The secondary aim was to determine whether acromegaly treatment affected glycaemic control in our cohort of patients.
Methods
We included ninety-five patients treated for acromegaly in University Hospital Wales, UK, between 1999 and 2020. Screening IGF-1 and nadir growth hormone following a 75g oral glucose tolerance test (OGTT) results were taken as evidence of diagnosis of acromegaly. HbA1c at the time of acromegaly diagnosis (Pre), post acromegaly treatment (Post) and most recent recording (Latest) were taken as a representation of glycaemic control. Analysis of this data and the graphs produced was done using Rstudio version 4.1.0, a statistical software.
Results
Nineteen patients were diagnosed and treated for diabetes mellitus before the diagnosis of acromegaly was made. Six patients were newly identified to have a blood glucose within diabetic range at OGTT (2 h plasma glucose $>=11.1$ mmol/l) and 5 of them underwent subsequent HbA1c testing. However, this was not the case for those with an impaired glucose regulation (IGR) (two-h glucose = 7.8 -11.1 mmol/l and/or fasting glucose = 6.1-6.9 mmol/l) with only 2 out of 16 having a HbA1c result recorded. From the sub-cohort of 26 patients who were identified as having a raised blood glucose measurement on OGTT and a HbA1c reading at acromegaly diagnosis, 15 (58%) had HbA1c reading done 3-6 months after surgical treatment. The results showed a decrease in mean HbA1c post treatment (mean Pre HbA1c = 63.5 mmol/mol, mean Post HbA1c = 45.7 mmol/mol, $P<0.005$). 22 out of 26 patients (85%) who had "Pre", "Post" and "Latest" HbA1c readings were analysed to determine if acromegaly treatment has a long-term effect on glycaemic control. This showed significant decrease between Pre HbA1c and Post HbA1c ($P=0.0210$). There was no significant difference between Post HbA1c and Latest HbA1c ($P=1.00$).
Conclsion
IGR is a risk factor for diabetes mellitus and cardiovascular disease. Our data showed that improvements could be made in the care of patients with IGR detected in the diagnostic OGTT for acromegaly and in the follow up HbA1c monitoring for those with established diabetes mellitus or IGR who underwent acromegaly treatment.

DOI: 10.1530/endoabs.81.P437

P652

Thinking horses, finding zebras: a rare case report of a giant cell tumor of the skull in a pediatric patient

Viviana Popa[2], Alexandru Florescu & Cristina Preda
"Sfantul Spiridon" Hospital, Iasi, Romania; [2]Saint Spiridon County Hospital, Endocrinology, Iaşi, Romania

Giant cell tumors are rare, benign but aggressive and locally invasive tumors that usually affect the long bones in the limbs, typically presenting during the 3rd or 4th decade of life. Giant cell tumors of the skull are exceedingly rare, and less than 150 cases have been reported to date, of which less than 10 were described in the pediatric population. Here, we present the case of a 14 year old female that progressively developed severe headaches, blurry vision and diplopia over approximately 4 months. She was initially directed to the Neurosurgery service, where imaging studies revealed a mass, initially presumed to be a craniopharyngioma, on the left cavernous sinus topography, that extended into the sella turcica and compressed the pituitary. Complete resection was impossible due to the close proximity of the mass with the internal carotid artery, so endoscopic transnasal partial resection and a biopsy were performed instead. Histopathological examination along with immunohistochemical staining suggested that the mass was a pituitary adenoma. Endocrinological examination revealed partial corticotroph and tireotroph insufficiency, and substitution treatment with hydrocortisone and levothyroxine was initiated, but the patient was non-adherent. Over the next 6 months, the patient's symptoms worsened, and she was readmitted to the Neurosurgery service, where imaging studies showed the remaining mass had grown to 3 centimeters maximum diameter. A second

endoscopic transnasal partial resection and biopsy were performed. Second biopsy results suggested a giant cell tumor, but recommended determining PTH levels to rule out a brown tumor. Subsequent endocrinological examination revealed moderately elevated PTH levels (*124 pg/ml),* and vitamin D deficiency (serum vitamin D = 10.32 ng/ml). PTH levels normalized (*64.9 pg/ml*) after 6 months of vitamind D treatment (2000 IU daily). Giant cell tumors of the skull bones are exceedingly rare, especially in the pediatric population, but should still be considered in the differential diagnosis of sellar and parasellar masses. This case report is an opportunity to go over the impact of this type of tumor on quality of life, the differential diagnosis process, as well as the therapeutic options and their indications and contraindications in the adult and pediatric population.

DOI: 10.1530/endoabs.81.P652

P653

Predicting hypogonadotropic hypogonadism persistence in male macroprolactinoma

Yaron Rudman[1,2], Hadar Duskin-Bitan[1,2], Hiba Masri-Iraqi[1,2], Amit Akirov[1,2] & Ilan Shimon[1,2]
[1]Beilinson Hospital, Rabin Medical Center, Institute of Endocrinology, Petah-Tikva, Israel; [2]Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

Objective
To study the baseline characteristics predicting hypogonadotropic hypogonadism (HH) persistence in men with macroprolactinoma following medical treatment with cabergoline.
Design
Retrospective cohort study conducted in a tertiary pituitary center.
Methods
Male patients diagnosed with macroprolactinoma and HH that received cabergoline treatment with subsequent prolactin normalization were included: men that achieved eugonadism, and men that remained hypogonadal. Patient's demographic, clinical and biochemical parameters, sellar magnetic resonance imaging (MRI) and visual fields tests were obtained. Univariate analyses and multivariate logistic regression models for HH persistence were developed to investigate the relative contribution of the predicting factors.
Results
Fifty-eight male patients (age, 49.2 ± 12.6 years) with a median baseline prolactin of 1154 ng/ml (IQR, 478-2763 ng/ml) and adenoma (maximal) diameter of 25.9 ± 14.8 mm were followed for a median of 5.6 years (IQR, 3.0-10.7). All men achieved normoprolactinemia with cabergoline treatment. 12 men (21%) suffered from HH persistence at the end of follow-up, and 46 men achieved eugonadism. Baseline testosterone (1.6 ± 0.7 vs 0.7 ± 0.6 ng/ml; $P < 0.01$), luteinizing-hormone (1.8 ± 1.5 vs 0.4 ± 0.2 mIU/ml; $P < 0.01$) and follicle stimulating-hormone (3.4 ± 2.9 vs 0.9 ± 0.7 mIU/ml; $P < 0.01$) were lower, and prolactinoma diameter (23.7 ± 12.8 vs 34.6 ± 18.9 mm; $P = 0.02$) was larger in men with HH persistence. In addition, suprasellar tumor invasion (RR = 6.6; 95% CI 1.6–27.8), visual field defect (RR = 3.8; 95% CI 1.5–9.3) and hypopituitarism (RR = 6.3; 95% CI 2.6–14.8) were associated with HH persistence. 42 out of 46 men (91%) accomplished eugonadism within the first year following prolactin normalization. In a multivariate logistic regression model, the presence of either VFD and/or hypopituitarism (OR = 11.5; 95% CI 1.88–71.32) and baseline testosterone levels (OR = 0.12; 95% CI 0.02–0.64) remained independent predictors of HH persistence. Adenoma maximal diameter (OR 1.02; 95% CI 0.96–1.07) did not predict HH persistence.
Conclusion
In our cohort of men with macroprolactinoma that reached prolactin normalization with cabergoline treatment, 21% had HH persistence. Low baseline testosterone levels, visual field defect and pituitary hormone deficiency were independently associated with HH persistence. 91% of men accomplished eugonadism within the first year following prolactin normalization. These findings support informed clinical decisions regarding testosterone replacement initiation in men with macroprolactinomas.

DOI: 10.1530/endoabs.81.P653

P654

Pre and post-surgical pituitary dysfunction increase the risk of mortality in patients with non-functioning pituitary tumors: A long-term cohort study

Arturo Beyhart[1,2], Karla Mariaca[2], Valeria Salva-Crespi[1], Daniela Díaz Catalán[1], Iban Aldecoa[3], Maria L Olondo[4], Bernardo Sanchez-Dalmau[5], Isam Alobid[6], Irene Halperin[2], Mireia Mora[1,2], Joaquim Enseñat[7] & Felicia Alexandra Hanzu[1,2]
[1]IDIBAPS, Group of Endocrine Disorders, Barcelona, Spain; [2]Hospital Clinic, Endocrinology and Metabolism, Barcelona, Spain; [3]Hospital Clinic, Pathological Anatomy Centre, Barcelona, Spain; [4]Hospital Clinic, Image Diagnostic Centre, Barcelona, Spain; [5]Hospital Clinic, Ophthalmology Department, Barcelona, Spain; [6]Hospital Clinic, Otorhinolaryngology, Barcelona, Spain; [7]Hospital Clinic, Surgery Department, Barcelona, Spain

Background
Long-term studies evaluating mortality in patients with non-functioning (NF) pituitary tumors (PitNets) are limited, although standardized mortality ratios (SMR) in these patients are reported to be higher than that of general population. There is also no agreement on predictive factors associated to the increased mortality apart from age at diagnosis and glucocorticoid substitution therapy dose.
Objective
To assess long-term mortality and associated predictive factors in a single-surgeon cohort of patients with NF PitNets.
Methods
Patients < 80 years at diagnosis with a NF PitNet surgically intervened between 2005 and 2015 in the Hospital Clínic Barcelona Spain ($n = 90$, 51 females) were followed until censored date (01 December 2021) exitus or loss of follow up. Standardized mortality ratios (SMRs) were calculated using Catalan death rates from included years. Proportional hazards of mortality predictors were assessed by cox regression models. All-cause mortality survival rates were assessed by Kaplan-Meier curves. All analyses were adjusted by age and sex.
Results
Median follow-up was 7 years (range: 1 month–13 years) with a total patient-years of 808. Fifteen patients (16.6%) (5 females) died during the study period at a mean age of 74 ± 11 years. At half of study follow up (93 months), survival rate was 93% for females and 76% for males ($P = 0.083$). Main causes of death were associated to infections, malignancy, and cardiovascular diseases. Gender, age at diagnosis, corticotroph deficiency at diagnosis, tumor extension to the sphenoid sinus, tumor contact with the optical chiasm and tirotroph affection due to surgery were associated to exitus in univariate analysis ($P < 0.03$). However, only corticotroph deficiency at diagnosis and tirotroph affection due to surgery remained independently associated in multivariate cox regression analysis with a hazard ratio of 2.96 (95% CI, 1.32-7.91) and 3.99 (95% CI, 1.87-18.23) respectively. Kaplan-Meir log rank factor comparison showed that corticotroph deficiency at diagnosis was also associated with a younger death age (73.3 vs 81.9 years, $P = 0.021$). Overall SMR adjusted by age and sex was 3.92 in the whole cohort with respect to Catalan population ($P < 0.001$) and higher SMR for patients with tirotroph affection due to surgery was found (9.02 ($P < 0.001$)).
Conclsion
Although NF PitNets have a benign behavior, patients maintain substantially higher mortality rates than general population. Affections of pituitary hormonal axes either due to the mass effect of the tumor or because of neurosurgery are key risk factors associated to increased and earlier mortality.

DOI: 10.1530/endoabs.81.P654

P655

Congenital combined pituitary hormone deficiency associated with primary ovarian insufficiency: a case report

Ameni terzi, Nadia Khessairi, yasmine mouelhi, Fatma Chaker & Melika Chihaoui
Rabta Hospital, Endocrinology, Tunis, Tunisia

Introduction
Congenital combined pituitary hormone deficiency (CCPHD) is a rare disorder characterized by an impaired production of two or more hormones of the anterior pituitary gland. It is linked to different genetic mutations and requires an early diagnosis to prevent burdensome developmental consequences. Primary ovarian insufficiency, disparately is the depletion of ovarian function with loss of functional primordial follicles before the age of 40 years due to multiple etiologies including genetic causes. The association between CCPHD and primary ovarian insufficiency has rarely been documented representing thus an uncommon and unexpected condition that merits case report herein.
Case presentation
A 14-year-old female was referred to our department for delayed growth. Born at term with no history of perinatal insult, she was diagnosed with central congenital hypothyroidism in a pediatric unit and L-thyroxine replacement therapy was started. Within the next few years, the patient presented a decrease in growth velocity. Short stature and delayed development were observed. The anthropometric measurements showed weight 28 kgs (between -3SDS and -2SDS) and

height 121 cms (-4SDS) with height genetic target of 175 cm. Her secondary sexual characters rated S1, P1 and A0 according to Tanner's classification. There were no dysmorphic features. She had delayed bone age in relation to chronological age (bone age according to Greulich and Pyle method: 9 years and 6 months). The evaluation of growth hormone (GH) secretion revealed GH deficiency (GH peak response to insulin: inferior to 0.25 mUI/l; GH peak response to glucagon: 0.51 mUI/l). The insulin tolerance test disclosed corticotropin deficiency. ACTH, Prolactin levels were respectively 21.6 pg/ml, 11µg/l. The further investigation of the pituitary gland via magnetic resonance imaging demonstrated congenital pituitary hypoplasia. The patient started consequently GH and glucocorticoid-supplementary therapy. When she was 16-years old, she had primary amenorrhea associated to absence of secondary sexual characters development. Gonadotropin levels were elevated: FSH was 72.9 UI/l and LH was 26.34 UI/l. Pelvic ultrasound showed uterine hypoplasia. The karyotype was 46 XX. Primary ovarian insufficiency was then diagnosed.
Conclusion
This report outlines an unprecedented coexistence of CCPHD (thyrotropin, somatotropin, corticotropin deficiencies in our sample) and primary ovarian insufficiency. A further genetic analysis is essential although the cause remains unidentified in the majority of cases. Early recognition of these disorders is paramount as delay in replacement therapy can have devastating consequences.

DOI: 10.1530/endoabs.81.P655

P656

Insulin resistance, glucose and lipid metabolism in patients with PROP 1 mutation –single center, long term observation

Łukasz Kluczyński[1], Bartosz Partyński[1], Damian Rogoziński[1], Anna Bogusławska[1], Agata Zygmunt-Górska[2], Małgorzata Wójcik[2], Jerzy Starzyk[2], Alicja Hubalewska-Dydejczyk[1] & Aleksandra Gilis-Januszewska[1]
[1]Chair and Department of Endocrinology, Faculty of Medicine, Jagiellonian University Medical College, Krakow, Poland; [2]Department of Pediatric and Adolescent Endocrinology, Chair of Pediatrics, Pediatric Institute, Jagiellonian University, Medical College, Krakow, Poland

Introduction
A mutation in the PROP-1 gene is a rare cause of childhood-onset hypopituitarism. Patients with the disorder usually present with multiple pituitary hormone deficits. The pattern of development and the course of insufficiencies of individual axes remain unclear and affect patients metabolic status. Growth hormone therapy and substitution of other hormones may influence on glucose and lipid metabolism as well.
Aim
To characterize the carbohydrate and lipid metabolism of patients with childhood onset of hypopituitarism caused by PROP-1 mutation on the basis of long term observation in the pediatric/adult endocrinology departments of our university. The mean time of follow-up was 38.3 years (SD 12.8) with the longest observation lasting 62 years.
Methods
A retrospective analysis of metabolic data of 21 patients (12W/9 M) with confirmed PROP-1 mutation was performed. The mean age at the diagnosis was 7.3 years (SD 3.5). All patients present with thyroid, gonadal and somatotropic axes insufficiencies, while secondary hypoadrenalism was diagnosed in 19 cases (in 2 patients – transient).
Results
Body mass index (BMI) was elevated in 11/21 of patients (6/21 – overweight, 5/21 – obesity). At least one lipid abnormality - increased level of total cholesterol (in 9/21, 42.8% of cases, mean value 5.6 mmol/l), low-density lipoprotein (LDL – in 13/21, 61.9% of cases, mean value 3.8 mmol/l) or triglycerides (in 5/21, 23.8% of cases, mean value 1.7) mmol/l or decreased concentration of high-density lipoprotein (HDL - in 7/21, 33.3% of cases, mean value 1.4 mmol/l) was detected in majority of cases (16/21, 76% of patients). All patients had correct levels of fasting glucose (mean value 4.6 mmol/l) and glycolyzed hemoglobin (HbA1c; mean value 5.3%). In one patient oral glucose tolerance test (complete data available for 17/21 of cases) revealed impaired glucose tolerance. Mean values of fasting insulin and C-peptide were 6.92 uU/ml (min. 1.76, max. 19.0), and 1.85 ng/ml (min. 0.73, max. 6.58), respectively. HOMA IR was elevated (>2) in 5 patients. BMI was positively correlated ($P<0.05$, calculated for 17/21 of cases) with level of triglycerides, fasting insulin, HOMA-IR and insulin area under curve (AUC) in OGTT as well as negatively associated with HDL values. Age was corelated positively with HbA1c and glucose AUC in OGTT. Moreover, a significant positive correlation was documented for insulin and TC, LDL as well as triglycerides.
Conclusions
Patients with PROP-1 mutation-induced hypopituitarism characterize with multiple metabolic disturbances. The specific group of patients requires multidisciplinary medical care.

DOI: 10.1530/endoabs.81.P656

P657

Ectopic lipid deposition and insulin resistance in patients with GH disorders before and after treatment

Mai C. Arlien-Søborg[1,2], Michael Alle Madsen[1], Jakob Dal[1], Thomas Krusenstjerna-Hafstrøm[1], Steffen Ringgaard[3], Nickolaj Skou[4], Morten Lyng Høgild[1] & Jens Otto Jorgensen[1,2]
[1]Aarhus University Hospital, Department of Endocrinology and Internal Medicine, Aarhus N, Denmark; [2]Aarhus University Hospital, Medical Research Laboratory, Department of Clinical Medicine, Aarhus N, Denmark; [3]Aarhus University Hospital, Department of Clinical Medicine - The MR Research Centre, Aarhus N, Denmark; [4]Aarhus University Hospital, Department of Radiology, Aarhus N, Denmark

Background
Insulin resistance as part of the metabolic syndrome is associated with ectopic lipid deposition. Growth hormone (GH) status also modulates ectopic lipid accumulation but how this associates with insulin resistance in patients with GH disorders is not well established.
Aim
To study body composition, ectopic lipid deposition and insulin sensitivity in acromegaly and adult GH-deficiency before and after treatment.
Subjects and Methods
Twenty-one patients newly diagnosed with acromegaly and twelve patients with adult GH deficiency (GHD) were studied at diagnosis and after treatment. A reference group of twelve subjects was studied on a single occasion. Each study day comprised assessment of body composition with dual-energy X-ray absorptiometry, ectopic lipid deposition in the liver and skeletal muscle by MR spectroscopy, and Homeostatic Model Assessment for Insulin Resistance (HOMA-IR).
Results
Disease control of acromegaly decreased lean body mass (LBM) ($P< 0.000$) and increased the percentage of total body fat (TBF) ($P< 0.000$). GH replacement increased LBM in the GHD patients ($P=0.007$) and decreased the percentage of TBF ($P=0.010$). The intrahepatic lipid content (IHL) increased after disease control in acromegaly ($P=0.004$) to levels resembling a reference group ($P=0.28$), whereas IHL did not change significantly after GH replacement in GHD ($P=0.34$). Insulin resistance (HOMA-IR) improved after disease control of acromegaly ($P<0.000$) and remained unaltered after GH replacement in the GHD patients ($P=0.829$). IHL and HOMA-IR correlated positively in the reference group ($r=0.75$, $P=0.005$) and in GHD patients before ($r=061$, $P=0.038$) and after ($r=0.66$, $P=0.020$) GH replacement, whereas in acromegaly the correlation only manifested after disease control ($r=0.52$, $P=0.038$).
Conclsions
1) GH status is a significant modulator of body composition and insulin sensitivity.
2) GH excess reduces total fat mass and intrahepatic lipid content together with induction of insulin resistance.

The data support the notion that GH-induced insulin resistance is unassociated with hepatic lipid accumulation.

DOI: 10.1530/endoabs.81.P657

P658

The diagnosis of recurrence during postoperative follow-up of Cushing's disease

Mattia Barbot, Alessandro Mondin, Filippo Ceccato, Pierluigi Mazzeo, Martina Lazzara, Daniela Regazzo & Carla Scaroni
University Hospital of Padova, Endocrinology Unit, Department of Medicine-DIMED, Padova, Italy

Introduction
Transsphenoidal surgery (TSS) is the first-choice treatment in Cushing's disease (CD) with an immediate success rate of 70-80%. Unfortunately, due to the high rate of post-operative recurrences, CD patients require life-long surveillance.

However, there is no consensus on how to follow these patients after TSS to early diagnose relapses. The aim of the study was to find reliable predictors of recurrence after neurosurgery in CD.
Material and methods
Fifty-five CD patients (f/m = 43/12, median age 39, IQR 32-49 years) in remission after TSS (median 100, range 36–146 months) were included. Remission was defined by the presence of at least 2 of the following criteria: i) low-undetectable postoperative serum cortisol; ii) prolonged glucocorticoid replacement therapy; iii) normal urinary free cortisol (UFC) and late-night salivary cortisol (LNSC) for at least 12 months after surgery; iv) serum cortisol <50 nmol/l after 1 mg-DST. All patients were submitted to desmopressin (DDAVP) test in the diagnostic phase and were re-tested, at least once, 6-12 month after surgery.
Results
Thirteen patients (24%) recurred after a median time of 43 months (IQR 18-65). There were no differences in age and disease severity at time of diagnosis between patients who recurred and those in long-term remission, whereas macroadenomas were more frequently found in recurrent patients ($P=0.003$). No differences in histological features were recorded. Early post-operative serum cortisol was markedly lower in patients who remained in remission [55.5 (32.3-97) vs 120 (57-250), $P=0.024$], even though there was some degree of overlap between groups. A threshold of 63 nmol/l for serum cortisol was able to identify patient at high risk of relapse with sensitivity (SE) of 77% and specificity (SP) of 69%. Patients with recurrence displayed a greater ACTH and cortisol response to DDAVP test compared to those in prolonged remission ($P<0.0001$). An absolute increase in ACTH >7.6 ng/l was identified (AUC = 0.8796; 95%CI:75–100) as the best predictor of recurrence, with SE of 85% and SP of 83%. At 6 and 12 months from TSS, no differences in UFC and LNSC were observed between groups.
Conclusions
The presence of corticotroph macroadenoma is a risk factor for CD relapse. Early post-operative serum cortisol level is a reliable indicator of surgical outcome but DDAVP test is far more accurate to predict future recurrence. The re-appearance of a positive response to this test precedes the increase in LNSC and UFC by several months, thus patients displaying such alteration should be closely monitored.

DOI: 10.1530/endoabs.81.P658

P659

Evaluation of copeptin levels during glucagon stimulation test in children with suspected growth hormone deficiency

Emanuele Ferrante[1], Federico Giacchetti[1], Rita Indirli[1,2], Eriselda Profka[1], Giulia Rodari[1], Claudia Giavoli[1,1], Giovanna Mantovani[1,2] & Maura Arosio[1,1]
[1]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Endocrinology Unit, Milano, Italy; [2]Department of Clinical Sciences and Community Health, University of Milan, Italy

Introduction
Glucagon stimulation test is one of the recommended growth hormone provocation tests for diagnosing growth hormone deficiency in children. In adult patients, recent data showed that glucagon administration is able to stimulate the release of copeptin, the stable C-terminal glycopeptide of the AVP prohormone whose evaluation during hypertonic saline infusion represents the gold standard for the differential diagnosis of polyuria/polydipsia. However, similar data on pediatric population are still lacking. Aim of this study was to evaluate copeptin levels during glucagon test in children with suspected GH deficiency and to correlate its secretion with that of glucose, GH and cortisol.
Methods
Twenty-one children (10 females, mean age 10.3 ± 2.9 years) with suspected growth hormone deficiency were studied during glucagon stimulation test (30 μg/Kg, maximum 1 mg intramuscolarly). Of these, 20 patients had normal posterior pituitary function, and one patient had well-established central diabetes insipidus. Blood samples for measurement of glucose, GH, cortisol and copeptin were taken at baseline and 60, 90 120, 150 and 180 minutes after glucagon administration.
Results
Median basal copeptin levels in 20 patients without diabetes insipidus were 4.1 pmol/l (interquartile range: 3.3-6.7). During glucagon test, a significant increase of copeptin was recorded 120, 150 and 180 minutes after stimulation (median: 8.1, 10.6 and 8.9 pmol/l, respectively, for all $P<0.01$ vs basal) with a peak after 150 minutes (median: 10.6 pmol/l, interquartile range: 5.4-17.9).
Correlation study for repeated measures showed that copeptin was directly associated with cortisol ($r=0.39$, $P<0.001$) and GH ($r=0.42$, $P<0.001$), and inversely associated with glucose ($r=-0.36$, $P<0.001$). In a multilevel mixed-effects regression model, copeptin was associated with cortisol ($\beta=0.375$, $P=0.01$) and time ($\beta=0.005$, $P<0.001$) but not with GH and glucose. No difference in median copeptin levels at any time point between patients with negative and positive response to glucagon test was found. The only patient with central diabetes insipidus showed low basal and stimulated copeptin levels (basal: 1.5 pmol/l, peak: 2.0 pmol/l)
Conclusion
glucagon administration represents a nonosmotic stimulus of the posterior pituitary also in children, as indicated by increased copeptin levels during the test. Copeptin peak is reached after 150 minutes and its trend seems to be related to cortisol secretion. Further studies are needed in order to clarify the mechanism behind the copeptin stimulation and to confirm the usefulness of this test for the assessment of posterior pituitary function.

DOI: 10.1530/endoabs.81.P659

P660

Soluble alpha klotho in adult patients with growth hormone deficiency

Junia Ribeiro de Oliveira Longo Schweizer[1,2], Katharina Schilbach[1], Michael Haenelt[1], Anica Gagliardo[1], Sylvere Störmann[3], Jochen Schopohl[3] & Martin Bidlingmaier[1]
[1]LMU Klinikum; Med. Klinik und Poliklinik IV/Endokrinologie, Munich, Germany, Endokrinologie, Endokrinologisches Labor, München, Germany; [2]LMU Klinikum; Med. Klinik und Poliklinik IV/Endokrinologie, Munich, Germany, München,; [3]LMU Klinikum; Med. Klinik und Poliklinik IV/Endokrinologie, Munich, Germany, München, Germany

Background
We recently have shown a close association of high concentrations of soluble alpha klotho (sαKL) to disease activity in acromegaly. Small pilot studies suggested that sαKL concentrations might be reduced in GH deficiency (GHD) and increase after recombinant human GH (rhGH) therapy. Our aim was to evaluate the potential of sαKL as a biomarker in GHD.
Methods
We evaluated sαKL in comparison to the classical biomarkers GH, IGF-I and IGFBP 3 in different cross-sectional cohorts: adult patients with GHD (AGHD) without ($n=80$; A) or with rhGH ($n=57$; B), patients without GHD having either NFPA ($n=20$; C) or prolactinoma ($n=30$; D), and in healthy subjects ($n=199$; E). Furthermore, 22 patients were evaluated longitudinally, before and during rhGH therapy.
Results
As expected, GH, IGF-I and IGFBP 3 were lower in AGHD without rhGH (A) compared to the non-AGHD groups (C, D and E), and increased with rhGH therapy (B) ($P<0.05$ for all comparisons). SαKL concentrations in the cohorts were as follows (median (interquartile ranges); all pg/ml: A: 612 (468-785), B: 668 (468-801), C: 853 (687-3-962), D: 1036 (827-1399) and E: 869 (720-1122). sαKL was significantly lower in AGHD without rhGH (A) compared to NFPAs (C), prolactinomas (D) and healthy subjects (E) ($P<0.05$ for all comparisons) but was not higher in AGHD patients with rhGH therapy (A vs. B, $P>0.99$). Instead, sαKL concentrations in AGHD patients with rhGH remained lower compared to patients with prolactinoma and healthy controls (B vs. D and E, $P<0.0001$), and tended to remain lower compared to NFPAs (B vs. C, $P=0.09$). However, in the longitudinal cohort, sαKL increased with rhGH (599 (469-762) vs. 728 (605-926)) as did IGF-I (μg/l): 48.5 (38.7-62.2) vs. 142 (108-162), and IGFBP 3 (μg/l): 2681 (1840-3524) vs. 3270 (2541-4257), $P<0.001$ for all).
Conclusion
Our study suggests that sαKL is lower in AGHD than in patients with prolactinoma, NFPA and healthy subjects. During longitudinal assessment in the same patients, a significant increase in sαKL is seen in GHD subjects treated with rhGH. However, in contrast to situations of GH excess, where sαKL is greatly elevated, in GHD before and after treatment with rhGH, it remains within the normal range also seen in normal subjects and patients with pituitary disorders without GHD.

DOI: 10.1530/endoabs.81.P660

P661

Metyrapone vs osilodrostat in the short-term therapy of endogenous Cushing's syndrome: results from a retrospective single center analysis

Mario Detomas[1], Barbara Altieri[1], Timo Deutschbein[1,2], Martin Fassnacht[1] & Ulrich Dischinger[1]
[1]University Hospital Würzburg, Würzburg, Germany; [2]MEDICOVER Oldenburg MVZ, Oldenburg, Germany

Background
Although surgery is considered the first-line treatment for patients with endogenous Cushing's syndrome (CS), medical therapy is often required to control severe hypercortisolism. Metyrapone and osilodrostat are inhibitors of 11β-hydroxylase that have not been directly compared yet.
Methods
Retrospective analysis of patients with adrenocorticotropin (ACTH)-dependent and ACTH-independent CS treated with metyrapone or osilodrostat (as monotherapy) for at least one month. Serum cortisol and 24h-urinary free cortisol (24h-UFC) were analyzed at baseline (T0), after 2 weeks (T1), 1 month (T2) and 3 months (T3) of therapy. Furthermore, serum potassium and blood pressure were evaluated.
Results
16 patients with CS (8 under metyrapone and 8 under osilodrostat) were identified. Despite heterogeneity, both groups showed comparable mean 24h-UFC levels at T0 (757.8 µg/24h under metyrapone vs 816.9 µg/24h under osilodrostat; n.s.). From T0 to T1, the decrease of 24h-UFC was less pronounced under metyrapone than osilodrostat (-21.3% vs -68.4%; median drug dose: 1000 mg vs 4 mg). This tendency persisted at T2 (-37.3% vs -50.1%; median drug dose: 1250 mg vs 6 mg). A substantial difference in potassium levels at T3 was identified (-10.9% under metyrapone vs +14.5% under osilodrostat from T0). Furthermore, a more prolonged QTc-interval was observed under osilodrostat than under metyrapone (455.3 ms vs 432.5 ms). From T0 to T2, the number of antihypertensive drugs decreased under osilodrostat.
Conclsion
Although both of the drugs are efficient in reducing cortisol levels, osilodrostat seems to induce a faster reduction of cortisol levels and a faster control of blood pressure.

DOI: 10.1530/endoabs.81.P661

P662

Inferior petrosal sinus sampling for pituitary neuroendocrine tumors localization in cushing's disease

Paloma Moreno-Moreno, M[a] Rosa Alhambra Expósito, Ángel Rebollo-Román, Aura D. Herrera-Martínez & María Ángeles Gálvez-Moreno
Reina Sofia University Hospital, Endocrinology and Nutrition, Córdoba, Spain

Objective
Cushing's disease (CD) is the most common cause of hypercortisolism after iatrogenic origin, it represents approximately 70% of patients with endogenous Cushing's syndrome (CS) and ectopic ACTH secretion (10%). CD is caused by a corticotropin-secreting pituitary neuroendocrine tumor (ACTH-secreting Pit-NETs), 95% of cases as a microadenoma. In ACTH-dependent CS, differential diagnosis between CD and ectopic CS must be established. 40% of CD cases, any tumor is observed in the contrast-enhanced pituitary magnetic resonance imaging (MRI), and among the detected lesions, 85-87% are microadenomas Objective: to evaluate the usefulness of inferior petrosal sinus catheterization in the diagnosis of Cushing's disease, the intrahypophyseal location of the ACTH-secreting Pit-NETs.
Patients and methods
A retrospective observational study was performed in all patients with CS that underwent bilateral inferior petrosal sinus catheterization (BIPSS) in a single center. Statistical analysis: Chi square test with Yate's correction s and Cohen's coefficient k were used as a measure of agreement between the exploratory techniques. Sensitivity, specificity, positive and negative predictive value, and positive and negative probability coefficient were also calculated. Chi-squared test was used to compare categorical data. Statistical analyses were performed using SPSS® statistical software version 20.
Results
BIPSS was performed in 33 patients, 75.8% women, age 41.79 ± 14.60 years. BIPSS achieved a sensitivity of 96.67 %, IC 95% (0.80 − 0.99) and a specificity 100%, IC 95% (0.31 − 0.96). Positive predictive value was 100%, IC 95% (0.85 − 0.99) and the negative predictive value was 75%, IC 95% (0.21 − 0.98). The global value or efficiency of the procedure 96.97% IC 95% (0.82 − 0.99). An intersinus gradient ≥ 1.4 was observed in 25 patients. In those who underwent surgery, tumor localization during surgery coincided with BIPSS results in 80% of cases; Kappa index was 0.658 (P 0.000), so there is good agreement between the lateralization result of the BIPSS and the location by surgery for the location of the ACTH-producing adenoma. No complications were recorded after BIPSS.
Conclusions
BIPSS plays a key role in the diagnosis of CD, and its results in the location of the tumor must be taken into account, since it shows good precision when compared with the surgical location of the tumor.

DOI: 10.1530/endoabs.81.P662

P663

GH-secreting pituitary adenoma: dura mater invasion is not a predictor of acromegaly persistence after trans-sphenoidal surgery

Nunzia Prencipe[1], Giuseppe Diperna[2], ALESSANDRO MARIA BERTON[1], Bianca Baldassarre[2], Chiara Bona[1], Raffaele De Marco[2], Fabio Bioletto[1], Silvia Grottoli[1] & Francesco Zenga[2]
[1]University of Turin, Department of Medical Sciences, Turin, Italy; [2]Neurosurgery, University of Turin, Department of Neuroscience, Turin, Italy

Background
Despite the benign nature of pituitary adenomas, microscopic examination of surgical specimens showed that dural invasion occurs in about 42-85% of cases. No studies about dura mater invasion were conducted specifically in acromegaly, so the aim of the present study was to evaluate the relationship between histologically verified dural invasion and the "aggressiveness" features of GH-secreting adenomas.
Methods
A prospective study included all consecutive acromegaly patients that underwent neurosurgery (NS) at the Division of Neurosurgery of the University of Turin, between 2017 and 2020. All patients were operated with a 3DHD endoscope using an endoscopic endonasal approach by a single skilled neurosurgeon. For each patient the fallowing data were collected: 1) clinical, biochemical and morphological data at diagnosis, three months and one year after NS; 2) pathological features (dura mater invasion, immunohistochemical analyses, proliferation index Ki67 and p53, granulation pattern; 3) radiological findings at RMI scan, in particular intensity on T2-wighted images.
Results
35 acromegaly patients enrolled. Eleven patients had dura invasion (31%), while 24 did not have (69%). No significant differences were found in gender and age at diagnosis between INV+ and INV-. No difference was found in IGF-1 levels (INV+: 752 ng/ml, [548-987] ng/ml vs INV-: 664 ng/ml, [394-894] ng/ml) and IGF-1/ULN (2.5, [2.3-3.3] vs 2.4, [1.68 - 3.1]). GH levels at diagnosis were higher in INV+ (84.5 ng/ml, [29-153] ng/ml vs 17.2 ng/ml, [4.4-36] ng/ml, $P=0.02$). ROC curve analysis for GH levels at diagnosis showed that GH > 27 ng/ml was able to distinguish patients with dura mater invasion (AUC 0.760;$P=0.006$, sensitivity 80% and specificity 73%) and patients with GH > 27 ng/ml at diagnosis had a 10 times higher risk of dura invasion (Odds ratio 10.7; IC 95% 1.74-65.27). No difference was found in morphological, radiological and pathological features. We also analysed predictive parameters of healing. IGF-1 levels at diagnosis (625.5 ng/ml; [391.5 -867.5] ng/ml vs 872 ng/ml; [812 − 1011.5]ng/ml, $P=0.03$) and proliferation activity (Ki-67≥3%) were significantly lower in cured patients (16% vs 67%, $P=0.03$), while disease remission rate at three months was greater (100% vs 44%, $P=0.002$) compared to persistent disease patients.
Conclusion
The only parameter significantly associated with the dura mater invasion is GH levels at diagnosis. The dura mater invasion does not affect the possibility of recovery from acromegaly at 12 months. We confirmed that lower IGF-1 levels at diagnosis and lower Ki-67 are significantly associated with healing after surgery.

DOI: 10.1530/endoabs.81.P663

P664

Impact of COVID-19 lockdown in patients with acromegaly: an Italian multicenter experience

Rosa Pirchio[1], Renata Simona Auriemma[1], Valeria Cambria[2], Federico Gatto[3], Giulia Carosi[4], Marta Ragonese[5], Valentina Guarnotta[6], Filippo Ceccato[7], Alessia Cozzolino[8], Laura Mongioi[9], Nunzia Prencipe[2], Federica Nista[3], Giulia Del Sindaco[4], Aldo Calogero[9], Andrea Isidori[8], Carla Scaroni[7], Carla Giordano[6], Francesco Ferraù[5], Giovanna Mantovani[4], Diego Ferone[3], Silvia Grottoli[2], Felice Iasevoli[10], Annamaria Colao[1,11] & Rosario Pivonello[1,11]
[1]Università "Federico II" di Napoli, Dipartimento di Medicina Clinica e Chirurgia, Sezione di Endocrinologia, Naples, Italy; [2]Università degli Studi di Torino, SC Endocrinologia, Diabetologia e Metabolismo U, Dipartimento di Scienze Mediche, Turin, Italy; [3]IRCCS Policlinico San Martino Università di Genova, Dipartimento di Medicina Interna & Specialità Mediche (DiMI), Genoa, Italy; [4]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Endocrinology Unit, Milan, Italy; [5]Università degli Studi di Messina, Dipartimento di Patologia Umana dell'adulto e dell'età evolutiva, Messina, Italy; [6]Universitàdegli Studi di Palermo, Dipartimento promise, UOC di Endocrinologia e Malattie metaboliche, Palermo, Italy; [7]University-Hospital of Padova, Endocrinology Unit, Department of Medicine, DIMED, Padua, Italy; [8]Università degli Studi di ROMA "Sapienza", Dipartimento di MEDICINA SPERIMENTALE, Rome, Italy; [9]Università di Catania, UOC di Andrologia e Endocrinologia, Policlinico "G. Rodolico", Dipartimento di Medicina Clinica e sperimentale, Catania, Italy; [10]University of Naples Federico II, Department of Neuroscience, Naples, Italy; [11]"Federico II" University, Unesco Chair for Health Education and Sustainable Development, Naples, Italy

Over the last two years, COVID-19 outbreak and lockdown have exerted a remarkable psychological burden in the general population. Such an impact is supposed to be even worse in acromegaly, known to induce a severe psychological impairment due to its somatic disfigurements and systemic comorbidities. The current observational study aimed at investigating the impact of COVID-19 outbreak and lockdown on psychological health in acromegalic patients as compared to non-acromegalic healthy control population. During the last three weeks of lockdown, 246 patients (110 males, 136 females, age 51.4 $\pm$ 11.7 years) with history of acromegaly or active acromegaly under treatment from 9 Italian acromegaly referral centers and 246 age, gender, and marital status-matched controls were telematically administered several psychological questionnaires, aiming at evaluating the spectrum of anxiety (GAD-7) and depression (PHQ-9), and perceived stress (PSS). For all questionnaires, higher score indicated greater psychological impairment. A questionnaire evaluating quality of life in acromegaly, AcroQol, for which the higher score indicates a better quality of life, was administered exclusively to patients. Compared to controls, patients showed a significantly higher prevalence of moderate ($P=0.046$) and severe depression ($P=0.015$), and severe anxiety ($P=0.024$). Both in patient and controls, females showed higher scores in the entire series of psychological tests performed compared to males ($P<0.001$). Moreover, male patients showed significantly higher anxiety ($P=0.001$), and depression ($P<0.001$) scores, whereas female patients showed higher anxiety ($P=0.003$) and perceived stress ($P=0.037$) scores compared to respective controls. Glucocorticoid replacement (GR) therapy was significantly associated with higher scores of anxiety ($P=0.01$), depression ($P=0.037$), and perceived stress ($P=0.003$), and lower score of AcroQol ($P=0.038$). Patients with anxiety, depression, and perceived stress were mostly females ($P<0.05$), and patients with anxiety and perceived stress were also associated with low-grade instruction ($P<0.01$) and GR therapy ($P<0.01$). In conclusions, patients who experienced acromegaly had a greater risk of depressive and anxiety disorders as well as perceived stress compared to controls during COVID-19 outbreak and lockdown, thus suggesting the importance of a strict psychological monitoring.

DOI: 10.1530/endoabs.81.P664

P665

Long-term follow up after remission of Cushing's disease - experience of a single centre

Bojana Popovic[1], Sanja Ognjanovic[1], Dusan Ilic[1], Valentina Elezovic[1], Milica Opalic[1], Lena Radic[2], Mihailo Milicevic[2] & Djuro P. Macut[1]
[1]Clinic for Endocrinology, Diabetes and Metabolic Diseases, University Clinical Centre of Serbia, Department for Endocrine Tumors and Hereditary Cancer Syndromes, Belgrade, Serbia; [2]Clinic for Neurosurgery, University Clinical Centre of Serbia, Centre for Neurooncology, Belgrade, Serbia

Introduction
Chronic endogenous hypercortisolism in Cushing's syndrome imposes a great clinical burden of comorbidities, some of which might persist even after disease remission. Our aim was to analyze factors that predict long-term comorbidities after surgical remission of Cushing's disease (CD).
Subjects and methods
We retrospectively analyzed 37 patents (91.9% females) aged 39.5 $\pm$ 13.9 years (10-70) with diagnosed CD, treated in our institutions, and followed up during 15 years. Each patient was evaluated for presence of comorbidities [overweight/-obesity, impaired glucose metabolism (impaired fasting glucose, IFG/impaired glucose tolerance, IGT/diabetes, DM), hypertension (HTA), dyslipidemia, osteoporosis, depression], at the time of diagnosis and during follow up of clinical remission. Spearman's rank correlation coefficient was used to test associations between comorbidities and age, BMI, biochemical parameters and hormonal levels (basal cortisol and ACTH level, midnight cortisol level). Multiple regression analysis was used to test predictors of long-term comorbidities after CD remission. Statistical analysis was performed by SPSS software.
Results
At diagnosis, dyslipidemia, HTA, overweight/obesity, osteopenia/osteoporosis, IFG/IGT/DM and depression were present in these patients with frequences of 86.5%, 73.0%, 64.9%, 59.5%, 51.4% and 21.6%, respectively. Aside of 4 patients (10.8%), all the other had 2 or more comorbidities. The number of comorbidities positively correlated with age ($P=0.009$), BMI ($P=0.003$), glycemia ($P=0.018$), and triglyceride levels ($P=0.032$), and negatively with HDL ($P=0.009$); there were no significant correlations wih hormonal levels ($P>0.05$). Majority of patients (81.8%) had pituitary microadenoma. Transsphenoidal surgery (TS) was performed in 34 patients (91.9%), with median of 3 $\pm$ 4 months after diagnosis. After initial surgical success rate of 82.4% (28 patients), 20 patients (58.8%) kept long-term remission. Remission was achieved by bilateral adrenalectomy in 2 additional patients (22 overall, 59.5%), with follow up of 76.9 $\pm$ 60.6 months (1-192). Clinical remission was associated with significant decrease in frequency of overweight/obesity ($P=0.006$), depression ($P=0.004$), and HTA ($P=0.051$) while no significant decrease in frequency of dyslipidemia, IFG/IGT/DM and osteoporosis ($P>0.05$) was observed. A number of comorbidites remained positively associated with age ($P=0.016$), BMI ($P=0.042$), glycemia ($P=0.048$), and level of triglycerides ($P=0.048$), and negatively with HDL ($P=0.019$). In sepwise linear regression analysis the strongest predictors of long-term morbidity were age (B=0.068, $P=0.019$, 95% CI 0.013-0.124) and HDL level (B=-1.218, $P=0.005$, 95% CI -2.434–0.001) at diagnosis of CD.
Conclusion
Cushing's disease is the most prevalent cause of endogenous hypercortisolism, causing significant morbidity in these patients that remains so even after long-term remission. Life-long follow up of cardiovascular outcomes is needed in these patients.

DOI: 10.1530/endoabs.81.P665

P666

Inferior petrosal sinus sampling in differential diagnosis of adreno-corticotropic hormone (ACTH)-dependent cushing's syndrome: a tertiary centre experience

Cátia Araújo[1], Mafalda Martins Ferreira[1], Joana Reis Guiomar[1], Carolina Moreno[1], patrícia oliveira[1], Carla Baptista[1], Leonor Gomes[1,2], dírcea rodrigues[1] & Isabel Paiva[1]
[1]Centro Hospitalar Universitário de Coimbra, Serviço de Endocrinologia, Diabetes e Metabolismo, Coimbra, Portugal; [2]Centro Hospitalar e Universitário de Coimbra, Serviço de Endocrinologia, Diabetes e Metabolismo, Coimbra, Portugal

Introduction
Inferior petrosal sinus sampling (IPSS) has been considered to be the gold standard for differential diagnosis of Cushing's Disease (CD) and ectopic ACTH secretion (EAS).
Aim
To describe the experience of our centre in performing IPSS, its safety and efficacy; assess remission rates from transphenoidal surgery and clinical course; approach to the difficulty in the etiological diagnosis of ACTH-dependent Cushing's Syndrome.

Methods
In this single centre retrospective study we included 14 patients diagnosed with ACTH-dependent Cushing's Syndrome which IPSS were performed between 2011-2021. The diagnosis of CD was made when the basal central/peripheral ACTH ratio was > 2 and/or the rate after CRH/desmopressin stimulation was > 3. With the inter-sinus ratio > 1.3, lateralization was determined.
Results
2 patients whose IPSS failed due to anatomical variation and vasovagal syncope were excluded. In 12 patients, 7 were female patients. Median age: 48.9 ±11.9 years. Sellar magnetic resonance imaging (MRI) demonstrated pituitary microadenoma in 10 cases. IPSS results were conclusive for diagnosis of CD in 83% of patients (10) and none of them indicated EAS. Lateralization by IPSS and MRI was concordant in 9 out of 10 cases with CD and microadenoma. Inconclusive results in 2 IPSS: 1) blood sample collection into non-EDTA tube; 2) absence of measurement of prolactin and impossibility of assessing correct sampling in the absence of basal central/peripheral ACTH ratio. In 10 of 12 patients whose IPSS showed CD diagnosis, correct lateralization was confirmed by the operation in one patient only. Pathology specimens did not show pituitary adenoma in the other 5 cases. The rate of remission after transsphenoidal surgery was 2 out 6 patients.
Conclusions
IPSS is a safe procedure and an effective test in the differential diagnosis of ACTH-dependent Cushing's Syndrome. In our study, the sensibility of IPSS assessed was 83%, similar to what is described in the previous studies. DDaVP stimulation was equivalent to CRH stimulation. We emphasize the possibility of procedural failures that must be identified. It should be noted that regardless of whether or not there is a pituitary adenoma image on an MRI, IPSS proved to be useful to confirm CD and suggest a lateralization of ACTH secretion.

DOI: 10.1530/endoabs.81.P666

P667

Pituitary adenoma in multiple endocrine neoplasia type 1 (MEN1) syndrome: a single-center study

Roberta Modica, Alessia Liccardi, Roberto Minotta, Giuseppe Cannavale, Elio Benevento & Annamaria Colao
University of Naples Federico II, Department of Clinical Medicine and Surgery, Endocrinology Unit, Naples, Italy

Background
Multiple endocrine neoplasia type 1 (MEN1), is an autosomal dominant inherited disorder with high penentrance, characterized by the onset of multiple tumors, mainly in parathyroid, pituitary gland and gastroenteropancreatic tract. During the course of the disease pituitary adenomas (PA) occur in 20-65%, rarely as first clinical manifestation, and are often described as larger, more aggressive, and more resistant to conventional therapy than their sporadic counterpart. The aim of this study is to analyse clinical characteristics of PA in a monocentric series of MEN1 patients.
Aim
The clinical charts of all patients with MEN1, referred to the Endocrinology Unit at the Federico II University of Naples from January 2000 to June 2021, were retrospectively evaluated, analyzing epidemiological and clinical data.
Results
We identified 91 MEN1 patients (F/M = 50/41). The prevalence of PA was 49.5% (45 patients) with a slight female preponderance (F/M = 1.36). PA was diagnosed in 92.2% of cases after the diagnosis of MEN1. The mean age at diagnosis of PA was 44.6y (13-75y), this was much lower when PA was identified as the first MEN1 manifestation (28y). PA were microadenoma in 60% (27 patients), and macroadenoma in 40% (18 patients). PA were non-secreting in 44.4% (20 patients), PRL-secreting in 42.2% (19 patients), GH-secreting in 2.2% (1 patients), PRL-GH secreting in 8.8% (4 patients), and ACTH-secreting in 2.2% (1 patients). Symptoms of hormonal hypersecretion and/or compression of adjacent structures were detected in 53.4% (24 patients). Among patients with prolactinomas the M:F ratio was 1/1.11 (11/12 patients), and all 12 affected females had associated symptoms (menstrual irregularities, galactorrhea); while only 2/11 male patients had hyperprolactinemia-related disorders (decreased libido, impotence). With regard to therapeutic treatment, cabergoline was used in 40% (18 patients) of PA, while octreotide was used only in 2.22% (1 patient). Transphenoidal surgery was performed in cases of refractoriness or macro-adenoma-related symptoms in 15.5% of cases (7 patients), and radiotherapy subsequently was necessary in 2.22% of cases (1 patient).
Conclusion
PA within MEN1, are more common in women and are rarely the first clinical manifestation of the syndrome. Importantly, our data suggest that PA do not seem to be more aggressive than sporadic forms and show good response to medical and surgical therapy. A multidisciplinary approach in specialized centers may improve the clinical history of these patients allowing early diagnosis.

DOI: 10.1530/endoabs.81.P667

P668

Ultrasound of the median nerve in acromegalic patients :changes at 1 year follow up

Ivana Ságová[1,2], Dušan Pávai[1], Marián Mokáň[2] & Peter Vaňuga[1]
[1]National Institute of Endocrinology and Diabetology, Department of Endocrinology, L'ubochňa, Slovakia; [2]Comenius University Jessenius Faculty of Medicine, 1st Department of Internal Medicine, University Hospital Martin, Martin, Slovakia

Background
The aim of our study was to asses changes in the cross sectional area (CSA) of the median nerve by ultrasound in newly diagnosed acromegalic patients 1 year after treatment of acromegaly (transsphenoidal surgery, somatostatine analogues).
Patients and methods
The study included 30 newly diagnosed acromegalic patients (18 females and 12 males) and 30 healthy controls (18 females and 12 males) matched for age, gender and body mass index. Clinical history, physical examinations, laboratory examinations and ultrasound evaluations were performed at baseline and 1 year after treatment of acromegaly.
Results
The CSA of the median nerve was increased in acromegalic patients compared with controls (13.3 ± 2.2 mm^2 vs. 7.6 ± 1.8 mm^2 $P < 0.001$). 1 year after the treatment of acromegaly a significant decrease of growth hormone (GH) and insulin-like growth factor I (IGF-I) levels were achieved. The CSA of the median nerve was significantly reduced 1 year after treatment to 11.7 ±1.8 mm^2 ($P < 0.001$). Positive correlation was found between the levels of IGF- I and CSA of the median nerve in acromegalic patients before treatment ($r = 0.492$, $P = 0.006$).
Conclusion
This study demonstrates reduction in median nerve CSA 1 year after treatment of acromegaly. This changes are closely associated with the reduction of IGF- I levels. Biochemical control of acromegaly is important factor for normalization of the median nerve size.
Keywords
acromegaly, cross sectional area of the median nerve, growth hormone, insulin-like growth factor I, ultrasound

DOI: 10.1530/endoabs.81.P668

P669

From silent to carcinoma: the genomic alterations landscape of whole spectrum macroadenoma corticotrope pituitary tumors and carcinoma

Keiko Taniguchi[1], Sergio Andonegui-Elguera[1], Gloria Elena Silva Román[1], Eduardo Peña-Martinez[1], Sandra Vela Patiño[1], Ilan Remba-Shapiro[1], Moises Mercado[1] & Daniel Marrero-Rodríguez[2]
[1]Hospital de Especialidades, Centro Medico Nacional Siglo XXI, Instituto Mexicano del Seguro Social., Unidad de Investigación Medica en Enfermedades Endocrinas, Mexico City, Mexico; [2]Hospital de Especialidades, Centro Medico Nacional Siglo XXI, Instituto Mexicano del Seguro Social., Unidad de Investigación Medica en Enfermedades Endocrinas, Mexico City, Mexico

Corticotrope cells give arise to utmost aggressive and to very rare pituitary neoplasias, including pituitary carcinomas, Crooke's cell adenomas (CCA), clinically non-functioning silent corticotrope adenomas (SCA) and the Cushing-provoking pituitary adenomas (CD). The molecular etiopathogenesis of these tumors are still poorly understood. Therefore, we carried out whole exome sequencing to better understand the full genomic landscape single nucleotide variants and copy number variations of the pituitary macroadenoma tumors from corticotrope lineage. Carcinomas show SNV in USP8, TP53, AURKA, EGFR, HSD3B1 and CDKN1A. Whereas in CCA SNV in HSD3B1 and CDKN1A where

common however TP53 and AURKA were present in one each. HSD3B1 and CDKN1A SNV were present in all SCA, followed by EGFR and AURKA. They did not show USP8 SNV. As for the CD only one show USP8 SNV, corresponding to an Nelson syndrome tumor. All CD show TP53 and HSD3B1 SNV. None of the corticotrope tumors showed USP48, BRAF, BRG1 nor CABLES1 SNV. Functioning tumors including carcinoma and CD showed more CNV gains than the non-functioning tumors, carcinoma shares 10q11.22 amplification with benign adenomas, whereas 17q12 characterizes only benign adenomas. The theoretical evolutive development of the corticotrope carcinoma starting from the silent adenomas, if that's the case, shows two main clades, the first and smallest, contain two SCA (2/3) and two CD (2/5), these four adenomas shared SNV profile, potentially indicating the genes needed to be altered to make a transition from silent to overt tumors. ATF7IP characterize this clade. The second and largest clade harbors the CCA (1/1), the carcinoma (1/1), one SCA (1/3) and three CD (3/5). Interestingly, in this clade the carcinoma showed a close relation to CCA and to a CD. This clade could represent the molecular alterations required to make the transition from overt adenoma to a carcinoma, or at least to a more aggressive tumor. In this clade there was clustered a Nelson syndrome CD and the carcinoma, which are very aggressive entities. MSH3 gene characterize this clade. Overall, pituitary carcinoma and CD showed more SNV and CNV genomic alterations compared against CCA and SCA.

DOI: 10.1530/endoabs.81.P669

P670

Abstract withdrawn

DOI: 10.1530/endoabs.81.P670

P671

Targeting invasive pituitary adenomas: in vitro studies and *in vivo* investigations in a murine model of invasive pituitary tumors obtained by orthotopic pituitary GC cells injection

Fanny Chasseloup[1], Etienne Lefevre[1], Alexandre Dormoy[1], Nataly Ladurelle[1], Tiphaine Mignot[1], Clément Janot[1], Mirella Hage[1], Say Viengchareun[1], Philippe Zizzari[2], Philippe Chanson[1,3], Michael Buchfelder[4] & Peter Kamenicky[1,3]
[1]Université Paris-Saclay, INSERM U1185 ≪ Physiologie et Physiopathologie Endocriniennes ≫, France; [2]Université de Bordeaux, INSERM U1215, Neurocentre Magendie, France; [3]AP-HP, Hôpital de Bicêtre, Service d'Endocrinologie et des Maladies de la Reproduction, Centre de Référence des Maladies Rares de l'Hypophyse, France; [4]Universitätsklinikum Erlangen, Department of Neurosurgery, Germany

Context
Surgical removal is the primary treatment option for pituitary adenomas. However, pituitary surgery is frequently incomplete because of invasion of extrasellar cerebral structures, notably, of the cavernous sinus. Our objective was to study the molecular basis of the cavernous sinus invasion by pituitary adenomas.
Methods
We analyzed a tissue collection of 19 invasive pituitary adenomas with a sample from the intrasellar portion and a sample from the portion invading the cavernous sinus of each adenoma. We used RNA-sequencing to compare gene expression patterns of the invading and intrasellar portions. The implication of one differentially expressed candidate gene in the invasive behavior was first analyzed *in vitro* in lactosomatotroph GH3 and gonadotroph LbT2 cells. We used Transwell Assay to analyze the impact of pharmacologic inhibition of the candidate gene on cell migration and invasion. To study the role of this gene on tumor growth and behavior *in vivo,* we elaborated a model of invasive pituitary adenomas by stereotactic injection of murine somatotroph GC cells into the pituitary gland of female Wistar Furth rats. Twelve adult rats received 20.000 GC cells in each pituitary lobe. Tumor development was assessed fortnightly by 7Tesla MRI. Six of the 12 rats were treated with the pharmacological inhibitor of the candidate gene. Rats were sacrificed 7 weeks after cell injection.
Results
RNA-sequencing identified 159 up-regulated genes and 11 down-regulated genes in the invasive adenoma portions. *In vitro* pharmacological inhibition of the selected candidate gene decreased cell migration and invasion in GH3 cells ($P=0.0205$ and$P=0.0038$) and LbT2 cell ($P=0.0345$ and$P=0.0131$). Amongst the 12 injected rats, 11 (92%) developed invasive pituitary tumors. Tumor growth was rapid, causing death from intracranial hypertensions before the end of the protocol in 7 animals. Pharmacological inhibition tended to slow tumor growth from 30.3 mm^3 /week to 7.8 mm^3 /week ($P=0.12$) and decreased cumulative mortality (83% in untreated animals *vs* 33% in treated animals, $P=0.08$).
Conclusion
We described the molecular signature associated with the invasive behavior of pituitary adenomas and identified a therapeutic target, which is related to pituitary cells migration and invasion in functional *in vitro*studies. Pharmacologic inhibition of this target tended to decrease tumor growth and mortality *in vivo*, however larger numbers of animals are necessary to confirm this pilot observation. Our original approach of orthotopic cell injection into rat pituitaries resulting in tumor development provides a new tool for molecular studies of pituitary tumorigenesis and for pharmacological screening.

DOI: 10.1530/endoabs.81.P671

P672

The role of HIF-1α and vegfa polymorphism (G634C) in the development of the aggressive pituitary adenomas

Zamira Khalimova[1] & Ozoda Azimova[2]
[1]Republican Specialized Scientific Medical Center of Endocrinology, Neuroendocrinology, Tashkent, Uzbekistan; [2]Republican Specialized Scientific Medical Center of Endocrinology, Neuroendocrinology, Tashkent, Uzbekistan

Introduction
Although pituitary adenomas are considered benign, some have invasive growth, which is one indicator of aggressiveness. Early prognostic markers of aggressiveness may influence the quality of life improvement in patients with aggressive pituitary adenomas
Objectives
To study the clinical-immunological, molecular-genetic aspects of aggressive pituitary adenomas and to develop new approaches to early diagnosis and treatment.
Materials and methods
83 patients diagnosed with pituitary adenoma were examined. All patients underwent clinical examination and magnetic resonance imaging (MRI), to determine the degree of adenoma invasion by Knops classification. Polymorphism of regions of studied genes in the VEGFA gene of position G634C (rs2010963 locus), the gene HIF-1α C/T (rs11549465 locus) and G-197A in the gene IL-17A, made by the allele method - determined by the PCR method.
Results
Genetic analysis of VEGFA polymorphism showed that heterozygote (G/C) mutation in patients with invasive adenomas was found to be twice as high as 32.7% ($n=17.2$) compared to a control group of 15.7% ($n=13$). Moreover, the C/C homozygote mutation is also observed more in the 7.7% invasive adenoma patient group ($n=4$), which supports the evidence that mechanistic progression of invasive adenomas contributes to angiogenesis mutation through the VEGFA pathway. A heterozygous C/T mutation of the HIF-1A gene was found to be significantly higher ($P=0.02$) in patients with invasive adenomas compared to controls, with 25% ($n=13$) and 9.8% ($n=8$), respectively. While in non-invasive adenomas, this mutation was observed about three times lower. Our results clearly support the argument for the regulatory role of HIF-1A within VEGFA in the development of aggressive pituitary adenoma flow.
Conclusions
Thus, genetic analysis can become a predictor of aggressive behavior of pituitary adenomas and the use of genetic markers in clinical practice will contribute to the prevention of complications of aggressive adenomas.

DOI: 10.1530/endoabs.81.P672

P673

Transition in endocrinology: predictors of drop-out in a heterogeneous population during long-term follow-up

Martina Romanisio[1], Sara Brasili[1], Tommaso Daffara[1], Alice Ferrero[1], Davide Vimercati[1], Francesca Pizzolitto[1], Rosa Pitino[1], Edoardo Luigi Maria Mollero[1], Marco Zavattaro[1], Simonetta Bellone[2], Marina Caputo[1,3], Gianluca Aimaretti[1] & Flavia Prodam[1,3]
[1]Endocrinology, Department of Translational Medicine, Università del Piemonte Orientale, Novara, Italy; [2]Division of Pediatrics, Department of Health Sciences, Università del Piemonte Orientale, Novara, Italy; [3]Department of Health Sciences, Università del Piemonte Orientale, Novara, Italy, Novara, Italy

Aim
To evaluate: 1) clinical and epidemiological characteristics of outpatients transitioned from Pediatrics Endocrine (PED) to Adult Endocrine Department (AED) in a tertiary Centre; 2) transition process characteristics, and predictive factors of drop-out.
Patients and methods
Demographic, clinical, and transition features of 170 consecutive patients with paediatric onset of chronic endocrine or metabolic disease (excluded type 1 diabetes) who transitioned from PED to AED (2007-2020) were retrospectively evaluated.
Results
The age at transition was 18.4 ± 4 years (F:M = 1.2: 1). 93.6% of patients were affected by endocrinopathies (19.4% on a genetic basis), while 6.4% were in follow-up only in a cancer-survivor surveillance protocol. 69.4% of patients had one endocrine disease, 20.0% had 2, and 4.2% of them had 3 or more. 40.0% of subjects suffered also from non-endocrine diseases. The total comorbidity burden was high: 37.1%, 20.6%, and 11.1% of patients had 2, 3, 4, or more diseases. The number of treatments progressively increased and was associated with the number of visits (r 0.349, $P < 0.0001$), and the age at the last visit (r 0.184, $P < 0.0.1$). The number of visits was positively associated with the number of endocrine diseases and the etiology (mainly in hypergonadotropic hypogonadism, hypopituitarism). Patients with obesity had the low number of visits ($\chi2 = 13.850$, $P < 0.05$). 64.7% of patients were adherent to the follow-up, mainly if they had a high number of comorbidities ($\chi2 = 14.473$, $P < 0.01$) or thyroid disorders ($\chi2 = 3.618$, $P < 0.04$). Having performed one visit only was predictive of drop-out ($\chi2 = 18.624$, $P < 0.009$), regardless of pathology. Among cancer survivors, patients treated for central nervous system tumors had the highest adherence.
Conclusions
This is the first study that analyzed a specific transition plan for chronic endocrine diseases on long-term follow-up. The proposed "*one size fits all model*" is not adequate in responding to the different needs of patients. A structured transition plan is an emerging cornerstone. The first visit is crucial in building a trusting relationship between patients and healthcare providers and plays an important role in a successful therapeutic intervention.

DOI: 10.1530/endoabs.81.P673

P674

Validation of a clinicopathological classification for the prediction of pituitary adenomas: a retrospective cohort study in a PTCOE from 2013 to 2020

Thalía Argüello Gordillo, José Miguel Castro García, Lucía Martinez Gauffin, Artem Kuptsov, Dolores Tejedo-Flors, María Eugenia Torregrosa-Quesada, Javier Abarca Olivas, Luis Concepción, Ignacio Aranda & Antonio Pico
General University Hospital of Alicantet, Alacant, Spain

Introduction
Because of the increase of brain image explorations, the prevalence of pituitary tumours has increased a lot. Although most of them have an indolent behaviour, some behave aggressively, demanding a lot of resources for their management. Therefore, it is very important to identify them as soon as possible. The recent WHO 2017 classification of pituitary tumours gives insights into improving their identification using the immunostaining (IS) of transcription factors (TF) but does not include severity indexes. Therefore, a clinicalpathological classification is necessary. In 2013, Trouillas *et al* proposed a clinical-pathological classification that considered pituitary tumour subtypes along with radiological characteristics of the tumours. However, the identification of the pituitary tumour subtypes was based on the IS of pituitary hormones that gives an inacceptable percentage of Null Cell and unusual plurihormonal tumours. The aim of the present study is to classify a series of pituitary tumours coming from a PTCOE, identified according to WHO 2017 recommendations, and using the clinicopathological classification proposed by Trouillas *et al* 2013.
Methods
A retrospective cohort study including 180 patients with pituitary tumors surgically treated (NES) in a PTCOE from 2013 to 2020. We collected the following information from the electronic medical records: function, IS features (pituitary hormones, Transcription Factors, MIB15 and p-53 IS and mitotic count), and MRI tumour characteristics: size, sinus invasion, optic chiasma displacement and T2 value. We have defined aggressiveness based on the presence of tumour invasiveness defined by pre-operative MRI/endoscopic intraoperative examination plus a Ki67 index $\geq$ 3%. We have analyzed the relative risk and adjusted RR for all variables through the Chi-squared test and logistic regression, respectively.
Results
From the 180 recruited patients we have excluded 64 patients due to lack of adequate MRI follow-up. Age 59 } 16 years, 52% males. Of the 116 patients included for analyses, 75% were non-functioning tumors and 35% were functioning. Of functioning tumors, 7.5% were CTs, 13.9% STs, 5.5% PRLs and 1% TTs. Of NFP tumors: 34.3% were silent gonadotroph tumors (SGT), 8% silent corticotroph tumors (SCT), 1% silent somatotroph tumors (SST), 1% silent lactotroph tumors (SLT) and 1.5% silent tirotroph tumors (STT). Recurrence rate in non-functioning and functioning pituitary tumors were 17.9% and 9.7% respectively. A higher risk of post-surgical recurrence was found in tumors with sinus invasion (RR 2.13 (IC95%: 1.6-2.7; $P < 0.001$)), a T2 ratio higher than 2 (RR 2.7 (IC95% 1.7-4.4, $P < 0.001$)). No statistical significance ($P > 0.05$) was found for Ki-67 index >3%, however when combine this last one with sinus invasion (Trouillas IIb) in multivariant analyses a higher degree of recurrence was found (RR 42 (IC95%: 3.0-586); $P < 0.05$). Regarding non-functioning invasive silent CT and GT, 60% and 15.2% showed recurrence, with relative risk of 4 (IC 95% 1.2-13.2) and 1.5 (IC 95% 1.2-1.9), respectively. ($P > 0.05$).
Conclusions
As expected tumors with high proliferation indexes and sinus invasion show worse behaviors and therefore should be managed more frequently and carefully. Therefore, the clinical pathological classification of pituitary tumors proposed by Trouillas *et al* is an important tool which should be used by all PTCOEs. As expected, SCT behaved more aggressively than SGT, highlighting the importance of a correct typification of the different pituitary tumors subtypes, using whenever is possible the IS of TF.

DOI: 10.1530/endoabs.81.P674

P675

Central diabetes insipidus following immunization with BNT162b2 mRNA Covid-19 vaccine

Bruno Bouça[1], Marisa Roldão[2], Paula Bogalho[1], Luís Cerqueira[3] & Jose Silva-Nunes[1]
[1]Centro Hospitalar Universitário de Lisboa Central, Department of Endocrinology, Diabetes and Metabolism, Lisbon, Portugal; [2]Centro Hospitalar do Médio Tejo, Department of Nephrology, Abrantes, Portugal; [3]Centro Hospitalar Universitário de Lisboa Central, Department of Neuroradiology, Lisbon, Portugal

Introduction
The endocrine complications of COVID-19 remain largely unknown. Cases of central diabetes insipidus (CDI) have been reported after COVID-19, with hypophysitis being the most likely cause. COVID-19 vaccines potential adverse effects may mimetize some of these complications. We present a case of a woman who developed CDI one week after the 2 nd dose of BNT162b2 mRNA COVID-19 vaccine.

Case Report
Female patient, 37 years old, with rheumatoid arthritis under a well tolerated therapy with adalimumab (40 mg twice a month) since December 2018. In October 2021, she reported intense thirst and polyuria starting 4 months earlier (7 days after second dose of BNT162b2 mRNA COVID-19 vaccine). She denied polyphagia, weight loss, foamy urine, macroscopic hematuria, peripheral or periorbital edema. Blood analysis: creatinine 0.7 mg/dl, glucose 95 mg/dl, Na+ 141 mEq/l, K+ 3.9 mEq/l, TSH 3.8 mcUI/l (0.38-5.33), FT4 0.9 ng/dl (0.6-1.1), cortisol 215.4 nmol/l (185-624), ACTH 21.9 pg/ml (6-48), osmolality 298.2 mOs/lg (250-325); Urine analysis: volume 10 200 mL/24h, osmolality 75 mOs/kg (300-900), density 1.002. She was admitted to the ward to perform a water restriction test: 0' − Serum osmolality 308.8 mOsm/kg vs. urine osmolality 61.0 mOsm/Kg; 60' - urine osmolality 102 mOsm/Kg; urine osmolality 1 h after desmopressine was 511 mOsm/kg. MRI of the pituitary gland revealed no abnormal signs consistent with hypophysitis except for the loss of the posterior pituitary bright spot on T1 weighted imaging. Diagnosis of CDI was assumed, and started therapy with desmopressine. Although pituitary biopsy was not conducted, other probable causes of CDI were ruled out. A report of potential adverse effect from BNT162b2 mRNA COVID-19 vaccine was addressed to national health authorities. On the last appointment (December 2021), she was under desmopressin 0.06 mg tid, had no polydipsia or polyuria, BP 110/80 mmHg, and analytical results showed: Serum osmolality 297.2 mOsm/kg, Urine osmolality 148.0 mOsm/kg, FSH 4.76 UI/l, LH 5.62 UI/l, estradiol 323 pmol/l, IGF1 74.8 ng/ml (88-209), PRL 24.7 mg/l (3.3-26.7). Desmopressin was titrated to 0.12 mg bid.
Conclusion
In hypophysitis MRI often shows loss of posterior pituitary bright spot on T1 weighted imaging, pituitary enlargement or stalk thickening but those findings were not present in this patient. However, the same lack of abnormal signs consistent with hypophysitis in MRI has also been reported in 2 cases of CDI following COVID-19 infection. To the best of our knowledge, CDI has never been reported following administration of a COVID-19 vaccine.

DOI: 10.1530/endoabs.81.P675

P676

Pheochromocytoma/paraganglioma metastatic potential prediction

Ewelina Rzepka[1], Anna Kurzyńska[1], Anna Grochowska[2], Magdalena Ulatowska-Białas[3], Anna Skalniak[4], Martyna Lech[3], Marta Opalinska[5], Anna Bogusławska[1], Elwira Przybylik-Mazurek[1], Anna Sowa-Staszczak[6], Aleksandra Gilis-Januszewska[1] & Alicja Hubalewska-Dydejczyk[1]
[1]Jagiellonian University, University Hospital, Endocrinology, Kraków, Poland; [2]Jagiellonian University, University Hospital, Radiology, Kraków, Poland; [3]Jagiellonian University, University Hospital, Pathomorphology, Kraków, Poland; [4]Jagiellonian University, University Hospital, Genetics, Kraków, Poland; [5]University Hospital in Krakow, Department of Endocrinology, Oncological Endocrinology and Nuclear Medicine, Kraków, Poland; [6]Jagiellonian University, University Hospital, Nuclear Medicine, Kraków, Poland

Pheochromocytoma and paraganglioma (PPGL) are rare neuroendocrine tumours, which derive from the chromaffin cells of the adrenal medulla or extra-adrenal sympathetic and parasympathetic ganglia. About 15-20% of those neoplasms could present malignant course. Prediction of PPGL metastatic potential still remains a great clinical challenge, since the sensitivity and specificity of proposed prediction systems are not satisfactory. We performed a retrospective database search for pheochromocytoma and paraganglioma patients, diagnosed and treated in Endocrinology Department, University Hospital in Cracow from 2005 to 2021. 206 patients with pheochromocytoma and 27 patients with paraganglioma were included to the analysis. The mean follow-up period was 59 months (range: 2-396 months). In the whole group, 5 metastatic pheochromocytomas and 2 metastatic paragangliomas have been found. Our objective was to investigate clinicopathological characteristics of the patients with malignant PPGLs in the light of current metastatic potential predictors. The group of patients with disseminated disease comprise 2 men and 5 women. Median patient age was 51 years (range 19-72). In two patients metastatic disease was observed at the moment of diagnosis, in remaining cases metastases developed 5 to 84 months after the diagnosis (median time 32 months). The most common localizations of metastases were lymph nodes and bones (71.4% for each). The leading symptom of metastatic disease was fatigue (86%). The median size of the primary tumour was 7.7 cm. Hormonal assessment revealed significantly elevated 24-h urinary fractionated metanephrines in 6 patients. The dominant catecholamine profile was adrenergic (57%). In all patients concentration of 3- metoxytyramine was elevated. In one patient with paraganglioma it was the only elevated metabolite in 24-h urine collection. Moreover, chromogranin A level was substantially increased in all cases (minimum 4.8- fold the normal upper limit) and it was positively correlated with the progression of the disease. PASS score was known in three patients with pheochromocytoma, in all cases it was higher than 6. In patients with PPGL, detailed analysis of histopathological, clinical, hormonal and imaging results is essential to properly predict the possible course of the disease. In our patients, the most commonly observed metastatic potential predictors were PASS score more than 6, tumour size more than 6 cm, elevation of dopamine metabolite level. A repetitive assessment of chromogranin A concentration during follow-up may have additional value in monitoring of the disease. Due to rarity of the PPGL, the establishment of a new predictive system is difficult and requires multicentre, long-term studies.

DOI: 10.1530/endoabs.81.P676

P677

Adrenal haemorrhage in a pheochromocytoma - a rare, life-threatening and challenging complication

Ewelina Rzepka[1], Joanna Kokoszka[1], Anna Grochowska[2], Magdalena Ulatowska-Białas[3], Martyna Lech[3], Marta Opalińska[1,4], Magdalena Godlewska[1], Elwira Przybylik-Mazurek[1], Aleksandra Gilis-Januszewska[1] & Alicja Hubalewska-Dydejczyk[1,4]
[1]Jagiellonian University, University Hospital, Endocrinology, Kraków, Poland; [2]Jagiellonian University, University Hospital, Radiology, Kraków, Poland; [3]Jagiellonian University, University Hospital, Pathomorphology, Kraków, Poland; [4]Jagiellonian University, University Hospital, Nuclear Medicine, Kraków, Poland

Adrenal haemorrhage is a rare, usually life-threating complication, most commonly connected with primary or metastatic adrenal tumour. Among them pheochromocytoma is the most common cause of spontaneous adrenal bleeding and accounts for nearly 50% of cases. We performed a database search for pheochromocytoma patients, diagnosed and treated in Endocrinology Department, University Hospital in Cracow from 2005 to 2021. 206 patients with pheochromocytoma were identified. Subsequently, 23 cases were excluded due to incomplete medical data necessary to rule out potential adrenal bleeding. Of the remaining 183 patients with histologically confirmed pheochromocytoma, 7 cases with adrenal bleeding were found (3.8% of cases). The group of patients comprise 4 men and 3 women. Median patient's age was 49 years (range: 36-78 years). The most common manifestation of adrenal bleeding was acute abdominal pain (71.4%). Two patients (28.6%) developed shock, in one case resulted in multiple organ failure (MOF). Hormonal assessment concerning pheochromocytoma were performed in five patients (71.4%). 24- h urinary fractionated metanephrines were significantly elevated in all of them. Most patients (85.7%) have had symptoms suggestive of pheochromocytoma before haemorrhage − most commonly paroxysmal hypertension (57.1%). Nevertheless, In four patients diagnosis of pheochromocytoma was made at the time of adrenal haemorrhage, based on severe clinical manifestation, hormonal status and imaging. One patient died, before the diagnosis of adrenal bleeding was made. In two patients pheochromocytoma was suspected before the episode of haemorrhage: two months and sixteen months, respectively. Six out of seven patients have diagnostic imaging performed: median largest diameter of the lesions was 7.4 cm (range: 5-11 cm). Five patients had elective surgery, preceded by two- week pharmacological treatment with alpha- receptor blockers. In one case, four-day alpha-receptor blockage was administered, followed by the urgent surgery. In all cases the diagnosis of pheochromocytoma was confirmed in postoperative histopathology or in autopsy. PASS score was defined in 5 patients - in three cases it was no higher than 3, in two cases it exceeded 3. In two another cases, because of massive haemorrhagic changes, it couldn't be determined. The perioperative survival rate was 85.7%. Adrenal bleeding is a rare complication of pheochromocytoma, which constitutes a diagnostic and therapeutic challenge. It might remain unrecognized with lethal consequences. Physicians should be aware of such diagnosis in patients with adrenal bleeding, especially with accompanying abdominal pain, hemodynamic shock and previous history of pheochromocytoma-associated symptoms.

DOI: 10.1530/endoabs.81.P677

P678

Treatment of cushing's disease (CD) after primary failure of pituitary surgery or recurrence: evaluation of long-term control by medical treatment

Adel Ghalawinji[1], Justine Cristante[1], Virginie Lefournier[2], Philippe Chaffanjon[3], Marie muller[1], Emmanuel Gay[4] & Chabre Olivier[1]
[1]Université Grenoble Alpes, Endocrinologie CHU Grenoble Alpes, GRENOBLE, France; [2]Clinique du Mail, Neuroradiologie, Grenoble, France; [3]Université Grenoble Alpes, Chirurgie Endocrine CHU Grenoble Alpes, GRENOBLE, France; [4]Université Grenoble Alpes, Neurochirurgie CHU Grenoble Alpes, GRENOBLE, France

Introduction
Pituitary surgery is the first line treatment for most patients with Cushing's disease (CD) but after failure or recurrence after surgery 3 main strategies can be proposed: medical treatment (MT), a 2 nd pituitary surgery, bilateral adrenalectomy (BA). Pituitary radiotherapy is a 4th strategy, generally combined with one of the 3 others. Medical treatment (MT) emerges as an attractive strategy but there are little data on long-term control after failure of pituitary surgery or recurrence.
Objective
To evaluate long term control of CD with MT after failure of pituitary surgery or recurrence.
Methods
Monocentric retrospective study of all 119 patients who had pituitary surgery for CD between 2001 and 2020 in our institution, with 36 patients candidates for a second line therapy, including 19 with pituitary failures (19/119 =16%, surgical remission rate 84%) and 17 with recurrences (17/100=17%)
Results
The second line treatment was medical treatment (MT) in 28/36 patients (78%) 2nd pituitary surgery in 5/36 patients (14%) and BA in 3/36 patients (8%). The long-term control was achieved by MT in 11/36 patients (30%), 2nd pituitary surgery in 8/36 patients (22%) and BA in 14 patients (39%), while 3/36 patients (8%) remained uncontrolled. During the whole follow-up 29 patients received at least one drug and 67 introductions of drug treatment were performed (average 29/67=1.7/patient), using inhibitors of steroidogenesis: ketoconazole (27), metyrapone (15), osilodrostat (8), mitotane (3) or inhibitors of ACTH secretion: cabergoline(11), pasireotide (3). On long term 11/29 (38%) patients were maintained on MT (group A, duration of treatment 49.6 months) while 18/29 (62%) patients abandoned MT (group B duration of treatment 20.8 months,) for lack of long-term efficiency (66%), intolerance and/or lack of compliance (34%). A normal Urinary Free Cortisol (UFC) was obtained at least one time during 38/67 introductions of treatment (57%), including 36/53 (68%) with steroidogenesis inhibitors and 2/14 (14%) with inhibitors of ACTH secretion. The last treatment used in group A was osilodrostat (6); ketoconazole (3) ketoconazole + metyrapone (1) metyrapone (1). Group A patients had a higher age (55.9 vs 47.9P=0.04), and a tendency toward more different treatments (2.5 vs 1.7P=0.06) but were no different regarding sex and initial UFC. All female patients under 35 years ended in-group B. In conclusion, in this study MT was a long-term solution for 38% of the patients who experienced failure or recurrence after pituitary surgery for CD. Steroidogenesis inhibitors appeared more efficient.

DOI: 10.1530/endoabs.81.P678

P679

Efficacy, safety and metabolic impact of long-term pegvisomant therapy in acromegaly: results from a 10-year single center experience

Rosa Pirchio[1], Renata Simona Auriemma[1], Maria Elena Montini[1], Alice Vergura[1], Rosario Pivonello[1,2] & Annamaria Colao[1,2]
[1]Università "Federico II" di Napoli, Dipartimento di Medicina Clinica e Chirurgia, Sezione di Endocrinologia, Naples, Italy; [2]Unesco Chair for Health Education and Sustainable Development, "Federico II" University, Naples, Italy

Pegvisomant (PEG) is effective in acromegaly control and exerts a positive impact on glucose metabolism. The current study aimed at investigating the effects of 10-years PEG treatment on disease control, pituitary adenoma size, and metabolic profile in patients with acromegaly resistant to somatostatin analogues (SRLs). Twenty-two patients (9 men,13 women, age 45.54 ± 12.83 years) treated with PEG for 10 years, in monotherapy or in combination with SRLs, were included in the current study. In the whole patient cohort, anthropometric (BMI, systolic and diastolic blood pressure), hormonal (GH, IGF-I), biochemical (fasting glucose and insulin, lipid profile) parameters, and maximal tumour diameter were evaluated before and after 10-years of PEG treatment. After10-years PEG therapy, IGF-I levels persisted significantly decreased in all the patients (P<0.0001) compared to baseline, with full normalization in 91%. No significant change in dose of either PEG or SRLs was required. Tumour maximal diameter slightly decreased in the whole cohort. Fasting glucose (FG) was significantly increased (P=0.035), whereas HbA1c and diabetes prevalence remained stable. Fasting insulin (FI) and HOMA-IR decreased, HOMA-β was significantly reduced (P=0.013), whereas $ISI_{0,}$ was increased. A significant decrease in total- (P=0.03) and LDL- (P=0.05) cholesterol, and a slight increase in triglycerides were found. At baseline, GH and IGF-I levels significantly correlated with systolic blood pressure (SBP), FI, HOMA-IR, HOMA-β, and ISI_0. Baseline IGF-I correlated with percent change after 10 years (Δ) of FI (r=-0.354, P=0.015), and HDL (r=0.045, P=0.045). PEG dose was directly correlated to BMI (r=0.509, P=0.016), and triglycerides (r=0.554, P=0.007), and inversely to age (r=-0.455, P=0.030). Disease duration before PEG was directly related to BMI (r=0.446, P=0.037), and inversely to 10-years HOMA-IR (r=-0.563, P=0.029), HDL (r=-0.424, P=0.049), ΔFG (r=-0.462, P=0.03), ΔFI (r=-0.546, P=0.05), and ΔTG (r=-0.445, P=0.034). Long-term PEG therapy is effective and safe, without requiring an increase in dose to maintain disease control even after a decade of therapy. PEG beneficial impact on both insulin and lipid metabolism persists after prolonged therapy**.** PEG treatment should be started as soon as possible in patients resistant to SRLs as the extent of the metabolic improvement is inversely correlated to disease duration before PEG introduction.

DOI: 10.1530/endoabs.81.P679

P680

Long-term pasireotide therapy: real life experience of a single referral center

Rosa Pirchio[1], Alice Vergura[1], Maria Elena Montini[1], Renata Simona Auriemma[1], Rosario Pivonello[1,2] & Annamaria Colao[1,2]
[1]Università "Federico II" di Napoli, Dipartimento di Medicina Clinica e Chirurgia, Sezione di Endocrinologia, Naples, Italy; [2]Unesco Chair for Health Education and Sustainable Development, "Federico II" University, Naples, Italy

Pasireotide is a second-line therapy for acromegaly, that allows to obtain disease control in patients previously uncontrolled. However, pasireotide-induced hyperglycemia is of major concern. Currently, few data concerning prolonged use of pasireotide are available. The current retrospective study aimed at investigating the efficacy and safety of long-term pasireotide therapy. Sixteen consecutive patients (5 males, 11 females, age 47 ± 11 years) undergoing pasireotide for a minimal period of 36 months, were considered for the current study. In these patients, hormonal (GH, IGF-I), biochemical (fasting glucose and HbA1c), and radiological parameters (tumour maximal diameter and volume) have been considered at baseline and at 6, 12, 36 months, and last follow-up (LFU), during pasireotide therapy. At baseline, GH levels were 4.56 ± 3.82 ng/ml, IGF-I levels were 1.74 ± 0.72 x ULN, resulting 13 patients (81.25%) uncontrolled. Diabetes mellitus (DM) was present in 7 (43.75%), and 4 patients (25%) showed an impaired fasting glucose (IFG). After 6 months of pasireotide, GH and IGF-I levels were significantly reduced compared to baseline (P=0.017 and$P$=0.001, respectively). At 12 months, all patients achieved disease control (P<0.0001), tumour maximal diameter and volume were significantly reduced (P=0.003 and$P$=0.019, respectively). Disease control was maintained at 36 months evaluation, being tumour volume significantly further reduced compared to 12 months (P=0.010). Twelve patients (75%) were treated with pasireotide for a longer period (range 42-66 months); all these patients were controlled with a stable size adenoma at LFU. At 6 months, an increase in dose was recorded in 4 patients (25%, P=0.046), no further dose variation have been required. Pasireotide starting dose was significantly inversely correlated to IGF-I at 36 months (r=-0.614, P=0.011). Fasting glucose (FG) significantly increased in the first year of pasireotide therapy, particularly in the first 6 months (P=0.005); without a consistent increase in HbA1c (P=0.303) and DM (P=0.285). FG at 6 months was significantly correlated to age (r=0.692, P=0.003), rather than pasireotide dose (r=0.417, P=0.108). After 6 months, 75% IFG patients developed DM. At 36 months, 80% euglycemic patients at baseline were diabetic, and 20% showed IFG. As consequence, a significant increase in DM (P=0.023), and in the number of

antidiabetic drugs used ($P=0.005$) were observed. Pasireotide therapy is effective in determining disease control, and tumour shrinkage, even after a long period of treatment. Change in FG mainly occur in the first period, depending on age and glycemic status before pasireotide starting.

DOI: 10.1530/endoabs.81.P680

P681

The burden of adult growth hormone deficiency diagnostic tests: results of a patient experience survey in the UK

Harry Lewis[1], Joanne Mumford[1], Pat McBride[2], Pauline Whittingham[2], Glenn Darley[3] & Nacima Chernai[3]
[1]Initiate Consultancy, Towcester, United Kingdom; [2]The Pituitary Foundation, United Kingdom; [3]Consilient Health, United Kingdom

Objectives
To collect qualitative and quantitative information on the burden of adult growth hormone deficiency (AGHD) diagnostic tests for the patient.
Methods
A survey was published on The Pituitary Foundation's website and social media pages; respondents completed it online using SmartSurvey over period of two months (October-November 2021). 105 respondents took the survey, with 9 screened out after the first question because they had never taken an AGHD diagnostic test.
Results
Of the 96 respondents who completed the survey, 66 answered questions about the insulin tolerance test (ITT), 23 about the glucagon test, and 7 about the GHRH-arginine test. The ITT, whose mechanism of action depends on induced hypoglycaemia, presented both the widest variety of symptoms and, according to scores given by respondents, the most severe, with 9 of the 13 prompted symptoms experienced by the majority of patients who answered questions about it. When ITT patients were asked to rate the severity of the side effects they experienced on a scale of 1-5 (with 5 being the most severe), 5 symptoms − sweating, shakiness, fatigue, feeling dizzy, and feeling weak − had an average score of 3 or above ('moderate' or 'severe'). Although the glucagon test and GHRH-arginine test were overall less burdensome, they still caused some prompted symptoms to be experienced by the majority of patients who underwent them. Only 44% of patients felt well-prepared for their test, and 34.4% did not think the information they received beforehand was thorough. The majority indicated that their test had impacted their daily life in the days following. Due to the difficulty of correctly managing hypoglycaemia and the level of training and experience required by the clinicians assigned to oversee the test, some patients experienced adverse events such as blood sugars taking longer than usual returning to normal, an unexpectedly strong reaction to the administration of insulin, and adrenal crisis. In some cases, patients needed to have their test repeated.
Conclusions
Taking any AGHD diagnostic test can be a very unpleasant experience for the patient, and adverse events are common; this is particularly true for the ITT, which is the most used test in the UK and the international 'gold standard'. Due to the complexity and length of the test procedures, clinicians do not always appear to be confident when administering them. There is variability in patients' understanding of these facts pre-test, as well as in clinical responses to any complications that occur.

DOI: 10.1530/endoabs.81.P681

P682

Berlin questionnaire and epworth sleepiness scale as screening tools of sleep apnea risk in patients with acromegaly: comparison of 144 patients and an age-and gender-matched health cohort

Rosa Pirchio[1], Raffaele Addato[1], Maria Elena Montini[1], Corina Valentina De Santis Ciacci[1], Alice Vergura[1], Renata Simona Auriemma[1], Rosario Pivonello[1,2] & Annamaria Colao[1,2]
[1]Università "Federico II" di Napoli, Dipartimento di Medicina Clinica e Chirurgia, Sezione di Endocrinologia, Naples, Italy; [2]Unesco Chair for Health Education and Sustainable Development, "Federico II" University, Naples, Italy

Sleep apnea (SA) is a common acromegaly comorbidity, influencing patients' quality of life and mortality risk. Despite its importance, SA frequently remains undiagnosed, and its real prevalence seems to be underestimated. The current observational study aimed at investigating the role of Berlin questionnaire (BQ) and Epworth sleepiness scale (ESS) in assessing the risk of SA in this high-risk population, and to compare the results with an age-and gender-matched health cohort. One hundred and forty-four patients with acromegaly (63 men, 81 women, age 56.37 $\pm$ 12.94 years), and an equal number of age-and gender-matched health controls were included in the present study. All the subjects had no previous diagnosis of SA. For BQ and ESS, higher score indicated greater SA risk. A questionnaire evaluating quality of life in acromegaly, AcroQol, for which the higher score indicates a better quality of life, was administered only to patients. Patients showed a significantly higher BMI than controls ($P<0.001$), whereas there was no difference about hypertension prevalence ($P=1$). Comparing patients and controls, no significant difference was found in ESS score ($P=0.761$), and prevalence of high SA risk estimated by BQ ($P=0.623$). Furthermore, questionnaire results were analyzed in acromegalic patients related to gender, BMI, and disease control. ESS score and the prevalence of high SA risk based on BQ were similar between men and women. No significant differences were found for both ESS and BQ score among patients according to the BMI categories. Patients with uncontrolled disease had no differences in questionnaires' score compared to controlled patients. Patient's therapy did not influence ESS and BQ results. Acromegaly patients defined at high risk of SA according to BQ presented a significantly higher prevalence of hypertension ($P=0.002$), and number of antihypertensive drugs used ($P<0.001$), and lower AcroQol ($P=0.019$), compared to those at low risk. No differences concerning anthropometric parameters, GH and IGF-I levels, age at diagnosis, and disease duration were found between this two groups. AcroQol was inversely correlated to ESS ($r=$-0.326, $P=0.012$) and BQ ($r=$-0.310, $P=0.018$) scores. No correlation was found with age both in patients and controls. ESS and BQ are scores validated for SA risk assessment in the general population. The results of this study show that these tools seem to be not suitable for assessing SA risk in patients with acromegaly. Probably acromegalic patients, at higher risk of developing this comorbidity compared to the general population, requires a proper questionnaire.

DOI: 10.1530/endoabs.81.P682

P683

Pallister-hall syndrome diagnosed in a young man after an acute adrenal crisis

Anis Grassa, Meriem Yazidi, Bel Hadj Sliman Chayma, Nadia Khessairi, Ibtissem Oueslati & Melika Chihaoui
Hospital Rabta, Endocrinology, Tunis, Tunisia

Introduction
Pallister-Hall syndrome (PHS) is a very rare congenital syndrome, and its exact prevalence is still unknown. The clinical diagnosis is usually made when a hypothalamic hamartoma is associated with polydactyly. Endocrine manifestations consist of hypopituitarism, hypopituitarism, which can affect one or more pituitary axes, and precocious puberty. Here, we report the case of an 18-year-old young man in whom the diagnosis of PHS was delayed until his hospitalization in the endocrinology department for acute adrenal insufficiency.
Observation
The patient was an 18 years old young man who presented to the emergency room with clinical and biological features of an adrenal crisis. The medical history revealed several surgeries: a corrective one for polydactyly, a surgery for testicular ectopia and for a hypothalamic tumour diagnosed at the age of three years complicated with hypopituitarism. He would have received growth hormone for two years from the age of twelve. He was on hormone replacement therapy for hypothyroidism and adrenal insufficiency, and he stopped his treatment for a week. He had no medical follow-up for several years. The patient's family history was unknown as he was an adopted child. Physical examination showed a height of 157 cm (-3SD), a weight of 68 kg and a BMI of 27.5 kg /m^2. We noted an inequality of the two lower limbs. External genitalia's examination revealed a micropenis and hypoplastic testes. PHS was suspected and further investigations were then performed. An otolaryngology examination showed bifid epiglottis and laryngeal cleft. X-rays of the left hand revealed a surgically corrected postaxial type A polydactyly. Pelvic x-ray showed bone demineralisation and Risser stage was 4. Ultrasounds of heart, abdomen and kidneys were normal. The pelvic ultrasound showed hypoplastic testes. Brain MRI revealed a sellar and suprasellar mass measuring 28x25x24 mm corresponding to hypothalamic hamartoma. On biochemical evaluation, the

renal and hepatic functions, blood count, serum calcium and serum phosphorus results were normal. The pituitary assessment showed a thyrotropin and gonadotropin deficiencies
Conclusion
This patient's presentation shows that PHS may be misdiagnosed given its extremely low prevalence. Practitioners who may see patients with PHS at the young age (pediatricians, surgeons) should be familiar with this disease to avoid late diagnosis which may compromise patient prognosis.

DOI: 10.1530/endoabs.81.P683

P684

Pituitary macroadenoma revealed by symptoms mimicking Hakim Adams triad

Anis Grassa, Meriem Yazidi, Youssef Gharbi, Ibtissem Oueslati, Fatma Chaker & Melika Chihaoui
Hospital Rabta, Endocrinology, Tunis, Tunisia

Introduction
The clinical presentation of a secretory pituitary macroadenoma usually consists of a tumor syndrome accompanied by visual disturbances with signs of pituitary insufficiency and/or hormonal hypersecretion. Herein we describe an unusual presentation of a mixed secretory adenoma.
Observation
A 69-year-old was referred to our department for the management of a pituitary macroadenoma revealed by a symptomatology mimicking the Hakim Adams triad with gait disorders, sphincter disorders and a dementia syndrome, as well as a right monocular blindness. His past medical history included type 2 diabetes mellitus and hypertension. Physical examination noted a dysmorphic syndrome suggestive of acromegaly. Hormonal investigations revealed a hyperprolactinemia at 4755 ng/ml, a baseline GH of 7.8 ng/ml (>1) with elevated IGF1 levels. Baseline cortisol was at 8.9 µg/dl (nr:5-18) with an ACTH at 36.16 pg/ml (nr:7.22-63.3). TSH and FT4 were at 0.143 mIU/l (nr:0.1- 4.5) and 0.67 ng/dl (0.7-1.5) respectively. FSH and LH were at 2.94 IU/l (nr:1-12) and 1.34 IU/l (nr:2-12) respectively. Brain MRI showed a 5 cm pituitary macroadenoma with supra sellar extension pushing back the optic chiasm and leading to lateral ventricles dilatation upstream and an invasion of the right cavernous sinus. Ophthalmological examination showed pallor and bilateral papillary atrophy. Visual acuity was very low. Visual field showed right monocular blindness and was agonic on the left. The patient was put under Cabergoline at the dose of 1.5 mg per week. The evolution after one week was spectacular with disappearance of the walking, sphincter, and memory disorders with visual improvement, being reduced to a right lateral homonymous hemianopia.
Conclsion
Symptoms mimicking Adams Hakim's triad are exceptionally in relation with a pituitary adenoma. In case of prolactinoma, medical treatment with dopaminergic agonists may be associated with resolution of those neurological symptoms.

DOI: 10.1530/endoabs.81.P684

P685

Immunotherapy-induced endocrinopathies: a case report

Radvilė Dobrovolskytė, Lina Panceraite, Karolina Prielaidaite, Kristina Semeniene & Birute Zilaitiene
Lithuanian University of Health Sciences, Medical Academy, Kaunas, Lithuania

Endocrinopathies are one of the most common side effects induced by immunotherapy. The side effects result from the activation of immune system, which affects not only cancerous but also healthy body cells. In most cases, only one endocrinopathy occurs, but in our presented case we describe multiple endocrinopathies that occurred to a one person. 53-years-old male patient was referred to the Emergency department due to severe hyperglycemia (37.13 mmol/l) and the following symptoms: frequent urination, thirst, general weakness. New-onset diabetes was diagnosed and the patient was admitted to the Department of Endocrinology. After clarification of past medical history oncological disease emerged. In 2013, metastatic right kidney cancer was diagnosed (the tumor was spread to the lungs), the right nephrectomy was performed. Histopathological analysis confirmed clear cell renal cell carcinoma (ccRCC, pT3aG3). Systemic therapy with Sunitinib has been initiated. During the course of treatment, in 2016, hypothyroidism appeared, LT4 treatment was necessary. In 2020, for the reason of disease progression, immunotherapy with nivolumab, as a second line treatment, was initiated and stereotactic radiotherapy for paraaortic lymph nodes was applied. In the Department of Endocrinology, for the treatment of newly diagnosed diabetes mellitus intensive insulin therapy was chosen (HbA1c 18.7%, anti-IA2 1.0k U/l, n 0-7.5k U/l, anti-GAD 0.57k U/l, n 0-5; suspected immunotherapy-induced autoimmune diabetes mellitus). Depending on the patient medical history, was decided to consider other possible immunotherapy-induced endocrinopathies. After additional investigation hypopituitarism, secondary adrenal insufficiency was confirmed (ACTH 0.4 pmol/l, n 1.63-14.15, morning cortisol 47.1 nmol/l, n 147-726). Hydrocortisone replacement therapywas started immediately. Repeated blood tests revealed low levels of testosterone (T 2.22 → 3.23, n 9.08-30.1). The patient completed an international index of erectile function (IIEF) questionnaire and was diagnosed with mild to moderate erectile dysfunction. Mixed hypogonadism was confirmed (hypogonadism due to hypothalamic/pituitary and testicular dysfunction; LH 4.0 IU/I n 1.7-11.2, FSH 10.2 IU/I n 2.1-18.6), testosterone replacement therapy was prescribed. During inpatient treatment, headache and visual disturbances appeared. In assessing the course of the disease, tests results, despite the fact that no changes in the pituitary gland were seen after MRI, hypohysitis was diagnosed. The patient was discussed at multidisciplinary team meeting and it was decided that after adjusting the patient's condition, immunotherapy can be resumed, continuing the active follow up at the Department of Endocrinology.
It is very important to monitor patients throughout and after the treatment of immunotherapy for possible side effects that can lead to serious, life-threatening complications if not diagnosed in time.

DOI: 10.1530/endoabs.81.P685

P686

Ruptured rathke's cleft cyst (RCC) with irritation of optic apparatus and rapidly evolving panhypopituitarism

Annalisa Montebello[1], Joan Grieve[2], Hani J Marcus[2], Katherine Miszkiel[3], Fernanda Valerio[4] & William Martyn Drake[1]
[1]St. Bartholomew's Hospital, Endocrinology, London, United Kingdom; [2]University College London Hospital, Neurosurgery, London, United Kingdom; [3]University College London Hospital, QS Diagnostic & Support Services, London, United Kingdom; [4]University College London Hospital, Department of Clinical and Movement Neurosciences, London, United Kingdom

Background
Rathke's cleft cysts (RCC) are benign intrasellar cysts that originate from the remnants of Rathke's pouch and contain mucoid material. Most are asymptomatic, but some may compress adjacent structures leading to visual disturbances and endocrinopathies.
Case Report
A 20-year-old gentleman had an MRI Head in view of headaches. This showed a 17.7 mm peripherally enhancing suprasellar lesion with no intrinsic T1 high signal pre- contrast. He presented acutely three weeks later with headaches, blurred vision, sudden onset polyuria, polydipsia, and lethargy. An MR Pituitary showed a 23 mm, lobulated, peripherally enhancing sellar/suprasellar mass with elevation of the optic chiasm. The right optic tract showed inflammatory changes. The normal pituitary tissue was displaced. Blood investigations showed a random cortisol of 93 nmol/l, TSH 0.5 mU/l, T4 8.6 pmol/l, FSH <1 unit/l, LH <1 unit/l, Testosterone <0.5 nmol/l and central diabetes insipidus with a serum sodium of 139 mmol/l, serum osmolality 295 mmol/kg and urine osmolality of 121 mmol/kg. Pituitary replacement therapy was initiated with hydrocortisone, thyroxine and desmopressin and he underwent urgent transsphenoidal debulking of the lesion. Histology revealed a cystic pituitary lesion with focal xanthogranulomatous inflammation in keeping with cyst rupture. His vision improved post operatively. An ophthalmic review showed 6/3.8 acuity in the right eye and 6/4.8 acuity in the left, mild loss of sensitivity in the temporal hemifield of the right but intact visual fields in the left eye. Repeat imaging in November 2021 showed a residual 16 mm sellar/suprasellar cyst with ongoing distortion of the anterior visual pathways, contact with the intracranial optic nerves and distortion of the optic chiasm. He represented in January 2022 with sudden onset blurred vision. Ophthalmic review showed 6/9 visual acuity in the left and 6/6 in the right eye, a new left relative afferent pupillary defect, and new bitemporal hemianopia.

An MR Pituitary showed enlargement of the residual cystic lesion and further encroachment of the optic tract. He underwent urgent redo transsphenoidal endoscopic drainage of the cyst. His vision improved significantly post operatively. Visual fields were normal to confrontation. Histology showed a fragment of pituitary gland containing granulation tissue and stratified epithelium compatible with elements of a residual RCC.
Conclusion
In most RCCs the development of pituitary dysfunction and neuro-ophthalmic deficit are chronic. We present a rare case of a ruptured RCC causing acute visual problems and panhypopituitarism which recurred within a short period after decompression. The patient will remain under close clinical and radiological follow-up.

DOI: 10.1530/endoabs.81.P686

P687

Plurihormonal pituitary macroadenoma, co −secreting TSH/GH/and prolactin: a clinical challenge

Ismene Bilbao Garay[1], Nerea Egaña[1], Maite Perez De Ciriza[2], Laura Chinchurreta[2], Cristina Elias[1], Inmaculada Venegas[1], Ane Amilibia[1], Cristina Garcia[1], Jorge Rojo[1] & Alfredo Yoldi[1]
[1]Donostia Unibertsitate Ospitalea, Donostia, Spain; [2]Zumarragako Ospitalea, Zumarraga, Spain

Background
Co secreting Thyrotropin/growth hormone pituitary adenomas are rare, and their clinical presentation and long term management may be challenging. Clinically, the majority of plurihormonal pituitary adenomas are silent and diagnosis almost always relies on immunohistochemical analysis of the tumor tissue. Early detection is key to optimize patient mamagement. We report a case of pituitary plurihormonal macroadenoma with overt clinical hyperthyroidism and minimal GH excess symptoms.
Case Report
A 68-year-old female patient was admitted to our university hospital for transesphenoidal surgery due to a Thyrotropinoma diagnosed by one of our colleagues in another hospital. She underwent a thyroidectomy 15 years prior to diagnosis due to multiple bilateral thyroid nodules and she was taking levothyroxine replacement, noting that she presented discordance TSH/T4 levels. On review of previous test she consistently had elevated TSH and free T4 levels, and there was no family history of thyroid disease. Slightly high prolactin, IGF-I and elevated pituitary glycoprotein αSubunit were found during investigation and magnetic resonance Imaging(MRI) showed a sellar mass consisting of a pituitary macroadenoma that measured 31x21x29 mm(trxAPXCC) invading both cavernus sinuses and causing compression and superior displacement on the optic chiasm. She underwent successful transphenoidal adenomectomy and histopathology displayed a negative p53, a low KI67 of 1% and positivity for prolactin, GH and TSH in immunostaining. The patient was rendered euthyroid on levothyroxine, with GH <0.1 and normal age-sex adjusted IGFI levels and she is being followed without any recurrence of pituitary tumor or thyrotoxicosis.
Conclusion
Co-secreting occurs in 30% of Thyrotropinomas, requiring diligent inmunohistochemical analyses of all pituitary hormones to make the correct diagnosis and to alert the clinicians to ensure the right follow up.

DOI: 10.1530/endoabs.81.P687

P688

Implications of the 2017 WHO classification in the characterization of GH-secreting pituitary tumors

Iulia Florentina Burcea[1,2], Valeria Nicoleta Nastase[3], Amalia Raluca Ceausu[4], Anda Dumitraşcu[5], Anca Maria Cimpean[4], Marius Raica[4] & Catalina Poiana[1,2]
[1]"C. I. Parhon" National Institute of Endocrinology, Reproductive and Developmental Endocrinology, Bucharest, Romania; [2]"Carol Davila" University of Medicine and Pharmacy, Endocrinology, Bucharest, Romania; [3]"C. I. Parhon" National Institute of Endocrinology, Pituitary and Neuroendocrine Pathology, Bucharest, Romania; [4]"Victor Babes" University of Medicine and Pharmacy, Department of Microscopic Morphology/Histology and Angiogenesis Research Center, Timisoara, Romania; [5]"C. I Parhon"National Institute of Endocrinoloy, Radiology and Medical Imaging, Bucharest, Romania

Introduction
Somatotroph pituitary adenomas (PAs) represent 10-15% of all resected PAs, exhibiting immunohistochemical (IHC) positivity for GH (growth hormone) and PIT-1 transcription factor (TF). The histopathological (HP) and IHC variability of each PA influences the phenotype, radiological features, and therapy response.
Materials and methods
The study included 33 patients with acromegaly, with men: women ratio of 17:16. The HP-IHC characteristics were correlated with the clinical, imaging and laboratory data. Tumour specimens were assessed for anterior pituitary hormones, PIT-1, TPIT and SF-1 TF, Ki-67 labelling index, vimentin and reticulin.
Results
Of all cases, 30 had GH hypersecretion, while 3 had GH and PRL co-secretion. The symptomatology at diagnosis was dominated by the increase in size of extremities, associated with facial changes. Regarding the complications, they were identified right from the diagnosis, almost 50% of patients being hypertensive. Over 90% were macroadenomas. The maximum tumour diameter at diagnosis was positively correlated with suprasellar extension (P 0.001), the latter being also correlated with tumour invasion ($P<0.0001$). The postoperative tumour size was positively correlated with the postoperative value of random GH (P 0.01), the postoperative control of the residual secretion having a negative correlation with the maximum initial diameter. Regarding the biochemical evaluation, a statistically significant correlation was observed between the initial diagnostic values of IGF-1 and nadir GH in OGTT (P 0.02), respectively random GH (P 0.01), correlation maintained postoperatively (P 0.004 and <0.001, respectively). Most PAs were acidophilic, all had a positive IHC expression for GH. As expected, 93.93% had positive expression for PIT-1. PAs with IHC expression positive exclusively for GH accounted for 36.36%, while 13 cases (39.39%) showed a positive expression also for PRL. The expression of the other adenohypophyseal hormones was 12.12% for TSH, 3.03% for ACTH, and 9.09% for LH, respectively. Four cases were plurihormonal PIT-1 positive PAs, all with positive expression for PIT-1. Four cases had unusual IHC hormonal combinations. A particular feature of these PAs was the positive expression of the transcription factor SF-1 in a fairly large number of patients (39.39%). Most had a Ki-67 value below 3%.
Conclusions
The IHC classification of PAs, as stated by the WHO 2017 classification criteria, associated with the radiological dimensions and extent influence disease control, and are, probably, the most accurate prognostic factors. The 4 plurihormonal PIT-1 positive PAs associated a good cell differentiation and strongly acidophilic tinctoriality, advocating for a well-differentiated, mature tumour variant.

DOI: 10.1530/endoabs.81.P688

P689

Peculiar presentation of a TSH-secreting pituitary adenoma: a possible new multiple endocrine syndrome?

Giovanni Goggi[1,2], Irene Campi[2], Elisa Delle Donne[1,2], Mirella Moro[2], Fabiana Guizzardi[2], Marco Bonomi[1,2] & Luca Persani[1,2]
[1]University of Milan, Department of Medical Biotechnology and Translational Medicine, Milan, Italy; [2]IRCCS Istituto Auxologico Italiano, Department of Endocrine and Metabolic Medicine and Lab of Endocrine and Metabolic Research, Milan, Italy

Introduction
TSH-secreting pituitary adenomas (TSHomas) are a rare cause of central hyperthyroidism, accounting for less than 1% of all pituitary adenomas, with a prevalence in the general population of 1-2 cases per million.
Case Presentation
A 45-year-old female patient presented in 2009 with hypertension and tachycardia: blood tests revealed an inappropriately normal TSH with high fT3/fT4 levels and primary hyperaldosteronism. She declined further investigations and was started on nebivolol and hydrochlorothiazide by her GP. In November 2021, aged 58 years, she came to our observation for a compressive multinodular goiter with intrathoracic extension requiring surgery. In spite of a persistent biochemical picture of central hyperthyroidism, she did not complain symptoms of thyrotoxicosis. We ruled out possible interferences in the thyroid function tests and started the appropriate workup.

Diagnostic Investigations
We found an absent TSH response to exogenous TRH stimulation, suggestive for a TSHoma with a MRI showing a 12 mm pituitary macroadenoma. The remaining pituitary function was normal. Moreover, a primary hyperaldosteronism and a mild normocalcemic hyperparathyroidism despite cholecalciferol supplementation were found. No hyperplastic parathyroid glands were found at US scan, while the abdomen CT scan showed a slightly enlarged left adrenal gland. Due to the co-occurrence of a TSH-secreting pituitary adenoma, hyperparathyroidism and adrenal hyperplasia, suggestive of MEN1-4, we performed molecular analysis, by a targeted-NGS sequencing custom panel. We did not find variants in the *CDNK1B* or *MEN1* gene, while a heterozygous variant in the glial-cell-line-derived neurotrophic factor (*GDNF*) gene, previously reported in Hirschsprung disease, substituting an Isoleucine with a Methionine (p.I211 M) was found.
Discussion and Conclusion
GDNF is a plausible candidate gene for multiple endocrine syndromes, as GDNF family members bind to the GDNF-family-receptor alphas (GFRαs), leading to RET dimerization. In addition, it is expressed in normal pituitary and parathyroid glands and in pituitary/parathyroid adenomas. Furthermore, somatic mutations have been reported in parathyroid adenomas/hyperplasia. Nevertheless, the impact of p.I211 M variant in the pathogenesis of this case remains unclear. Previous studies showed that this *GDNF* variant retained its ability to induce RET tyrosine phosphorylation. These results suggest that the p.I211 M variant might act as a disease modifier in conjunction with other genetic lesions (Eketjall, 2002) still not identified in our patient. The curious association of central hyperthyroidism with primary hyperaldosteronism and hyperparathyroidism is suggestive of a novel MEN syndrome variant.

DOI: 10.1530/endoabs.81.P689

P690

Clinical characteristics at diagnosis and diagnostic delay among newly-diagnosed patients with acromegaly- single-center, pilot study

Magdalena Godlewska, Anna Bogusławska, Łukasz Kluczyński, Ewelina Rzepka, Alicja Hubalewska-Dydejczyk & Aleksandra Gilis-Januszewska
Jagiellonian University Medical College, Department of Endocrinology, Kraków, Poland

Introduction
Diagnostic delay remains significant among the patients with acromegaly, even though the disease awareness has improved over the years.
Aim
The aim was to investigate the diagnostic delay and symptoms present at diagnosis of acromegaly among the newly-diagnosed patients.
Material and methods
72 consecutive patients diagnosed with acromegaly between 01.2014 and 12.2021 were evaluated. Division into groups based on: gender, age upon diagnosis ($\leq$30 and $>$30 years of age) and age at the retrospectively estimated onset of symptoms ($\leq$30 and $>$30 years of age) was made. Clinical and biochemical data at diagnosis were analyzed with IBM SPSS Statistics ver. 27. The study was approved by local Bioethics Committee.
Results
63 patients (56.6% females, mean age 41.13+/- 14.03 years) were included in the study. Pituitary tumor was accidentally discovered in 24.2%, the median diagnostic delay was 4 years (IQR 4.0-7.0). There were no statistically significant differences in diagnostic delay, accidental diagnosis between genders and age groups. Acral enlargement was the most frequently reported symptom (90.3% of patients). Headaches, reported by 45.2% patients, were more frequent in females (42.86%) than in males (29.63%)($P=0.031$). Snoring was more common among patients with onset $>$30 years of age than in early onset (28.13% vs 0%, $P=0.018$). 25.85% patients had visual field impairment due to optic chiasm compression. Menstrual abnormalities were present in 37.14% females; 25.92% males reported decreased libido, with no statistical differences. Those symptoms were more common among patients with onset of symptoms $\leq$ 30 years of age than in those with later onset (50% vs 21.88%, $P=0.041$). Hypogonadotropic hypogonadism was more common in males (74.1%) than in females (16.7%)($P<0.001$). 42.8% of females and 29.6% of males suffered from hyperprolactinemia. Secondary hypothyroidism was present in 14.28% of women and 18.5% men. Adrenal axis insufficiency was discovered in only 2 males (7.4%). Nobody was diagnosed with diabetes insipidus. There was no statistically significant relationship between the diagnostic delay and any of the symptoms or any of the pituitary axis insufficiency.
Conclusions
In our study, males tend to underreport the symptoms of hypogonadotropic hypogonadism. Menstrual irregularities or decreased libido are more frequently reported in younger age, while headaches are more common in females. Diagnostic delay did not statistically depend on presence of any of the symptoms nor pituitary insufficiency.

DOI: 10.1530/endoabs.81.P690

P691

Very-low-calorie-ketogenic-diet (VLCKD) approach to manage obesity in craniopharingioma patients

Oana Ruxandra Cotta[1], Ylenia Alessi[1], Rosaria Certo[1], Alessandra Piccione[1], Rosalinda Casablanca[1], Giuseppe Paola[1], Martina Buda[2], Monica Scaramuzzo[1], Francesco Ferrau'[1,2] & Salvatore Cannavo'[1,2]
[1]University of Messina, Unit of Endocrinology, Messina, Italy; [2]University of Messina, Department of Human Pathology of Adulthood and Childhood "G. Barresi", Italy

Background
Craniopharingioma patients frequently experience severe obesity, unresponsive to caloric restriction or lifestyle modifications. Recently very-low-ketogenic-diets (VLCKD) proved to be a promising lifestyle intervention for obesity management, but no data are available regarding their effect on hypothalamic obesity (HO).
Introduction
We present the outcome of VLCKD protocol applied in young patients with HO following neurosurgery for craniopharingioma.
Methods
Three patients who developed HO after surgery for craniopharingioma (1 male, mean weight 125±2.8 kg, mean BMI 43.9±3.9 kg/m^2) were treated with VLCKD protocol. All patients had previously undergone largely unsuccessful dietary interventions. BMI, weight, waist circumference changes and adverse effects were assessed during a follow-up period of 7.5±7.3 months (range 3-16 months).
Results
The two female patients presented panhypopituitarism and diabetes insipidus, while the male had multiple pituitary deficiencies (central hypothyroidism, hypogonadotropic hypogonadism and growth hormone deficiency); all patients were on adequate replacement therapy. Both female patients presented visual field impairment. All patients showed non-alcoholic steatoepatitis, hyperinsulinism but not diabetes mellitus, while the male patient also presented hyperuricemia. VLCKD resulted in a significant weight loss (125±2.8 kg vs 112.4±3.6 kg, *P*0.008) as well as waist circumference reduction (111.7±3.8 vs 102.3±3.0, *P*0.029). At last follow-up, BMI (43.9±3.9 kg/m^2 vs 39.4±2.8 kg/m^2 *P*0.17) and HOMA Index (9.66±2.6 vs 5.12±3.5, *P*0.14) remarkably decreased, although not significantly. The only side effect registered was persistent hyponatriemia in one female patient, normalising after VLCKD suspension, corticosteroid and desmopressin replacement treatment adjusting.
Conclusions
The use of VLCKD protocol is a promising, safe and effective treatment option for HO in craniopharingioma patients. Frequent control of electrolytes is mandatory.

DOI: 10.1530/endoabs.81.P691

P692

Analysis of the frequency of relapses according to the national registry cushing' s syndrome in Republic of Uzbekistan

Umida A. Mirsaidova & Zamira Khalimova
Republican Specialized Scientific Practical Medical Center of Endocrinology of Republic of Uzbekistan named by Ya.Kh.Turakulov, Tashkent, Uzbekistan

Transsphenoidal pituitary surgery is the method of choice in the treatment of ACTH-DCS, although to date, according to a number of researchers, the method is not ideal. Despite the achievement of immediate postoperative remission in 69-

98% of cases, with an increase in the duration of follow-up after TSS from 5 to 10 years, an increase in the frequency of relapses from 15 to 66% is observed. In this regard, we analyzed cases of ACTH DCS subjected to TSS for 2003-2021, included in the national register. Thus, according to the registry data, over a 18-year period, 222 patients with ACTH DCS were under dynamic observation, of which 128(57.6%). The remaining 94(42.4%) patients were on medication - 54 cases (24.4%), adrenalectomy - 36 (16.2%), including 3 patients (1.3%) in combination with RT, on radiation therapy -4 patients (1.8%). Every year, there are 2-3 cases of relapse, which aggravate both the course and outcome of the disease. In view of this, the this stage of our research was the search and analysis of possible causes of the development of relapses of the disease in ACTH-DCS. The analysis revealed that a total of 53 (41.4%) patients out of 128 treated with TSS developed a relapse in the period 2003-2021. Of these women, the overwhelming majority - 48 (90%) and 5 men (10%). The mean age of the patients was 34.3 ± 0.26 years. The average duration of the remission period was 3.25 ± 0.04 years. Due to the development of recurrence and failure to achieve in 33 cases (62.3%), repeated TSS was performed in 11 patients, radiation therapy in 5 and adrenalectomy in 15 patients, which caused the development of pituitary complications in the form of diabetes insipidus in 2 (3.7 %) and panhypopituitarism in 2 (3.7%). Thus, in a cohort of 53 (42.9%) patients with ACTH-DCS, who developed a relapse of the disease after TSS, they were aged 34.3 ± 0.16, consisted mainly of females (90%), were characterized by microadenomas (88.6%), insufficient decrease in ACTH and cortisol levels in the early postoperative period (by 1.5 and 1.7 times, respectively), persistence of arterial hypertension (26.4%), impaired BMD (63.4%), 26.3%), the presence of central diabetes insipidus (3.7%) and panhypopituitarism (3.7%). As the results of the analysis show, the very state of remission in patients with ACTH-DCS is unstable and, for various reasons, they may develop a relapse, the frequency of which increases with an increase in the observation period.

DOI: 10.1530/endoabs.81.P692

P693

Multimodal treatment including temozolomide (TMZ) and pasireotide for aggressive, giant silent corticotroph PiTNET in a young patient

Anna Bogusławska, Łukasz Kluczyński, Magdalena Godlewska, Ewelina Rzepka, Alicja Hubalewska-Dydejczyk & Aleksandra Gilis-Januszewska
Department of Endocrinology, Endocrine Oncology and Nuclear Medicine, Jagiellonian University Medical College, Cracow, Poland

Silent corticotroph pituitary neuroendocrine tumours (PiTNETs) are a subtype of nonfunctioning PiTNETs, that present positive immunostaining for adrenocorticotropin (ACTH) and/or show the expression of the transcription factor T-PIT without clinical signs of hypercortisolemia. They constitute 20% of all corticotroph PitNETs and manifest in most cases as macroadenoma with suprasellar extension and a higher tendency to apoplexy. We present a 33-year-old male with aggressive course of silent corticotroph PitNET. The patient was admitted to Emergency Department due to severe headaches and vomiting. Headaches (8-9/10 using numbering rating score (NRS)) and worsening vision loss were present one year before the surgery. In computer tomography, a sellar tumour mass (39x33x55 mm) was found with extrasellar extension, causing pressure on the cerebral aqueduct of the third ventricle, involving left sphenoid sinus. Additionally, features of cerebral edema were described. The patient was transferred to Neurosurgery Department and, external ventricular drainage was performed due to obstructive hydrocephalus. Two days later, debulking transsphenoidal surgery (TSS) was performed. Histopathology results showed silent adenoma subtype 1 (densely granulated), Ki67 $< 1\%$. Genetic testing was negative for *AIP* and *MEN1* mutations. However, 3 months later, magnetic resonance imaging (MRI) showed progression of PitNET (40x39x30 mm) with increasing hydrocephalus. Subsequently, second TSS was performed, complicated with cerebrospinal fluid leak. Biochemically, persistent multiple pituitary hormone deficiencies and diabetes insipidus were diagnosed. Clinically, severe headaches (9-10/10 using NRS) without improvement after analgesic and worsening vision loss were observed. The patient was consulted by multidisciplinary pituitary tumour board and radiotherapy was planned. Pasireotide (10 mg) monthly and 0.5 mg of cabergoline weekly were scheduled, however, due to rapid progression of the tumour and the compression of optic chiasm, emergency TSS (05.2021) with the decompression of the optic nerves was performed. After surgery, chemotherapy with temozolomide (starting dose of 150 mg/m^2) for 5 days was introduced. After first cycles, adjuvant stereotactic fractionated radiotherapy (total dose 50.4 Gy in 28 cycles) was performed. Temozolomide at the dose of 200 mg/m^2 for 5 days every 4 weeks was continued. Severe headaches (9-10/10 using NRS) without improvement after analgesic were still present. Pasireotide (increasing dose from 10 to 40 mg/month) was reimplemented, decrease of headaches from (initially 9-10 to none /10 using NRS) has been observed. In last MRI, after 5 cycles of temozolomide, and during pasireotide and cabergoline treatment, regression of the pituitary tumour (current measurements: 20x30x29 mm) was observed. Additionally, patients is in a very good general condition, reports no headaches.

DOI: 10.1530/endoabs.81.P693

P694

Radiological classification of craniopharyngioma based on its origin

Tanja Skoric Polovina[1], David Ozretic[2], Mirsala Solak[1], Ivana Kraljevic[1], Tina Dusek[1], Annemarie Balasko[1], Karin Zibar Tomšić[1] & Darko Kastelan[1]
[1]Clinical Hospital Center Zagreb, Dpt of Endocrinology, ZAGREB, Croatia; [2]Clinical Hospital Center Zagreb, Dpt of Neuroradiology, Zagreb, Croatia

Recognizing the site of origin of craniopharyngioma (CP) along the hypothalamus-pituitary axis according to pre-operative MR is helpful to understand its growth pattern in relation to hypothalamus, which is critical in the prediction of hypothalamic injury and planning of treatment. We retrospectively classified 29 CP according to MR pre-operative image study using modified classification of Tang *et al*. (Nature, 8:10215, 2018). According to its relation to pituitary stalk, CP were classified into two types: central and peripheral. Peripheral type was further subdivided into three subtypes: hypothalamic stalk, suprasellar stalk and intrasellar stalk. Central type and hypothalamic stalk peripheral subtype CP were considered to be of hypothalamic origin. We compared types of CP with the development of cognitive dysfunction and obesity after the treatment as markers of hypothalamic injury. Of the 29 CP examined in this study, five were classified as central type, and 24 as peripheral type. Twelve of peripheral type were subclassified as hypothalamic stalk CP, four as suprasellar stalk CP, and eight as intrasellar stalk CP. Cognitive dysfunction was found significantly more often in patients with central CP and hypothalamic stalk CP (3/5 and 4/12, respectively) in comparison to patients with suprasellar and intrasellar stalk CP who did not developed cognitive impairment ($P = 0.012$). Obesity developed in 3 of 5 patients with central CP, 4 of 12 with hypothalamic stalk CP, 1 of 4 with suprasellar stalk CP, and 1 of 8 with intrasellar stalk CP, with no statistical difference between CP types. Our results showed that cognitive impairment as a marker of hypothalamic damage was found only in CPs of hypothalamic origin (classified as central and hypothalamic stalk CP). We conclude that this classification, based on preoperative MR findings, can predict hypothalamic damage. Suprasellar and intrasellar stalk CP may not involve the hypothalamus and therefore can be safely resected with no hypothalamic damage.

DOI: 10.1530/endoabs.81.P694

Reproductive and Developmental Endocrinology

P180

European Registries for Rare Endocrine Conditions (EuRRECa): results from the e-Reporting platform for rare conditions (e-REC)

Salma Rashid Ali[1,2], Jillian Bryce[2], Ana Luisa Priego Zurita[3], Martine Cools[4], Thomas Danne[5], Harshini Katugampola[6], Olaf M. Dekkers[7], Olaf Hiort[8], Agnès Linglart[9], Irene Netchine[10], Anna Nordenström[11], Attila Patócs[12], Alberto M Pereira[3], Luca Persani[13,14], Nicole Reisch[15], Arelene Smyth[2], Zdenek Sumnik[16], Domenica Taruscio[17], Edward Visser[18], Natasha Appelman-Dijkstra[19] & Faisal Ahmed[1,2,3]
[1]Developmental Endocrinology Research Group, School of Medicine, Dentistry & Nursing, University of Glasgow, UK; [2]Office for Rare Conditions, Royal Hospital for Children & Queen Elizabeth University Hospital, Glasgow, UK; [3]Dept of Medicine, Division of Endocrinology, Leiden University Medical Center, Leiden, Netherlands; [4]Department of Internal Medicine and Paediatrics, Ghent University, Belgium, Department of Paediatric Endocrinology, Ghent University Hospital, Ghent, Belgium;

[5]Diabetes Center AUF DER BULT, Hannover, Germany; [6]Genetics and Genomic Medicine Programme, UCL GOS Institute of Child Health, 30 Guilford Street, London WC1 N 1EH; [7]Departments of Medicine & Clinical Epidemiology, Leiden University Medical Centre, Leiden, Netherlands; [8]Division of Paediatric Endocrinology and Diabetes, Department of Paediatrics and Adolescent Medicine, University of Lübeck, Lübeck, Germany; [9]APHP, Bicêtre Paris Sud, le Kremlin Bicêtre, France; [10]Sorbonne Université, Inserm, Centre de recherche Sainte Antoine, APHP, Hôpital des Enfants Armand Trousseau, Paris, France; [11]Pediatric Endocrinology and Inborn Errors of Metabolism, Karolinska University Hospital, S-17176 Stockholm Sweden; [12]Clinical Genetics and Endocrinology Laboratory, Department of Laboratory Medicine, Semmelweis University, Budapest, Hungary; [13]Dept of Biotechnology and Experimental Medicine, University of Milan, 20122 Milan, Italy; [14]Division of Endocrine and Metabolic Diseases, Istituto Auxologico Italiano, 20145 Milan, Italy; [15]Med. Klinik und Poliklinik IV, Klinikum der Universität München, Munich, Germany; [16]Department of Pediatrics, Motol University Hospital, Prague, Czech Republic; [17]National Centre for Rare Diseases, Istituto Superiore di Sanità, Rome, Italy; [18]Erasmus Medical Centre, Department of Internal Medicine, Academic Centre for Thyroid Diseases, Rotterdam, Netherlands; [19]Leiden University Medical Center, Leien, Netherlands

Background
EuRRECa (eurreca.net) is a web-based project that supports professional networks such as European Reference Networks (ERNs) in capturing standardised clinical information. The project includes an e-reporting registry (e-REC), which can be used to perform regular surveillance of specific events. Since 2018, e-REC has been used by the ERN for rare endocrine conditions (Endo-ERN) to understand the number of new clinical encounters at centres within this network.
Methods
Electronic reporting cards were issued through a simple bespoke reporting platform on a monthly basis to clinicians who had registered to participate in e-REC from July 2018 to June 2021. Clinicians were asked to report any newly encountered cases of any of the conditions that have been included in Endo-ERN.
Results
The number of centres reporting on e-REC has increased over a 3 year period from July 2018 to June 2021 when, a total of 60 centres from 22 countries had reported cases. Over this period, a median of 24 (range 10, 37) paediatric centres and 24 (12, 38) adult centres had reported cases on a monthly basis. A total of 7.860 and 3.771 new cases were reported in adults and children, respectively. Amongst paediatric cases, conditions within the sex development condition group were most commonly reported, comprising 44% of all reported conditions, with a trend towards more cases being reported on an annual basis. Overall, the median number of cases reported per centre was 30 (10, 137) and transgender (male to female) cases comprised the most commonly reported condition (58% of cases). Amongst adults, pituitary and thyroid conditions were most commonly reported, comprising 45% and 20% of all conditions, respectively. An increasing number of pituitary cases were reported over the 3 year period; a median of 79 (6, 255) pituitary cases were reported per centre. The reporting of thyroid cases remained constant; a median of 43 (5, 75) thyroid cases were reported per centre. Amongst conditions within the pituitary and thyroid groups, pituitary adenomas and non-metastatic thyroid carcinomas were the most commonly reported conditions, comprising 69% and 97% of cases, respectively.
Conclusion
There is increasing acceptability of the e-REC platform which can be used to capture brief and simple information to improve our understanding regarding new encounters of rare endocrine conditions. The platform can be adapted to serve the needs of several networks that are interested in understanding the occurrence of rare conditions.

DOI: 10.1530/endoabs.81.P180

P181

Hormonal treatment modification during the long term follow-up of transwomen and transmen individuals: a retrospective observational Italian study

Marta Cacciani[1,2], Giorgia Spaggiari[1], Antonio R. M. Granata[1], Manuela Simoni[1,2] & Daniele Santi[1,2]
[1]Unit of Endocrinology, Department of Medical Specialties, Azienda Ospedaliero-Universitaria of Modena, Modena, Italy; [2]University of Modena and Reggio Emilia, Department of Biomedical, Metabolic and Neural Sciences, Modena, Italy

Background
Persons with assigned either male (AMAB) or female (AFAB) sex at birth might wish to obtain feminization or masculinization, respectively. To this purpose, hormonal treatment with sex hormones must be tailored to each subject. Several studies and the European Society of Endocrinology guidelines tried to identify the optimal hormonal treatment in both AMAB and AFAB subjects. However, the clinical management in the long term follow-up remains challenging. Many treatment adjustments and/or shifts are clinically performed to reach the therapeutic goal, i.e. phenotypic characteristics of the perceived gender, minimizing adverse events.
Aim of the study
To evaluate treatment modifications/shifts required in the long term follow-up of AMAB and AFAB subjects treated with guideline-based hormone therapy adjusted according to biochemical results.
Methods
A retrospective, longitudinal, observational clinical study was carried out at the Andrology Unit of Modena (Italy). All AMAB and AFAB subjects evaluated since 2006 were considered eligible. All clinical consultations performed until January 2022 were collected, including data regarding previous medical history, comorbidities, physical examination, blood examinations, hormonal assessment, and therapeutic choice.
Results
A total of 120 subjects were enrolled, 69 AMAB (57%) and 51 AFAB (43%). AFAB subjects were significantly older (41.1+9.1 *vs* 33.9+8.8 years, $P<0.001$) and followed-up for longer time (36.8+42.0 *vs*23.4+31.2 months, $P<0.001$) than AMAB.
In AFAB subjects, treatment modifications were performed 60 times (26.5%) during the follow-up and the dropout rate was 2.0% (1 subject). Mean testosterone serum levels during follow-up were 6.7+6.4 ng/ml. Therapy modifications were neither predicted by testosterone serum levels, nor comorbidities number, nor drug number (Cox logistic regression: 0.384, $P=0.061$). In AMAB group, hormonal treatment was modified 164 times (45.1%) during follow-up, with a dropout rate of 24.6% (17 subjects). Mean oestradiol serum levels at follow-up were 49.8+45.1 pg/ml. While therapy changes were not predicted by oestradiol serum levels (Cox logistic regression: 0.778, $P=0.194$), they resulted directly related with the number of comorbidities (Cox logistic regression: 0.585, $P=0.025$).
Conclusion
Our retrospective long term analysis on AFAB and AMAB subjects highlighted a comprehensive maintenance of sex hormones levels within therapeutic ranges burdened by frequent therapy modifications. These drug adjustments resulted more evident in AMAB subjects, in which treatment changes seemed related to the presence of comorbidities. Considering also the higher dropout rate compared to AFAB, AMAB subjects seem to require a more stringent clinical management during follow-up.

DOI: 10.1530/endoabs.81.P181

P182

Defining reference ranges for serum anti-Müllerian hormone (AMH) on a large cohort of normozoospermic adult men highlights new potential physiological functions of AMH on FSH secretion and sperm motility

Hamza Benderradji[1,2], Barbotin Anne-Laure[2,3], Leroy-Billiard Maryse[4], Prasivoravong Julie[1], Marcelli François[1], Decanter Christine[4], Robin Geoffroy[1], Mitchell Valérie[1], Rigot Jean-Marc[1], Bongiovanni Antonino[5], Sauve Florent[2], Buée Luc[2], Maurage Claude-Alain[2,6], Cartigny Maryse[7], Villers Arnauld[1], Prevot Vincent[2], Catteau-Jonard Sophie[2,4], Sergeant Nicolas[2], Giacobini Paolo[2], Pigny Pascal[8,9] & Leroy Clara[1,7]
[1]University of Lille, CHU Lille, Department of Andrology, Urology and Renal Transplantation, Lille, France; [2]University of Lille, Inserm, CHU Lille, Lille Neuroscience & Cognition, UMR-S1172, Lille, France; [3]University of Lille, CHU Lille, Department of Reproductive Biology-Spermiology-CECOS, LILLE, France; [4]University of Lille, CHU Lille, Department of Endocrine Gynecology and Reproductive Medicine, Lille, France; [5]University of Lille, CNRS, Inserm, CHU Lille, Institut Pasteur de Lille, US 41 - UMS 2014-PLBS, BioImaging Center Lille, Lille, France; [6]University of Lille, CHU Lille, Department of Pathological Anatomy, Lille, France; [7]University of Lille, CHU Lille, Department of Pediatric Endocrinology, DevGen, Reference Centre for Genital Development Abnormalities, Lille, France; [8]Department of Biochemistry & Hormonology, Lille, France; [9]University of Lille, CHU Lille, Inserm, UMR-S 1277, Lille, France

Background
Few studies to date have attempted to measure serum anti-Müllerian hormone (AMH) levels in adult men, and solid references ranges have not yet been defined on a large cohort.
Objective
In this study, we aimed to first establish the reference ranges for serum AMH and AMH-to-total testosterone ratio (AMH/tT) in adult males. Secondly, we investigated the relationship between serum AMH and both reproductive hormones and semen parameters.
Methods
This single-center retrospective study included 578 normozoospermic adult men. Serum AMH concentrations were determined with an automated sandwich chemiluminescent immunoassay.
Results
The median serum AMH was 43.5 pmol/l. The 2.5th and 97.5th percentile values for serum AMH and AMH/tT were 16.4 pmol/l − 90.3 pmol/l, and 0.45 − 3.43, respectively. AMH was positively correlated with inhibin B and sperm concentration, and negatively correlated with age, FSH and progressive sperm motility. Interestingly, using immunofluorescence, we documented for the first time that AMH type-II receptor (AMH-R2) is expressed in ejaculated human spermatozoa and gonadotrophic cells in postmortem pituitaries.
Conclusions
A new age-specific reference range for serum AMH and AMH/tT was established. Moreover, AMH-R2 expression in human spermatozoa and gonadotrophic cells, together with the relationship between serum AMH levels and sperm motility or mean FSH levels, highlight new potential functions of AMH in regulating sperm motility or FSH secretion in adult men.

DOI: 10.1530/endoabs.81.P182

P183

Intranasal kisspeptin administration stimulates reproductive hormone secretion in healthy volunteers and patients with hypogonadism

Edouard Mills[1], Magda Swedrowska[2], Layla Thurston[1], Maria Phylactou[1], Bijal Patel[1], Lisa Yang[1], Sophie Clarke[1], Beatrice Muzi[1], Emma Alexander[1], Muhammad Choudhury[1], Paul Bech[1], Ali Abbara[1], Ben Forbes[2], Alexander Comninos[1] & Waljit Dhillo[1]
[1]Imperial College London, Hammersmith Campus, Section of Endocrinology and Investigative Medicine, London, United Kingdom; [2]King's College London, Institute of Pharmaceutical Science, London, United Kingdom

Background
Kisspeptin is a critical activator of hypothalamic gonadotrophin releasing hormone (GnRH) neurons and has significant potential to treat common reproductive disorders. To date, kisspeptin has solely been administered to humans via the intravenous or subcutaneous routes, however intranasal administration could offer a novel non-invasive delivery route. We therefore sought to determine the effects of intranasal kisspeptin on reproductive hormone release in humans for the first time.
Methods
Randomised, double-blinded, placebo-controlled, cross-over study in 12 healthy men (mean ± SEM age 28.3 ± 1.7 years; BMI 24.5 ± 0.7 kg/m^2). After monitored self-administration of intranasal kisspeptin-54 (3.2, 6.4, 12.8 and 25.6 nmol/kg) or 0.9% saline, serum reproductive hormone levels were measured every 15 minutes for four h. Subsequently, four women (mean age 29.8 ± 3.7 years; BMI 21.2 ± 1.1 kg/m^2) with hypothalamic amenorrhoea (HA) attended for the same protocol comparing intranasal kisspeptin-54 (12.8 nmol/kg) and 0.9% saline. Mean ± SEM was presented. Time profiles of hormone levels were compared using two-way ANOVA, and multiple means using one-way ANOVA.
Results
In healthy men, intranasal kisspeptin dose-dependently increased mean luteinising hormone (LH) levels at doses between 3.2-12.8 nmol/kg ($P = 0.008$ and < 0.0001 for 6.4 and 12.8 nmol/kg vs saline, respectively), with the maximal rises occurring 30-45 minutes post-administration. The maximal LH change from baseline was significantly elevated following all kisspeptin doses vs saline (*saline:* 1.54 ± 0.30 IU/l; *3.2 nmol/kg:* 2.46 ± 0.30 IU/l [p = 0.01]; *6.4 nmol/kg:* 3.08 ± 0.48 IU/l [p = 0.04]; *12.8 nmol/kg:* 4.45 ± 0.59 IU/l [p = 0.002]; *25.6 nmol/kg:* 4.07 ± 0.66 IU/l [p = 0.003]). Follicle stimulating hormone (FSH) levels followed a similar trajectory to LH. Kisspeptin at 12.8 nmol/kg increased serum testosterone from 120 minutes onwards ($P = 0.02$), with a maximal change from baseline of 4.9 ± 0.7 nmol/l ($P = 0.03$). In women with HA, intranasal kisspeptin increased mean LH ($P = 0.002$ vs saline), with the peak levels occurring 30-45 minutes post-administration. The maximal LH change from baseline was 4.06 ± 0.89 IU/l, compared with 0.20 ± 0.38 IU/l for saline ($P = 0.03$). Intranasal kisspeptin increased mean FSH ($P = 0.01$ vs saline). No significant changes in downstream serum oestradiol or progesterone were observed during the acute four-h study.
Conclusion
We report the first investigation of the effects of intranasal kisspeptin delivery on reproductive hormone release. Our results demonstrate that intranasal kisspeptin robustly and dose-dependently stimulates reproductive hormone release in healthy men and in a patient-group of women with hypogonadism. Given the ongoing development of kisspeptin therapeutics, intranasal kisspeptin offers a novel, safe, effective and non-invasive route of administration for the management of reproductive disorders that would be preferred by patients and clinicians alike.

DOI: 10.1530/endoabs.81.P183

P184

Effects of testosterone therapy on bone turnover markers and bone mineral density in obese males with type 2 diabetes and functional hypogonadism

Kristina Groti Antonic
Ljubljana, Endocrinology, Ljubljana, Slovenia

Aims
Both functional hypogonadism (FH) and type 2 diabetes (T2D) negatively affect bone mineral density (BMD). We aimed to evaluate changes on bone turnover markers (BTMs) and BMD in obese males with FH and T2D due to testosterone therapy (TTh).
Research Design and Methods
55 obese males with FH and T2D participated in a two-year (first year double-blind, placebo-controlled study, second year follow-up) clinical trial. Participants were randomized into two groups. Group T ($n = 28$) received 1000 mg testosterone undecanoate (TU) both years of the study while group P ($n = 27$) received placebo first year and TU second year. BTMs C-telopeptide of type I collagen (CTX) and procollagen I N-terminal propeptide (PINP), estradiol, 25-hydroxyvitamin D, total, calculated free and calculated bioavailable testosterone levels were assessed at baseline, 12 and 24 months. BMD changes were evaluated at baseline and after 24 months using dual-energy x-ray absorptiometry (DXA).
Results
Results show decrease in median CTX from baseline of 1055 (676 to 1344) pmol/l to 911 (556 to 1152) pmol/l after one year of placebo ($P = .012$), then to 453 (365 to 665) pmol/l after one year of TTh ($P < .001$) in group P and from 887 (648 to 1496) pmol/l to 504 (262 to 804) pmol/l after first year of TTh ($P < .001$), then to 372 (165 to 599) after second year of TRT ($P < .001$) in group T. Median PINP did not change from 31.4 (27.1 to 40.3) µg/l baseline at statistically significant level after one year of placebo ($P = .469$) in group *P*but decreased to 28.0 (23.6 to 32.0) µg/l after one year of TTh ($P = .009$); in group T a decrease from 30.9 (21.9 to 35.3) µg/l to 26.2 (18.6 to 32.1) µg/l was observed after first year of TTh ($P = .005$), then to 20.1 (17.8 to 26.5) µg/l after second year of TRT ($P < .001$). DXA showed no changes in femoral neck BMD in 32 patients from both groups *P* ($n = 16$) or T ($n = 16$) while a statistically significant increase in lumbar spine BMD by.075 ± .114 g/cm^2 (95% CI:.014 to.136; $P = .019$) has been observed in group T following two years of TTh.
Conclsions
BTMs decreased significantly after TU and improvement of lumbar spine BMD was observed after two years of TTh in obese males with FH and T2D.

DOI: 10.1530/endoabs.81.P184

P185

Management of 46, XY 17 alpha-hydroxylase deficiency: a case report

Bruno Bouça[1], Mariana Cascão[2], Pedro Fiúza[3], Sara Amaral[1], Paula Bogalho[1] & Jose Silva-Nunes[1]

[1]Centro Hospitalar Universitário de Lisboa Central, Department of Endocrinology, Diabetes and Metabolism, Lisbon, Portugal; [2]Centro Hospitalar Universitário de Lisboa Central, Intensive Care Unit, Lisbon, Portugal; [3]Centro Hospitalar Universitário de Lisboa Central, Department of Internal Medicine, Lisbon, Portugal

Introduction

17 alpha-hydroxylase deficiency (17OHD) is a rare autosomal recessive disease caused by mutations in the CYP17A gene, representing 1% of cases of Congenital Adrenal Hyperplasia (CAH). The accumulation of mineralocorticoids and the glucocorticoid effect of corticosterone induce high blood pressure (HBP) and hypokalemia.

Clinical Case

A 44 year-old female reporting HBP since the age of 20 years and without chronic medication, presented at the emergency department (ED) complaining of generalized asthenia and polyarthralgia for about two weeks. On examination, she was hypertensive (174/100 mmHg); blood analysis revealed severe hypokalemia − K^+ 1.2 mEq/l (3.5-5.1). In the ED, she had an episode of ventricular tachycardia evolving to asystole. After resuscitation, she was transferred to the Intensive Care Unit with rapid clinical improvement under antihypertensive therapy and hydrocortisone. Further laboratory evaluation showed: cortisol <0.4 mg/dl (3.7-19.4), ACTH 213 pg/ml (<46), aldosterone (decubitus) 27.4 ng/dl (1-16), renin <1.8 mcUI/ml (2.8-39.9). Due to these findings, she was transferred to the Endocrinology ward. On examination, she had an uncharacteristic morphotype, BMI 16.7 kg/m^2 (175 cm; 51.2 kg), cutaneous hyperpigmentation and Tanner stage M1P1. Hormonal evaluation showed: LH 64 mIU/ml (follicular phase 1.8-11.8), FSH 97 mIU/ml (3.03-8.08), estradiol 17 pg/ml (21-251), progesterone 5.2 ng/ml (0.1-0.3), 17-OHP 0.19 ng/ml (0.21-1.45), total testosterone 0.03 ng/ml (0.11-0.56). CT scan revealed bilateral adrenal hyperplasia (right width 11.5 mm; left width 12.9 mm) and absence of female internal genitalia (explaining primary amenorrhea referred by the patient). Genetic diagnosis was confirmed by the identification of the c.3G>A p.(Met1?) variant in homozygosity in the CYP17A1 gene. Karyotype analysis was compatible with 46 XY. At the last appointment, the patient was normotensive under dexamethasone 0.5 mg id, spironolactone 50 mg id, olmesartan 40 mg id, nifedipine 60 mg bid and nebivolol 5 mg id; blood analysis showed K+ 4.7 mEq/l and aldosterone 20.4 ng/dl.

Conclusion

The association of severe hypokalemia, hypertension, hypocortisolism, oligo/amenorrhea and the absence of secondary sexual characteristics favored the diagnosis of 17OHD, confirmed by genetic testing. As in other published cases, diagnosis outside pediatric age is not rare and should be considered in cases of severe hypokalaemia in hypertensive adults and lack of secondary sexual development.

DOI: 10.1530/endoabs.81.P185

P186

Glycaemic and metabolic effects of testosterone replacement in hypogonadal men with uncontrolled type 2 diabetes − a randomised double blinded placebo controlled trial − stride study

Preethi Mohan Rao[1,2], Daniel M Kelly[2,3] & T. Hugh Jones[1,2]

[1]Barnsley Hospital NHS Foundation Trust, Robert Hague Centre for Diabetes and Endocrinology, United Kingdom; [2]The University of Sheffield, Human Metabolism and Oncology, United Kingdom; [3]Sheffield Hallam University, Biomolecular Research Centre, United Kingdom

The objective of the study was to assess the effect of intra-muscular testosterone on glycemic control, metabolic parameters and hypogonadal symptoms in men with hypogonadism and poorly controlled type 2 diabetes. This is a randomised double-blinded placebo-controlled add-on trial of intramuscular-testosterone undecanoate(Nebido®) administered every 12 weeks in 65 hypogonadal men with poorly-controlled diabetes. Phase-1 patients were randomly assigned to either treatment or placebo arm for 6 months of TRT. Phase-2 was an open-labelled phase for 6 months and patients on placebo moved on to the treatment group wherein patients in the treatment group continued. Anthropometric measurements, questionnaires and biochemical parameters were assessed at baseline and every three months for a year. Mean age of the cohort was 59 ± 8.98 years(mean $\pm$ SD). Mean duration since diagnosis of diabetes was 8.6 years. 17(26%) were on insulin. Baseline cohorts were comparable. There was no improvement in mean HbA1c or fasting plasma glucose(FBG) between the active and placebo groups after 6 months of TRT. No difference was found in HbA1c or FBG at 12 months compared to baseline in the active group either. Our study also showed a significant decrease in serum triglycerides(-0.497 ± 0.213 mmol/l, $P=0.023$) and improvement in left hand grip strength($P=0.025$) at 6 months post treatment in the active group compared to placebo group. There was no significant difference in the mean weight, BMI, WC, WHR, fat mass, fat percentage or fat free mass between the groups. Our study is the first ever RCT to show a significant improvement in total AMS(aging male symptom)scores from baseline after 6 months of TU treatment compared to placebo group($P<0.05$) in a cohort with poorly-controlled type 2 diabetes and hypogonadism. Another key finding is that the proportion of patients with severe symptoms moving to a less severe category(low/mild/moderate severity) was 46% in the active vs only 28% in placebo($P=0.0024$). Our study concludes that TRT did not have a significant improvement in glycaemic control at 6 months between the active/placebo groups and at 12 months within the active group and may need longer duration to see the positive effects especially in cohort of people who have had long duration of diabetes. There was a significant reduction in triglyceride levels and increase muscular-strength after 6 months of TRT. STRIDE study is the first ever RCT to show a significant improvement in clinical symptoms and symptom severity following testosterone treatment in patients with hypogonadism and type 2 diabetes after 6 months of TRT.

DOI: 10.1530/endoabs.81.P186

P187

Overall impact of gender affirming hormone therapy: the portuguese experience

Miguel Saraiva[1], Rafael Santos[2], Zélia Figueiredo[3], Carolina Lemos[4] & Isabel Palma[1]

[1]Centro Hospitalar Universitário do Porto - Hospital de Santo António, Endocrinology, Diabetes and Metabolism, Porto,; [2]Instituto de Ciências Biomédicas Abel Salazar, Universidade do Porto; [3]Hospital de Magalhães Lemos; [4]i3S-Instituto de Investigação e Inovação em Saúde, Universidade do Porto, Porto

Introduction

The prevalence of Transgender individuals seeking gender affirming hormone therapy (GAHT) has been increasing. This therapy has been known to be highly effective in the treatment of gender dysphoria and enhancing mental health in this population.

Aim

To evaluate the overall impact of GAHT on self-esteem, well-being and social/familial relations in the Portuguese adult transgender population

Methods

Cross-sectional study conducted in March 2021. Data collected through an *online* questionnaire that was delivered to adult transgender people living in Portugal who had been under GAHT for at least one year. To answer some of the items on the questionnaire, an ordinal scale ranging from 0 (worst result) to 6 (best result) was used.

Results

A total of 142 individuals (Group T) answered the questionnaire: 101 under masculinizing GAHT (Group M) and 41 under feminizing GAHT (Group F), with a median age of 25.0(21.0−33.0) years. The overall satisfaction with GAHT was evaluated with a median of 5.0 (5.0-6.0) points, with no differences between subgroups ($P=0.681$).

Discussion

This study reinforces that transgender people report high grades of satisfaction with both the physical and psychological effects of GAHT. This therapy seems to significantly enhance self-esteem, body wellbeing and social/familial relations and to reduce suicidal ideation, having an overall great impact on the quality of life of transgender people.

DOI: 10.1530/endoabs.81.P187

Table 1

Variable		Group T			Group M			Group F	
	N	Median (P25-P75)	*P*	*n*	Median (P25-P75)	*P*	*n*	Median (P25-P75)	*P*
Self-esteem									
Before	114	1.5 (1.0 – 2.0)	<0.001	87	1.0 (0.0 – 2.0)	<0.001	27	2.0 (1.0 – 2.0)	<0.001
After		1.5 (1.0 – 2.0)			5.0 (4.0 – 6.0)			5.0 (4.0 – 6.0)	
Body well-being	114	1.0 (0.0 – 2.0)	<0.001	87	1.0 (0.0 – 2.0)	<0.001	27	1.0 (0.0 – 2.0)	<0.001
Before									
After		5.0 (4.0 – 5.0)			4.0 (3.0 – 5.0)			5.0 (4.0 – 6.0)	
Suicidal ideation	114	3.0 (1.0 – 5.0)	<0.001	87	3.0 (1.0 – 5.0)	<0.001	27	3.0 (1.0 – 5.0)	0.406
Before									
After		5.0 (2.0 – 6.0)			5.0 (3.0 – 6.0)			3.0 (2.0 – 6.0)	
Social relations	113	3.0 (1.0 – 4.0)	<0.001	86	3.0 (1.0 – 5.0)	<0.001	27	3.0 (1.0 – 4.0)	0.003
Before									
After		5.0 (3.0 – 6.0)			5.0 (3.0 – 6.0)			5.0 (3.0 – 6.0)	
Familial relations	114	3.0 (1.0 – 4.3)	<0.001	87	3.0 (2.0 – 5.0)	<0.001	27	3.0 (2.0 – 4.0)	0.019
Before									
After		4.0 (3.0 – 5.0)			4.0 (3.0 – 5.0)			5.0 (3.0 – 5.0)	

P188

The effect of testosterone on quality of life, constitutional symptoms, sexual function and memory − randomised placebo-controlled study in hypogonadal men with uncontrolled type 2 diabetes − stride study

Preethi Mohan Rao[1,2] & T. Hugh Jones[1,2]
[1]Barnsley Hospital NHS Foundation Trust, Robert Hague Centre for Diabetes and Endocrinology, Barnsley, United Kingdom; [2]The University of Sheffield, Human Metabolism and Oncology, Sheffield, United Kingdom

The objective of the study was to assess the effect of intra-muscular testosterone on constitutional symptoms, sexual symptoms, memory and in men with hypogonadism and poorly-controlled type-2 diabetes. This is a randomised double-blinded placebo-controlled add-on trial of intramuscular testosterone undecanoate(Nebido®) administered every 12 weeks in 65 hypogonadal men with poorly-controlled diabetes. Phase-1 patients were randomly assigned to either treatment or placebo arm for 6 months of TRT. Phase-2 was an open-labelled phase for 6 months and patients on placebo moved on to the treatment group wherein patients in the treatment group continued. Outcomes(AMS, SF-36, IIEF-5 questionnaires, MMSE, Barnsley and NERI questionnaires) were assessed at baseline and every 3 months. Mean age of the cohort was 59 ± 8.98 years(mean ± SD). Baseline characteristics were comparable between active/placebo groups. Our study is the first ever RCT to show a significant reduction in the mean total AMS score from baseline of 48.34 ± 13.13 to score of 37.72 ± 12.25 at 6 months after testosterone treatment vs from 48.34 ± 12.69 to score of 42.78 ± 13.48 in the placebo group($P < 0.05$) in a cohort with type 2 diabetes and hypogonadism. Our study also showed that the proportion of patients with severe symptoms moving to a less severe category(low/mild/moderate severity) was 46% in the active vs only 28% in placebo group($P = 0.0024$). There was no significant difference in either the SF-36 scores, MMSE scores, BDHQ, NERI or IIEF scores or its domains at baseline and after 6 months of TRT. In phase-2 of the trial, there was a statistically significant reduction in the AMS total score all its subscales before and after TRT in the active arm at 12 months. A significant improvement in libido was also demonstrated. There was a significant reduction in the BDHQ total score($P = 0.07$) and two of its sub-domains − Sexual-wellbeing and Emotional-wellbeing($P = 0.002$ and$P = 0.011$ respectively) within the active arm before and after treatment of testosterone at baseline(0), 3,6,9 and 12 months post treatment. There was significant improvement in the mean scores of physical health domain and health change in over 1-year domain of SF-36 questionnaire($P = 0.019$, $P = 0.019$ respectively) and significant improvement in the mean scores of delayed verbal recall domain of MMSE which was highly significant($P = 0.0004$) before and after treatment in the active arm at baseline(0), 3,6,9 and 12 months post treatment. Our trial is the first RCT to show a significant improvement in constitutional symptoms, sexual symptoms, libido, symptom severity, and delayed verbal recall with TRT in a cohort with poorly-controlled type-2 diabetes and hypogonadism

DOI: 10.1530/endoabs.81.P188

P189

Is there a link between polycystic ovary syndrome and transgenerational transmission of a reproductive and metabolic function in male offspring?

Sanjiv Risal[1], Congru Li[2], Qing Luo[2], Romina Fornes[2], Maria Manti[2], Haojiang Lu[2], Gustaw Eriksson[2], Claes Ohlsson[3], Eva Lindgren[2], Nicolas Crisosto[4], Manuel Maliqueo[5], Barbara Echiburú[5], Sergio Recabarren[5], Teresa Sir Petermann[5], Anna Benrick[6], Nele Brusselaers[7], Jie Qiao[8], Qiaolin Deng[9] & Elisabet Stener-Victorin[9]
[1]Karolinska Institute, Department of Physiology and Pharmacology, Stockholm, Sweden; [1]Karolinska Institute, Department of Physiology and Pharmacology, Stockholm, Sweden; [3]University of Gothenburg, Centre for Bone and Arthritis Research, Department of Internal Medicine and Clinical Nutrition, Institute of Medicine, Sahlgrenska Academy; [4]University of Chile, Endocrinology and Metabolism Laboratory, West Division, School of Medicine, University of Chile, Carlos Schachtebeck 299, Interior Quinta Normal, Santiago, Chile; [5]Laboratory of Animal Physiology and Endocrinology, Faculty of Veterinary Sciences, University of Concepción, Chillán, Chile; [6]Department of Physiology, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden; [7]Department of Microbiology, Tumor and Cell Biology, Karolinska Institutet, Stockholm, Sweden; [8]Center of Reproductive Medicine, Department of Obstetrics and Gynecology, Peking University Third Hospital, Beijing 100191, China; [9]Karolinska Institute, Department of Physiology and Pharmacology, Sweden

Our previous study showed that polycystic ovary syndrome (PCOS)-like reproductive and metabolic phenotypes induced by maternal dihydrotestosterone (DHT)-exposure, can be passed on in mice from mothers (F_0) to daughters (F_1),

granddaughters (F_2), and even to great-granddaughters (F_3). The female transmission is independent of diet-induced obesity and is mediated by transcriptional and mitochondrial perturbations of oocytes accompany. How maternal DHT-exposure and obesity affect their male progeny across generations is less known. Based on two clinical studies: a Swedish nationwide register and a Chilean case-control study, we found that sons of mothers with PCOS are more obese and have dyslipidemia. Next, we investigated whether diet-induced maternal obesity and/or prenatal DHT-exposure in mice, mimicking both the lean and the obese PCOS phenotype, result in transgenerational transmission of a PCOS-like phenotype in male offspring via male germline. We find a transmission of reproductive and metabolic dysfunction in F_1 and F_3 male offspring in both androgenized and obese lineages, respectively, but with stronger phenotype in the obese lineage. Small non-coding RNAs (sncRNAs) sequencing of sperm from F_1 and F_3 male offspring revealed common differential expressed sncRNAs (DEsncRNAs) across generations in androgenized, obese, and obese and androgenized lineages, with distinct regulatory patterns among lineages. Three of the predicted targets of PIWI-interacting RNA and micro RNAs were also differentially expressed in serum from sons of PCOS mothers. Our results reveal a previously unknown risk of reproductive and metabolic dysfunction in male progeny of PCOS mothers, which is likely caused by epigenetic germline changes by sncRNAs.

DOI: 10.1530/endoabs.81.P189

P190

The role of B cells in immune cell activation in polycystic ovary syndrome

Angelo Ascani[1], Sara Torstensson[2], Sanjiv Risal[2], Haojiang Lu[2], Sabrina Teschl[1], Gustaw Eriksson[2], Congru Li[2], Joana Menezes[2], Katalin Sandor[2], Camilla Svensson[2], Martin Stradner[1], Barbara Obermayer-Pietsch[1] & Elisabet Stener-Victorin[2]
[1]Medical University of Graz, Department of Internal Medicine, Graz, Austria; [2]Karolinska Institutet, Department of Physiology and Pharmacology, Stockholm, Sweden

Objective
Age-associated double negative (DN) B memory cells lacking surface expression of CD27 and immunoglobulin D (IgD) are associated with proinflammatory characteristics and higher disease activity in autoimmune diseases. We first characterized B cells phenotypes in women with and without polycystic ovary syndrome (PCOS). We then took an *in vivo* approach, transferring purified IgG extracted from serum of hyperandrogenic women with PCOS to mice to establish whether self-reactive B cells have a causal effect on the development of a PCOS-like phenotype.
Methods
We initially characterized major B cell lineages in serum of hyperandrogenic women with PCOS and of women without PCOS (controls). We purified IgG from the serum of women with PCOS (PCOS IgG) and controls which was injected intraperitoneally into immunocompetent wild type (WT) female mice and thereafter into age paired mice lacking both B and T cells (RAG1-/-). Reproductive function was tested by measuring anogenital distance and estrous cyclicity. Body composition and metabolic functions were assessed combining EchoMRI, metabolic cages and oral glucose tolerance test. Serum was collected for analysis of sex steroids by liquid chromatography mass spectrometry. Comprehensive flow cytometric analysis of lymphocytes and myeloid cells was applied in whole blood, spleen, lymph node, ovary, endometrium, visceral adipose tissue.
Results
Immunophenotypic analyses showed a significant remodeling of B cell repertoire in women with PCOS compared with controls: higher frequencies of DN B memory cells were found in PCOS patients ($P=0.002$), with declined IgD^+ B memory cells ($P=0.011$). Total testosterone was an independent predicting variable for IgM variability ($P=0.01$). Transfer of human PCOS IgG into female WT mice resulted in PCOS-like phenotype with higher circulating estrogens and trend of increased androgens, as well as higher body weight ($P<0.05$). Preliminary results from immune profiling showed an overall increase of DN B cells in mice receiving PCOS IgG, particularly DN2 subsets with a $CD21^-$ phenotype, with increased frequencies of active naïve cells and neutrophils in ovary.
Conclsions
Women with PCOS display an increased peripheral expansion of DN B cells. Exposing mice with IgG from women with PCOS rapidly induced an altered immune cell profile with increased body weight and circulating sex steroids. PCOS may represent a state of inflammatory-cell hypersensitivity and chronic inflammation, resulting in remodeling of the lymphocytes. The ongoing transfer of purified B cells from prepubertal hyperandrogenic mouse model into mice B cell deficient mice (muMt-) will define the overall impact of androgen exposure on B cell phenotypes.

DOI: 10.1530/endoabs.81.P190

P191

FSH and bone: comparison between males with central vs primary hypogonadism

Luca Giovanelli[1,2,3], Biagio Cangiano[1,2], Stefano Colombo[4], Luca Persani[1,2], Richard Quinton[3,5], Marco Bonomi[1,2] & Iacopo Chiodini[1,2]
[1]University of Milan, Department of Medical Biotechnology and Translational Medicine, Milan, Italy; [2]Istituto Auxologico Italiano, Department of Endocrine and Metabolic Medicine, Milan, Italy; [3]Newcastle-upon-Tyne Hospitals, Department of Endocrinology, Diabetes & Metabolism, Newcastle upon Tyne, United Kingdom; [4]University of Milan, Milan, Italy; [5]University of Newcastle-upon-Tyne, Translational & Clinical Research Institute, Newcastle upon Tyne, United Kingdom

Background
Recent data suggest a direct effect of follicle stimulating hormone (FSH) on the skeletal metabolism. Particularly, it can encourage bone resorption and also inhibit osteoblast differentiation. High FSH levels have been found to correlate with impaired bone health in females, whilst evidence in males remains somewhat poor and conflicting. Intriguingly, men with primary and central hypogonadism might represent a novel study model in this context.
Aims
To investigate the possible association of FSH excess with male osteoporosis.
Patients and Methods
119 men, consecutively referred to Istituto Auxologico Italiano and Newcastle upon Tyne Hospitals, were enrolled in this prospective cross-sectional observational study at the time of the first diagnosis of hypogonadism. All participants had spontaneous pubertal development. Regarding those with hypergonadotropic hypogonadism (Hyper Hypo), patients with a pre-pubertal onset form (PPO) (i.e., Klinefelter syndrome) were distinguished from the ones with an adult-onset form (AO) based on the onset of FSH elevation. Bone mineral density (BMD) at both lumbar spine (LS) and femoral neck (FN) was measured using dual-energy X-ray absorptiometry. The prevalence of morphometric vertebral fractures (VFx) was evaluated by performing spinal radiographs.
Results
Across the whole cohort, LS and FN BMD were directly associated with age at diagnosis and body mass index (BMI), respectively. After adjusting for potential confounders (age at diagnosis, BMI, smoking habits, calculated free testosterone (cfT) and 25OH vitamin D levels) by means of General Linear Model analysis, AO-Hyper Hypo patients showed significantly lower LS BMD and tended to show lower FN BMD values, as compared to those with hypogonadotropic hypogonadism (Hypo Hypo). In men with PPO-Hyper Hypo LS BMD was significantly lower than in AO-Hyper Hypo ones. No significant differences in the prevalence of VFx were found between the groups.
Conclusions
This is the first prospective study comparing men with primary and central hypogonadism in order to better delineate the putative role of FSH on the male bone health. These findings indicate a potential negative effect of FSH excess on the male bone mass, especially at spine. The duration of high FSH levels may also play a part in this setting. Longitudinal studies, involving hypogonadal men on testosterone replacement therapy, are required. Indeed, it would be crucial to identify new risk factors and mediators of male bone

fragility, with a view to ultimately reducing the huge public health burden related to fractures.

DOI: 10.1530/endoabs.81.P191

P192

Simulation via instant messaging – birmingham advance (SIMBA) as a tool to bridge gaps in clinical knowledge and expectations between physicians and patients with polycystic ovary syndrome

Pavithra Sakthivel[1], Eka Melson[2,3], Fatema Rezai[1], Carina Synn Cuen Pan[1], Jameela Sheikh[1], Harjeet Kaur[1], Catherine Cooper[4], Farah Abdelhameed[5], Francesca Pang[1], Shreya Bhatt[1], Dania Shabbir[6], Meri Davitadze[7], Helena Gleeson[8], Konstantinos Manolopoulos[3], Justin Chu[3,9], Michael O' Reilly[3,10], Wiebke Arlt[3,8], Caroline Gillett[3], Punith Kempegowda[3,8] & Simba Team[3]

[1]University of Birmingham, College of Medical and Dental Sciences, Birmingham, United Kingdom; [2]Ninewells Hospital, NHS Tayside, Dundee, United Kingdom; [3]Institute of Metabolism and Systems Research, University of Birmingham, College of Medical and Dental Sciences, Birmingham, United Kingdom; [4]Walsall Manor Hospital, Walsall Healthcare NHS Trust, West Midlands, United Kingdom; [5]University of Warwick, Coventry, United Kingdom; [6]Jinnah Medical and Dental College, Karachi, Pakistan; [7]Georgian-American Family Medicine Clinic "Medical House", Tbilisi, Georgia; [8]Queen Elizabeth Hospital, University Hospitals Birmingham NHS Foundation Trust, Birmingham, United Kingdom; [9]Birmingham Women's Hospital, Birmingham Women's and Children's NHS Foundation Trust, Birmingham, United Kingdom; [10]Royal College of Surgeons in Ireland, University of Medicine and Health Sciences, Dublin, Ireland

Introduction
Polycystic Ovary Syndrome (PCOS) is the most common endocrinopathy in women. Studies exploring the experiences of people with PCOS reveal inadequate patient access to information and limited insight into healthcare professionals' (HCP) attitudes regarding the condition. Simulation via Instant Messaging-Birmingham Advance (SIMBA) is a virtual simulation platform proven to increase learners' confidence in their approach to simulated cases with a high acceptance rate and reproducibility. However, participation in previous SIMBA sessions has been limited to HCPs.
Objectives
To assess the effectiveness of SIMBA in improving HCPs' knowledge on diagnosis and management of health conditions related to PCOS and recognise areas of disparity in knowledge and clinical expectations between HCPs and patients with PCOS.
Methods
Anonymised transcripts based on real-life cases were prepared with expert input and used to train moderators. The transcripts were used to deliver WhatsApp-based simulation to HCPs and parallel Zoom-based workshops to people with PCOS. HCPs were guided through the cases by moderators to elicit history, propose diagnoses, and management plans. People with PCOS discussed the same cases and reflected upon case management based on personal experiences. Patients and HCPs convened for a Q&A discussion at the end of the session where cases were discussed by experts and patient reflections were shared. Participants filled in pre and post SIMBA surveys.
Results
25 HCPs and 15 patients participated in the session. HCPs reported a 41% and 40% increase in confidence in the management of simulated cases (skin, weight, fertility and menstrual periods related issues in PCOS; $P<0.001$) and non-simulated cases (metabolic outcomes, menopause, mental health and endometrial cancer; $P<0.001$), respectively. HCPs reported that SIMBA improved their professionalism (28%) and communication skills (40%) and had a positive personal (84%) and professional (92%) impact. Patients reported a 17.7% increase in confidence regarding HCPs' awareness of management options for all cases following the session ($P=0.0002$). Thematic analysis of patient feedback revealed that 83.3% found the session engaging, organised and insightful. 90% of HCPs agreed that the session improved patients' understanding of the diagnosis and management of PCOS and 100% believed that the session improved their own understanding of patient experiences.
Conclusion
SIMBA is proven to be an effective educational tool that reduces discrepancies in clinical expectations between HCPs and patients and improves HCPs' confidence in managing simulated cases. It promotes transparent discussion of clinical practice and patient experiences, thereby strengthening doctor-patient relationships.

DOI: 10.1530/endoabs.81.P192

P193

Efficacy of very low calorie ketogenic diet in obese PCOS: a randomized controlled study

Srdjan Pandurevic[1], Paola Dionese[1], Ilaria Mancini[2], Dmitri Mitselman[1], Matteo Magagnoli[1], Rita Teglia[1], Domenica Gazineo[3], Lea Godino[3], Flaminia Fanelli[1], Maria Cristina Meriggiola[2], Uberto Pagotto[1] & Alessandra Gambineri[1]

[1]IRCCS Azienda Ospedaliero-Universitaria di Bologna, Division of Endocrinology and Diabetes Prevention and Care, Bologna, Italy; [2]IRCCS Azienda Ospedaliero-Universitaria di Bologna, Unit of Gynecology and Obstetrics, Bologna, Italy; [3]S. Orsola Teaching Hospital, Bologna, Italy

Background
Very low-calorie ketogenic diet (VLCKD) was shown to be effective in reducing weight and insulin resistance (IR) in obese patients. Considering that IR is very common in women with polycystic ovary syndrome (PCOS), and that IR worsens hyperandrogenism, ovulatory disfunction, and body fat accumulation, conceivably VLCKD could alleviate PCOS manifestations in the obese phenotype.
Objective
This study compared the effects of a commercial VLCKD ("PnK® method") and the control low calorie standard diet (LCD) on body weight and composition, insulin resistance, ovulation and hyperandrogenism in a population of obese PCOS.
Methods
This is an open-label, monocentric, randomized controlled trial (NCT04801173), supported by Pronokal Health group S.L. Women aged 18-45 years with PCOS diagnosed using the NIH criteria were randomized into the VLCKD or LCD group (15 vs 15). VLCKD group followed the VLCKD for 8 weeks, switching to the LCD for 8 weeks more, while the LCD group followed the LCD for 16 weeks. Ovulation monitoring by progesterone measurement and pelvic ultrasound was done at baseline and at the end of the study (week 16), while a clinical exam, bioelectrical impedance analysis (BIA) anthropometry, and biochemical analyses were performed at baseline, at week 8, and at week 16 of the study. Androgens were measured by tandem liquid chromatography-mass spectrometry. Free testosterone (freeT) was calculated using the Vermeulen formula. Repeated measures general linear model was used to evaluate within- and between-group differences for continuous variables.
Results
2 dropouts occurred in the VLCKD group, 1 in the LCD group. Body weight decreased significantly in both groups, but more so in the VLCKD group – average difference 12.4 kg (-13.6%) vs 4.7 kg (-5.3%) ($P<0.001$). Significant differences between the VLCKD and LCD groups were also seen in waist circumference (-8.1% vs -2.2%), BIA-measured body fat (-15.1% vs -8.5%), and freeT (-30.3% vs +10.6%), over the course of the study ($P=0.004$, $P=0.02$, and$P=0.002$, respectively). HOMA-IR index also decreased more in the VLCKD group during the first 8 weeks (-36.1% vs -26.1%, $P=0.02$). At baseline, 5/13 (38.5%) participants in the VLCKD group and 2/14 (14.3%) participants in the LCD group had ovulatory cycles, which differentially increased to 11/13 (84.6%) and 5/14 (35.7%) at post-intervention monitoring, respectively (McNemar, $P=0.031$).

Conclusion
This data shows that VLCKD is a valid method for reducing body fat and rapidly ameliorating hyperandrogenism and ovulatory dysfunction in obese PCOS women.

DOI: 10.1530/endoabs.81.P193

P194

Abstract withdrawn

DOI: 10.1530/endoabs.81.P194

P195

The effect of dihydrotestosterone on the immune profile in a mouse model of Polycystic Ovary Syndrome

Sara Torstensson[1], Angelo Ascani[2], Haojiang Lu[1], Sanjiv Risal[1], Gustaw Eriksson[1], Congru Li[1], Anna Benrick[3], Barbara Obermayer-Pietsch[2] & Elisabet Stener-Victorin[1]
[1]Karolinska Institutet, Department of Physiology and Pharmacology, Stockholm, Sweden; [2]Medical University of Graz, Department of Internal Medicine, Austria; [3]University of Gothenburg, Department of Physiology, Sweden

Polycystic Ovary Syndrome (PCOS) is an endocrine disorder affecting 10-15% of women worldwide, characterized by high androgen levels, anovulation and/or polycystic ovarian morphology. Chronic low-grade inflammation is associated with the disorder as well as many of its comorbidities, such as obesity and type-2 diabetes. To determine the role of the immune system in the pathophysiology of PCOS, we characterized the immune profile of the dihydrotestosterone (DHT)-induced PCOS-like mouse model. Prepubertal female mice implanted with a DHT-pellet displayed reproductive dysfunction, with a disrupted estrous cyclicity and increased anogenital distance, and a metabolic phenotype similar to the comorbidities seen in women with PCOS, with increased body weight and fat mass (EchoMRI), higher fasting glucose and impaired glucose uptake following oral glucose tolerance test. The immune profiles of reproductive, immunological, and metabolic tissues were analyzed by flowcytometry. The number of eosinophils in endometrium was decreased in the DHT-induced PCOS model compared to control, whereas infiltration of peripheral NK cells was increased. Moreover, an overall shift towards a pro-inflammatory M1 phenotype was seen among macrophages in endometrium of DHT exposed mice, indicated by a higher proportion of macrophages expressing MHC-II, and a trend suggested an increased total number of macrophages. The same effect on eosinophils was seen in visceral adipose tissue (VAT), with no effect on circulating eosinophils. Macrophage immune-phenotype and number followed the same pattern in VAT as in endometrium. Next, an increased number of NK cells was found in the spleen as in endometrium, while there was no difference in number of NK cells in blood in DHT-exposed mice. Strikingly, these mice had a clear reduction in CD8+ cytotoxic T cells in the spleen and in blood, as well as an overall reduction in the CD3+ lymphocyte population in blood. Interestingly, there was no difference in the number of CD4+ T helper cells, neither in blood nor spleen. The altered T cell populations could be due to androgen receptor activation on thymic epithelial cells as androgens suppress thymopoiesis in male mice. This hypothesis is supported by the decreased thymic weight in the DHT-induced PCOS model. In summary, we show that the prepubertal PCOS-like model displays an altered immune profile in a wide range of tissues. Whether these alterations are a result of androgen receptor activation and/or a result of metabolic dysfunctions remains to be elucidated, and it remains to define what impact these immune alterations have on reproductive and metabolic function.

DOI: 10.1530/endoabs.81.P195

P196

Effects of octamethylcyclotetrasiloxane and decamethylcyclopentasiloxane on female reproductive systems in rat

Jimin Lee, KangMin Kim, Minsu Lee, YongIn Kim & Eui-Bae Jeung
Chungbuk National University, College of Veterinary Medicine, Cheongju-si, Chungcheongbuk-do, Rep. of South Korea

In our daily life, humans are exposed to lots of chemicals. Among those chemicals, octamethylcyclotetrasiloxane (D4) and decamethylcyclopentasiloxane (D5) have been widely used in cosmetics for their functions such as softening, wetting, and viscosity control. However, the effect of these chemicals on the female reproductive systems has not been clearly elucidated. In the case of D4, it was recently recognized as an endocrine disrupting chemical (EDC), but the effect of D5 has been unknown. *In vitro* study, the human uterus epithelial-like Ishikawa cells, were treated with D4 and D5 to measure cell viability. In both D4 and D5 showed, decreased in cell viability at the 10^{-4} M. It means both chemicals are toxic in uterus. *In vivo* study, female Sprague Dawley rats were exposed to D4 and D5 diluted in corn oil for 2 weeks. At this time corn oil (Vehicle), 60 mg/kg/day (D4), and 100 mg/kg/day (D5) were administrated by using oral injection. Result shows there was no significant difference in uterine epithelial and stromal marker gene expression. On the other hand, ovary folliculogenesis and steroidogenesis gene expression were varied. HE staining results showed that increased uterine glands and ovary follicles number. Therefore, this study suggests that D4 and D5 aggravated female reproductivity such as miscarriage and implantation failure.
Acknowledgement
This work was supported by the National Research Foundation of Korea(NRF) grant funded by the Korea government(MSIT) (No. 2021R1A2C2093275).

DOI: 10.1530/endoabs.81.P196

P197

Functional analysis of anti-mullerian hormone variants in patients with polycystic ovary syndrome

Li Meng, Anke McLuskey & Jenny Visser
Erasmus MC, University Medical Center Rotterdam, Department. of Internal Medicine, Rotterdam, Netherlands

Objective
Recently rare heterozogous AMH genetic variants have been identified in women with polycystic ovary syndrome (PCOS) that result in reduced AMH signaling. However, the exact functional mechanism remains unknown. Therefore, we have performed functional analyses to analyze the processing, secretion and signaling of these PCOS-specific AMH rare variants.
Methods
Six PCOS-specific AMH variants containing mutations (V12G, P151S, P270S, P352S, P362S, H506Q) were selected based on previous findings. The variants were introduced in an AMH expression vector containing either a wild type (AMH-RAQR) or optimized cleavage site (AMH-RARR) and co-expressed with the BRE-Luc reporter in the mouse granulosa cell line KK-1. The AMH expression vectors were stably expressed in HEK293 cells for Western Blot analysis and ELISA.
Results
Expression of AMH-P151S and AMH-H506Q decreased AMH signaling by ~90% ($P<0.001$), depending on the presence of a RAQR or RARR cleavage site. Signaling of the other four variants was comparable to wild-type (wt)-AMH. Coexpression of the variants with wt-AMH at equal amounts confirmed that AMH-P151S and AMH-H506Q significantly inhibited the signaling activity of wt-AMH by ~30% ($P<0.001$). Transfection of increasing amounts of these two variants resulted in a further inhibition, which was independent of the cleavage site. To explain this dominant negative effect, we next analyzed the impact of AMH cleavage on AMH signaling. Cells were transfected with an AMH construct containing an inactive cleavage site (AMH-RAGA) in combination with exogenous AMH treatment. We observed that exogenous AMH-induced signaling was suppressed by 30% ($P<0.01$) in the presence of AMH-RAGA. In contrast, exogenous AMH-induced signaling was not affected when AMH-P151S or AMH-H506Q was transfected. Indeed, Western blot analysis showed that AMH-P151S and AMH-H506Q proteins were only detected in the cell lysate but not in the supernatant, even in the presence of RARR cleavage site. In contrast, wt-AMH and the P352S and P362S variant were detected in both the cell lysate and the supernatant. Further supporting these results, confocal image analysis showed that cells expressing AMH-P151S and AMH-H506Q retained significantly higher cellular AMH protein levels with a highly abnormal

subcellular localization in the ER compared to the cells expressing wt-AMH and AMH-P352S.
Conclusions
Our results show that the PCOS-specific AMH variants P151S and H506Q disrupt normal processing and secretion of AMH. Our results further suggest that these AMH variants hamper secretion of wt-AMH, explaining the dominant negative effect of these variants on AMH signaling.

DOI: 10.1530/endoabs.81.P197

P198

Blue Morpho: An international survey investigating differences in emotional and psychosexual wellbeing by ethnicity and birthplace in women with polycystic ovary syndrome

Jameela Sheikh[1], Halimah Khalil[1], Salomi Shaikh[2], Meghnaa Hebbar[1], Nawal Zia[1], Saskia Wicks[3], Sindoora Jayaprakash[4], Anuradhaa Subramanian[5], Rachel Chapman[6], Helena Gleeson[7], Lynee Robinson[8], Justin J. Chu[8], Tejal Lathia[9], Chitra Selvan[10], Michael O'Reilly[11,12], Konstantinos Manolopoulos[11], Wiebke Arlt[7,11] & Punith Kempegowda[7,11]
[1]University of Birmingham, College of Medical and Dental Sciences, Birmingham, United Kingdom; [2]D Y Patil University - School of Medicine, Navi Mumbai, India; [3]Barts Health NHS Foundation Trust, London, United Kingdom; [4]The Dudley Group NHS Foundation Trust, Dudley, United Kingdom; [5]University of Birmingham, Institute of Applied Health Research, Birmingham, United Kingdom; [6]University Hospitals Coventry and Warwickshire NHS Trust, Coventry, United Kingdom; [7]University Hospitals Birmingham NHS Foundation Trust, Birmingham, United Kingdom; [8]Birmingham Women's and Children's NHS Foundation Trust, Birmingham, United Kingdom; [9]Apollo Hospitals, Navi Mumbai, India; [10]MS Ramaiah Medical College, Department of Endocrinology, Bengaluru, India; [11]University of Birmingham, Institute of Metabolism and Systems Research, Birmingham, United Kingdom; [12]Royal College of Surgeons in Ireland (RCSI) University of Medicine and Health Sciences, Department of Medicine, Birmingham, United Kingdom

Objective
This study investigated the association between ethnicity, birthplace and emotional and psychosexual wellbeing in women with Polycystic Ovary Syndrome (PCOS) in the community.
Design
International cross-sectional study.
Methods
Women with a self-reported PCOS diagnosis by a healthcare professional were invited to complete an online Blue Morpho questionnaire between September-October 2020 (UK) and May-June 2021 (India). Four validated questionnaires were included: Hospital Anxiety and Depression Scale (HADS) to examine anxiety and depression; Body Image Concern Inventory (BICI) to assess dysmorphic appearance concerns; Beliefs About Obese Persons Scale (BAOP) to investigate beliefs about causes of obesity; and Female Sexual Function Index (FSFI) to assess domains of sexual function (desire, arousal, lubrication, orgasm, satisfaction and pain). Adjusted linear and logistic regression models were used to evaluate the relationship between ethnicity (White vs Non-white) and country of birth (UK vs India), and questionnaires scores and outcomes (Anxiety and/or Depression [HADS $\geq$11]) and Body Dysmorphic Disorder [BDD; BICI $\geq$72]). Adjustments were made for age category, level of education, marital status and parity.
Results
1008 women with PCOS completed the questionnaire. 44.8% were in the 26-35 age category, 44.9% had an undergraduate degree, 53.9% were single and 84.1% did not have children. The prevalence of anxiety and depression was 60.6% and 24.3%, respectively. Women of non-white ethnicity (60.7%; $n=611$) reported higher prevalence of depression (OR 1.96 [95% CI 1.41-2.73]) but lower BDD (OR 0.57 [95% CI 0.41-0.79]) prevalence compared to white ethnic women (38.9%; $n=392$). Similarly, women born in India (44.9%; $n=453$) had higher prevalence of anxiety (OR 1.57 [95% CI 1.00-2.46]) and depression (OR 2.20 [95% CI 1.52-3.18]) but lower BDD prevalence (OR 0.42 [95% CI 0.29-0.61]) compared to women born in the UK (43.0%; $n=433$). Both groups of white ethnic women and women born in the UK reported higher psychological illbeing; higher BICI and BAOP scores. However, overall sexual wellbeing and all FSFI sexual domains, excluding desire, were significantly impaired for both groups of non-white ethnic women and women born in India.
Conclusion
This study reveals the significant influence of ethnicity and birthplace on emotional and psychosexual wellbeing among women with PCOS, focusing on poor body image, weight stigma and sexual dysfunction. This highlights the importance of providing an individualised, holistic multidisciplinary approach alongside clinical care for women with PCOS and improving awareness of the significant influence of ethnicity and birthplace on PCOS related outcomes amongst primary healthcare providers to improve patient care.

DOI: 10.1530/endoabs.81.P198

P199

Is N-terminal prohormone of B-type natriuretic peptide (NT-proBNP) disturbed in polycystic ovary syndrome?

Małgorzata Kałużna[1], Pola Kompf[1], Katarzyna Ziemnicka[1], Krauze Tomasz[2], Katarzyna Wachowiak-Ochmańska[3], Andrzej Wykrętowicz[2], Przemyslaw Guzik[2] & Marek Ruchala[1]
[1]Poznan Univeristy of Medical Sciences, Department of Endocrinology, Metabolism and Internal Diseases; [2]Poznan Univeristy of Medical Sciences, Department of Cardiology - Intensive Therapy, Poland; [3]Heliodor Swiecicki University Hospital, Endocrinology, Metabolism and Internal Diseases Ward, Poland

Introduction
Polycystic ovary syndrome (PCOS) patients present with or without biochemical hyperandrogenism (HAPCOS or non-HAPCOS, respectively). Although cardiometabolic and hormonal abnormalities have been reported in women with PCOS, particularly those with hypertension, direct comparisons between normotensive (blood pressure (BP) $<$140/90 mmHg) patients with HAPCOS and non-HAPCOS are scarce. Data on N-terminal prohormone of B-type natriuretic peptide (NT-proBNP) in PCOS are inconclusive.
Methods/design
We compared various cardiovascular (CV), anthropometric, metabolic, and hormonal features of normotensive PCOS patients and healthy women. This case-control observational study involved 249 normotensive PCOS and 85 healthy eumenorrheic women. Based on blood androgen concentrations, PCOS patients were divided into HAPCOS ($n=69$) or non-HAPCOS ($n=180$) groups. NT-proBNP was measured using Cobas 6000 Analyzer with electrochemiluminescence sandwich immunoassays (Roche Diagnostics GmbH, Germany).
Results
HAPCOS patients had significantly ($P<0.05$) lower NT-proBNP concentration than non-HAPCOS women (34.57 vs. 39.77 pg/ml;$P=0.021$) and controls (41.58 pg/ml;$P=0.01$). NT-proBNP levels were comparable between non-HAPCOS and controls. HAPCOS patients had also significantly higher peripheral and central systolic BP and pulse pressure (PP), C-reactive protein, low-density lipoprotein cholesterol, triglycerides, glucose, and insulin than non-HAPCOS and healthy women. Still, these results were within normal ranges. However, body mass index (BMI) of HAPCOS subjects was over 4 kg/m^2 higher than in non-HAPCOS patients and nearly 6 kg/m^2 higher than in controls. Except for BMI, statistical differences in the cardiometabolic profile were of little clinical relevance. Higher amounts of adipose tissue in HAPCOS patients may be an explanation for the coexistence of higher BP and lower NT-proBNP concentration. A negative correlation between parameters of biochemical hyperandrogenism (free testosterone, dehydroepiandrosterone sulfate, androstenedione, dihydrotestosterone), and NT-proBNP was observed, suggesting a role of androgens in influencing NT-proBNP levels. It is likely that a combination of several abnormalities in HAPCOS women, like: excess fat tissue, hyperandrogenism, hyperinsulinemia, and insulin resistance, may be responsible for the relatively lower NT-proBNP levels and higher systolic BP and PP among this patient population.
Conclusions
Normotensive women with HAPCOS have a worse cardiometabolic profile but a lower NT-proBNP concentration than non-HAPCOS patients. Features of this profile in both PCOS groups are within normal ranges typical for healthy women. Increased BMI may be the only clinically relevant parameter differentiating hyperandrogenic from non-hyperandrogenic PCOS patients and healthy women.

DOI: 10.1530/endoabs.81.P199

P438

Central precocious puberty developed after treatment of leydig cell tumor: case report

Bouguerra Hadjer[1], Khellaf Amina[1], Amel Adimi[2] & Zakia Arbouche[1]
[1]Department of Endocrinology, Beni Messous UHC, Algiers, Algeria;
[2]Department of Endocrinology, Bab El Oued UHC, Algiers, Algeria

Background
Leydig cell tumors (LCTs) are the most prevalent hormone-secreting testicular tumors, but overall, a rare testicular tumor subtype. Surgery is the main therapy with a favorable prognosis. Nevertheless, the development of central precocious puberty after surgery of the tumor has been observed on rare occasions.
Case Report
An 8.5-year-old boy presented with symptoms of sexual precocity dating back to 4 years. He had pubic hair (P4), enlarged left testis (G3: right testis 4 cc, left testis 10 cc with a palpable nodule), and stature advance. The hormonal evaluation revealed high levels of testosterone and estradiol and low levels of FSH and LH. Ultrasound of the testis showed an inhomogeneous hypoechoic tumor of the left testis. An inguinal radical orchiectomy managed this mass. The pathological diagnosis was a benign LCT. Three months after surgery, the patient presented persistent physical signs of sexual precocity, enlarged right testis, and stature gain of 8.5 cm. His hormonal values confirmed central precocious puberty: the testosterone level stayed high at 2.57 ng/ml facing LH and FSH levels at 3.26 UI/l and 4.55 UI/l respectively. Ultrasonography ruled out testicular tumor recurrence and brain magnetic resonance imaging excluded a tumor of the hypothalamus or pituitary gland. We started treatment with triptorelin (GnRH analog). After 3 months of treatment, we observed clinical regression of physical signs and stabilized growth velocity. After 6 months, hormonal assessment showed testosterone returned to prepuberal range (0.15 ng/ml), FSH and LH levels were 0.11 UI/l and 0.43 UI/l respectively. At the last follow-up (1 year from the beginning of triptorelin), we note a stature gain of 2 cm and a stabilization of the bone age with no adverse effects.
Discussion and conclusion
Eleven other cases of gonadotropin-dependent precocious puberty after successful treatment of LCTs have been reported in the litterature[1,2,3]. The mechanism is unknown but is hypothesized due to the rebound secretion of LH after surgery of LCTs and subsequent reduction in androgens, which suppressed the adenohypophysis. The true incidence of central precocious puberty remains unclear because long-term follow-up of children with LCTs is not available. GnRH analog therapy appears to be the most effective medical treatment in such cases.
Keyboards
LCTs, central precocious puberty, GnRH analog.
References
1. Akilan K *et al*. *Can Urol Assoc J*. 2020;14(7): E343-E346.
2. Verrotti A *et al*, Front Pediatr. 2015 Nov 2;3:93.
3. Luckie TM *et al*, J Pediatr Hematol Oncol. 2019 Jan;41(1):74-76.

DOI: 10.1530/endoabs.81.P438

P439

Coexistence of 46, XX testicular disorder of sex development and 11β-hydroxylase deficiency: *In Vivo* and *In Vitro* Studies

Bang Sun, Xi Wang, Jiangfeng Mao, Xueyan Wu & Min Nie
Peking Union Medical College Hospital, Beijing, China

Background
46, XX testicular disorder of sex development (DSD) and 11β-hydroxylase deficiency (11β-OHD) are two extremely rare types of disorder of sex development. No coexistence has been reported yet.
Case Description
Here we reported the first patient diagnosed as the coexistence of 11β-OHD and 46, XX testicular DSD basing on clinical, biochemical, molecular, cytogenetic, and functional experiment findings. A 22-year-old male showed small testes and gynecomastia for 2 years. At the age of 3, he was diagnosed as congenital adrenal hyperplasia (CAH). Adrenal ultrasound suggested the bilateral adrenal hyperplasia (both length*width = 2.4*0.9 cm) and X ray showed accelerated bone age (12.5 years old). Irregular cortisone acetate 6.25 mg per day was administrated since then. At the age of 18, he was sent to emergency for aortic aneurysm rupture and heart failure, and diagnosed as 11β-OHD. Sanger sequencing revealed that he carried compound heterozygous variants in *CYP11B1* gene: NM_000497.4: c.905_907delinsTT and NM_000497.4: c.954 + 7C > T, which were respectively inherited from his father and mother. According to American College of Medical Genetics and Genomics (ACMG) guideline, c.905_907delinsTT was identified as pathogenic variant, and c.954 + 7C > T, the novel one, was defined as variant of unknown significance. Pathogenicity of c.954 + 7C > T were further verified in COS7, CHO, and 273T cell lines by minigene methods, which turned out to cause the gain of a cryptic one at the 5bp downstream of the original one. The patient was treated by neoplasty of thoracic aortic aneurysm and added anti-hypertension drugs in addition to glucocorticoid after surgery. Unexpectedly, small testes and gynecomastia came into notice recently. Laboratory tests revealed hypergonadotropic hypogonadism and azoospermia. Scrotum ultrasound showed bilateral testicular dysplasia. To figure out these unexplainable results, whole exome sequencing was performed and revealed two copy number variants: duplication of Xp22.33-q28 spanning 151.32 Mb and deletion of Yp11.2-q11.23 spanning 23.34 Mb. Karyotype test by culturing blood lymphocytes showed 46, XX (100/100). Another disease, 46, XX testicular DSD, was diagnosed. Fluorescence *in situ* hybridization (FISH) revealed the presence of *SRY*gene translocating into the short arm of X chromosome. Under the coaction of two diseases, testosterone level was in male normal range, and replacement was unnecessary. Assisted reproduction was advised to start early.
Conclusion
To our knowledge, this is the first report of the coexistence of 46, XX testicular DSD and 11β-OHD in the same individual. The case illustrates the complexity that might be encountered in the diagnosis of DSD when different genetic defects affecting sex development exist.

DOI: 10.1530/endoabs.81.P439

P440

Cardiometabolic risk factors and diabetes mellitus are related with the severity of menopausal symptoms in middle-aged women

Elena Armeni[1], Stylianos Kopanos[1,2], Eleni Verykouki[3], Areti Augoulea[1], Stavroula A. Paschou[1], Demetrios Rizos[4], George Kaparos[5], Makarios Eleftheriades[1], Anna-Bettina Haidich[3], Dimitrios Goulis[2], Nikolaos Vlahos[1] & Irene Lambrinoudaki[1]
[1]National and Kapodistrian University of Athens, 2 nd Department of Obstetrics and Gynecology, Aretaieio Hospital, Athens, Greece; [2]Unit of Reproductive Endocrinology, Medical School, Aristotle University of Thessaloniki, 1st Department of Obstetrics and Gynecology, Thessaloniki, Greece; [3]Faculty of Health Sciences, School of Medicine, Aristotle University of Thessaloniki, University Campus, Department of Hygiene, Social-Preventive Medicine and Medical Statistics, Thessaloniki, Greece; [4]National and Kapodistrian University of Athens, Hormonal Laboratory, Aretaieion Hospital, Athens, Greece; [5]National and Kapodistrian University of Athens, Aretaieion Hospital, Biochemical Laboratory, Athens, Greece

Background
Both surgical and spontaneous menopause are associated with increased cardiovascular disease (CVD) risk. Recent evidence reported that clusters of menopausal symptoms are associated with accumulation of cardiometabolic risk factors. Climacteric symptoms are also known to be affected by lifestyle parameters, ethnicity, the geographical location as well as by the overall health status at the time of the menopausal transition.
Aim
This study aimed to evaluate the association between menopausal symptoms, and lifestyle as well as cardiometabolic risk factors, in a cohort of apparently healthy middle-aged women.
Methods
This study consisted of 2.793 peri- and postmenopausal women (menopausal-age $\leq$ 15 years), not on menopausal hormone therapy, retrieved from the outpatient Menopause Clinic of the 2nd Department of Obstetrics and Gynecology, National and Kapodistrian University of Athens, Greece. We assessed demographic and athropometric parameters (including body mass index, BMI), and obtained fasting blood samples for evaluation of biochemical/hormonal data. The severity of menopausal symptoms was evaluated by the Greene Climacteric scale (GCS).
Results
Mixed effect models showed that the total GCS-score associated with BMI (b = 0.12, 95%CI: 0.04 to 0.20), diagnosis of type 2 diabetes (T2DM, b = 2.10, 95%CI: 0.06 to 4.15), older age at menopause (menopausal age > 7 years vs 2 to 7 years, b = -1.24.95% CI: -2.17 to -0.33). Physical GCS score associated with BMI (b = 0.06, 95%CI: 0.03 to 0.09), central obesity (b = 0.18, 95%CI: 0.02 to 0.34), menopausal status (2 to 7 years vs > 7 years after the final menstrual period *vs.* perimenopause, b = -0.36, 95%CI: -0.59 to -0.13 and b = -0.65, 95%CI: -0.97 to -0.34, respectively). Psychological GCS-score associated with values of BMI (b = 0.06, 95% CI: 0.00 to 0.11). All previous GCS-scores associated negatively with age. Vasomotor GCS-score associated negatively with menopause-age > 7 years vs younger menopausal age. Poisson mixed models showed that GCS-sexual

score associated with a younger menopausal age (menopause age 2 to 7 years vs > 7 years, incidence rate ratio (IRR) = 1.53, 95%CI: 1.21 to 1.94), central obesity (IRR = 1.18, 95%CI: 1.00 to 1.39), smoking, diastolic blood pressure, age.
Conclusions
The results of this study indicate that the severity of menopausal symptoms is associated with obesity, smoking and T2DM, in a large sample of peri- and postmenopausal women.

DOI: 10.1530/endoabs.81.P440

P441

Usefulness of routine assessment of free testosterone for the diagnosis of functional male hypogonadism

Paolo Facondo[1], Elena Di Lodovico[1], Letizia Chiara Pezzaioli[1], Carlo Cappelli[1], Alberto Ferlin[2] & Andrea Delbarba[3]
[1]University of Brescia (Italy), Department of Clinical and Experimental Sciences; [2]Unit of Andrology and Reproductive Medicine, University of Padova, Padova, Italy, Department of Medicine; [3]Unit of Endocrinology and Metabolism, ASST Spedali Civili, Brescia, Italy

Objective
To investigate whether routine assessment of free testosterone improves the diagnostic accuracy of functional male hypogonadism.
Methods
Total and free testosterone (calculated through SHBG assessment) were determined in 372 male patients (median age 44) referring to our department for sexual symptoms symptoms (188 patients) or infertility (184 men). Low total and free testosterone were defined as < 2.31 ng/ml and <63 pg/ml, respectively.
Results
Hypogonadism, as calculated free testosterone <63 pg/ml, was found in 47/188 (25.0%) patients with sexual symptoms and in 21/184 (11.4%) with infertility. Total testosterone determination misdiagnosed hypogonadism in 8.4% (12/143) of men with sexual symptoms and in 2% (3/152) with infertility. In subjects with borderline total testosterone (between 2.31 and 3.5 ng/ml), only 24.7% (19/77) had hypogonadism confirmed by free testosterone levels. No subjects had known conditions altering SHBG. Free testosterone levels significantly correlated with age, haematocrit, gonadotropins, gynecomastia, BMI, and number of co-morbidities, whereas total testosterone associated only with the latter two. Moreover age, haematocrit, erectile dysfunction, BMI, and low libido were significantly different between men with normal and low free testosterone, whereas only BMI and low libido were significantly different between patients with normal and low total testosterone.
Conclusion
This is the first study evaluating the impact of FT assessment to diagnose functional hypogonadism in men with hypogonadal symptoms or infertility. Routine assessment of free testosterone allows a more accurate diagnosis of functional hypogonadism, especially in men with sexual symptoms. Free testosterone levels associate with clinical and biochemical parameters of androgen deficiency better than total testosterone levels. A first-line assessment of SHBG and calculated free testosterone levels should be performed in all men with symptoms of male hypogonadism, to improve our diagnostic performance.

DOI: 10.1530/endoabs.81.P441

P442

Energy deficit as a cause of transient male hypogonadotropic hypogonadism: a successful resolution of a primary infertility

Vânia Benido Silva[1], Maria Teresa Pereira[1], Nuno Rossano Louro[2] & Márcia Barreiro[3]
[1]Centro Hospitalar Universitário do Porto, Endocrinology, Diabetes and Metabolism, Porto, Portugal; [2]Centro Hospitalar Universitário do Porto, Urology, Porto, Portugal; [3]Centro Hospitalar Universitário do Porto, Gynecology/Medically Assisted Procreation Center, Porto, Portugal

Introduction
Caloric restriction combined with overtraining can result in a total body energy deficit, which in turn is associated with multiple deleterious endocrine consequences, including hypogonadotropic hypogonadism. This can be a reversible cause of primary infertility, but its occurrence in men is still poorly recognized.
Case Report
We report a case of a 39-year-old male evaluated in an urology appointment for primary infertility. He had a history of psoriasis, previous parotitis with no documented testicular involvement and obesity 4 years earlier (weight:110 kg, height: 1.79 m, Body mass index[BMI]:34.3 kg/m^2). For that reason, he made lifestyle changes, performing a restricted calories and carbohydrates diet combined with 2 h daily intense physical exercise, with significant and rapid weight loss (currently, weight: 71 kg, BMI 22.2 kg/m^2). For at least 1 year, he had a marked decrease in libido, rare sexual intercourses, vaginal anejaculation since the beginning of attempts at procreation, and significant asthenia, which he associated with work stress and physical activity. No changes in erection were valued. Objectively, he presented hairy distribution according to age and sex, absence of gynecomastia. The vas deferens were bilaterally palpable, the testes were of normal volume, with no apparent lesions and no varicocele, and the penis was without alterations. From further investigation, the analytical study proved hypogonadotropic hypogonadism (Total Testosterone [TT] 2.21 ng/ml [Reference Range (RR): 2.8-8.0]; LH 1.4 mIU/ml[RR:1.6-8.6], SHBG 41.7 nmol/l [RR:13-71]). Prolactin (7.5 ng/ml [RR:4.04-15.2]) and TSH (2.11 µIU/ml [RR: 0.30 - 3.18]) were normal. The spermogram showed asthenoteratozoospermia and the scrotal ultrasound showed no changes. The pituitary MRI was normal. The study carried out with the female element did not identify any changes. The hypothesis of hypogonadotropic hypogonadism secondary to caloric restriction and concomitant excessive daily energy expenditure was raised and the patient progressively increased the dietary intake of carbohydrates while maintaining the same frequency and intensity of physical exercise. After 3 months of this modification, the patient reported more energy, complete resolution of libido complaints and greater frequency of sexual intercourse. Analytically, testosterone and gonadotropin levels normalized (TT 2.90 ng/ml[RR:2.8-8.0]; FSH 4.6 mIU/ml[1.5-12.4], LH 1.6 mIU/ml[RR:1.6-8.6]) and a pregnancy spontaneously occurred.
Conclusion
The male reproductive axis is very sensitive to caloric deprivation, with clinical and analytical repercussions. This case alerts to this male cause of hypogonadotropic hypogonadism, often overlooked in the investigation of primary infertility. Given its functional nature, this condition is reversible and treated with increased energy intake.

DOI: 10.1530/endoabs.81.P442

P443

Y-chromosome disomy and sexual ambiguity

Yosra Hasni[1,2], Oumayma Zarrouk[1], Samia Tilouche[2,3], Hamza Elfekih[1,2], Hayfa Farid[1], Amel Maaroufi[1,2], Maha Kacem[1,2], Molka Chadli Chaieb[1,2] & Koussay Ach[1,2]
[1]Farhat-Hached University Hospital, Endocrinology-Diabetology Department, Sousse, Tunisia; [2]Faculty of Medicine Ibn El Jazzar, University of Sousse, Sousse, Tunisia; [3]Farhat-Hached University Hospital, Pediatrics department, Sousse, Tunisia

Introduction
Chromosomal abnormality 47, XYY, despite being present in approximately 1 in 1000 newborn boys, remains less known phenotypically and more than 85% of men are never diagnosed. Males with 47, XYY syndrome are described to be phenotypically normal. They present often a developmental delay, behavioral difficulties and learning disabilities that may be associated with accelerated growth rate and taller stature in adulthood. Endocrine disorders, especially pubertal delay, are rarely described in patients with this karyotype. We report the case of a boy who had at birth sexual ambiguity revealing a 47, XYY karyotype.
Observation
A 13-year-old boy was found at birth to have sexual ambiguity with a 1.5 cm micropenis and empty scrotum. Imaging ruled out the presence of female external genitalia and concluded to bilateral cryptorchidism. 17-OH Progesterone was normal at 0.5 ng/ml ruling out 21-hydroxylase deficiency. Testosterone, DHT, delta 4-androstenedione and DHEA-sulfate were normal with a testosterone/DHT ratio < 20. Genetic analysis revealed 47, XYY karyotype. He received βHCG injections and had a surgery for the micropenis and bilateral cryptorchidism. The child does not have psychomotor or growth disorders. He is still prepubescent (Tanner staging: P1/G1) with a penis size of 4.5 cm. Hormonal exploration revealed FSH = 0.9 mUI/ml, LH = 0.4 mUI/ml with testosterone < 0.1 ng/ml and a bone age less than 13 years, requiring monitoring to detect early a possible pubertal delay.
Discussion
47, XYY karyotype is a rare anomaly in which gonadal function is generally intact. However, a higher incidence of infertility was noted in men who carry this genetic abnormality. The association of this karyotype with micropenis and

pubertal delay was also described in the literature as a possible cause of this chromosomal anomaly.

DOI: 10.1530/endoabs.81.P443

P444

Use of selective venous vein sampling in postmenopausal women with hyperandrogenism of unclear aetiology

Ana Romero Gregori[1], Olga Giménez[1], Ismael Capel[1], David Subías[1], Saad Marcouchi[1], Laura Costa[2], Juan Perendreu[3], Eugenio Berlanga[4] & Mercedes Rigla[1]
[1]Hospital Parc Taulí de Sabadell, Endocrinology, Sabadell, Spain; [2]Hospital Parc Taulí de Sabadell, Obstetrics and Gynecology, Sabadell, Spain; [3]Hospital Parc Taulí de Sabadell, Interventional Radiology, Sabadell, Spain; [4]Hospital Parc Taulí de Sabadell, Laboratory, Sabadell, Spain

Background
Hyperandrogenism is infrequent in menopause, being the most common cause benign pathologies. However, it can also be produced by an ovarian or adrenal tumour. Correct diagnosis and location can be challenging because small lesions may not be visible with modern imaging studies. We report a case of ovarian stromal hyperplasia where selective venous catheterization and hormonal sampling were performed to find the origin of excessive androgen production.
Case report
A 74-year-old woman was referred to our hospital with high serum testosterone level and hirsutism. Her medical history included obesity (IMC 34 kg/m^2), type 2 diabetes, dyslipidaemia and OSAS. Her symptoms had begun five years previously with 8 kg weight gain, frontal alopecia and hirsutism on her chest, arms and abdomen. Ferriman-Gallwey scored 21. Laboratory examination revealed severe hyperandrogenism with a total testosterone of 2.27 ng/ml (normal range 0.03-0.41 ng/ml) and free testosterone of 5.1 pg/ml (normal range 0-3.7 ng/ml). Dehydroepiandrosterone sulfate, androstenedione, 17-hydroxyprogesterone, prolactin, IGF-1 and thyroid hormones were all within normal range. Urinary free cortisol was normal in two determinations. An overnight 1 mg dexamethasone suppression test showed normal suppression of serum cortisol. Transvaginal ultrasonography showed that both ovaries were of normal size with no detectable masses. Adrenal computed tomography did not detect enlargement or tumour formation in either adrenal gland. Pelvic magnetic resonance did not show any remarkable findings. An ovarian androgen production was suspected. Selective vein catheterization and hormonal sampling from both ovarian and adrenal veins were performed before and after stimulation with 250 mg $ACTH_{1-24}$. Serum testosterone levels from left and right ovarian vein were remarkably higher than in the other veins, 387 ng/dl and 52.80 ng/dl respectively. Right ovarian vein sampling was uncertain because of anatomic difficulties. Owing to the fact the patient was menopausal, she underwent a laparoscopic bilateral oophorectomy. Final pathology demonstrated ovarian stromal hyperplasia. Postoperatively, her total testosterone levels decreased to 0.10 ng/ml. Four months after the surgery there was a clear improvement in hirsutism and frontal alopecia.
Conclsion
Selective ovarian and adrenal venous sampling is useful to localize the androgen producing source when imaging technique findings are inconclusive. In our case, an ovarian origin was confirmed. Due to the fact that the patient was menopausal and the right ovarian vein sampling was uncertain, a bilateral oophorectomy was preferred. However, selective venous sampling is especially important in women on reproductive age to avoid bilateral oophorectomy.

DOI: 10.1530/endoabs.81.P444

P445

Kisspeptin improves sexual brain processing in women with low sexual desire

Layla Thurston[1], Tia Hunjan[1], Natalie Ertl[1,2], Matt B Wall[1,2], Edouard Mills[1], Sofiya Suladze[1], Bijal Patel[1], Emma Alexander[1], Beatrice Muzi[1], Eugenii A Rabiner[2], Paul Bech[1], David Goldmeier[3], Ali Abbara[1], Alexander Comninos[1,4] & Waljit Dhillo[1,4]
[1]Imperial College London, Endocrinology and Investigative Medicine, London, United Kingdom; [2]Invicro, London, United Kingdom; [3]Imperial College Healthcare NHS Trust, Sexual Medicine, London, United Kingdom; [4]Imperial College Healthcare NHS Trust, Endocrinology, London, United Kingdom

Introduction
Sexual desire is a key component of the sexual response model. Absence or deficiency of sexual desire can lead to marked distress or interpersonal difficulty, termed 'hypoactive sexual desire disorder' (HSDD). HSDD is the most common female sexual health complaint worldwide, affecting up to 10% of women. Despite its detrimental impact on psychological well-being and quality of life, treatment options are currently limited. The hormone kisspeptin is a key endogenous activator of the hypothalamic-pituitary-gonadal axis, with emerging roles in sexual and emotional behaviour, and thus could serve as a novel treatment option in women with HSDD.
Methods
We performed a randomized, double-blind, two-way crossover, placebo-controlled study in 32 premenopausal women with HSDD. We used psychometric, functional neuroimaging, and hormonal analyses to investigate the effects of kisspeptin administration on brain activity, in response to erotic stimuli (erotic videos) and facial attraction (images of faces of varying attractiveness).
Results
Kisspeptin administration resulted in an increase in self-reported ratings of feeling 'sexy', compared to placebo, measured using the Sexual Arousal and Desire Inventory ($t[32]=2.27$, $P=0.03$). On functional MRI, kisspeptin administration deactivated the left inferior frontal gyrus and activated the postcentral and supramarginal gyrus in response to erotic videos ($Z=2.3$, $P<0.05$). Kisspeptin administration deactivated the secondary somatosensory cortex ($Z=2.3$, $P<0.05$) and enhanced activation in the posterior cingulate cortex on viewing male faces, which correlated with a reduction in self-reported sexual aversion ($r=0.476$, $P=0.005$). Kisspeptin resulted in a mean increase in LH of 2.75 iU/l ($F(1, 62)=6.084$, $P=0.02$) and FSH of 0.37 iU/l ($F(1, 62)=4.030$, $P=0.05$) across the 75-minute duration of the study as expected, with no effect observed on downstream circulating estradiol, progesterone or testosterone levels.
Discussion
Our results demonstrate that kisspeptin administration to women with HSDD increases their self-reported ratings of feeling 'sexy'. Our brain activity changes provide mechanistic insight for this, with deactivation of the left inferior frontal gyrus, likely serving to reduce internal monologue and response inhibition. Furthermore, kisspeptin's deactivation of the secondary somatosensory cortex can reduce a woman's focus on herself, her body image, and related negative thoughts, thus augmenting her judgement of male facial attractiveness. Finally, kisspeptin's actions in the posterior cingulate cortex can serve to increase feelings of romantic love and reward processing, thereby reducing sexual aversion and increasing sexual desire. These behavioural and mechanistic findings in women with HSDD lay the foundations for clinical applications for kisspeptin in psychosexual disorders.

DOI: 10.1530/endoabs.81.P445

P446

The effect of gastric sleeve resection on menstrual pattern and ovulation in premenopausal women with class III-IV obesity

Tetiana Tatarchuk[1], Ivan Todurov[2], Panagiotis Anagnostis[3], Tetiana Tutchenko[1], Natalia Pedachenko[4], Marina Glamazda[1], Natalia Koseii[1] & Svetlana Regeda[1]
[1]Institute of Pediatrics, Obstetrics and Gynecology of the Academy of Medical Sciences of Ukraine, Kiev, Ukraine; [2]Center for Innovative Medical Technologies, Academy of Sciences of Ukraine, Kiev, Ukraine; [3]Aristotle University of Thessaloniki, Unit of Reproductive Endocrinology, 1st Department of Obstetrics and Gynecology, Medical School, Thessaloniki, Greece; [4]Department of Obstetrics, Gynecology and Perinatology, P.L. Shupik National Healthcare University of Ukraine

Purpose
Bariatric surgery is very efficacious in treating severe obesity. However, its effect of menstruation and ovulation is currently unknown. The purpose of this study was to assess the effect of gastric sleeve resection (GSR) on menstrual pattern in women with stage III-IV obesity and ovulatory dysfunction compared with conventional management.
Methods
This was a prospective, multicentre, non-randomized trial, in premenopausal women, who fulfilled the criteria for gastric sleeve resection (GSR). Both women with and without polycystic ovary syndrome (PCOS) were evaluated at three, six, nine, 12 and 15 months post-surgery.
Results
Menstrual cycle irregularities were identified in 122 severely obese women (60 with PCOS; 62 non-PCOS). The % total weight loss was greater with GSR than

with conventional management (33.4% *vs*. 3.6% in PCOS; 24.8% *vs*. 3.6% in non-PCOS, respectively). Intermenstrual interval was shortened towards normal length ($\leq$35 days) both in PCOS and non-PCOS GSR groups, by the 6th and 12th post-surgical month, respectively. Furthermore, ovulation at six months was achieved in 63.6% of PCOS and 45% of non-PCOS subjects post-GSR, which was higher than in controls (11.1% and 13.6%, respectively; $P<0.05$). This percentage rose to 75.7% and 81.8% at 12 and 15 months in PCOS, respectively, but not in the non-PCOS group (55% and 52.5%, respectively; $P<0.05$).
Conclusions
Weight reduction after GSR improved menstrual irregularity towards normality in women with severe obesity. Ovulation dysfunction was also resumed in more than half of these patients at 6-15 months. These effects were more evident in women with PCOS.

DOI: 10.1530/endoabs.81.P446

P447

Interplay between estrogen signaling and notch pathway in rodent Sertoli cells

Sylwia Lustofin, Alicja Kamińska, Małgorzata Brzoskwinia, Joanna Cyran, Barbara Bilińska & Anna Hejmej
Jagiellonian University, Institute of Zoology and Biomedical Research, Department of Endocrinology, Krakow, Poland

Somatic cells of the seminiferous epithelium, called Sertoli cells, play a key role in germ cell development and maintenance of proper course of spermatogenesis. Although androgens are considered the main regulators of Sertoli cell activity, recent studies indicate that their metabolites, estrogens, also influence Sertoli cell function. Estrogens, act mainly through nuclear estrogen receptors α and β (ERα, ERβ), however non-classical signaling *via* membrane G protein-coupled estrogen receptor 1 (GPER) was also confirmed. It is well established that direct interactions between the cells in the seminiferous epithelium, including the Notch pathway, are essential for undisrupted spermatogenesis. Notch pathway is activated by binding membranous ligands Delta-like (DLL) or Jagged (JAG) of one cell to surface Notch receptors of the neighboring cell. The aim of this study was to explore the role of estrogens and their receptors in the control of the expression of Notch pathway ligands in Sertoli cells. Experiments were performed on primary Sertoli cells cultures isolated from rat testis (PSC) and mouse Sertoli cell line (TM4). First, the effect of estrogenic stimulation or estrogen action inhibition were examined using 17β-estradiol or estrogen receptor antagonists (ICI 182.780; G-15), respectively. Next, to determine the precise role of each receptor, siRNA silencing was conducted to knockdown the expression of ERα, ERβ, or GPER. qRT-PCR, western blot and immunofluorescence were employed to analyze the expression of DLL1, DLL4 and JAG1. The expression of all studied ligands was increased after stimulation by 17β-estradiol. The increase of either JAG1 or DLL1 expression in estrogen-stimulated cells was inhibited only by ICI 182.780. Knockdown experiments revealed that ERα silencing entirely abolished the effect of 17β-estradiol on both JAG1 and DLL1 expression. Exposure to ICI 182.780 and G-15 decreased DLL4 protein expression in 17β-estradiol-stimulated Sertoli cells. Silencing experiments demonstrated that ERβ and GPER knockdown effectively blocked estrogen influence on DLL4 protein expression. In summary, our results indicate that the expression of Notch pathway ligands in Sertoli cells is regulated by estrogens. JAG1 and DLL1 expression is controlled mainly *via* ERα, while DLL4 expression is dependent on ERβ and GPER signaling. Thus, the cooperation between classical and non-classical estrogen signaling pathways may be important for the communication within the seminiferous epithelium *via* Notch signaling, and thereby for proper spermatogenesis. This study was supported by a grant N18/MNW/000022 (Jagiellonian University, Faculty of Biology). The conference attendance supported by "Jagiellonian Interdisciplinary PhD Programme" POWR.03.05.00-00-Z309/17-00 (The European Social Fund).

DOI: 10.1530/endoabs.81.P447

P448

Finasteride inhibits epinephrine synthesis in humans: implication for sexual dysfunction

Silvia Giatti[1], Silvia Diviccaro[1], Alessandro Di Domizio[2], Lucia Cioffi[1], Eva Falvo[1], Donatella Caruso[1], Alessandro Contini[3] & Roberto Cosimo Melcangi[1]
[1]Università degli Studi di Milano, Department of Pharmacological and Biomolecular Sciences, Milano, Italy; [2]Spillo Project, Paderno Dugnano, Italy; [3]Università degli Studi di Milano, DISFARM, Milano, Italy

Finasteride is a 5alpha-reductase (5α-R) inhibitor used in clinics to treat androgen-dependent conditions, such as benign prostate hyperplasia and androgenetic alopecia (AGA). Its use has been associated with several adverse effects, including sexual complaints. However, to date, no hypothesis to explain such adverse effects has been proposed. This is a consequence of the still incomplete knowledge of the intricate network of motivational, psychological, and molecular inputs that are involved in sexual behavior. In this work, a multidisciplinary approach has been used to evaluate whether finasteride may interact with targets different from 5α-R (i.e., off-target proteins − OTPs). *In silico* analysis (SPILLO-PBBS software and docking/molecular dynamics) indicated that the enzyme phenylethanolamine N-methyltransferase (PNMT), the limiting enzyme in epinephrine production, might be a finasteride OTP. This is interesting, since epinephrine and norepinephrine are involved in erection (Becker *et al*., 2000, J Urol), and alterations in their levels has been observed in patient with erectile dysfunction (Becker *et al*., 2002, Urology). An inhibitory assay developed *in vitro* confirmed that finasteride blocks the human PNMT. Finally, to verify the *in vivo* interaction, adult male rats were treated with finasteride (1 mg/rat/day s.c. daily for 20 days). *Ex vivo* analysis indicated that epinephrine levels were decreased by finasteride treatment in adrenal glands, while those of norepinephrine were increased. This, together with no variation in PNMT protein levels, confirmed the hypothesis of a block in epinephrine synthesis. Therefore, we explored if corpora cavernosa (CC) of finasteride-treated rats presented molecular alterations. A decreased protein level of estrogen receptor beta was observed in CC of finasteride-treated rats, in line with evidence in aging and diabetic rats with erectile dysfunction (Shirai *et al*., 2004, Urology). Moreover, the levels of dopamine, which improve the penis relaxation, were significant decreased in CC tissue after finasteride administration. Overall, the data here presented indicate that finasteride affects epinephrine synthesis by blocking PNMT enzymatic activity in humans. This block can have an impact in sexual behavior, as suggested in an animal model treated with finasteride. In addition, the alterations observed in CC indicate possible impairment of erectile function. Our results suggest possible mechanisms for the sexual dysfunction observed after finasteride treatment in humans and add a piece of knowledge on the mechanisms controlling sexual function in mammals.

DOI: 10.1530/endoabs.81.P448

P449

Global impact of PCOS awareness month: challenges and opportunities

Kashish Malhotra[1], Carina Synn Cuen Pan[2], Meri Davitadze[3], Konstantinos Manolopoulos[4], Michael O'Reilly[5], Wiebke Arlt[6,7] & Punith Kempegowda[6,7]
[1]Dayanand Medical College and Hospital, Ludhiana, Punjab, India; [2]College of Medical and Dental Sciences, University of Birmingham, United Kingdom; [3]Georgian-American Family Medicine Clinic 'Medical House', Georgia; [4]Henry Dunant Hospital Center, Athens, Greece; [5]Royal College of Surgeons in Ireland (RCSI) University of Medicine and Health Sciences, Department of Medicine, Ireland; [6]University Hospitals Birmingham NHS Foundation Trust, United Kingdom; [7]Institute of Metabolism and Systems Research, University of Birmingham, United Kingdom

Background
September is celebrated as PCOS awareness month worldwide and is aimed at improving the lives of those with PCOS, promoting research, and strengthening advocacy efforts. While significant financial and human resources are invested in promotions during this month, to the best of our knowledge, there is no evidence to show the impact of this initiative. In our study, we evaluated the global digital impact of PCOS Awareness Month, tracking commonly used hashtags as surrogate markers, patterns of associated emotions and identifying key players, collaborations and trending topics associated with PCOS Awareness Month.
Methods
We utilised several online tools (Symplur, SocioViz.net, Sprout Social, Sentiment Viz, and Google trends) to study the global impact of PCOS Awareness Month using #PCOS, #PCOSawareness, #PCOSawarenessmonth, and a corresponding search query. Network and sentiment analysis was done on the last day of PCOS awareness month to identify common themes and associated topics with the tweets. Google Trends was used to study the web and news search popularity globally to get an overall idea of the internet search trends beyond social media platforms.

Results
While we found a growing trend for #PCOS and related hashtags from 2014 to 2020, we noticed a decline in 2021. In each of these years, the largest spike of both impressions and users for #PCOS was seen at the start of September with a declining trend for the rest of the month. Verified users, who have notably more influence, have shown consistently increasing support for the PCOS Awareness Month from 2014 to 2021. On network analysis, the most commonly associated hashtags with the #PCOS were #endometriosis, #fertility, #womenshealth, #pcossupport, and #infertility. Sentiment analysis revealed most of the tweets were linked to subdued but pleasant emotions. 76% of top influencers collaborated with at least one other person during PCOS Awareness Month activities. Geographically, we noted limited engagement in African, Asian, and non-English speaking European countries
Conclsions
PCOS Awareness Month is an effective strategy to raise awareness with social media playing a crucial role in amplifying the message especially with the usage of hashtags. Further gains can be made by enhancing collaborations between like-minded individuals and organisations to make concerted efforts during PCOS Awareness Month. Our findings also provide an opportunity to understand the current perceptions and expectations amongst the public, which can influence future healthcare investment and research.

DOI: 10.1530/endoabs.81.P449

P450

Influence of polycystic ovary syndrome on in vitro fertilization and relationship with the Asn680Ser polymorphism in FSHR gene

Inês Vieira[1], Ana Filipa Ferreira[2], Alexandra Carvalho[2], Conceição Dias[2], Silvana Fernandes[2], Dírcea Rodrigues[1], Paulo Cortesão[2], Teresa Almeida Santos[2] & Isabel Paiva[1]
[1]Coimbra Hospital and University Center, Endocrinology, Diabetes and Metabolism; [2]Coimbra Hospital and University Center, Gynecology, Obstetrics, Reproduction and Neonatology

Introduction
Polycystic ovary syndrome (PCOS) is a frequent cause of infertility. Its influence on the results of in vitro fertilization (IVF) is controversial, and generally not isolated from the effect of obesity. A relationship between the FSH receptor (*FSHR*) polymorphism *Asn680Ser* and the risk and phenotype of PCOS has been studied with conflicting results.
Objectives
To analyze the influence of obesity and PCOS on the gonadal axis and IVF results. To assess the influence of *Asn680Ser* on the risk of PCOS and IVF.
Material and Methods
Retrospective analysis of patients with PCOS by Rotterdam criteria with and without obesity and controls with tubal infertility, undergoing 1st IVF after a short ovarian stimulation cycle with GnRH antagonist.
Results
Sample with 212 patients: 72 without obesity, with PCOS (group A); 75 without obesity or PCOS (B); 36 with obesity and PCOS (C); 29 with obesity, without PCOS (D). Mean age 33.5 ± 3.7 years with homogeneous distribution between groups ($P=0.207$) and similar body mass index in the non-obese (A 23.8 ± 2.9 vs B 23.3 ± 2.7 kg/m2, $P=0.203$) and in the obese groups (C 33.9 ± 3.0 *vs* D 33.1 ± 2.1 kg/m2, $P=0.305$). The PCOS groups had: higher gonadotropins, LH/FSH ratio, testosterone, antral follicle count and anti-Mullerian hormone; lower luteal phase estradiol and progesterone ($P<0.001$ for all analyses). In the IVF results, the differences were more pronounced in the groups with *vs* without obesity, C and D (*vs* A and B) had: fewer mature oocytes (6.3 ± 5.3 and 5.7 ± 2.9 *vs* 9,1 ± 6.8 and 6.7 ± 5.2, $P=0.035$), less blastocysts (1.1 ± 1.6 and 0.5 ± 0.8 *vs* 1.7 ± 2.3 and 1.6 ± 2.2$P=0.031$) and lower embryo transfer rate (45.7 and 41.4 *vs* 68.8% and 69.3, $P=0.007$). In those who transferred embryos, the probability of pregnancy did not differ ($P=0.197$). In multivariate analysis, only obesity had an individual contribution to the transfer probability ($P=0.001$). The *Asn680Ser*polymorphism (analyzed in 113 cases) was present at a similar rate in patients with and without PCOS (65.7 *vs*54.4%, $P=0.225$) and was not associated with the likelihood of embryo transfer or pregnancy ($P=0.452$ and 0.174, respectively).
Discussion
Differences in IVF results were particularly related to obesity, suggesting that, although the hormonal changes associated with PCOS can be overcome by controlled ovarian stimulation, addressing obesity is essential for the success of IVF. In this population, *Asn680Ser*was not associated with the risk of PCOS or IVF outcomes.

DOI: 10.1530/endoabs.81.P450

P451

Association between basal androgen concentrations and number of follicles on the day of triggering final oocyte maturation in poor responders undergoing IVF - a prospective study

Julia Bosdou[1], Panagiotis Anagnostis[2], Despoina Savvaidou[1], Leonidas Zepiridis[1], Dimitrios Goulis[2], Grigorios Grimbizis[1] & Efstratios Kolibianakis[1]
[1]Aristotle University of Thessaloniki, Medical School, 1st Department of Obstetrics and Gynecology, Unit for Human Reproduction, Thessaloniki, Greece; [2]Aristotle University of Thessaloniki, Medical School, 1st Department of Obstetrics and Gynecology, Unit of Reproductive Endocrinology, Thessaloniki, Greece

Purpose
Androgens promote early follicular development and granulosa cell proliferation by augmenting follicle-stimulating hormone (FSH) receptor expression in granulosa cells. Several retrospective studies have evaluated the association between basal androgen concentrations and follicular development in women undergoing ovarian stimulation for in vitro fertilization (IVF) with conflicting results. The aim of this study was to investigate whether basal androgen concentrations are associated with the number of follicles on the day of triggering final oocyte maturation in poor responders undergoing IVF.
Methods
This prospective study was performed between 02/2020 and 01/2022 in 103 poor responders according to the Bologna criteria. Androgens, including total testosterone, sex hormone-binding globulin (SHBG), dehydroepiandrosterone sulfate (DHEAS), Δ4-androstenedione and 17-OH progesterone (17-OHP), were measured at the initiation of ovarian stimulation. Ovarian stimulation was performed using a fixed dose of 300 IU of recombinant gonadotrophins and gonadotrophin releasing hormone (GnRH) analogues. Triggering of final oocyte maturation was performed in the presence of three follicles of ≥ 17 mm. Primary outcome measure was the number of follicles ≥ 11 mm on the day of triggering final oocyte maturation. The association between androgen concentrations and the number of follicles ≥ 11 mm on the day of triggering was evaluated using generalized estimating equations, accounting for female age and body mass index (BMI). Values were expressed as a coefficient (coef) or mean (95% confidence interval).
Results
Female age was 41.9 (41.2-42.6) years, while BMI was 26.1 (24.9-27.3) kg/m^2. The number of follicles ≥11 mm on the day of triggering final oocyte maturation was 6.1 (5.3-7.0). The number of COCs retrieved was 3.9 (3.2-4.6), the number of MII oocytes was 3.4 (2.8-3.9) and the number of 2pn oocytes was 2.5 (2.1-2.8). No significant association was found between basal testosterone (coef: -0.008, -0.019 to +0.003, $P=0.17$), 17-OHP (coef: -0.044, -0.391 to +0.303, $P=0.80$), SHBG (coef: -0.002, -0.007 to +0.002, $P=0.25$), Δ4-androstenedione (coef: -0.101, -0.306 to +0.104, $P=0.33$) concentrations and the number of follicles ≥11 mm. In contrast, a significant negative association was found between basal DHEAS (coef: -0.011, -0.019 to -0.003, $P=0.007$) concentrations and the number of follicles ≥11 mm on the day of triggering final oocyte maturation.
Conclusions
Higher DHEAS concentrations were associated with the development of fewer follicles ≥ 11 mm. Given the significant negative association between DHEAS concentrations and the number of follicles on the day of triggering final oocyte maturation, future studies on DHEA supplementation should consider basal DHEAS concentrations.

DOI: 10.1530/endoabs.81.P451

P452

A need for transgender care education among polish endocrinologists

Katarzyna Matwiej[1], Karolina Zawadzka[1], Grzegorz Sokolowski[2], Alicja Hubalewska-Dydejczyk[2] & Malgorzata Trofimiuk-Muldner[2]
[1]Jagiellonian University Medical College, Students' Scientific Group at the Department of Endocrinology, Kraków, Poland; [2]Jagiellonian University Medical College, Chair and Department of Endocrinology, Kraków, Poland

Background
A significant body of research indicates that transgender and gender-nonconforming persons represent an underserved population susceptible to health care disparities. The attitudes and knowledge of medical doctors toward transgender people have important implications for the future quality of healthcare for transgender patients.

Specific Aim
The aim of this study was an assessment of coverage of transgender care issues in training curricula of endocrinologists in Poland, including educational and practical experience while providing health care to transgender persons.
Methods
An anonymous survey was sent via electronic mail to the members of the Polish Society of Endocrinology. Survey questions were designed to assess the transgender health issues coverage during training, personal experience with transgender patients and attitudes toward gender-affirming interventions.
Results
A total of 110 endocrinologists responded to the online survey, 74 fully answered questionnaires (67.27%) were analysed. The majority of respondents were between the age of 35-54 ($n=50$; 67.57%) with minimal 10 years seniority. Years in practice were not associated with the level of transgender care training. Among respondents, 21 doctors (28.28%) provided hormonal gender-affirming interventions for transgender patients. The vast majority of endocrinologists did not receive during residency any training on the care of transgender patients, including communication skills ($n=54$; 72.97%) and therapeutic recommendations ($n=37$; 50.00%). Assessment of willingness to provide health care to transgender persons revealed that 22 respondents (29.73%) have concerns in this area. In this group, most doctors ($n=15$; 68.18%) did not have any previous experience with transgender patients. The main indicated obstacle was lack of experience and competence ($n=19$; 82.61%). Endocrinologists, who provide hormonal gender-affirming interventions represent a higher level of participation in training on the care of transgender patients (OR = 4.0, $P<0.003$) and acceptance of hormone interventions as well as surgical procedures (OR = 6.6, $P<0.002$).
Conclusion
Medical school and residency curricula are lacking in the content of transgender care. As a result, personal and professional comfort levels while providing medical care to transgender and gender non-conforming persons could be inadequate. Efforts should be made to provide the proper education on health care issues related to gender incongruence.

DOI: 10.1530/endoabs.81.P452

P453

Crosstalk between androgen-ZIP9 signalling and key regulators of mitochondrial dynamics in rodent leydig cells

Małgorzata Brzoskwinia, Alicja Kamińska, Sylwia Lustofin, Anna Hejmej & Barbara Bilińska
Jagiellonian University, Institute of Zoology and Biomedical Research, Department of Endocrinology, Krakow, Poland

Androgen signalling plays a central role in the regulation of male reproduction. Androgens act predominantly by activating the classical intracellular androgen receptor (AR). In addition, alternative pathways may account for rapid effects of androgens via cytoplasmic or membrane-localized androgen receptor − ZIP9. In the testis, the main source of androgens, in particular testosterone, are Leydig cells. The proper synthesis of testosterone depends on the structural condition of Leydig cells, and any disturbance in the biosynthesis and availability of steroids may affect the secretory activity of these cells. The initial steps of steroidogenesis occur in the Leydig cells mitochondria, which need to be fully functional. It should be noted that the dynamic changes in the mitochondria (their fission and fusion) are associated with the steroidogenic activity of Leydig cells. Therefore, the aim of this study was to test whether the disruption of androgen signalling may have an effect on the expression of mitochondrial dynamics-involved proteins Drp1, Mfn2 and Tom20 in rodent Leydig cells. Experiments were performed using rat primary Leydig cells and mouse TM3 Leydig cell line. To determine the role of AR signalling in the mitochondria dynamics, pharmacological antagonists − hydroxyflutamide (HF) and bicalutamide (BIC) were used to inhibit activation of AR, and ZIP9 (i) or/and siRNA was used to knockdown the expression of these receptors (ii). Immunofluorescence, western blot, qRT-PCR were used for detection Drp1, Mfn2, and Tom20 expression. We found that testosterone increased the expression of Mfn2 and Drp1, whereas the expression of Tom20 decreased in both primary Leydig cells and TM3 cells. HF, BIC, and both androgen receptors silencing partly blocked testosterone effect on Mfn2 expression, which indicates that Mfn2 is controlled by both receptors. The increase of Drp1 expression was inhibited only by BIC and ZIP9 silencing, which suggests that in Leydig cells Drp1 expression is regulated by ZIP9. In contrast, only HF and AR silencing blocked the effect of testosterone on Tom20 expression demonstrating that this protein is dependent on AR signalling. The above findings were confirmed by the results of immunofluorescence analysis. Collectively, our results indicate a crosstalk between androgen and mitochondrial protein expression in Leydig cells and point to cooperation of classical and non-classical androgen signalling pathways in controlling Leydig cell function. This study was supported by a research Grant OPUS 12 2016/23/B/NZ4/01788 from the National Science Centre. The conference attendance was supported by "Jagiellonian Interdisciplinary PhD Programme" (POWR.03.05.00-00-Z309/17-00) funded by the European Union.

DOI: 10.1530/endoabs.81.P453

P454

Different grade of obesity influences the association between 25-hydroxyvitamin and Testosterone levels: A cross-sectional study in young Spanish men with Obesity

Hatim Boughanem[1,2], Miguel Damas-Fuentes[1,2], Maria Molina Vega[1,2], Francisco José Tinahones Madueño[1,2], Jose Carlos Fernandez Garcia[1] & Manuel Macias[1,2]
[1]Hospital Universitario Virgen de la Victoria, Endocrinology and Nutrition, Málaga, Spain; [2]Biomedical Research Institute of Malaga (IBIMA), Cellular and Molecular Endocrinology, Malaga, Spain

Backgrounds
One of the most observations in subjects with obesity, is a high prevalence of vitamin D deficiency, which, in turn, it has been implicated with decreased testosterone levels and an increased hypogonadism risk. Testosterone deficiency is a very common feature in males with obesity. However, only few studies have investigated the effect of vitamin D on testosterone in the context of obesity, and controversial results has been found.
Hypothesis
We hypothesized that a low serum 25-hydroxyvitamin D (25(OH)D) levels may be associated with a decreased testosterone levels in males with obesity. In addition, we also hypothesized that 25(OH)D levels may differ notably according to the different grade of obesity, as a result/consequence of variations in the body mass index (BMI).
Objectives
The aim of the present study was to investigate the relationship between serum 25(OH)D and testosterone levels in young Spanish men with different grade of obesity.
Methods
The study cohort consisted of 269 healthy young men with obesity Men (BMI $\geq$ 30 kg/m^2) aged between 18 and 49 years old, and recruited in Málaga (Spain), between June 2013 to June 2015. Participants were divided under the 50th percentile of serum 25(OH)D levels (134 subjects with vitamin D sufficiency and 135 with vitamin D deficiency). We have measured serum 25(OH)D and sex-related hormones. The associations between 25(OH)D and reproductive hormones and hypogonadism were analyzed using linear regression and binary logistic regression analyses, respectively.
Results
The 25(OH)D deficiency group had significantly decreased both serum total and free testosterone levels and increased serum androstenedione levels when compared to the 25(OH)D sufficiency group ($P<0.05$). Using multivariable lineal regression analyses, 25(OH)D was correlated with the majority of sex-related hormones. However, this significant association disappeared when we adjusted this model by BMI. Further, we analyzed the effect that BMI exerted on the association between 25(OH)D and testosterone, analyzing different grade of obesity. We found that subjects with obesity type III, and adjusted by age, smoking status and BMI, showed that both total testosterone and SHBG were significantly and positively associated with 25(OH)D. Using a mediation analysis, we observed a partial effect of BMI on the association between 25(OH)D and total testosterone levels, indicating that 25(OH)D influence total testosterone levels, and BMI partially mediated this association.
Conclusions
Serum 25(OH)D is associated with total testosterone levels in those subjects with morbid obesity.

DOI: 10.1530/endoabs.81.P454

P455

Analysis of follicle-stimulating hormone receptor (FSHR)/g-protein coupled estrogen receptor (GPER) complex internalization through early and late endosomes

Clara Lazzaretti[1], Beatrice Casadei Garofani[1], Elia Paradiso[1], Sara D'Alessandro[1,2], Samantha Sperduti[1,3], Neena Roy[1], Elisa Mascolo[1], Lara Baschieri[1,2], Claudia Anzivino[1,3], Manuela Simoni[1,3,4] & Livio Casarini[1,3]

[1]University of Modena and Reggio Emilia, Unit of Endocrinology, Department of Biomedical, Metabolic and Neural Sciences, Modena, Italy; [2]University of Modena and Reggio Emilia, International PhD School in Clinical and Experimental Medicine (CEM), Modena, Italy; [3]University of Modena and Reggio Emilia, Center for Genomic Research, Modena, Italy; [4]Azienda Ospedaliero-Universitaria di Modena, Department of Medicine, Endocrinology, Metabolism and Geriatrics, Modena, Italy

Introduction
Follicle-stimulating hormone (FSH) is a glycoprotein that support reproduction by regulating ovarian follicular growth and development. Recent studies demonstrated that proliferative signals mediating folliculogenesis are mediated by the G protein-coupled estrogen receptor (GPER) expressed in ovarian tissues throughout the follicular phase. In granulosa cells, GPER forms heteromers with FSHR, reprogramming cAMP-induced death signals to AKT-dependent, anti-apoptotic/-proliferative events, fundamental to sustain oocyte survival. Since GPER is mainly located in the endoplasmic reticulum, we may hypothesize it modulates FSH signals *via* heteromerization and retention of FSHR in the cytoplasm.
Aim
In this study, we analysed FSHR/GPER heteromers trafficking through early and late endosomes and its impact on FSH-mediated signalling from endocytic compartments.
Methods
HEK293 cells were transfected with FSHR- and GPER-coding plasmids and treated by 10 nM FSH, in the presence or absence of receptor internalization blockade by Dynasore. cAMP production and FSHR interaction with specific endosomal markers, i.e. Ras-related proteins (Rab) 5, 7 and 11, were evaluated at different time-points (0-20 min) by bioluminescence resonance energy transfer (BRET). Results were compared by Kruskal-Wallis test and Dunn's post-hoc test ($P<0.05$; $n=5$) and showed as means $\pm$ SEM.
Results
FSH treatment of FSHR only-expressing cells resulted in the receptor internalization mediated by β-arrestins, and in FSHR localization into Rab7-positive endosomes, addressing it to lysosomes. No FSH-induced compartmentalization of the receptor into early- and recycling-endosomes (Rab5 and Rab11 markers) was found. Conversely, FSHR/GPER co-expression reduces the basal FSHR trafficking through Rab5 and Rab11-marked endosomes, prevents FSH-induced FSHR-Rab7 interaction and drives FSHR internalization mainly through β-arrestin recruitment (FSHR- *vs* FSHR/GPER-expressing cells; $P<0.05$). This event might be essential for FSH-induced signalling modulation. Indeed, as previously described, the FSH treatment of FSHR-expressing cells induces intracellular cAMP increase, while it does not in FSHR/GPER co-expressing cells (AUC FSHR $=85.51\pm8.4$ *vs* AUC FSHR+GPER $=30.6\pm7.4$; $P<0.05$). Interestingly, in FSHR/GPER co-expressing cells where internalization was inhibited by Dynasore, FSH induces a cAMP response, oppositely to what demonstrated in Dynasore-untreated cells (AUC Dynasore-treated FSHR+GPER $=101.1\pm16.11$; $P<0.05$) and suggesting the requirement of the heteromer internalization to inhibit cAMP production.
Conclusion
In conclusion, these results suggest that GPER blocks FSHR-mediated cAMP production *via* compartmentalization of receptors into specific endosomes. These data strengthen the existence of FSHR membrane partners modulating its mode of action, possibly impacting ovarian physiology.

DOI: 10.1530/endoabs.81.P455

P456

Common and unique transcriptional regulation in target tissues and oocytes across polycystic ovary syndrome-like mouse models

Qiaolin Deng[1], Yu Pei[1,2], Sanjiv Risal[1], Hong Jiang[1] & Elisabet Stener-Victorin[4]
[1]Karolinska Institutet, Physiology and Pharmacology, Stockholm, Sweden; [2]Center for Molecular Medicine, Karolinksa University Hospital, Stockholm, Sweden

Yu Pei and Sanjiv Risal are joint first authors. Elisabet Stener-Victorin and Qiaolin Deng are joint corresponding authors. Polycystic ovary syndrome (PCOS) affects around 15% of women of reproductive age and the key feature of the syndrome is hyperandrogenism. To understand the complex pathophysiology of PCOS, more than 30 PCOS-like animal models have been developed to mimic certain pathophysiological features. So far, not much is known about the common and unique molecular and cellular features among the most used PCOS-like mouse models. The overall aim of this study is to compare three hyperandrogenic PCOS-like mice models that are commonly used to understand the molecular pathology across inflicted tissues: hypothalamus, subcutaneous adipose tissue, ovary, and metaphase II (MII) oocytes among the prenatal androgenized (PNA) model (F1 offspring), the prepubertal androgenized (PPA) model, and the theca-cell specific nerve growth factor overexpressing mouse model (17 NF). We performed bulk RNA sequencing of tissues and single-cell RNA sequencing of MII oocytes across the models and identified differential expressed genes (DEGs) in each tissue and model. The greatest number of DEGs was found in the ovary, followed by adipose tissue whereas hypothalamus is least affected in all models. In addition, ovary and adipose tissue were most affected in PPA model compared to other models. We found several common DEGs were involved in lipid metabolism and steroid hormone biogenies among ovary, adipose tissue and hypothalamus in all models. Moreover, we conducted weighted gene correlation network analysis (WGCNA) method to identify functional correlated gene modules across all models and revealed common biological pathways for hub genes including gonadal development, cell-cell communication, hormonal metabolism and lipid metabolism in ovary and adipose tissue. Notably, greatest transcriptional alteration was also observed in MII oocytes in the PNA model, with DEGs in gonad development and germ cell development, likely due to fetal programming effects. Currently, we are investigating crosstalk between tissues and oocytes and comparing these finding with relevant human tissues.

DOI: 10.1530/endoabs.81.P456

P457

A systematic review and meta-analysis assessing psychosexual wellbeing in people with polycystic ovary syndrome

Halimah Khalil[1], Kashish Malhotra[2], Jameela Sheikh[1], Meghnaa Hebbar[1], Nawal Zia[1], Sindoora Jayaprakash[3], Saskia Wicks[4], Anuradhaa Subramanian[5], Rachel Chapman[6], Helena Gleeson[7], Lynne Robinson[8], Justin Chu[8], Tejal Lathia[9], Chitra Selvan[10], Michael W. O'Reilly[11,12], Konstantinos Manolopoulos[11], Wiebke Arlt[7,11] & Punith Kempegowda[7,11]
[1]University of Birmingham, College of Medical and Dental Sciences, Birmingham, United Kingdom; [2]Dayanand Medical College, Ludhiana, India; [3]The Dudley Group NHS Foundation Trust, Dudley, United Kingdom; [4]Barts Health NHS Foundation Trust, London, United Kingdom; [5]University of Birmingham, Institute of Applied Health Research, Birmingham, United Kingdom; [6]University Hospitals Coventry and Warwickshire NHS Trust, Birmingham, United Kingdom; [7]Queen Elizabeth Hospital, University Hospitals Birmingham NHS Foundation Trust, Birmingham, United Kingdom; [8]Birmingham Women's Hospital, Birmingham Women's and Children's NHS Foundation Trust, Birmingham, United Kingdom; [9]Apollo Hospitals, Navi Mumbai, India; [10]MS Ramaiah Medical College, Department of Endocrinology, Bengaluru, United Kingdom; [11]University of Birmingham, Institute of Metabolism and Systems Research, Birmingham, United Kingdom; [12]Royal College of Surgeons in Ireland (RCSI) University of Medicine and Health Sciences, Department of Medicine, Dublin, Ireland

Background
Polycystic ovarian syndrome (PCOS) is a common endocrine disorder, with an estimated prevalence of 10-15% worldwide. PCOS can have adverse consequences on the emotional wellbeing of the patient. However, evidence exploring the relationship between PCOS and psychosexual wellbeing, specifically sexual function, and dysmorphic appearance concerns, is largely inconclusive.
Aim
A systematic review and meta-analysis were undertaken to assess differences in sexual function and dysmorphic appearance concerns among people with and without PCOS.
Methods
Electronic databases (MEDLINE, EMBASE, APA PsycInfo, PUBMED, Web-of-Science Core Collection, and CENTRAL) were searched through August 2021. Observational studies (cross-sectional, case-control, cohort) and Randomised Control Trials (RCTs) were included. Outcome measures included validated questionnaires or Visual Analogue Scales (VAS) reporting on sexual function or dysmorphic appearance concerns. Methodological quality was assessed by adaptation to the Newcastle-Ottawa Quality Assessment Scale (NOS). The inverse variance method, based on a random- or fixed-effects model (Review Manager, Version 5) was used to perform meta-analyses.
Results
The search yielded 5964 publications and 53 full-text articles were included, of which 38 (71.7%) assessed sexual function outcomes, and 15 (39.5%) assessed dysmorphic appearance concerns using validated scales, in people with PCOS.
27 studies used the Female Sexual Function Index (FSFI) to assess domains of sexual function (desire, arousal, lubrication, orgasm, satisfaction, and pain). Meta-analysis of 11 comparative cohort studies (793 PCOS women and 1507 controls) revealed no significant differences between PCOS and controls in sexual desire ($P=0.11$); satisfaction ($P=0.05$); pain ($P=0.56$); arousal ($P=0.05$) and total

FSFI score ($P=0.27$). PCOS women scored significantly lower on lubrication (SMD $=-0.16$; $P=0.001$) and orgasm (SMD $=-0.16$; $P=0.02$), indicating impaired sexual function. Included studies used 13 different validated scales to assess dysmorphic appearance concerns among people with PCOS. Meta-analysis of 3 comparative cohort studies (406 PCOS women and 394 controls) using the Multidimensional Body-Self Relations Questionnaire Appearance Scales (MBSRQ-AS) to assess appearance concerns was performed. PCOS women scored significantly lower on the appearance evaluation (SMD $=-0.78$; $P<0.00001$) and significantly higher on appearance orientation (SMD $=0.22$; $P=0.0004$), indicating higher overall dissatisfaction with physical appearance.
Conclusions
People with PCOS experience a greater degree of sexual dysfunction and body image concerns implying psychosexual wellbeing needs to feature in clinical assessment of people with PCOS. Further studies are needed to identify ways to minimise this impact.

DOI: 10.1530/endoabs.81.P457

P695

Andrological effects of SARS-Cov2 infection: a systematic review and meta-analysis

Walter Vena[1], Giovanni Corona[2], Alessandro Pizzocaro[1], Francesco Pallotti[3], Donatella Paoli[3], Giulia Rastrelli[4], Elisabetta Baldi[4], Nicola Cilloni[5], Federico Semeraro[5], Andrea Salonia[6], Suks Minhas[7], Rosario Pivonello[8], Alessandra Sforza[2], Linda Vignozzi[4], Andrea Marcello Isidori[3], Andrea Lenzi[3], Mario Maggi[9] & Francesco Lombardo[3]
[1]Humanitas Research Hospital, Endocrinology, Diabetology and Andrology Unit, Rozzano (MI), Italy; [2]Azienda Usl, Maggiore-Bellaria Hospital, Endocrinology Unit, Medical Department, Bologna, Italy; [3]Sapienza University of Rome, Department of Experimental Medicine, Roma, Italy; [4]University of Florence, Department of Experimental and Clinical Biomedical Science - Andrology, Women's Endocrinology and Gender Incongruence Unit, Florence, Italy; [5]Maggiore Bellaria Hospital, Department of Anaesthesia, Intensive Care and EMS, Bologna, Italy; [6]University Vita-Salute San Raffaele, Department of Urology, Milan, Italy; [7]Imperial Healthcare NHS Trust, Department of Urology, Charing Cross Hospital, London, United Kingdom; [8]Federico II University of Naples, Staff of UNESCO Chair for Health Education and Sustainable Development, Naples, Italy; [9]University of Florence, Endocrinology Unit, "Mario Serio" Department of Experimental and Clinical Biomedical Sciences, Florence, Italy

Background
Since the preliminary epidemiological data concerning the coronavirus disease 2019 (COVID-19) has been availabe, clear sex disparity has been evident, with males, although not more frequently affected, often experiencing worse outcomes when compared to women. The short and long term andrological effects of coronavirus disease 2019 (COVID-19) have not been clarified. The aim of the present study is to systematically review and meta-analyze all available data regarding possible short- and long-term andrological effects of COVID-19. In addition, information regarding the safety of the COVID-19 vaccines on sperm quality was investigated.
Methods
All prospective and retrospective observational studies reporting information on severe acute respiratory syndrome coronavirus 2 (SARS-CoV2) mRNA semen and male genitalia tract detection, as well as those reporting data on semen analysis and hormonal parameters in infected/recovered patients without any arbitrary restriction were included.
Results
Out of 204 retrieved articles, 35 were considered, including 2.092 patients and 1.138 controls with a mean age of 44.1 ± 12.6 years, and mean follow up 24.3 ± 18.9 days. SARS-CoV-2 mRNA can be localized in male genitalia tracts during the acute phase of the disease; mean crude detection rate (DR) was 8[5;12]%. Meta-regression analysis showed that DR was not influenced by patient age or by disease severity or associated morbidities. DR was significantly higher in those studies assessing the viral mRNA presence in the semen less than 11 days after the diagnosis ($P=0.02$). When all studies were considered, COVID-19 was associated with a significant reduction of total sperm count, sperm concentration and total sperm motility, whereas no difference in sperm morphology or progressive motility was observed. Moreover, SARS-CoV2 infected patients were characterized by reduced total T levels, whereas no difference in either LH or FSH levels was observed. Sensitivity analyses confirmed the negative effects of SARS-CoV2 infection on T levels only for those studies that included patients in the acute phase (mean difference in total T levels -2.19 [-7.08;-1.20] nmol/l;$P=0.01$).
Conclusions
COVID-19 can result in short-term impaired sperm and T production. Available data cannot clarify long-term andrological effects. Low T observed in the acute phase of the disease is associated with an increased risk of being admitted to the Intensive Care Unit or death. The use of mRNA COVID-19 vaccines does not seem to affect sperm quality.

DOI: 10.1530/endoabs.81.P695

P696

Comparison of three different AMH assays with AMH levels and follicle count in women with polycystic ovary syndrome

Loes Moolhuijsen[1], Yvonne Louwers[2], Joop Laven[2] & Jenny Visser[1]
[1]Erasmus MC, Department of Internal Medicine, Rotterdam, Netherlands; [2]Erasmus MC, Div. of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynaecology, Rotterdam, Netherlands

Anti-Müllerian hormone (AMH) levels strongly correlate with the number of antral follicles in the ovary. In women with polycystic ovary syndrome (PCOS), this is reflected by significantly increased serum AMH levels. AMH levels are therefore suggested as a proxy for polycystic ovary morphology (PCOM) in PCOS diagnosis. Different assays are available to measure serum AMH levels. However, lack of a golden standard and the use of different antibodies to detect AMH, have led to inter-assay variability. Little is known about inter-assay correlation in women with increased AMH levels, especially in PCOS. Hence, our aim was to investigate the correlation of AMH values between different AMH assays and with total follicle count (TFC) in a large cohort of PCOS patients. Serum AMH levels were measured in 1660 PCOS patients, diagnosed using the Rotterdam criteria. AMH levels were measured by three different AMH assays: (1) Gen II ELISA [Beckman Coulter]; (2) picoAMH assay [AnshLabs]; and (3) Automated Elecsys assay [Roche]. Patients were divided in subgroups based on the reported AMH cutoff values for PCOM: low AMH (<2.80 ng/ml), mid AMH ($2.80-7.04$ ng/ml) and high AMH level (>7.04 ng/ml). Passing Bablok regression was used for the comparison between assay methods. Spearman's correlation rank was used to assess the correlation between AMH levels and TFC. The inter-assay correlations over the total range of AMH levels were: Gen II vs Elecsys: 0.81; picoAMH vs Gen II: 0.81; picoAMH vs Elecsys: 0.94. Stratification in three AMH subgroups revealed an AMH level dependent inter-assay correlation. A strong inter-assay correlation was present in both low and high AMH subgroups, ranging from $0.62-0.86$. The correlation in the mid AMH level subgroup was only moderate, with correlation coefficients ranging between $0.28-0.56$. A positive correlation was present over the total range of AMH levels and TFC, with correlation values ranging from $0.57-0.62$. However, subgroup analysis showed that independently of assay method used, the correlation decreased in all three AMH subgroups and became moderate at best with coefficients ranging between $0.11-0.45$. In conclusion, in our cohort of PCOS patients both inter-assay correlation and correlation between AMH level and follicle count depend on the range of serum AMH level. While a high AMH level may reflect the presence of PCOM, our results suggest that it does not accurately reflect the total number of follicles in PCOS. This once more emphasizes the need of a standardization of AMH measurement.

DOI: 10.1530/endoabs.81.P696

P697

Clinical/biochemical characteristics of functioning gonadotroph adenomas in women presenting with ovarian hyperstimulation

Nikoleta Papanikolaou[1], Amy Coulden[2], Nina Parker[1], Sit Lee[3], Chris Kelly[4], Richard Anderson[5], Aled Rees[6], Jeremy Cox[1], Waljit Dhillo[1], Karim Meeran[1], Maya Al-Memar[1], Niki Karavitaki[2] & Channa Jayasena[1]
[1]Imperial College Healthcare NHS Trust, London, United Kingdom; [2]University Hospitals Birmingham NHS Foundation Trust, Birmingham, United Kingdom; [3]The Royal Infirmary of Edinburgh, Edinburgh, United Kingdom; [4]NHS Forth Valley, United Kingdom; [5]University of Edinburgh Medical School, United Kingdom; [6]Cardiff University, Cardiff, United Kingdom

Background
Functioning gonadotroph adenomas (FGA) are rare benign pituitary tumours. Several case reports suggest that FGA may present with features of ovarian hyperstimulation in women. However, a lack of aggregated clinical experience of FGA precludes the meaningful guidance of management in affected women.

Methods
Case series of 7 women presenting at different UK sites with FGA induced ovarian hyperstimulation syndrome (OHSS).
Results
Mean age was 31.6 years (range: 16-48) at diagnosis. 3/7 women underwent ovarian surgery prior to diagnosis of FGA. Two of those presented acutely unwell with abdominal pain, distention and palpable mass requiring oophorectomy for torted ovary/ruptured cyst. OHSS was classified as mild or moderate in all other cases. Abdominal pain, irregular periods, headache, visual disturbances, were also reported at presentation by 100%, 71%, 57%, 43% of women, respectively. Visual field defects were present in 6/7 women. Median follicle stimulating hormone (FSH) levels were 26.1 U/l (range:8.3-33), but luteinizing hormone (LH) was <2.5 U/l in all cases. Estradiol (E2) far exceeded the reference range in 5/7 women (2990 to >18000 pmol/L); E2 was at the upper limit of reference range in the remaining 2/7 women (960-1450 pmol/L). Hyperprolactinemia and deficiencies of other pituitary hormones were noted in 6/7 and 4/7 women, respectively. One woman had elevated thyroid stimulating hormone (TSH) and free thyroid hormones; histopathology subsequently confirmed a plurihormonal adenoma expressing TSH and FSH**.** Two patients were given lanreotide prior to surgical management but neither FSH, E2 nor tumour size responded to treatment. Duration of treatment was 6 and 12 weeks. Transsphenoidal surgery was performed in 6/7 women; resection was incomplete but OHSS symptoms and biochemistry improved post-operatively in all cases. The case with longest follow-up period had five transsphenoidal surgeries and radiotherapy twice over a period of 24 years.
Conclusion
This is the largest series of FGA in women. Transsphenoidal surgery remains the only effective treatment improving clinical and biochemical features of OHSS with FGA. Long-term clinical follow-up is required owing risk of adenoma recurrence. The long-term prognosis remains unclear for fertility in women diagnosed with FGA.

DOI: 10.1530/endoabs.81.P697

P698

The biochemical investigation of PCOS: a UK wide survey of laboratory practice

James M Hawley[1], Rachel Marrington[2], Finlay MacKenzie[2], Jo Adaway[1], Angela Taylor[3], Wiebke Arlt[3] & Brian Keevil[1]
[1]Wythenshawe Hospital, Biochemistry, Wythenshawe, United Kingdom; [2]Birmingham Quality UK NEQAS, Birmingham, United Kingdom; [3]University of Birmingham, Institute of Metabolism and Systems Research, Birmingham, United Kingdom

Background
Polycystic ovary syndrome (PCOS) is a heterogenous condition that affects approximately 12% of females. The diagnosis can be complex and biochemistry tests are routinely relied upon to help identify hyperandrogenaemia and to exclude other conditions. However, although national and international guidelines advocate the use biochemistry tests, little information is provided as to which tests should be used and which other endocrinopathies should be excluded.
Objectives
To gather information about what tests UK laboratories routinely use to investigate PCOS, what reference ranges are applied, and which other conditions are routinely excluded.
Design
A national survey consisting of 32 questions was compiled by clinical scientists and clinicians. This was circulated to NHS clinical laboratories via UK NEQAS and The British Endocrine Society with online access available between June – December 2021. Supplementary to the survey, UK NEQAS distributed three cases for interpretation to complement their steroid hormone scheme.
Results
The survey attracted responses from 81 participants. Of these, 90% identified that testosterone would be included in an initial screen with only 50% using it in combination with SHBG to provide a free androgen index. Of the conditions that are not routinely excluded; 74% would not add TSH to investigate hypothyroidism and 84% would not consider adding 17OHP to exclude late onset CAH. Testosterone analysis is commonly performed by immunoassay in the UK with only 12% of respondents using LC-MS/MS. Reference ranges for testosterone varied with the most commonly used being a manufacturer derived <1.7 nmol/l and the highest reported being a luteal upper limit of 6.0 nmol/L. Several participants (64%) identified that they would send high testosterones to an LC-MS/MS laboratory for confirmation, the concentration at which this occurred ranged from >1.2 nmol/l to >5 nmol/l. Androstenedione was only included by 16% of participants in the initial screen with the majority using LC-MS/MS for its measurement and the upper limit of normal ranging from 4.6 to 14.3 nmol/l. The results from the clinical interpretation provided varied responses.
Conclusions
There is significant variation across the UK in the investigation of PCOS. This is apparent in which tests are offered by biochemistry laboratories, what reference ranges are used and, as a direct consequence of these, what interpretation is applied. This potentially further complicates the investigation and diagnosis of PCOS and represents an inequality across the healthcare system. There is a requirement for clear guidance on what tests should be used to investigate PCOS.

DOI: 10.1530/endoabs.81.P698

P699

Cyproterone associated meningioma in a polycystic ovarian syndrome patient- a rare occurrence in our cohort

Ali Al Jumaah[1,2], Narendra Reddy[1,2], Miles J Levy[1,2], Ragini Bhake[1] & Shailesh Gohil[1,2]
[1]Department of Endocrinology, Leicester Royal Infirmary, Leicester, United Kingdom; [2]University of Leicester, Leicester, United Kingdom

Introduction
Meningiomas are the most common brain tumours and they express progesterone receptors. Cyproterone acetate (CPA) is a synthetic progestogen approved for use as an anti-androgen in Polycystic Ovarian Syndrome (PCOS). We report a case of meningioma probably resulting from long-term CPA treatment and a review of our PCOS cohort for further cases.
Case report
A 47-year-old lady with PCOS was treated with CPA 100 mg once daily for hirsutism and androgenic alopecia for 15 years (cumulative dose-exposure = 193g). She developed reduced vision in left eye; an MRI brain revealed a 6-cm left supra-orbital meningioma alongside 2 small separate lesions (0.8 cm & 0.3 cm). CPA was stopped and large mass was resected; histology confirmed Grade 2 meningioma. Smaller lesions were conservatively managed.
Quality Improvement project
To identify further cases of meningioma, a retrospective electronic records' review of consecutive PCOS patients who were on either CPA or Dianette (CPA 2 mg + Ethinyl Estradiol 35 mg) in University Hospitals of Leicester from 1980 to 2021 was undertaken. $n=1302$ patients received either CPA or Dianette as current or past treatment (CPA = 508; Dianette = 794) with a cumulative dose-exposure of 56g/patient. 78/508 CPA patients are currently under active follow-up; 20 are currently on CPA (100 mg = 14; 50 mg = 6). CPA was stopped in rest due to lack of efficacy, tolerability, compliance, and/or lost to follow-up. Up-to-date imaging & records review of 508 CPA-cohort detected one meningioma occurrence which is described above. No meningioma cases were noted in the Dianette cohort.
Discussion
First described in 2008 and confirmed in a recent French study, there is a 11-fold higher dose-dependent risk of meningioma with 36g to 60g cumulative CPA dose-exposure compared to <3g. In June 2020, Medicines and Healthcare products Regulatory Agency (MHRA) issued guidance to minimise risk of meningioma, limiting high dose (50-100 mg) license for only prostate cancer and male hypersexuality. It is plausible that meningioma is co-incidental in our patient as incidence is 6-10 in 100.000 background population. However, recognised association, potent progestogenic effect and high-dose exposure may potentially incriminate CPA. Given solitary incidence in our cohort, remaining 19 CPA patients are closely monitored, MHRA guidance explained with an option offered to swap to alternate treatment.
Learning points
1) To be aware of meningioma side effect risk in high dose CPA (>50 mg/day) treated patients and consider cessation/swapping to alternate treatment.
2) CPA should be stopped in high risk patients such as PMH of meningioma, radiotherapy or Neurofibromatosis-2 genetic mutation.

DOI: 10.1530/endoabs.81.P699

P700

Fetal exposure to anti-müllerian hormone triggers a transgenerational epigenetic transmission of polycystic ovary syndrome (PCOS) defects in adulthood

Mimouni Nour El Houda[1], Isabel Paiva[2], Anne-Laure Barbotin[1], Fatima Ezzahra Timzoura[1], Damien Plassard[3], Stephanie Le Gras[3], Gaetan Ternier[1], Pascal Pigny[4], Sophie Catteau-Jonard[5], Virginie Simon[5], Vincent Prevot[1], Anne-Laurence Boutillier[2] & Paolo Giacobini[1]

[1]Univ. Lille, Inserm, CHU Lille, U1172 - LilNCog - Lille Neuroscience & Cognition, Lille, France; [2]Université de Strasbourg, UMR 7364 CNRS, Laboratoire de Neurosciences Cognitives et Adaptatives (LNCA), Strasbourg, France; [3]CNRS UMR 7104, Inserm U1258, GenomEast Platform, Institut de Génétique et de Biologie Moléculaire et Cellulaire (IGBMC), Université de Strasbourg, Illkirch, Strasbourg, France; [4]CHU Lille, Service de Biochimie et Hormonologie, Centre de Biologie Pathologie, Lille, France; [5]CHU Lille, Service de Gynécologie Médicale, Hôpital Jeanne de Flandre, Lille, France

Polycystic ovary syndrome (PCOS) is the most common endocrine and metabolic disorder affecting women in reproductive age. Women with PCOS exhibit 2-3x higher levels of circulating Anti-Müllerian Hormone (AMH) as compared to healthy women and it is unclear if the elevation of AMH is a bystander effect or is driving the condition. Moreover, PCOS has a strong heritable component, however the etiopathology of the disease and the mechanisms underlying its transmission remain to be elucidated. Therefore, it is crucial to unravel contributions of intrauterine environmental factors that might induce epigenetic changes leading to increased susceptibility to PCOS later in life. We have previously measured AMH levels in a cohort of pregnant women with PCOS and control women revealing that AMH is significantly more elevated in the former group vs the latter. Pregnant mice were treated with AMH to model our clinical findings and investigate the neuroendocrine phenotype of their female progeny across multiple generations. Using this new preclinical PCOS model showed that fetal exposure to excess AMH drives a transgenerational transmission of the major reproductive and metabolic PCOS alterations across multiple generations via altered landscapes of DNA methylation. Furthermore, these findings revealed the existence of common epigenetic signature in a cohort of mothers and their daughters suffering from PCOS as well as in PCOS-like mice, which could serve as markers for early diagnosis of the syndrome. Furthermore, the efficiency of an epigenetic-based therapy used in this preclinical model of PCOS, offers a promising therapeutic avenue to improve the management of PCOS patients. Collectively, our results challenge the concept of PCOS originating *in utero* and appear to consolidate the role of AMH as a trigger of the pathogenesis. This work further points to PCOS-like mouse model as an excellent preclinical tool to investigate both neuroendocrine disturbances of PCOS and how developmental programming effects are transmitted, while offering a therapeutic avenue for the treatment of the disease.
Key words: PCOS, Fetal programming, AMH, GnRH, Transgenerational Transmission

DOI: 10.1530/endoabs.81.P700

P701

Evolution of congenital hypothyroidism with *in situ* thyroid gland in children and adolescents

Luisa Pignata, Brunella Bagattini, Lucia Montanelli, Patrizia Agretti, Giuseppina De Marco, Eleonora Ferrarini, Francesca Orsolini & Massimo Tonacchera
University of Pisa, Department of Endocrinology and Metabolism, Pisa, Italy

Background
In recent years, increasing cases of congenital hypothyroidism (CH) with *in situ* thyroid gland are identified. Outcome of children affected from CH with normally sited thyroid of normal size is still unknown. The objective of our study is to describe the natural history of this specific form of CH. Patients and methods: We retrospectively evaluated clinical, biochemical and instrumental data of 74 patients with diagnosis of CH with *in situ* thyroid gland, referred to our center after positive neonatal screening. After 3 years of age, 48 patients performed a clinical reassessment after withdrawal of levothyroxine (L-T4) therapy, through biochemical evaluation with thyroid function profile, imaging evaluation with neck ultrasound and, in most cases, a scintiscan with 123-I and perchlorate discharge test. We evaluated the need for L-T4 therapy at retesting and during follow-up.
Results
48 patients performed clinical reassessment: 10 had overt hypothyroidism (20.8%), 20 showed hyperthyrotropinemia (41.7%) and 18 were euthyroid (37.5%) after L-T4 withdrawal for 4 weeks. 32 patients performed a scintiscan with 123-I and perchlorate discharge test: 6 patients presented a partial iodine organification defect, while 4 patients had a total defect. 28 children (58.3%) resumed therapy immediately after clinical reassessment, while 20 (41.7%) suspended it. Follow-up data after retesting (median duration of 10) were available in 44 patients. Between children who had suspended therapy at retesting, 4 resumed therapy during follow-up, while in the group of children who had resumed therapy at retesting, 9 suspended it. At the end of follow-up, 22 patients (50%) were untreated and 22 (50%) were still taking therapy. We observed no statistical differences between CH children who suspended or continued L-T4 in first serum TSH levels, sex ratio, or birth weight. Serum TSH at clinical reassessment showed a significant difference between two groups.
Conclusions
over a third of patients had a normal thyroid function off L-T4 therapy when retested after 3 years of age. During subsequent follow-up, half of our patients underwent to suspension of L-T4. Therefore, a clinical reassessment after 3 years of age should be performed to evaluate the need of L-T4 substitution and avoid unnecessary prolonged treatment. However, it is not possible to predict whether these subjects will need therapy again, so long-term follow-up studies are needed.

DOI: 10.1530/endoabs.81.P701

P702

Non-alcoholic fatty liver disease prevalence in Klinefelter syndrome

Lucia Digitale Selvaggio, Rosa Di Fraia, Francesca Allosso, Aldo Marrone & Daniela Pasquali
University of Campania L. Vanvitelli, Advanced Medical and Surgical Sciences, Napoli, Italy

Non-alcoholic fatty liver disease (NAFLD) is becoming more common over the world. Its predisposition for evolving to cirrhosis and hepatocellular cancer, as well as its link to extrahepatic symptoms, puts patients and clinicians under a double burden. Several studies have found a link between NAFLD and many endocrinopathies, demonstrating a substantial bi-directional link between NAFLD and hypogonadism, in both men and women. In man with T2DM, NAFLD is linked to reduced total testosterone, however this is owing to a common soil of insulin resistance/obesity rather than the degree of liver necroinflammation or fibrosis. No data are available regarding Klinefelter syndrome (KS), the most common chromosomal condition associated with hypogonadism and NAFLD.
Methods
Thirty-five KS on Testosterone (T) replacement treatment were recruited. All patients underwent physical examination, full liver function tests, fasting glucose, triglycerides, cholesterol, blood cell counts, viral markers (HBV, HCV, HIV) and liver ultrasonography. The presence of autoimmune liver disease was assessed. The body mass index (BMI: kg/m2) was recorded for all patients. Insulin resistance index (HOMA-IR), and renal function were calculated. Conventional ultrasonography was performed to assess liver dimension, hyper echogenicity as compared to the right kidney parenchyma, distal attenuation, and the presence of areas of focal sparing. Prevalence of steatosis, using non-invasive methods in relation to anthropometric, biochemical, virological and ultrasound was estimated.
Results
Prevalence of steatosis in KS was 51%. BMI was 28.4 ± 1.3 and HOMA-IR 3.8 ± 1.0(Mean ± SEM). T, 393.3 ± 22 ng/dl, and SHBG, 31 ± 2 nmol/l, serum levels were in the normal range. AMA, ANA and ASMA were negative. AST, ALT, and gamma GT were slightly increased in 11.1%, 44.4% and 31.1%, respectively. No patient shows signs of advanced liver disease. Total and LDL cholesterol were normal (174 ± 9 and 112 ± 7, Mean ± SEM, respectively). Serologic markers for HBV, HCV, HAV infection were negative.
Conclusions
The prevalence of NAFLD increases by up to 80-90% in cohorts of individuals with dysmetabolic conditions such as overweight/obesity, T2DM, and metabolic syndrome, underscoring the primary role of metabolic factors in its development. These data are consistent with our preliminary findings in KS patients in whom the prevalence of steatosis was relevant in 51% of cases. The presence of autoimmune liver disease was excluded, and viral markers were negative, while KS were overweight and exhibited insulin resistance, despite normal T levels. However, the main pathophysiological mechanisms linking hypogonadism to NAFLD are complex and still under investigation, and more data are needed to better understand this condition.

DOI: 10.1530/endoabs.81.P702

P703

Early changes in androgen hormones in individuals with spinal cord injury: a longitudinal study

Oche Adam Itodo[1,2,3], Peter Francis Raguindin[2,3,4], Gion Frankl[4,5], Jens Wöllner[6], Inge Eriks-Hoogland[6], Xavier Jordan[7], Margret Hund-Georgiadis[8], Taulant Muka[2], Jürgen Pannek[6], Jivko Stoyanov[4] & Marija Glisic[2,4]
[1]Swiss Paraplegic Research, Spinal Cord Injury Biobanking and Translational Medicince, Nottwil, Switzerland; [2]Institute of Social and Preventive Medicine (ISPM), Bern, Switzerland; [3]Graduate School for Health Sciences, Bern, Switzerland; [4]Swiss Paraplegic Research, Nottwil, Switzerland; [5]Graduate School for Cellular and Biomedical Sciences, Bern, Switzerland; [6]Swiss Paraplegic Centre, Nottwil, Switzerland; [7]Clinique romande de réadaptation, Sion, Switzerland; [8]REHAB Basel, Basel, Switzerland

Background
Individuals with spinal cord injury (SCI) are in increased risk of hypothalamic−pituitary−gonadal axis disruption. We aimed to explore changes in androgen hormones during first impatient rehabilitation and identify factors associated with their levels among participants from the Swiss Spinal Cord Injury Cohort (SwiSCI) cohort.
Methods
We measured sex hormones using Enyzyme Linked Immunosorbent Assay in persons with a newly aquired SCI that participated in the SwiSCI study. We used univariable linear regression analysis to explore the association between clinical and injury characteristics and androgen hormones (total testosterone (TT), free testosterone (FT), sex hormone-binding globulin (SHBG), dehydroepiandrosterone (DHEA), and dehydroepiandrosterone sulfate (DHEAS))) at baseline. Longitudinal changes were explored using linear mixed models adjusted for age, body anthropometrics, injury characteristics, and medication use. Analyses were stratified by sex.
Results
We analyzed paired samples of 86 individuals with SCI [70 males (81%), 16 females (19%)] with median age of 51 years (IQR 36-64) and median rehabilitation duration of 5.6 months (IQR 4.2-7.5). At baseline, increasing age and longer time since injury in men were associated with lower FT, SHBG, DHEA, and DHEAS and higher SHBG respectively. Increased upper extremity spasticity was linked with lower TT, DHEA and DHEAs and higher handgrip strength was associated with higher FT. TT in males in the beginning of the rehabilitation was in low normal range. At the end of rehabilitation, TT and DHEAS increased in males. We found no differences in hormone levels among individuals with different injury etiology, body composition, nor total spinal cord independence measure (SCIM). Due to limited number of women, female-specific findings should be interpreted with caution (**Table 1**).
Conclusions
We observed gradual increase in androgen hormones over a period of rehabilitation which was linked with improved functional recovery. Future studies to explore whether testosterone and DHEA supplementation may improve neurological and functional recovery as well as metabolic parameters during first inpatient rehabilitation.

DOI: 10.1530/endoabs.81.P703

P704

Intracranial idiopathic hypertension in a maletranssexual patient after testosterone overdosing

Francisco Javier Martinez Martin, Alba Hernandez-Lazaro, Ricardo de Leon-Durango, Agnieszka Kuzior, Paula Gonzalez-Diaz, Esperanza Perdomo-Herrera, Alba Lucia Tocino-Hernandez, Claudia Arnas-Leon, Carmen Acosta-Calero & Maria del Pino Perez-Garcia
Hospital Universitario de Gran Canaria Dr. Negrin, Endocrinology and Nutrition, Las Palmas de Gran Canaria, Spain

Introduction
Intracranial Idiopathic Hypertension (IIH) is a rare complication of testosterone therapy. It is usually benign, but may result and permanent blindness. Its diagnosis is based on a high CSF (> 25 cm H_2O) pressure, in the absence of specific causes. The androgen receptor is expressed in the human choroid plexus, and may enhance the activity of Na+/K+-ATPase, and therefore CSF secretion.
Methods
Review of the patient's clinical record.
Results
A 24-year old female-to-male transsexual patient had been treated for 4 years with 60 mg of testosterone gel daily, using a dispenser which supplied 20 mg/pulse. He was satisfied with the treatment, his secondary male sexual characters were well developed, his hormonal levels and hematocrit were adequate and he had not suffered any adverse effects except mild acne. The availability of the testosterone dispenser was interrupted and the patient was changed to a different testosterone gel formulation but due to a dispensation error the total daily dose of testosterone was increased to 200 mg. After 2 months the patient was admitted in the Neurology Ward for the workup of an excruciating holocranial headache, poorly responding to common analgesics, which severely limited his daily activities. Tinnitus or visual disturbances were not reported. An intracranial tumor was suspected but the cranial CT scan and MNR were negative and funduscopy did not show significant oedema. Two lumbar punctures revealed CSF pressures on 36 and 29 cm H2O, but otherwise were normal. Total plasma testosterone levels were above the measurable range (> 34.6 ng/ml, normal 2.8 - 10.7 ng/ml) and hematocrit was mildly elevated (52.7%). Testosterone was withdrawn and acetazolamide 500 mg BID was prescribed for a week. The patient was asymptomatic at discharge. One month after the discharge, transdermal testosterone was reinstated, with a daily dose of 50 mg, with no adverse effects, recovery of the target hormonal levels and normal hematocrit.
Conclusions
IIH is a rare complication of testosterone therapy, which we had not previously found in our extensive experience with testosterone treated transsexual patients. In our patient it was related to accidental overdosing, but it has occasionally been reported with standard treatment. It is a potentially severe complication, which may impair the patient's daily activities and in the worst case scenario cause permanent blindness. The risk of IIH must be considered in male transexual patients but only very rarely may result in a contraindication for gender-affirming therapy.

DOI: 10.1530/endoabs.81.P704

P705

Lessons from a patient with the 48XXXY karyotype: Not just another case of Klinefelter's syndrome

Agnieszka Kuzior[1,2], Alba Hernandez-Lazaro[1], Ricardo de Leon-Durango[1], Carlos Ríos-Gomez[1], Claudia Arnas-Leon[1], Carmen Acosta-Calero[3], Paula Maria Fernandez-Trujillo-Comenge[1], Ana Delia Santana-Suarez[1], Paula Gonzalez-Diaz[4] & Francisco Javier Martinez Martin[1,2]
[1]University Hospital of Gran Canaria Dr. Negrin, Endocrinology and Nutrition Clinic, Las Palmas de Gran Canaria, Spain; [2]Hospitales Universitarios San Roque | Las Palmas de G.C., Endocrinology and Nutrition Clinic, Las Palmas de Gran Canaria, Spain; [3]University Hospital of Gran Canaria Dr. Negrin, Cardiology Clinic, Las Palmas de Gran Canaria, Spain; [4]University Hospital of Gran Canaria Dr. Negrin, Emergency Dpt., Las Palmas de Gran Canaria, Spain

Introduction
The 48XXXY karyotype is an infrequent (incidence about 1/50000 male births) sporadic aneuploidy of the sex chromosomes, classically considered as a variant of the Klinefelter syndrome (47XXY). Although many of their characteristics are shared, patients with the 48XXXY karyotype suffer from additional endocrinological and neuropsychological disturbances which are not part of the classic Klinefelter syndrome. Hereby we present a clinical case.
Methods
Review of the patient's clinical records and of the relevant literature.
Case Presentation
A male, 27 year old patient, previously diagnosed of left renal agenesis, hypertriglyceridemia and cognitive impairment of unknown etiology with a 66% legal disability was referred to our Endocrinology Clinic from the Urology Dept, for workup of testosterone deficiency. He had undergone a standard vasectomy, but his testicles were reported as partially atrophic and his total testosterone was 0.96 ng/ml (normal range 2.8 - 10.7 ng/ml). The anamnesis disclosed cognitive impairment since childhood, with speech development at the age of 4 years and enuresis until 12 years. Growth was normal, having reached target adult height, and the development of secondary sexual characters was normal except for absence of facial hair. The patient had normal erections and maintained regular sexual activity. The physical examination disclosed dysmorphic facial features, bilateral gynecomastia, penis of normal size, testicular volume of 10-12 mL, scarce pubic and axillary hair, gynecoid fat distribution, short trunk with long limbs and bilateral cubitus valgus. Lab tests were compatible with hypergonadotropic hypogonadism, with total testosterone 0.82 ng/ml, FSH 36 mU/ml and LH 24 mU/ml. The workup was completed by the karyotype 48XXXY.
Conclusions
Some of the peculiarities of our patient, such as cognitive impairment, genital hypoplasia and dysmorphic features are characteristic of the 48XXXY syndrome,

while others such as unilateral renal agenesis are less often associated with it. Other developmental abnormalities involving the cardiac, neurological and genitourinary systems may be present. This case underscores the heterogeneity of the syndrome. The early diagnosis of the 48XXXY syndrome is highly desirable because it is significantly more complex than the classic Klinefelter syndrome (47XXY) with additional somatic and cognitive disturbances, and usually requires multidisciplinary care and follow-up.

DOI: 10.1530/endoabs.81.P705

P706

Alterations in lipid composition are linked with decreased motility in human spermatozoa

Bárbara Guerra-Carvalho[1,2,3], Marco G Alves[1], Soraia Pinto[4], Alberto Barros[4,5,6], Rita Ferreira[2], Rui A Carvalho[3], Pedro Domingues[7] & Pedro F Oliveira[2]
[1]Department of Anatomy and UMIB - Unit for Multidisciplinary Research in Biomedicine, ICBAS - School of Medicine and Biomedical Sciences, University of Porto, Porto, Portugal; [2]QOPNA & LAQV, Department of Chemistry, University of Aveiro, Aveiro, Portugal; [3]Department of Life Sciences, Faculty of Sciences and Technology, University of Coimbra, Coimbra, Portugal; [4]Centre for Reproductive Genetics Professor Alberto Barros, Porto, Portugal; [5]Department of Genetics, Faculty of Medicine, University of Porto, Porto, Portugal; [6]i3S – Instituto de Investigação e Inovação em Saúde, University of Porto, Porto, Portugal; [7]Mass Spectrometry Centre, LAQV-REQUIMTE, Department of Chemistry, University of Aveiro, Aveiro, Portugal

Infertility is a growing concern in Western countries. Several factors, including lifestyle habits and increased prevalence of chronic disorders associated with hormonal alterations, increased chronic inflammation and systemic oxidative stress (such as obesity and diabetes mellitus), are contributing to the reduction of reproductive potential among males in modern societies. Evidence suggests these factors negatively impact human sperm quality resulting in a combination of alterations in specific sperm features, namely in its motility. Asthenozoospermia is a common cause of fertility reduction and is characterized by a reduction in sperm motility (sperm total motility $<40\%$). Sperm lipid metabolism is crucial for sperm motility and morphology as well as for sperm-oocyte interactions, although the relevance of lipid content of human spermatozoa is poorly understood. In this work, we aimed to compare sperm lipidome from asthenozoospermic and normozoospermic men and to identify lipid metabolites that correlate with sperm motility. Sperm samples from the male partner of couples seeking fertility counselling ($n=57$) were collected and sperm parameters were assessed accordingly to WHO guidelines. Sperm polar lipid content from asthenozoospermic ($n=17$) and normozoospermic ($n=39$) men was analysed by liquid chromatography-mass spectrometry. A total of 245 lipid molecular species were identified and quantified in sperm samples from both groups. Using a PCA model, we found a distinct lipid profile between asthenozoospermic and normozoospermic men. Sperm lipid analysis showed an increase in the lysophospholipid (LPL) content in asthenozoospermic men, whereas the phosphatidylethanolamine (PE) content was increased in normozoospermic men. The levels of several lipids, including lysophosphatidylcholine (LPC) 18:0, 18:1, 20:1, O(16:1) and O(18:2), and lysophosphatidylethanolamine (LPE) 20:1 and O(20:2) negatively correlated with sperm total motility. Contrarily, some PE lipids, including PE-P(36:4), PE-O(38:6), PE-O(38:7), PE-O(40:9), and PE(38:6), as well as acyl-carnitine (26:6) and fatty acid (20:3);3O showed a positive correlation with total sperm motility. Overall, our data show a different lipidomic profile in sperm from asthenozoospermic men. Asthenozoospermic sperm content in LPLs suggests altered lipid metabolism in these men, which might be associated with alterations in sperm membrane fluidity and consequent decrease in sperm motility. Moreover, LPL levels suggest that increased inflammation and oxidative status might be in the aetiology of asthenozoospermia. Our results suggest that alterations in lipid metabolism might be a potential cause for chronic disorders-related decreased sperm motility and male infertility.

DOI: 10.1530/endoabs.81.P706

P707

The role of hypothalamic markers in the development of POI following COVID-19

Nilufar Baqoyeva[1] & Feruza Xaydarova[2]
[1]Y.X.Turakulov Republican Specialized Scientific and Practical Medical Center of Endocrinology, Polyclinic, Tashkent, Uzbekistan; [2]Y.X.Turakulov Republican Specialized Scientific and Practical Medical Center of Endocrinology, Administration, Tashkent, Uzbekistan

Introduction
Premature ovarian insufficiency (POI) is a pathological condition, which accompanying with loss of ovarian function in women under the age of 40. This is manifested by hypergonadotropic amenorrhea, infertility and estrogen deficiency. POI affects 1% of women. The specific causes can be genetic disorders, autoimmune, infectious-toxic and iatrogenic factors, but the exact mechanism is unclear yet. According to different authors, the idiopathic form accounts for 50 to 90% of cases. Increased cases of menstrual irregularities (amenorrhea), following infection with COVID-19. This abstract review the study conducted on the role of hypothalamic peptides such as kisspeptin and BDNF in the pathogenesis of premature ovarian insufficiency as a consequence of COVID-19. The pandemic has significantly impacted the mental health of women, and it can affect women's reproductive health. This is due to stress during the pandemic. It is very important to identify markers of menstrual disorders after covid-19. The aim of the study was to study the concentrations of kisspeptin and BDNF in blood plasma in patients with POI following coronavirus disease.
Methods and results
The study included 2 groups: 44 women with diagnosed POI following COVID-19 (age 30 $\pm$ 2 years) and 15 women with regular menstrual cycle as control group (age 33 $\pm$ 3). The KISS1 and BDNF levels were measured using enzyme linked immunosorbent assay kit (ELISA KIT). In control group tests were performed in follicular phase (days 3-5). In the group with POI the level of kisspeptin was lower (268.35 $\pm$ 16.7 pg/ml) than in control group (312.95 $\pm$ 31.84 pg/ml, $P<0.005$) The concentration of BDNF was also lower in group with POI (215.48 $\pm$ 37.67 pg/ml) than in control group (402.91 $\pm$ 34.12 pg/ml). The kisspeptin and BDNF plasma levels are correlated negatively with period of amenorrhea. Decreased levels of kisspeptin and BDNF in the blood correlated with the occurrence of premature ovarian insufficiency and were as risk factor for its occurrence. It showed that patients with POI were more likely to have deficiency of kisspeptin and BDNF and higher levels of FSH.
Conclusion
This study confirms the relationship between kisspeptin, BDNF and the occurrence of POI in women following COVID-19. This study provides important potential opportunities for understanding the pathology of POI.

DOI: 10.1530/endoabs.81.P707

P708

The medical treatment of polycystic ovary syndrome: effects of inositol isomers and metformin on clinical, metabolic and hormonal profile

Nunzia Verde[1], Bianca Pellegrini[1], Lucia Auriemma[1], Alessia Baratto[1], Cristina De Angelis[1], Francesco Garifalos[1], Davide Menafra[1], Michele Castoro[1], Chiara Simeoli[1], Annamaria Colao[1,2], Rosario Pivonello[1,2] & Renata Simona Auriemma[1]
[1]Università Federico II di Napoli, Dipartimento di Medicina Clinica e Chirurgia, Sezione di Endocrinologia, Unità di Andrologia e Medicina della Riproduzione e della Sessualità Maschile e Femminile (FERTISEX-CARES), Naples, Italy; [2]Federico II University of Naples, Unesco Chair for Health Education and Sustainable Development, Naples, Italy

Polycystic ovary syndrome (PCOS) is characterized by menstrual irregularities and clinical and biochemical hyperandrogenism, and is associated with insulin resistance, visceral obesity and metabolic disorders. The aim of the current study was to compare the effects of inositol isomers (INO) and metformin (MET) on the clinical, metabolic and hormonal aspects of PCOS. In 94 PCOS women, clinical (weight, BMI, waist circumference - WC, menstrual intervals, Ferriman-Gallway score - FGS), metabolic (fasting glucose and insulin, HOMA-IR, HOMA-beta, lipid profile) and hormonal [FSH, LH, estradiol (E2), androstenedione (A), testosterone (T)] parameters were retrospectively investigated before (T0) and after 6 months (T6) of treatment with INO (Group 1, $n=36$) or MET (Group 2, $n=58$). INO was administered in the 3 following formulations (F): F1, myo-inositol 1000 mg + D-chiro-inositol 200 mg; F2, myo-inositol 1100 mg + D-chiro-inositol 27.6 mg; F3, myo-inositol 1000 mg + alpha-lipoic acid 800 mg. At T0, FGS and hormonal profile were similar between Group 1 and Group 2, except for HDL ($P=0.002$) and FSH ($P=0.02$), which were higher in Group 1, whereas weight ($P<0.0001$), BMI ($P<0.0001$), WC ($P<0.0001$), menstrual intervals ($P=0.011$), fasting insulin ($P=0.001$), HOMA-IR ($P=0.001$), HOMA-beta ($P=0.001$) and triglycerides ($P=0.001$) were higher in Group 2. At T6, in Group 1, menstrual intervals ($P=0.005$), FGS ($P<0.0001$) and testosterone ($P=0.021$) were significantly reduced compared to baseline, with a trend to a decrease for weight, BMI, A, HOMA-IR and triglycerides. The effects of INO

formulations were similar, except for percent increase in E2, which was significantly higher ($P=0.027$) in F1, compared to F3. At T6, in Group 2, weight ($P<0.0001$), BMI ($P<0.0001$), WC ($P<0.0001$), menstrual intervals ($P<0.0001$), FGS ($P<0.0001$), HOMA-IR ($P=0.002$), total cholesterol ($P=0.001$), LDL ($P<0.0001$), triglycerides ($P<0.0001$), A ($P=0.003$) and T ($P=0.005$) were significantly reduced, whereas HDL ($P<0.0001$) and HOMA-beta ($P<0.0001$) were significantly increased, compared to baseline. Noteworthy, percent decrease in weight ($P<0.0001$), BMI ($P<0.0001$) WC ($P=0.018$), HOMA-IR ($P<0.0001$), total cholesterol ($P=0.046$), LDL ($P=0.015$) and triglycerides ($P=0.041$), and percent increase in HDL ($P=0.012$), were significantly higher in Group 2, compared to Group 1. In conclusion, INO and MET are effective treatments for menstrual irregularities and clinical and biochemical hyperandrogenism in women with PCOS, with different formulations of INO displaying similar efficacy, and MET displaying an apparent greater efficacy over INO on insulin resistance, lipid metabolism, and visceral obesity.

DOI: 10.1530/endoabs.81.P708

P709

Serum testosterone mirrors inflammation parameteres in females admitted with covid-19 disease

Maria Francesca Birtolo[1], Walter Vena[1], Alessandro Pizzocaro[1], Simona Jaafar[1], Antea Ciafardini[1], Alessandro Brunetti[1], Stella Pigni[1], Gherardo Mazziotti[1,2] & Andrea Lania[1,2]
[1]IRCCS Humanitas Research Hospital, Endocrinology, Diabetology and Andrology Unit, Rozzano, Italy; [2]Humanitas University, Department of Biomedical Sciences, Pieve Emanuele, Italy

Background
Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection is showing a rapid and continuous evolution in terms of new waves, the spread of variants and the evidence of reinfections. The growing heterogeneity of clinical presentation requires the identification of underlying pathogenic mechanisms to allow a better risk stratification. Previous studies analysed the role of sex hormones in disease severity demonstrating in male patients the association of low testosterone (T) levels with unfavorable outcome of COVID-19. Conversely, data concerning the role of T in women with SARS CoV-2 infection are scant and limited to small cohorts.
Purpose
To investigate the relationship between serum T values and clinical presentation and outcome of SARS-CoV2-related pneumonia in a population of adult females admitted to hospital due to coronavirus-disease 19 (COVID-19).
Methods
All adult females hospitalized for COVID-19 in our Institution during the period between November 1st 2020 and February 28th 2021 were evaluated for arterial partial pressure oxygen (PaO2)/fraction of inspired oxygen (Fio2) ratio, serum T and inflammatory parameters (IL-6 and procalcitonin) at study entry, need of ventilation during hospital stay and in-hospital mortality. Berlin criteria were used to define acute respiratory insufficiency (ARI).
Results
The study included 101 women (mean age 76.8 $\pm$ 13.8 years, mean BMI 27.3 $\pm$ 6.3 kg/m^2 and mean T 1.333 $\pm$ 1.3 nmol/l). A significant correlation was observed between serum T levels and IL-6 ($P<0.044$) and procalcitonin ($P<0.001$). At hospital admission 55% ($n=56$) of subjects were diagnosed with ARI. No significant association was found between serum T levels and ARI ($P=0.227$) . Mean duration for hospital stay was 14.2 $\pm$ 9.9 days, and mortality was 23% ($n=25$). Subjects who died had significantly higher age (83.7 $\pm$ 10, 5 vs 74.6 $\pm$ 14.1; $P=0.033$), IL-6 (89.3 $\pm$ 95.3 vs 35.9 $\pm$ 39.2;$P=0.021$) and procalcitonin levels (1.7 $\pm$ 4.0 vs 0.3 $\pm$ 1.7; $P=0.001$) as well as significantly lower fT3 levels (2.89 $\pm$ 0.55 vs 3.70 $\pm$ 0.80;$P=0.007$) as compared to survivors. No significant difference was observed in serum T levels among the two groups ($P=0.604$).
Conclusion
Oppositely to what observed in male subjects, this study provides a first preliminary evidence about the role of higher serum T levels in female as a mirror of higher inflammatory phenotype and worse COVID-19 disease course, possibly reflecting a massive adrenal cortex activation in response to systemic inflammation.

DOI: 10.1530/endoabs.81.P709

P710

Age- and body mass index-adjusted association between insulin sensitivity and risk factors for cardiovascular disease in polycystic ovary syndrome

Małgorzata Kałużna[1], Tomasz Krauze[2], Pola Kompf[1], Katarzyna Ziemnicka[1], Wykretowicz Andrzej[2], Marek Ruchala[1] & Przemyslaw Guzik[2]
[1]Poznan Univeristy of Medical Sciences, Department of Endocrinology, Metabolism and Internal Diseases, Poznan, Poland; [2]Poznan Univeristy of Medical Sciences, Department of Cardiology - Intensive Therapy, Poznan, Poland

Introduction
Impaired insulin sensitivity accompanies polycystic ovary syndrome (PCOS). Women with PCOS are usually at risk of premature cardiovascular disease, which increases with age and body weight. We studied the link between insulin sensitivity measured by the Matsuda Insulin Sensitivity Index (MISI) adjusted to body mass index (BMI) and age in otherwise healthy PCOS women.
Methods
250 adult women with PCOS of reproductive age (18-43 years old) underwent measurements of MISI, lipid profile, resting heart rate, peripheral and central systolic and diastolic blood pressure. Patients were divided into tertiles of MISI (T1 (<4.74), T2 (4.74-8.35) and T3 (>8.35), respectively). Their data were compared by the Analysis of Covariance (ANCOVA) adjusted for patients' BMI and age. Only the results with a P-value <0.05 are shown as Estimated Marginal Means +/- Standard Error in the following order: T1, T2 and T3.
Results
Better insulin sensitivity (patients with higher MISI values) was associated with lower plasma concentration of total cholesterol (188.2+/-3.8, 175.3+/-3.5 and 176.2+/-3.6 mg/dl), low-density lipoprotein cholesterol (106.0+/-3.4, 93.6+/-3.1 and 91.8+/-3.2 mg/dl), triglycerides (96.3+/-5.3, 77.5+/-4.8 and 76.2+/-5.0 mg/dl), and resting heart rate (76.9+/-1.5, 73.1+/-1.4 and 70.0+/-1.4 beats/minute) independent of age and BMI. Similar associations were not found for high-density lipoprotein cholesterol, peripheral and central systolic and diastolic blood pressure.
Conclusions
A less atherogenic lipid profile and lower heart rate, regardless of the effects of age and BMI, are observed in PCOS women with better insulin sensitivity. The clinical meaning of these findings requires further studies.

DOI: 10.1530/endoabs.81.P710

P711

Demographic trends and morbidity in the basque country transgender population (2009-2020)

Pedro González Fernández[1,2], María del Carmen Fernández López[1], Susana Ponce de León Sáenz de Navarrete[1], María Gema Grau Bolado[1,2], María Luisa Guadilla Fernández[1] & Itxaso Rica Echevarría[1,2]
[1]Hospital Universitario Cruces, Barakaldo, Spain; [2]Biocruces Bizkaia Health Research Institute, Barakaldo, Spain

Introduction
The number of transgender men and women who seek gender-affirming therapy is rapidly increasing worldwide. It is still a population at high risk for several morbidities. The Basque Country Gender Identity Clinic was created in 2009 to centralize their medical care in the region.
Aim
To determine the proportion of transgender individuals in the Basque Country, the prevalence of several morbidities in this transgender population, their evolution, and their trends since 2009.
Methods
Cross-sectional study. We selected all transgender men and women who requested therapy at our clinic and registered their demographic and clinical data. We compared the population who was first attended in the years 2009-2014 vs those first attended in 2015-2020. We compared the prevalence of several diseases between the transgender population and the Basque general population as recorded in public registries.
Results
The proportion of transgender people in the Basque Country is 2.4 per 10.000. Transgender men consume more psychoactive drugs than the general male population (9.9% vs 5.0%, $P=0.001$), while transgender women have a higher prevalence of smoking (31.5% vs 21.3%, $P=0.001$), a higher prevalence of HIV infection (3.4% vs 0.003%, $P=0.001$) and lower bone mass density (lumbar Z-score -0.87 SD, femoral neck Z-score -0.44 SD) than the general female

population. Transgender individuals first attended between 2015-2020 were younger (28 vs 17 years, $P=0.001$), had a higher academic level (secondary education or higher in 85.5% vs 37.5%, $P=0.001$) and consume less anxiolytics than those first attended the precedent years (2009-2014).
Conclusions
The proportion of transgender people in the Basque Country is 2.4 per 10.000. Transgender population in the Basque Country is at risk for several morbidities. Individuals who have sought gender-affirming therapy between 2015-2020 have a better profile at baseline (younger age, higher academic level, and less psychoactive drugs use) than those first attended between 2009-2014, which likely reflects the positive changes that have taken place in our area regarding integration and improved medical care to this population.

DOI: 10.1530/endoabs.81.P711

P712

Phenotypic and genotypic heterogeneity of sexual development disorders 46, XY in the Tunisian population

Faten Haj Kacem Akid[1], Mohamed Abdellahi Mohamed Ahmed[1], Dhieb Nessrine[1], Benrhouma B[2], Kammoun T[3], Hachicha M[3], Kallel N[4], Belguith N[2], Mouna Mnif[1] & Mohamed Abid[1]
[1]Department of Endocrinology and Diabetology CHU Hedi Chaker, Sfax, Tunisia; [2]Human Genetics Department, CHU Hedi Chaker, Sfax, Tunisia; [3]Pediatric Department, CHU Hedi Chaker Sfax, Tunisia; [4]Department of Internal Medicine, Gabes, Tunisia

Introduction
Sexual disorders 46 XY DSD are responsible for a range of phenotypic disorders, ranging from an ambiguous phenotype to a complete female phenotype. In this context, we report a cohort of 22 46 XY patients with a female phenotype in order to establish a phenotype-genotype correlation.
Results
The average age at diagnosis was 15.5 years (E: 7 days-33 years). The reason for consultation was primary amenorrhea in 16 cases (72.7%), sexual ambiguity in 5 cases and inguinal hernia in 1 case. The standard karyotype showed a homogeneous chromosomal formula compatible with a male genetic sex, i.e. 46 XY, in 95% of cases and a mosaic formula, i.e. 46, XY/45, X in two cases. The diagnosis of gonadal dysgenesis was chosen in 4 patients (18.18%) in front of a completely female phenotype with ectopic gonads and frankly low levels of testosterone and HMA compared to age contrasting with increased FSH. Full LH resistance was retained in 3 patients with a female complete phenotype and low testosterone levels contrasting with high LH levels with histological Leydig cell agenesis, the biomolecular study of LH resistance confirmed the presence of a nonsense mutation Q525X in the second extracellular loop. A testicular steroidogenesis abnormality affecting the conversion of Δ4-androstenedione to testosterone was reported in 8 patients with a TESTO/Δ4-A <0.8 ratio after HCG, a molecular abnormality of the 17â-HSD3 gene was confirmed as homozygous in (c618C $>$ A) in 4 patients and as heterozygous composite (Pc206X/Pg133R) in 4 others. A biomolecular abnormality of androgen resistance with the presence of a homozygous mutation of exon 5 (R753X) was identified in 5 patients with an evocative phenotype associated with high levels of testosterone and LH. Finally, a biomolecular abnormality of the 5° reductase gene was mentioned in 2 patients with an ambiguous phenotype associated with a base-increased Testo/DHT ratio and after HCG. A homozygous mutation of exon 4 (pC222T) was confirmed in a single patient.
Conclusion
The abnormalities of sexual differentiation cover a wide spectrum of phenotypic and genotypic abnormalities and pose a real problem of etiological diagnosis. To be sure, advances in molecular biology are of great value in understanding the etiopathological links between clinical aspects and the cascade of sexual differentiation.

DOI: 10.1530/endoabs.81.P712

P713

Molecular and functional studies of novel genetic variants of TP63 an SAMD11 genes unravel their potential role in the pathogenesis of primary ovarian insufficiency

Raffaella Rossetti[1], Silvia Moleri[1], Fabiana Guizzardi[1,2], Marco Bonomi[1,3], Anna Marozzi[3], Francesco Brancati[4,5] & Luca Persani[1,3]
[1]IRCCS Istituto Auxologico Italiano, Department of Endocrine and Metabolic Diseases and Lab of Endocrine and Metabolic Research, Milan, Italy; [2]IRCCS Istituto Auxologico Italiano, Molecular Biology Laboratory, Cusano Milanino, Italy; [3]University of Milan, Department of Medical Biotechnologies and Translational Medicine, Milan, Italy; [4]University of L'Aquila, Medical Genetics, Department of Life, Health and Environmental Sciences, L'Aquila, Italy; [5]IRCCS San Raffaele Pisana, Human Functional Genomics, Rome, Italy

Primary ovarian insufficiency (POI) is one of the major causes of female infertility, affecting about 3.7% of women before the age of 40. POI is associated with the premature loss of ovarian function and can manifest with primary amenorrhea (PA) or post-pubertal secondary amenorrhea (SA), with elevated gonadotropins and hypoestrogenism. Several evidence established a clear genetic component to POI, albeit heterogeneous. In search of novel causative genes, we screened 64 POI patients through a customized next generation sequencing panel, which includes known and novel candidate genes potentially involved in POI pathogenesis. Among the novel rare variants identified in genes belonging to pathways relevant in ovarian physiology, we focused our functional studies on a nonsense variant (c.1927C $>$ T) in *TP63* gene, that was identified in two sisters with PA, and a frameshift insertion (c.682_683insT) in *SAMD11* gene, that was identified in 6 unrelated SA patients. The longest isoform of *TP63* gene, TAp63α, is almost exclusively expressed in the nucleus of oocytes after meiotic double-stranded DNA break repair and protect germ line fidelity during meiosis. We investigated the contribution to POI of the *TP63* variant through luciferase reporter assays in Saos-2 cell line using the firefly luciferase gene under the control of three different human promoters, direct targets of p63: *BAX*, involved in cell cycle and apoptosis; *K14*, regulating differentiation; and *IRF6*, required for cell cycle exit and tissue development. *TP63* variant falls in the transactivation inhibitory domain, which inhibits the transactivation domain of the protein. The presence of this variant showed an increment of transcriptional activity on both *K14* and *IRF6* promoters but a slight reduction on *BAX*, which is partially recovered in presence of the wild-type counterpart. The pathogenic consequences of this variant could be the overexpression of dosage-sensible genes involved in differentiation and development of the ovarian follicle and the haploinsufficiency of *TP63* in cell cycle regulation. *SAMD11*gene encodes for a transcriptional modulator that might slightly promote cell proliferation. We observed an enrichment of the frequency of *SAMD11*variant in the POI cohort with respect to the female population worldwide. We observed by immunoblotting that the frameshift generates a truncated protein which can still be produced and possibly further degraded. Moreover, proliferation assay in HEK293T showed a reduced cell growth both at homo- and heterozygous state. *SAMD11*has never been associated to ovarian phenotypes, however, our results suggest this variation might be considered as a POI predisposing factor.

DOI: 10.1530/endoabs.81.P713

P714

Serum concentrations of 17-hydroxyprogesterone and dehydroepiandrosterone sulfate in women with polycystic ovary syndrome and their relation to the parameters of glucose metabolism

Ewa Stogowska[1], Anna Krentowska[1], Agnieszka Adamska[2], Agnieszka Lebkowska[1] & Irina Kowalska[1]
[1]Medical University of Białystok, Department of Internal Medicine and Metabolic Diseases, Poland; [2]Medical University of Białystok, Department of Endocrinology, Diabetology and Internal Medicine, Poland

Introduction
Polycystic ovary syndrome (PCOS) is characterized by menstrual disorders, hyperandrogenism and polycystic ovaries on ultrasonography. This hormonal disorder is also strongly associated with insulin resistance. The diagnosis of PCOS can be established after the exclusion of other causes of mentioned symptoms, such as non-classic congenital adrenal hyperplasia (NCAH). To date, several studies suggest the increased serum concentration of 17-hydroxyprogesterone (17-OHP) in PCOS, even in the absence of NCAH; however, its impact on glucose metabolism has not been discussed widely in the literature.
Aim of the study
The aim of the study was the evaluation of serum 17-OHP and dehydroepiandrosterone sulfate (DHEA-S) concentrations in women with PCOS and the assessment of their relation to the parameters of glucose metabolism.
Materials and methods
We analyzed 35 PCOS women and 19 control subjects, matched for BMI (24.87 ± 4.51 kg/m2) and age (25.35 ± 4.56 y.o.). In women with PCOS, NCAH was excluded by the ACTH stimulation test. The participants were reviewed for

anthropometric measurements, the clinical signs of hyperandrogenism, complex hormonal profile, oral glucose tolerance test (OGTT) and ovarian ultrasound parameters. The increase in 17-OHP concentrations in the ACTH-stimulation test (17-OHP delta value), the homeostasis model assessment of insulin resistance (HOMA-IR), Matsuda index and free androgen index (FAI) were calculated.
Results
The women with PCOS were distinguished by statistically higher baseline concentration of 17-OHP, FAI, the level of DHEA-S, serum glucose concentrations at 60 min and 120 min of OGTT, as well as insulin concentration at 120 min of OGTT (all $P<0.01$) and higher testosterone level ($P=0.014$) in comparison to the control group. In PCOS-affected women, we found the correlation between the 17-OHP delta value and Matsuda index ($r=$-0.77, $P=0.002$), as well as testosterone and insulin at 60 min of OGTT ($r=0.5$, $P=0.042$). Moreover, we observed that FAI correlated with fasting insulin concentration ($r=0.76$, $P<0.001$), as well as HOMA-IR ($r=0.67$, $P=0.005$). Additionally, in a whole study group, we observed the correlation between glucose concentration at 60 min of OGTT and baseline level of 17-OHP ($r=0.39$, $P=0.006$), 17-OHP delta value ($r=0.44$, $P=0.017$), testosterone ($r=0.29$, $P=0.048$), FAI ($r=0.4$, $P=0.016$) and DHEA-S ($r=0.34$, $P=0.049$). We also found the relationship between DHEA-S and insulin concentration at 120 min of OGTT ($r=0.34$, $P=0.049$), as well as the baseline level of 17-OHP ($r=0.48$, $P=0.004$) in a whole study group.
Conclusion
Serum 17-OHP and DHEA-S concentrations are elevated in PCOS-affected women and their levels might be related to the parameters of glucose metabolism.

DOI: 10.1530/endoabs.81.P714

P715

Early career clinicians' knowledge about lifestyle management of PCOS and the current practices of implementing it in clinical practice - does more need to be done?

Nawal Zia[1], Jameela Sheikh[1], Halimah Khalil[1], Alisha Narendran[2], Meghnaa Hebbar[1], Saskia Wicks[3], Sindoora Jayaprakash[4], Punith Kempegowda[5] & Pcos SEva Team[6]
[1]Birmingham, College of Medical and Dental Sciences, University of Birmingham, Birmingham, United Kingdom; [2]Birmingham, King Edward VI High School for Girls, Birmingham, United Kingdom; [3]Barts Health NHS Foundation Trust, London, United Kingdom; [4]The Dudley Group NHS Foundation Trust, Dudley, United Kingdom; [5]Queen Elizabeth Hospital, University Hospitals Birmingham NHS Foundation Trust, Birmingham, United Kingdom; [6]Institute of Metabolism and Systems Research, University of Birmingham, Birmingham, United Kingdom

Objective
Polycystic Ovary Syndrome (PCOS) is one of the most common endocrine conditions affecting women of reproductive age. Current estimates place the condition as more common than Type 2 Diabetes Mellitus (T2DM). Recent studies have shown several long term comorbidities associated with PCOS, thus making it essential that all physicians, regardless of training and speciality, understand and empower women with PCOS to adopt evidence-based behavioural changes. This study set out to establish an understanding of evidence-based lifestyle management of PCOS and the current practices of implementing it in clinical practice amongst final year medical students and newly graduated healthcare professionals.
Design
A survey was constructed using evidence-based recommendations in the international guidelines for PCOS.
Method
We invited final year medical students and non-specialist junior doctors in the UK to complete an online survey between September 2020 and January 2021. The findings were reported as frequency and proportion.
Results
A total 67 participants took part in the survey (41 female and 25 male; medical students (21%), foundation doctors (64%) and senior house officers (15%); 34% from London deanery and 27% from the West Midlands deanery). 54% ($n=36$) knew the correct prevalence of PCOS. Although 70% ($n=47$) knew biochemical androgen excess is a sign of PCOS, only 43% ($n=28$) and 1% ($n=1$) knew free testosterone and free androgen index respectively, were the tests of choice to diagnose this. Instead, androstenedione (52% ($n=35$) and DHEAS (43% ($n=29$) were the most common biochemical tests of choice by this cohort. Interestingly, 55% (n37) said they would use AMH as a test to diagnose PCOS. Although most of the participants knew that BMI 94% ($n=63$) and waist circumference 95% ($n=64$) required routine monitoring between 6-12 months for PCOS, only 6% ($n=4$) were aware of the national recommendations for exercise. 36% ($n=26$) identified obesity and T2DM as the most common long term effects of PCOS.
Conclusion
Effective evidence-based lifestyle advice and patient empowerment are crucial for enhanced clinical outcomes in people with PCOS. Our study highlights that physicians and medical students have a limited understanding of the international evidence-based recommendations for PCOS. Our future work will focus on understanding the current educational opportunities for medical students and junior doctors about lifestyle advice and patient empowerment. With this information, we will work with all involved stakeholders to improve access to these programmes for medical students and early career clinicians.

DOI: 10.1530/endoabs.81.P715

Thyroid

P200

Thyroid dysfunction related to SARS-CoV-2 vaccination: the experience of a single center in Milan

Ilaria Muller[1,2], Francesco Di Marco[3], Maura Arosio[1,2] & Mario Salvi[2]
[1]University of Milan, Department of Clinical Sciences and Community Health, Milan,; [2]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico di Milano, Endocrinology, Milan,; [3]University of Milan, Milan, Italy

Background
The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic disease (Covid-19) has caused millions of deaths worldwide, thus a massive SARS-CoV-2 vaccination campaign has been launched since the end of 2020. Viruses and vaccines can induce adverse thyroid effects; SARS-CoV-2 infection and vaccines have been associated with several thyroid disorders, especially subacute thyroiditis (SAT) and Graves' disease (GD). We aimed to study the occurrence of thyroid diseases following SARS-CoV-2 vaccination in our Centre.
Methods
From February 2020 onwards we have recorded all consecutive cases of SAT of any cause, noting if occurred shortly after SARS-CoV-2 infection or vaccines. We have also retrospectively extended this analysis to GD and Graves' orbitopathy (GO). Our patients underwent blood tests for thyroid function, inflammatory markers, anti-SARS-CoV-2 antibodies and thyroid ultrasound scan.
Results
Up to December 2021 we have registered 15 patients with thyroid dysfunction occurring shortly after SARS-CoV-2 vaccination: 8 SAT and 7 GD, of which 3/7 (43%) also developed GO and 1/7 (14%) associated autoimmune acute hepatitis. Importantly, we observed an increased number of SAT diagnoses from June 2021 onwards, when the vaccination campaign was extended to the Italian general population. Patients' mean age was 53 years (range 23-83 years) and females were 9/15 (60%). 3/15 (20%) patients had a previous history of thyroid disease (one subclinical hypothyroidism, one transient gestational hypothyroidism and one Hashimoto's thyroiditis) and 10/15 (67%) patients had a positive family history of thyroid disorders. Patients received all SARS-CoV-2 vaccination types (8 Pfizer, 5 AstraZeneca, 1 Johnson&Johnson, 1 Moderna); symptoms were developed following the first dose (mean +15 days) in 10/15 (67%), the second (mean +6 days) in 4/15 (27%) and the third (mean +14 days) in 1/15 (7%) patients. A previous documented SARS-CoV-2 infection occurred in 4/15 (27%) patients several months before the vaccination.
Conclusions
SARS-CoV-2 vaccines seem to be associated with the onset of SAT or GD. Possible mechanisms involve the interaction of the spike protein with the ACE-II receptor expressed in thyroid tissue, a cross-reactivity of the spike protein with thyroid self-proteins or an immune reaction induced by adjuvants (ASIA syndrome). The majority of patients had a positive family history for thyroid disorders, thus a genetic predisposition is likely involved. Until more safety data about SARS-CoV-2 vaccines will be available, caution and strict monitoring of individuals predisposed to thyroid disorders or autoimmunity is suggested, especially those with low risk factors for Covid-19 disease.

DOI: 10.1530/endoabs.81.P200

P201

Indications and extended follow-up of radiofrequency ablation for treatment of hyperthyroidism caused by solitary autonomous functioning thyroid nodules

Manon van der Meeren[1,2], Frank Joosten[2], Hans de Boer[1], Laura Deden[2] & Wim J.G. Oyen[2]
[1]Rijnstate Hospital, Internal Medicine, Arnhem, Netherlands; [2] Rijnstate Hospital, Radiology and Nuclear Medicine, Arnhem, Netherlands

Background
Hyperthyroidism caused by autonomous functioning thyroid nodules (ATN) is usually treated with I-131. Recently, radiofrequency ablation (RFA) has emerged as a promising alternative but it is not yet incorporated in guidelines.
Aims
Assessment of efficacy of RFA treatment in patients with hyperthyroidism caused by ATN and factors that may affect treatment success.
Methods
Retrospective analysis of patients treated for hyperthyroidism caused by ATN with RFA, when follow-up of at least one year was available. Results of patients with a single toxic adenoma (STA) are compared with patients with a toxic multinodular goitre (TMG) and a dominant hyperactive nodule on scintigraphy and ultrasound. Proportions were compared by the chi-squared test. Cure was defined as thyroid medication-free biochemical euthyroidism.
Results
48 patients (36 STA, 12 TMG) were included, 85% were female, mean age was 55 (range 27-80). The median nodule volume was 12 ml at baseline. Median energy delivered during RFA was 0.6 kCal/ml. One year post RFA 29 patients (60.4%) were cured after a median of 3.2 months (range 0.1-11). Median volume reduction was 68% (range 21-99). One patient, with a history of hemithyroidectomy, developed hypothyroidism. 18 patients (37.5%) were hyperthyroid one year post RFA. Baseline and RFA parameters were similar for STA and TMG patients. The one-year cure rate was higher among STA patients compared to TMG: 72% vs 25% ($P<0.05$), respectively. 13 patients with persistent hyperthyroidism received re-RFA. 9 (69%) of them were cured at last follow-up (median 12 months post re-RFA). Extended follow-up was available for 31 patients (25 STA and 6 TMG). 3 STA and 1 TMG patients developed late recurrent hyperthyroidism between 24-37 months post-RFA. Of all 48 patients, cure was achieved in 86% of STA patients and in 33% of TMG patients after 1 or 2 RFA sessions at last available follow-up after first intervention (median 20 months after first intervention).
Conclusion and discussion
The efficacy of single session RFA session was nearly 3 times higher in STA patients compared to TMG. These data confirm that RFA is an effective treatment for STA. Further analysis is required to assess the role of RFA in TMG. Follow-up after RFA should be at least 2 years since late recurrences are observed.

DOI: 10.1530/endoabs.81.P201

P202

Deiodinase Type I regulation in fatty liver disease

Nuria López Alcántara[1], Cathleen Geißler[2], Alison-Michelle Naujack[2], Yingfu Chen[3], Natalie Taege[2], Jan H. Britsemmer[2], Leonardo Vinicius Monteiro De Assis[4], Henrik Oster[4], Joachim Spranger[3], Eva Wirth[3], Rubén Nogueiras[5], Henriette Kirchner[2] & Jens Mittag[1]
[1]University of Lubeck, Center of Brain, Behavior and Metabolism (CBBM), Institute of Endocrinology, Lübeck, Germany; [2] University of Lubeck, Center of Brain, Behavior and Metabolism (CBBM), Institute of Human genetics. Section Epigenetics and Metabolism, Lübeck, Germany; [3]Charité - Universitätsmedizin Berlin, Center for Cardiovascular Research, Berlin, Germany; [4]University of Lubeck, Center of Brain, Behavior and Metabolism (CBBM), Institute of Neurobiology, Lübeck, Germany; [5]University of Santiago de Compostela, Molecular Metabolism, Santiago de Compostela, Spain

Background and Aim
Hepatic thyroid hormone (TH) signalling plays an important role in onset and progression of liver diseases. Patients with altered thyroid hormone regulation in the liver, leading to a local hypothyroid, are at higher risk of developing non-alcoholic fatty liver disease (NAFLD). Treatment with thyroid hormones proved to be a promising therapy for these patients, slowing the progression of NAFLD to non-alcoholic steatohepatitis (NASH), a more advanced stage of the disease characterized by inflammation and occasional fibrosis. The action of thyroid hormone in the liver is regulated by TH transporters, deiodinases, and receptors. Among these, deiodinase type 1 (*Dio1*) is a major player, converting the prohormone thyroxine (T4) directly to the bioactive form T3 in the hepatocytes. However, the exact regulation of *Dio1* in liver disease is not yet fully understood.
Methods
We studied *Dio1* expression in several hepatic disease models, including male C57BL/6 mice fed with high-fat diet (HFD) during 18 weeks and treated with metformin for the last two weeks of treatment, male C57BL/6 mice fed with methionine-choline-deficient HFD for 2 weeks, male C57BL/6 mice fed with choline-deficient HFD for 4 and 8 weeks at thermoneutrality, and finally male C57BL/6 mice treated with carbon tetrachloride to induce liver failure.
Results
Expression of *Dio1* was rapidly increased in animals fed with HFD and remained elevated throughout the treatment without changes induced by metformin treatment. Remarkably, some of the other conditions did not resulted in an increase in *Dio1*, although lipid deposition in the liver was similar.
Conclusion
Our results show that *Dio1* is rapidly induced by HFD, an effect that seems to be independent of insulin sensitivity, as it was not reversed by metformin treatment. However, *Dio1* induction was restrained in other animal models with similar degree of hepatic lipid deposition, suggesting that other factors such as liver inflammation may prevent the HFD induced *Dio1* induction.

DOI: 10.1530/endoabs.81.P202

P203

Transoral endoscopic thyroidectomy (TOETVA) in thyroid cancer, our view as endocrinologists

Susana Mallea-Gil[1,1], Yamila Sanchez[1], Bibiana Coca[1], Maria de los Angeles Sosa[1], Adriana Palazzo[1], Javier Rossi[2], Maria Marta Aparicio[1], Silvina Sankowicz[1], Samanta Estevez[3] & Carolina Ballarino[1]
[1]Hospital Militar Central, Endocrinology, Buenos Aires, Argentina; [2] Hospital Militar Central, Surgery, Buenos Aires, Argentina; [3] Hospital Militar Central, Pathology, Buenos Aires, Argentina

Recent progress in surgical technology has resulted in new techniques as transoral endoscopic thyroidectomy (TOETVA) that is an option for patients' cosmetic requests. We evaluated patients with thyroid cancer who underwent thyroidectomy by TOETVA approach and their follow-up. Retrospective study, 5 patients were included, Bethesda classification in FNAC resulted: 2 patients with VI category (CAT), 2: V CAT and 1: III CAT. All patients were operated by TOETVA between 2020-2021. Median age: 48 years (36-64). Median nodules size was: 13.5 mm (7.7-23). No patients presented adenopathies. Total thyroidectomy was performed by TOETVA in 4 patients, one patient required conversion to open thyroidectomy. Hemithyroidectomy was performed in the patient with III CAT, the pathology report resulted in follicular carcinoma and she was later operated by conventional approach. Median size of malignant tumors was 14.7 mm (12-21). Of the 2 patients with VI CAT: 1 had a classical papillary carcinoma, the other one had a follicular variant of papillary carcinoma. Of the two patients with V CAT, 1 had a classical follicular carcinoma and the other one had a nodular goiter; the patient with III CAT had a clear cell variant of follicular carcinoma. In 3 patients the thyroid capsule was absent in some areas, predominantly in the posterior margin. In 4 patients we observed electrocautery effects and tissue attrition. Postoperative complications were: inferior lip insensitivity (5/5), hypogeusia (4/5), mild to soft pain and hematoma in the neck (5/5), suffocating hematoma (1/5), hypoparathyroidism (3/5); all complications were transient. Four patients underwent I-131 therapy; post-therapeutic WBS showed higher and nodular uptake in the neck compared with the patients with conventional thyroidectomy. Stimulated thyroglobulin (TG) was normal in 3 patients and 1 had elevated TG. In the follow-up, only the patient with clear cell variant of follicular carcinoma had increased TG and presented recurrence in the neck, so she was operated again and later received radiotherapy. The remaining patients had normal ultrasonography and TG below 1.
Conclusions
patient selection is very important in TOETVA approach. The cosmetic objective of TOETVA was reached; the complications were different, probably related to the learning curve required for surgeons. Except the patient with the aggressive follicular carcinoma, the patients' follow-up was satisfactory. However, we need more patients and longer follow-ups to determine if the higher and different RAI uptake in the neck scan and the histological findings have an impact in the long follow-up of these patients.

DOI: 10.1530/endoabs.81.P203

P204

Thyrotoxicosis due to African herbal supplements: does iodine contamination play a role?

Eugénie Van Mieghem[1], Bernaerts Kim[2] & Verhelst Johan[2]
[1]Antwerp University Hospital, Department of Internal Medicine, Edegem, Belgium; [2] ZNA Middelheim, Department of Endocrinology, Antwerpen, Belgium

Introduction
In thyrotoxicosis, the clinical syndrome of excess circulating thyroid hormones, differentiation must be made between thyrotoxicosis with increased or decreased radio-iodine tracer uptake on thyroid scintigraphy. A cause of thyrotoxicosis with decreased radio-iodine uptake is iodine excess. In patients not taking any medication and without any history of recent radiological imaging studies, the confirmation of iodine excess as the cause of the thyrotoxicosis is difficult. Especially in patients with a penchant for traditional medicine and natural supplements, a thorough inquiry about supplement use is key to establishing a correct diagnosis.
Case Presentation
In our endocrinology outpatient clinic, in the period between September 2017 and October 2021, six patients, originally from Western Africa, were referred due to abnormal thyroid function tests with suppressed TSH and elevated fT3 and/or fT4. In all patients thyroid antibodies were negative. No fever, painful swelling of the thyroid or recent URTI were reported. The patients hadn't used any medication containing iodine nor had recently underwent a radiological study. On thyroid scintigraphy, in all patients a reduced to absent radio-iodine uptake could be seen. Ultimately, it came to light that all six patients had been taking African natural supplements. In one patient a complete 24-h urinary iodine excretion was performed, which was significantly elevated with a value of 1115.8 µg iodine per 24 hours (783 µg/l), confirming iodine excess. After discontinuation of the supplements, in all patients a normalization of the thyroid function tests could be seen.
Discussion/conclusion
Some herbal remedies used in traditional African medicine seem to cause hyperthyroidism. Characteristics of this kind of hyperthyroidism are reduced to absent radio-iodine uptake on thyroid scintigraphy, absent thyroid autoimmunity, a normal thyroid ultrasound and a spontaneous restoration of euthyroid state with discontinuation of the supplements. Our hypothesis is that this type of thyrotoxicosis is caused by an increased iodine exposure due to use of natural supplements used in traditional African medicine. We suspect that the African supplements, imported from Western Africa to Europe, are treated with iodine-containing compounds to improve the preservability. Iodine-induced hyperthyroidism, or the Jod-Basedow syndrome, is therefore a cause of thyrotoxicosis that therefore must certainly be kept in mind in certain ethnic groups. If a thorough questioning of the supplement use doesn't reveal the intake of natural remedies, then an urinary iodine excretion can sometimes provide a conclusive answer if iodine excess is suspectedly involved in the thyrotoxicosis.

DOI: 10.1530/endoabs.81.P204

P205

Association between thyroid autoimmunity and gestational diabetes mellitus in euthyroid women

Georgiana Sitoris[1], Kris Poppe[1], Flora Veltri[1], Malika Ichiche[1], Pierre Kleynen[1], Jean-Philippe Praet[2] & Serge Rozenberg[3]
[1]Centre Hospitalier Universitaire Saint-Pierre, Université Libre de Bruxelles (ULB), Endocrine Unit, Bruxelles, Belgium; [2] Centre Hospitalier Universitaire Saint-Pierre, Université Libre de Bruxelles (ULB), Departement of Internal Medicine, Bruxelles, Belgium; [3] Centre Hospitalier Universitaire Saint-Pierre, Université Libre de Bruxelles (ULB), Departement of Gynecology and Obstetrics, Bruxelles, Belgium

Objective
Pregnant women with autoimmune (subclinical) hypothyroidism have an increased risk of developing gestational diabetes mellitus (GDM). However, this association remains controversial in euthyroid women with thyroid autoimmunity (TAI). Therefore, the aim of the study was to determine the association between TAI and GDM in euthyroid women in a logistic regression analysis with adjustments for baseline/demographic parameters.
Methods
Cross-sectional study in 1447 euthyroid women who performed their entire clinical/biological work-up and oral glucose tolerance test (OGTT) in our center. At median 13 (11-17) weeks of gestation, TSH, free T4 and thyroid peroxidase antibodies (TPOAb) were measured, baseline characteristics recorded and an OGTT was performed between 24-28 weeks of pregnancy. Exclusion criteria were pre-pregnancy diabetes, assisted pregnancies, and women with (treated) thyroid dysfunction before or after screening. The diagnosis of GDM was based on 2013 WHO criteria.
Results
Two hundred eighty women were diagnosed with GDM (19.4%), 26.1% in women with TAI and 18.9% in women without TAI ($P=0.096$). TAI was associated with GDM (adjusted odds ratio (aOR) 1.69 (95% CI, 1.01-2.82); $P=0.046$). Maternal age >30 years, pre-pregnancy BMI ≥ 30 kg/m^2 and another than Caucasian background were also associated with GDM; aOR 1.93 (95% CI, 1.46-2.56); $P<0.001$, 2.03 (95% CI, 1.46-2.81); $P<0.001$ and 1.46 (95% CI, 1.03-2.06);$P=0.034$, respectively.
Conclusions
In our cohort, the presence of TAI in euthyroid pregnant women was associated with gestational diabetes. In line with literature data, higher age and obesity were associated too. Future studies should focus on treatment options that might decrease the development of GDM in euthyroid women with TAI.

DOI: 10.1530/endoabs.81.P205

P206

Discordance between fT4 and TSH concentrations during levothyroxine treatment

Heleen Jansen[1], Marijn Bult[1], Peter H. Bisschop[2], Anita Boelen[1], Annemieke C Heijboer[1] & Jacquelien Hillebrand[1]
[1]Amsterdam UMC, Vrije Universiteit Amsterdam and University of Amsterdam, Amsterdam Gastroenterology Endocrinology & Metabolism, Department of Clinical Chemistry, Endocrine Laboratory, Amsterdam, Netherlands; [2] Amsterdam UMC, University of Amsterdam, Department of Endocrinology and Metabolism, Amsterdam, Netherlands

Introduction
Physicians in our hospital notified the laboratory staff of a number of patients at the outpatient clinic with increased free T4 (fT4) concentrations without (complete) suppression of thyroid stimulating hormone (TSH). This phenomenon appeared to occur more frequently following implementation of a new automated fT4 immunoassay. The discordance between fT4 and TSH concentrations may be explained by analytical issues (not further explained here), incorrect reference intervals, or patient-related factors (e.g. medication, population). We aimed to establish the contribution of the possible factors involved.
Methods
First, reference intervals of the current Cobas (Roche) and former Delfia (Perkin Elmer) fT4 immunoassay were re-evaluated using blood samples of healthy volunteers. Second, TSH (Cobas, Roche) and fT4 requests and the frequency of discordant pairings (i.e. fT4 above the upper limit of normal and TSH 0.02 − 5.0 mU/l) of patients from Amsterdam UMC were retrospectively analysed using a Delfia fT4 and Cobas fT4 cohort. Third, we performed a literature search to assess whether time of blood draw and time of levothyroxine (L-T4) ingestion may contribute to higher fT4 concentrations in L-T4 users.
Results
The original reference intervals belonging to the Delfia and Cobas assay were confirmed. The Delfia ($n=176$, 5.5%) and Cobas cohort ($n=295$, 8.6%) showed comparable frequencies of discordance. Interestingly, approximately 80% of the discordant results belonged to L-T4 users. Review of the literature showed that fT4 concentrations may vary depending on time of blood draw and, therefore, time of L-T4 intake. Besides, fT3/fT4 ratios are different in L-T4 users vs healthy controls and indicate an adapted regulation of the thyroid axis in those patients.
Conclusion
Discordance between fT4 and TSH concentrations was not related to the introduction of a new fT4 immunoassay. The increased fT4 concentrations with discordant TSH could not be explained by analytical issues or incorrect reference intervals, but may be explained by L-T4 intake. Physicians and laboratory specialists should be aware that patients treated with L-T4 may have fT4 concentrations above the reference interval with normal or slightly decreased TSH concentrations, to avoid questioning the assay's performance, or worse, adapting L-T4 dose in patients.

DOI: 10.1530/endoabs.81.P206

P207

Thyroid autoimmunity observed in a local center hospital of northeast Japan − Association with the nuclear power plant accidents

Takao Kunori & Hiroshi Yoshida
Iwaki-City Medical Center, Surgery, Iwaki, Japan

Background
Our hospital is located 40 km from the nuclear power plants(Tokyo Electric Daiichi; NPP) exploded in northern east Japan disaster (2010.3). After the explosion, yearly radiation dose reached to 1-10 mSV in our city and 10-50 mSV in most poluted areas (next to our city). In former ESE congress, we reported cytological analysis of nodular goiter (NOD). In the present study, patients' thyroid autoimmunity was analyzed whether there is any difference between pre- and post-NPP accidents. Patients and methods: 1.625 new patients (pts; 6.242 exams; 2007-2021). Ultra-sonogram (US) and hormonal assay for anti-thyroglobulin (aTg), thyroid peroxidase antibody (TPO), anti-TSH receptor antibody (TSH-R) and, in case of HY, thyroid stimulating antibody (TS), were performed at their visits. Fine needle aspiration cytology (FNA) was, if necessary, performed for NOD. Clinical diagnosis: Hyperthytroidism (HY), 420 pts (26%, 1.592 exams). chronic thyroiditis (HA), 160 (10%, 642), NOD 1.045 (65%:solid 27%, cyst 12%, multiple 15%). Data was compared between pre-NPP (A, 2007-2009) and post-NPP period(B1-B3, 2010- 2021). Significance was determined by Kai2 or student-t test (significance $P<0.05$).
Results
1) Age: A, 55 ± 18 years ($n=1.295$); B1(2010-2013), 55 ± 16 ($n=1.796$); B2 (2014-2017) 59 ± 16 ($n=1.495$); B3 (2018-2021) 57 ± 17. (B2B3>A, $P=0.01$). 2) Gender: female(%), A 21.4%; B1 29.6%; B2 23.6%; B3 5.1%(B>A, $P<0.0001$).3)Autoimmunity(%) : a) All periods; TP(aTg+ TPO+) 10%, Tp(aTg+ TPO-) 3.9%, tP(aTg- TPO+) 3.8%, tp(aTg- TPO-) 25%.b) Period A-B (new pts): TP(aTg+ TPO+); A 18%; B1 18%;B2 29%;B3 25%. (A< B2B3:$P=0.004$).c) Period A-B (all pts): TP (aTg+ TPO+); A 20%($n=97$), B 123%($n=147$), B2 24%($n=153$), B3 28%($n=253$). (B>A, $P=0.0001$). 4) TSH-R positive(%): A 34%($n=206$), B1 27%($n=232$), B2 21%($n=151$), B2 22% +21%($n=196$). (A>B, <0.0001). 5) NOD: Antibody positive(%): Solid, 41%, cyst 52% a) aTg+: A 12%($n=162$), B1 42%($n=246$), B2 13%($n=230$), B3 44%($n=298$). (A<B1B3, $P<0.0001$). b)TSH-R+: A 5.5%($n=162$), B1 4%($n=246$), B2 14%($n=230$), B3 9.1%($n=296$). (A<B, $P<0.0001$).
Discussion
There was a slight increase of aTg+ TPO+ pts and decrease of TSH-R+ pts. This phenomenon is similar to the results of Chernobyl inhabitants' analysis. However, there are various factors influencing autoimmunity, aging, gendar, residence or some others.
Conclusions
No apparent effect of NPP accidents was observed in thyroid immunity. To confirm the radiation effects, more elaborated environmental study is needed.

DOI: 10.1530/endoabs.81.P207

P208

Estimating incidence and case fatality of thyroid storm in Germany between 2007 and 2017: A claims data analysis

Arulmani Thiyagarajan[1], Katharina Platzbecker[1], Till Ittermann[2], Henry Völzke[2] & Ulrike Haug[1,3]
[1]Leibniz Institute for Prevention Research and Epidemiology-BIPS, Department of Clinical Epidemiology, Bremen, Germany; [2] University Medicine Greifswald, Institute for Community Medicine, Greifswald, Germany; [3] University of Bremen, Faculty of Human and Health Sciences, Bremen, Germany

Background
Given the general lack of descriptive epidemiological studies on thyroid storm, we aimed to estimate the incidence rate and case fatality of thyroid storm in Germany based on a large claims database.
Methods
Using the German Pharmacoepidemiological Research Database (GePaRD) we identified patients with at least one inpatient discharge diagnosis of thyroid storm (International Statistical Classification of Diseases and Related Health Problems, 10th revision, German modification; ICD-10-GM E05.5) between 2007 and 2017 and calculated age-standardized and age-specific incidence rates in males and females. We defined deaths occurring within 30 days of the diagnosis as thyroid storm-associated and determined case fatality by sex and age group.
Results
Overall, we identified 1.690 patients with an incident diagnosis of thyroid storm (72% females). Mean age was 60 years (standard deviation: 18.6 years). The age-standardized incidence rate per 100.000 persons per year was 1.4 (95% confidence interval [CI] 1.2 to 1.7) in females and 0.7 (95% CI 0.5 to 0.9) in males. In females ≤60 and >60 years of age, the incidence rate was 0.9 (males 0.4) and 2.7 (males 1.7), respectively. The case fatality of thyroid storm was 1.0% in males ≤60 years (females: 1.4%) and 16.7% in males >60 years of age (females: 10.9%).
Conclusion
Incidence rates of thyroid storm were markedly higher in females than in males and were three times higher in persons >60 years compared to younger age groups. Case fatality was below 2% in persons aged ≤60 years and markedly higher in older persons (males: 17 times, females: 8 times).
Keywords: thyroid storm; incidence; case fatality; Germany

DOI: 10.1530/endoabs.81.P208

P209

Patients with autoimmune thyroiditis present similar immunological response to COVID-19 BNT162b2 mRNA vaccine with healthy subjects, but vaccination may affect thyroid function

Stavroula A. Paschou[1], Vangelis Karalis[2], Theodora Psaltopoulou[3], Vasiliki Vasileiou[4], Ioanna Charitaki[3], Tina Bagratuni[3], Vassiliki Ktena[4], Fotini Papandroulaki[4], Sentiljana Gumeni[5], Georgia N. Kassi[4], Ioannis P. Trougakos[5], Evangelos Terpos[3] & Meletios-Athanasios Dimopoulos[3]
[1]Endocrine Unit and Diabetes Center, Department of Clinical Therapeutics, Alexandra Hospital, School of Medicine, National and Kapodistrian University of Athens, Athens, Greece; [2] Faculty of Pharmacy, School of Health Sciences, National and Kapodistrian University of Athens, Athens, Greece; [3] Department of Clinical Therapeutics, Alexandra Hospital, School of Medicine, National and Kapodistrian University of Athens, Athens, Greece; [4] Department of Endocrinology, Alexandra Hospital, Athens, Greece; [5] Department of Cell Biology and Biophysics, Faculty of Biology, National and Kapodistrian University of Athens, Athens, Greece

Background
This is the first study, that aimed: a) to compare immune response, namely the kinetics of neutralizing antibodies (Nabs), after vaccination with BNT162b2 mRNA vaccine between patients with autoimmune thyroiditis and controls, and b) to investigate changes in thyroid function in healthy subjects with no history of thyroid dysfunction before and after vaccination.
Methods
The entire study consisted of two sub-studies. In the first sub-study, NAbs levels after BNT162b2 mRNA vaccination were compared between 56 patients with autoimmune thyroiditis and 56 age and gender-matched healthy controls from the day of the first vaccination until a period of up to three months after the second vaccination. In the second sub-study, thyroid hormones (T3, T4, TSH) and thyroid auto-antibodies levels (anti-TG, anti-TPO) of 72 healthy subjects with no history of thyroid disease were examined before (D1) and one month after completion of the second vaccination (D50).
Results
Among patients with autoimmune thyroiditis, the median neutralizing inhibition on D22, immediately before second vaccination, was 62.5%. One month later (D50), values increased to 96.7%, while three months after the second vaccination NAbs titers remained almost the same (94.5%). In the healthy group, median NAbs levels at D22 were 53.6%. On D50 the median inhibition values increased to 95.1%, while after three months they were 89.2%. The statistical analysis did not show significant differences between two groups (P-values 0.164, 0.390, 0.105 for D22, D50 and three months). Regarding changes in thyroid function, the mean value for T4 before vaccination was 89.797 nmol/l and one month after the second vaccination was 89.11 nmol/l (P-value=0.649). On D1 the mean T3 value was 1.464 nmol/l, which dropped to 1.389 nmol/l on D50 (P-value=0.004). For TSH, mean levels were 2.064 mIU/ml on D1 and fell to 1.840 mIU/ml one month after the second vaccination (P-value=0.037). Despite decrease, all thyroid hormone levels remained within the normal range. No changes were found for anti-TPO or anti-TG.
Conclsions
This study provided evidence that patients with autoimmune thyroiditis present similar immunological response to COVID-19 BNT162b2 mRNA vaccination with healthy subjects, while vaccination may affect thyroid function.

DOI: 10.1530/endoabs.81.P209

P210

Surgical outcomes and related complications in Graves' disease (GD)

Miguel Paja Fano[1,2], Ignacio Merlo-Pascual[3], Josune Rodríguez-Soto[3], Natalia C. Iglesias-Hernández[3], Jon Izquierdo-Coca[3], Iñigo Hernando-Alday[3], Ana J. Isusquiza-Etxezárraga[3], Estíbaliz Ugarte-Abásolo[3], Cristina Moreno-Rengel[3], Aitzol Lizarraga-Zufiaurre[3], Javier Espiga-

Alzola[3], M. Teresa Gutiérrez-Rodríguez[4], Amaya Expósito-Rodríguez[4] & Amelia Oleaga-Alday[3]
[1]OSI Bilbao-Basurto. Basurto University Hospital, Endocrinology, Bilbao, Spain; [2] Basque Country University (UPV-EHU), Medicine, Spain; [3] OSI Bilbao-Basurto. Basurto University Hospital, Endocrinology, Bilbao, Spain; [4] OSI Bilbao-Basurto. Basurto University Hospital, Endocrine Surgery, Bilbao, Spain

Despite being the most successful definitive treatment for GD and offering the best response in terms of quality of life, thyroidectomy is rarely performed worldwide. Few studies evaluate its complication rate and potential prognostic factors for complications. We report our last ten years' experience. Incidence of temporary and permanent hypoparathyroidism, temporary and permanent recurrent laryngeal nerve (RLN) injury and incidental malignancy were recorded, looking for predictors of their occurrence. Biochemical trends of TSI and TSH levels after surgery were also examined. From 1798 thyroid surgeries, 162 patients undergoing total thyroidectomy for GD were collected. Median age was 44.4 years and 78.4% were female. Thirty percent of the patients needed calcitriol at discharge, and one year later this rate was 5.2%. Twelve percent of patients had injury to one RLN following surgery, with permanent damage in 1.9%. Active Graves' orbitopathy (GO) was the second leading reason for surgery (26 cases). GO activity improved in 50% but worsened after thyroidectomy in 6 cases. Mean thyroid weight was 41.4 g and 13 glands showed incidental malignancy, all but one PTC. Prior to surgery, 94.8% of patients had measurable TSI titres (ELISA) and these were persistent 6 and 12 months after surgery in 86% and 62%, with lower titres. Median time to halve TSI titres was four months. One month after surgery, previously suppressed TSH was detectable in 75.2% of patients. There were no recurrences of hyperthyroidism. Univariate analysis showed that glandular weight, lower postoperative calcium, higher preoperative alkaline phosphatase, and parathyroid tissue in the surgical specimen were associated with immediate postoperative hypoparathyroidism, whereas higher TSI titres were associated with a higher incidence of RLN damage. Incidental carcinomas were associated with the presence of severe OG. In multivariate logistic regression, only perioperative PTH and calcium dynamics predicted the need for calcitriol, whereas preoperative [TSI] maintained the predictive value of RLN damage (OR per 1 IU/l: 1.07). OG lost predictive value for the detection of incidental cancers. Neither the finding of incidental malignancy nor the presence of parathyroid glands, nodular disease or germinal centres in histological specimen were associated with increased complication rates. Underused thyroidectomy is a safe alternative to radioiodine in GD, with a low rate of complications. It discloses occult carcinoma in 8% of GD. Surgical hypoparathyroidism is associated with perioperative calcium and PTH dynamics and this study finds a novel association between preoperative TSI level and transient LNR damage.

DOI: 10.1530/endoabs.81.P210

P211

SARS-CoV-2 Vaccine-Associated Subacute Thyroiditis: Insights from a Systematic Review

Silvia Ippolito[1], Daniela Gallo[1], Alessandro Rossini[2], Bohdan Patera[3], Nicola Lanzo[3], Gaia Francesca Maria Fazzino[1,3], Eliana Piantanida[1,3] & Maria Laura Tanda[1,3]
[1]ASST Sette Laghi, Endocrine Unit, Varese, Italy; [2] ASST Papa Giovanni XXIII, Endocrine Unit, Bergamo, Italy; [3] University of Insubria, Medicine and Surgery, Varese, Italy

Introduction
subacute thyroiditis (SAT) is an inflammatory disease of the thyroid gland causing transient thyrotoxicosis, characterized by neck pain and symptoms of thyroid hormones excess. Viral infections are considered the main trigger of SAT. SAT has also been described after vaccination against H1 N1 vaccine, seasonal influenza virus vaccine, Human Papillomavirus vaccine, and hepatitis B vaccination; more recently, a rising number of cases of SAT following SARS-CoV-2 vaccination has also been reported.
Purpose
perform a systematic review on published cases of subacute thyroiditis secondary to SARS-CoV-2 vaccination, to highlight main features and increase the awareness of this condition.
Methods
original reports of SAT developed after SARS-CoV-2 vaccination (mRNA, viral vector, or inactivated virus vaccines) were retrieved from a search of electronic databases. Individual patient data on demographics, medical history, type of vaccine, workup and therapies were collected. Wilcoxon rank-sum, Kruskal-Wallis and chi-squared tests were employed for comparisons.
Results
29 articles including 48 reports were retrieved, 3 additional cases evaluated by the Authors were described and included for analysis. Of the 51 patients, 38 (74.5%) were women, median age was 39.5 years (IQR 34-47). Patients developed SAT after a median of 10 days (IQR 4-14) after the vaccine shot. Baseline thyroid exams revealed thyrotoxicosis in 88.2% of patients, decreasing at 31.6% at follow-up. Corticosteroids were used in 56.4% of treated patients. Patients undergoing non-mRNA vaccines were most frequently Asian ($P=0.019$) and reported more frequently weight loss ($P=0.021$). All patients with a previous diagnosis of thyroid disease belonged to the mRNA vaccine group.
Conclusions
SARS-CoV-2 vaccine-associated SAT is a novel entity, that should be acknowledged by physicians. Previous history of thyroid disease may predispose to develop SAT after mRNA vaccines, but further studies and larger cohorts are needed to verify this suggestion. SARS-CoV-2 vaccine-associated SAT is usually of mild/moderate severity and could be easily treated in most cases, thus it should not raise any concern regarding the need to be vaccinated.

DOI: 10.1530/endoabs.81.P211

P212

Identifying the use of clinical and radiological parameters to assess moderate-severe Graves' Orbitopathy − a multi-centre analysis of the characteristics of patients with Graves' Orbitopathy

Nicole George[1], Vickie Lee[2], Claire Feeney[2], Kunwar Bhatia[2] & Amina Ali[1]
[1]Imperial College London, School of Medicine, London, United Kingdom; [2]Imperial College Healthcare NHS Trust, United Kingdom

Background
Early diagnosis and surveillance of Graves' Orbitopathy (GO) is essential to prevent severe, sight-threatening complications and long-term disability; therefore, it is highly desirable to identify risk factors and early predictors of severe disease. GO is clinically assessed using the Clinical Activity Score (CAS) and the EUGOGO Severity Scale (ESS), which are subjective, qualitative tests that are used to evaluate the activity and severity at the anterior orbit. However, we propose the use of radiological characteristics, such as specific muscle enlargement, to predict the progression to severe disease. Therefore, we evaluated the clinical and radiological features of GO in patients presenting to multi-centre multidisciplinary teams in London and identified factors predictive of severe disease.
Method
A retrospective patient-cohort study of 356 patients referred to three multi-disciplinary (MDT) clinics in London between 2012 and 2021 was investigated. Patient characteristics were statistically analysed to investigate group-wise differences and correlations to help predict subsequent disease activity. From this analysis, odds ratios were produced for both clinical and radiological parameters.
Results
Median age was 46.0 years (interquartile range: 36-55), 79.2% female, 41.2% Asian. Out of 356 patients, 43.0% had moderate-severe or sight-threatening disease. On odds ratio analysis, clinical parameters of older age (OR 1.96 (1.07-3.59)), male gender (OR 2.03 (1.19-3.45)), hyperthyroidism (OR 3.64 (2.08-6.38)) were associated with more severe disease. On analysis of radiological parameters, superior rectus-levator complex muscle involvement was also associated with more severe disease (OR 1.90 (1.03-3.50)).
Conclusion
These results suggest that cases of higher severity disease were more prevalent in the older demographic and the male population. The presence of radiological superior rectus-levator muscle involvement was associated with a higher incidence of moderate-to-severe disease. This provides an additional significant radiological criterion for diagnosing moderate-to-severe disease and providing all-important early intervention for these patients. This highlights the merit of both clinical and radiological assessment for the diagnosis and surveillance of Graves' Ophthalmology.

DOI: 10.1530/endoabs.81.P212

P213

Tuberculosis and myxedema coma − clinical case

Miguel Saraiva, Ariana Maia, Guilherme Assunção, Cláudia Amaral, Cláudia Freitas & André Couto de Carvalho

Centro Hospitalar Universitário do Porto, Endocrinology, Diabetes and Metabolism, Porto, Portugal

Introduction
Myxedema coma is the ultimate stage of severe long-standing hypothyroidism, representing a true endocrinological emergency. Many precipitating factors have been identified, including the initiation of certain drugs.
Case report
An 89-year-old woman was admitted to our emergency department due to an inaugural seizure. There was a history of progressive functional deterioration in the last 7 weeks, short after being diagnosed with lymph node tuberculosis (8 weeks before). There was no known history of previous thyroid disease. She suffered from atrial fibrillation, under chronic treatment with amiodarone, and she had undergone scalp radiotherapy for *tinea capitis* during her childhood. The patient presented with marked psychomotor lentification, hypothermia (33.4º C), hypotension (75/25 mmHg) and hypoglycemia (41 mg/dl). Her blood sample revealed normocytic normochromic anemia (9.5 g/dl), mild hyponatremia (133 mmol/l), marked rhabdomyolysis (creatine kinase 610.6 U/l; myoglobin 789.0 µg/L) and primary hypothyroidism (TSH 288.0 µUI/ml; fT4 0.23 ng/dl) with negative antithyroid antibodies titer. There was no evidence of respiratory failure, ongoing acute infection or ischemic event. The brain CT revealed signs of chronic ischemic leukoencephalopathy. Confirming the diagnosis and its severity, the patient scored a total of 95 points in the Diagnostic Scoring System for Myxedema Coma. It is likely that the patient's hypothyroidism was due to a *Wolf-Chaikoff* effect to amiodarone but the precipitating factor myxedema coma seemed to be the initiation of the antitubercular medication, namely rifampicin, which is a known inducer of CYP450 with a potential effect by increasing thyroid hormones' metabolism. During hospitalization, the patient responded well to levothyroxine supplementation, gradually resolving every organic disfunction and was discharged under oral levothyroxine, 36 days after admission.
Discussion
Myxedema coma is a serious clinical condition with high morbidity and mortality. When introducing medications that may alter the metabolism of thyroid hormones, namely CYP450 inducers or inhibitors, it is important to monitor thyroid function. This case highlights that this should be a routine procedure not only for patients with known hypothyroidism but also for those with risk factors for thyroid dysfunction.

DOI: 10.1530/endoabs.81.P213

P214

Severe refractory active thyroid eye disease: an unmet clinical need in Europe

Ploutarchos Tzoulis[1,2] & Chrysoula Dosiou[3]
[1]IASO General Clinic, Department of Endocrinology, Marousi, Greece; [2] University College London, Department of Experimental and Translational Medicine, London, United Kingdom; [3] Stanford University School of Medicine, Division of Endocrinology, Stanford CA, United States

Introduction
Moderate to severe thyroid eye disease (TED) has a significant impact on quality of life. In some cases, TED is resistant to systemic glucocorticoids, the mainstay of treatment since the 1950s, requiring alternative therapies. We describe here a patient with active severe TED who is refractory to various treatments.
Case presentation
A 48-year-old non-smoker male, with a long history of psoriasis, vitiligo and atrophic gastritis, presented in May 2019 with Graves' thyrotoxicosis and was treated with methimazole. In July 2020, following 14 months of euthyroidism, he started experiencing eye pain, proptosis, and diplopia, with a clinical activity score (CAS) of 6/7. TSI (thyroid stimulated immunoglobulin) levels were 16.2 IU/l (normal range $<$ 1.75 IU/l). He was treated with oral methylprednisolone for 3 months, showing a small response in eyelid swelling, but developed a 15 kg weight gain, proximal myopathy, peripheral edema, restlessness, and insomnia. In November 2020, he underwent total thyroidectomy. After a brief period of hypothyroidism, which was corrected with levothyroxine, he had TED improvement (CAS 4/7) and TSI normalization. In March 2021, a few weeks after COVID vaccination, his TED deteriorated significantly (CAS 6/7), while TSI rose to 4.45 IU/l. Administration of a total dose of 4.5 gr methylprednisolone in 12 weekly intravenous infusions resulted in slight reduction of eyelid swelling, some pain relief, and TSI normalization. Throughout this period, he received artificial tears and oral selenium, while he remained euthyroid. However, he gradually developed worsening diplopia and several side effects, including a 7 kg weight gain, irritability, and insomnia. Tocilizumab, a monoclonal antibody against interleukin-6 (IL-6) receptor, was started intravenously (8 mg/kg). After three monthly infusions, there was significant improvement in eyelid swelling and pain, but no effect on proptosis and diplopia (CAS 5/7). Severe arthralgias and intractable pruritus necessitated discontinuation of treatment.
Conclusion
This case illustrates the therapeutic challenges around severe refractory active TED. Glucocorticoids and tocilizumab improved soft-tissue inflammation, but had minimal impact on proptosis and diplopia. There is an unmet clinical need in Europe for therapies with efficacy against proptosis and diplopia, such as teprotumumab, a monoclonal antibody against the insulin-like growth factor-I receptor. Teprotumumab, approved in 2020 by the US Food and Drug Administration for TED, is still not routinely available in Europe. In a rapidly evolving treatment landscape of TED, it is essential to ensure patient access to therapeutic advances targeting the underlying pathogenetic mechanisms in order to improve patient outcomes.

DOI: 10.1530/endoabs.81.P214

P215

Is there a familial predisposition to severe amiodarone-induced thyrotoxicosis? Report of two cases

Blanca Bernaldo Madrid[1], Sara Mera Carreiro[1], Xavier Pérez Candel[1], Celia Lopez Nevado[1], Patricia Espinosa De Los Monteros[1], Fernando Hernández Olmeda[1], Santiago Ochagavia Camara[1], Isabel Runkle[1], Jorge Gabriel Ruiz Sánchez[2] & Mario Pazos Guerra[1]
[1]Hospital Clinico Universitario San Carlos, Madrid, Spain; [2] Hospital Universitario Fundación Jiménez Díaz, Madrid, Spain

Introduction
Amiodarone-induced thyrotoxicosis (AIT) occurs in up to 6% of patients taking this medication in iodine sufficient areas and in up to 10% of patients in iodine deficient areas and has a high rate of mortality, that can reach 50% in untreated severe forms. There are two main types (1 and 2) described, although usually we find mixed types, with both components. Below, we describe the cases of two brothers that developed severe mixed forms of amiodarone-induced thyrotoxicosis.
Case-Report
The first case was a 61-year-old male with ischemic cardiomyopathy and atrial fibrillation which was successfully ablated in 2017 and was treated with amiodarone until September 2018. In April 2019, he was admitted to hospital because of a severe mixed AIT with initially good response to medication, which enabled discharge home with continued medical management. However, he was immediately re-admitted to the hospital due to worsening symptoms and increasing levels of thyroid hormones and required amiodarone continuous infusion and urgent total thyroidectomy. The second case was a 60-year-old male with recurrence of atrial fibrillation successfully ablated a few years prior and also treated with amiodarone until December 2020. In August 2021 he began to experience palpitations and independently decided to start amiodarone for 2 weeks. Two months later he was admitted with severe AIT, despite medical treatment. He was treated with amiodarone continuous infusion and two sessions of plasmapheresis before total thyroidectomy.
Discussion
We report two cases in the same family with severe mixed AIT. They both needed urgent thyroidectomy and amiodarone continuous infusion, useful four days before surgery to rapidly block conversion between T4 and T3, decreasing the active form of the hormone. Furthermore, in one of the cases plasmapheresis was used, being a procedure that decreases blood levels of thyroid hormone up to 40-50%.
Although both cases could be explained by underlying thyroid autonomy or iodine deficiency and a Job-Basedow phenomenon, we can't rule out the existence of familiar predisposition to AIT. There is not literature describing genetic alterations potentially involved in increasing production of thyroid hormones secondary to amiodarone administration. For that reason, it would be useful to report those familiar cases of AIT, from now on, so that we can investigate which factors are involved.

DOI: 10.1530/endoabs.81.P215

P216

Keep calm and call the surgeon: a case series of urgent thyroidectomy in thyrotoxicosis

Tanja Rezic[1], Tomislav Novosel[2], Mirjana Kardum-Pejic[1], Ivan Oreski[1], Drago Boscic[2], Srecko Marusic[1] & Vlatka Pandzic Jaksic[1]

[1]Clinical Hospital Dubrava, Endocrinology, Diabetes and Clinical Pharmacology, Zagreb, Croatia; [2] Clinical Hospital Dubrava, Zagreb, Croatia

Introduction
The standard management of Graves' disease includes initial use of antithyroid drugs, while radioactive iodine ablation or thyroid surgery are later definitive treatment options. Management of thyrotoxicosis secondary to the use of amiodarone can be challenging as patients may not promptly respond to antithyroid or corticosteroid therapy, and thyrotoxicosis may be more harmful in those patients owing to the underlying cardiac disease. In rare thyrotoxicosis cases, conventional treatment fails, and urgent thyroidectomy is the way to restore euthyroid state. Case series: We report three patients with thyrotoxicosis who underwent successful urgent thyroidectomy with rapid preoperative preparation. Two patients with Graves' disease were treated with methimazole which led to severe agranulocytosis in the first, and severe cholestatic hepatotoxicity in the second patient. In addition to propranolol and corticosteroids, potassium iodine (Lugol's solution) was used to render these patients euthyroid before thyroidectomy. Finally, third patient with severe cardiomyopathy requiring cardiac transplantation presented with type II amiodarone-induced thyrotoxicosis. Plasma exchange was performed to reduce thyroid hormones and to allow stabilisation of this patient prior to urgent thyroid surgery.
Conclusion
Urgent thyroidectomy is the only option for treatment of thyrotoxicosis in selected patients and careful preoperative preparation is essential to optimise surgical outcomes.

DOI: 10.1530/endoabs.81.P216

P217

A combining pre-surgical thyroid risk score (TRS) for nodules with indeterminate cytology

Carla Colombo[1], Guia Vannucchi[2], Marina Muzza[3], Gabriele Pogliaghi[4], Sonia Palazzo[5], Gianlorenzo Dionigi[6], Luca Persani[7], Giacomo Gazzano[5] & Laura Fugazzola[1]
[1]Department of Pathophysiology and Transplantation, University of Milan; Division of Endocrine and Metabolic Diseases, Istituto Auxologico Italiano IRCCS, Milan, Italy; [2] Division of Endocrine and Metabolic Diseases, Istituto Auxologico Italiano IRCCS, Milan, Italy; [3] Laboratory of Endocrine and Metabolic Research, Istituto Auxologico Italiano IRCCS Milan, Milan, Italy; [4] Department of Pathophysiology and Transplantation, University of Milan;Laboratory of Endocrine and Metabolic Research, Istituto Auxologico Italiano IRCCS, Milan, Italy; [5] Pathology Unit, Istituto Auxologico Italiano IRCCS, Milan, Italy, Milan, Italy; [6] Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy; Endocrine Surgery Unit, Istituto Auxologico Italiano IRCCS, Milan, Milan, Italy; [7] Department of Medical Biotechnology and Translational Medicine, University of Milan, Milan, Italy; Division of Endocrine and Metabolic Diseases, Istituto Auxologico Italiano IRCCS; Laboratory of Endocrine and Metabolic Research, Istituto Auxologico Italiano IRCCS, Milan, Italy

Background
Cytology is the gold standard method for the differential diagnosis of thyroid nodules, though 25−30% of them are classified as indeterminate and, in some cases, surgery is required for a definitive diagnosis.
Aim
In order to reduce unnecessary thyroid surgeries, we set up a 'thyroid risk score' (TRS) to increase the diagnostic accuracy in a large series of patients with indeterminate cytology and to apply it to a validation series.
Methods
The pre-surgical TRS derived from the sum of the scores assigned at cytology, namely EU-TIRADS classification, nodule measurement, and molecular characterization (24 different genetic alterations, including point mutations and gene fusions, analysed by our customized assay PTC-MA assay until recently and, currently, from a Next-Generation Sequencing-NGS panel). We prospectively tested 136 indeterminate thyroid nodules for the model evaluation, while further 50 patients have been enrolled to date for the model validation.
Results
66/136 analyzed nodules underwent surgery and 20/66 (30.3%) were malignant. The risk of malignancy (ROM) increased paralleling the score: in the category >4 and ≤ 6 (low suspicion), $>6 \leq 8$ (intermediate suspicion), and >8 (high suspicion) ROM was 10, 47 and 100%, respectively. ROC curves selected the score >6.5 as the best threshold to differentiate between malignant and benign nodules ($P< 0.001$). The TRS $>$ 6.5 had a better performance than the single parameters evaluated separately, with an accuracy of 77% and 82% upon inclusion of noninvasive follicular thyroid neoplasm with papillary-like nuclear features among malignant or benign cases, respectively. In the new series, 12/50 nodules with TRS $>$ 6 will undergo surgery in order to confirm TRS cut-off.
Conclusions
In conclusion, for the first time, we generated and applied a score combining a cost-effective molecular assay with already validated tools, harboring different specificities and sensitivities. The combination of different parameters reduced the number of false negatives inherent to each classification system. The TRS $>$ 6.5 was highly suggestive for malignancy and retained a high accuracy in the identification of patients to be submitted to surgery. A proper role of the TRS can be also predicted in the evaluation of large nodules routed to surgery in most cases. Indeed, in the era of mini-invasive procedures, a low TRS could favor the possibility to submit older patients and cases with co-morbidities to these techniques. The validation series will give more insights into the accuracy of our present TRS cut-off.

DOI: 10.1530/endoabs.81.P217

P218

Results of radioiodine remnant ablation with 30 mci dose in low-risk differentiated thyroid carcinoma (dtc)

Irene De Lara-Rodriguez[1], Suset Dueñas Disotuar[1], Ana R. Romero Lluch[1], Juan Luis Tirado-Hospital[2], Ana Piñar Gutiérrez[1] & Elena Navarro[1]
[1]Virgen del Rocío University Hospital, Endocrinology, Sevilla, Spain; [2]Virgen del Rocío University Hospital, Nuclear Medicine, Sevilla, Spain

Background
The indication of ablation with I131 in low-risk DTC is controversial. The exact dose needed for thyroid remnant ablation is still a matter of debate in low-risk DTC patients. However, low dose has been found to be equally effective as high dose in terms of recurrence rate in recent studies. Taking this into account the current trend is to administer lower doses, although some studies describe a higher rate of retreatment.
Aims
1. To examine whether there is difference in the response to treatment with 30 vs $>$30 mCi dose in patients with low-risk DTC.
2. To study if there are predictor variables for needing a second I131 dose in low-risk DTC

Material and method
This is a cohort study of pre-ablation low-risk DTC patients undergoing treatment with 30 mCi vs $>$ 30 mCi of 131I between 2017 and 2020. Tumor variables, biochemical characteristics, response after ablation (at one year), and need for a second 131I dose were analyzed. Qualitative variables are expressed as n(%) and quantitative variables as median [IQR]. We used Chi-square and the Kruskal-Wallis test for independent samples to compare both groups.
Results
Both groups are comparable. There were no differences in the type of response and the need for a second dose between groups. However, pre-ablation Tg, stimulated Tg, and pre-ablation AbTg were significantly higher in patients requiring a second dose (P 0.01, P 0.001, and P 0.04, respectively).

		30 mCi	>30 mCi
Median dose (mCi)		30[30-30]	80[80-80]
N		74	62
Women		64(86.5%)	50(80.6%)
Age (years)		55[42-64]	54[45-66]
Tumor type	Papillary	73(98.6%)	58(93.5%)
	Follicular	1(1.4%)	3(4.6%)
Tumor size	T1	34(46%)	23(37%)
	T2	33(44.5%)	30(48.3%)
Excellent response		53(71.7%)	48(77.4%)
Second dose		16(21.6%)	9(14.5%)

Second dose	pre-ablation Tg (ng/ml)	stimulated Tg (ng/ml)	pre-ablation AbTg (UI/ml)
No	0.20 [0.04-0.79]	0.55 [0.06-1.70]	10[10-11.7]
Yes	0.44[0.22-1.54]	2.30[0.79-5.53]	10.35[10-196]

Conclusions
In low-risk DTC patients, the response to treatment with 30 mCi is like that with higher doses. High pre-ablation Tg and AbTg should guide us to use higher doses of I131.

DOI: 10.1530/endoabs.81.P218

P219

Utility of liquid biopsy in indeterminate thyroid nodules

Soham Tarafdar, Susmita Dutta, Pradip Mukhopadhyay, Nitai P. Bhattacharyya & Sujoy Ghosh
IPGME&R and SSKM Hospital, Dept of Endocrinology and Metabolism, Kolkata, India

Background
Indeterminate thyroid nodules pose a diagnostic dilemma and the patients often undergo unnecessary surgeries or repeat surgery. Currently different molecular methods for detection of driver mutations are being used for better characterisation of these nodules. These methods are costly and not widely available all over the world. Currently use of liquid biopsy by measurement of cell-free DNA (cfDNA) levels from plasma has been useful in diagnosis and follow up of cancers of other organs/tissues. We have analysed cfDNA levels in patients with thyroid nodules to explore the possibility of establishing a cut-off for identification of malignancy and its application in the indeterminate category of nodules.
Methods
Patients underwent ultrasonography (USG) and USG-guided fine needle aspiration as well as surgery, where indicated. CfDNA was extracted from plasma by using a commercially available kit. Quantification and purity of the isolated cfDNA was measured by determining absorbance at 260 nm and 280 nm in duplicate using a Nano Drop Spectrophotometer. Surgical biopsy and histopathology were taken as gold standard for diagnosis. In initial analysis (determination of cut-off), cfDNA levels were compared between Bethesda 2 and Bethesda 5 &6 to establish a cut-off value that could differentiate malignant from benign nodules. In the subsequent analysis, the aforementioned cut-off was applied (validation of cut-off) to those with indeterminate nodules to check ability to predict malignancy.
Results
Fine needle aspiration ($n=207$) yielded patients with Bethesda 2 ($n=112$) Bethesda 5 & 6 ($n=34$) who underwent histopathological confirmation. Cell-free DNA levels in these 2 groups were 23.09 $\pm$ 8.47 and 90.26 $\pm$ 9.00 (ng/ml) respectively. A cfDNA cut-off of 64.05 ng/ml, with area under the curve of 0.993 (95% CI, 0.98-1.0) with 100% sensitivity and 96.4% specificity was established to identify malignant lesions. Indeterminate group (Bethesda 3 & 4 $n=61$) underwent surgery (malignant $n=33$), (benign $n=28$), and using the previously identified cut-off for cfDNA, we were able to identify malignant lesions with a sensitivity of 100% and specificity of 96.43%. There was a very strong agreement between cfDNA-based classification with histopathology-based classification of benign and malignant nodules (Cohen's kappa 0.96; $P < 0.001$).
Conclusion
Liquid biopsy by using plasma cfDNA could be a useful test in differentiating benign and malignant nodules in indeterminate category and help in better management.

DOI: 10.1530/endoabs.81.P219

P220

Alpelisib-induced thyroiditis in a patient with metastatic breast carcinoma

Anusha Prem Kumar[1], Calvin Flynn[2], Michaela J Higgins[2], Rachel K Crowley[1], Donal O'Shea[1] & Aoife Garrahy[1]
[1]St. Vincent's University Hospital, Department of Endocrinology, Ireland; [2]St. Vincent's University Hospital, Department of Oncology, Ireland

Background
Alpelisib is a novel phosphotidylinositol 3-kinase (PI3K) inhibitor which, in combination with fulvestrant, has been shown to increase progression-free survival in patients with HR+/HER2-/*PI3KCA* mutated advanced breast cancer[1]. Hyperglycaemia, including alpelisib-induced diabetic ketoacidosis is a known adverse effect, along with rash, diarrhoea and stomatitis. No other associated endocrinopathy has been reported to date. Case presentation: We present the case of a 50-year-old woman with metastatic breast cancer was referred from the Oncology service with a two-week history of fatigue, tremors, palpitations, sweats and myalgia, associated with raised free T4 and free T3, and suppressed TSH. Two months prior, she had been commenced on the novel Phosphotidylinositol 3-kinase (PI3K) inhibitor, alpelisib, combined with fulvestrant, due to progression of her disease on first and second-line therapies. Alpelisib was held once abnormal thyroid function was noted. On examination the patient was tachycardic and tremulous. The thyroid was tender to palpation without a discernible goitre. TSH <0.02 mIU/l(0.27-4.20), FT4 62.4 pmol/l (12.0-22.0), FT3 25.1 pmol/l (3.1-6.8). Anti-TSH receptor and anti-thyroid peroxidase antibodies were undetectable. She was commenced on propanolol for symptom relief. Ultrasound thyroid showed a diffusely heterogenous gland without increased vascularity. Technetium 99 m radionuclide uptake scan showed diffusely reduced radiotracer uptake, consistent with thyroiditis. Although her hyperthyroidism initially improved with cessation of alpelisib, it deteriorated again with recommencement. The patient was commenced on prednisolone 30 mg once daily. This was weaned as her thyroid function improved, allowing for recommencement of alpelisib treatment. She currently remains euthyroid. Summary: This is the first reported case of alpelisib-induced thyroiditis in a patient treated for metastatic breast carcinoma. We have demonstrated efficacy in treatment with steroid therapy, allowing for continued treatment with this agent. Activation of the PI3K pathway has been shown to inhibit sodium-iodide symporter expression and function within thyroid follicular cells[2]. However, the pathophysiology of alpelisib-induced thyroiditis remains to be elucidated.
Bibliography
1. Andre, F., *et al*., Alpelisib for PIK3CA-Mutated, Hormone Receptor-Positive Advanced Breast Cancer. N Engl J Med, 2019. **380**(20): p. 1929-1940.
2. Garcia, B. and P. Santisteban, PI3K is involved in the IGF-I inhibition of TSH-induced sodium/iodide symporter gene expression. Mol Endocrinol, 2002. **16**(2): p. 342-52.

DOI: 10.1530/endoabs.81.P220

P221

Levothyroxine absorption test results in patients with resistant hypothyroidism

Anis Grassa, Ibtissem Oueslati, Elyes Kamoun, Meriem Yazidi & Melika Chihaoui
La Rabta University hospital, Department of Endocrinology, Tunis, Tunisia

Introduction
Hypothyroidism is a very common condition, and its treatment is relatively easy with levothyroxine (LT4). However, cases of resistant hypothyroidism were reported despite high doses of levothyroxine. The aim of this study was to evaluate the usefulness of the levothyroxine absorption test to confirm or exclude a disorder of thyroid hormone absorption.
Methods
This was a retrospective study including patients who were admitted to our department between January 2018 and December 2021 for resistant hypothyroidism under high-dose of levothyroxine ($\geq$ 2.7µg/kg/day). Levothyroxine absorption test was performed on all patients. The percentage of levothyroxine absorption was calculated using the following formula: % LT4 absorption = [(peak ΔT4 $\times$ volume distribution) / administered dose of LT4 (µg)] $\times$ 100 (Volume distribution (dL)=4.42 $\times$ body mass index). Normal absorption was defied by a % LT4 absorption > 60 %.
Results
Seven patients (5 women and 2 men) were enrolled in this study. Their mean age was of 39 $\pm$ 11.3 years [27-62]. Their mean body weight was 85.4 kg [72-98] with a mean body mass index of 30.3 kg/m^2 [25.4-36]. The average duration of hypothyroidism was 10 years [2-20]. The mean dose of levothyroxine was 5.3 µg/kg/day. At baseline (T0), the mean TSH level was 278.8 mIU/l (nr: 0.35- 4.95) and the mean FT4 level was 0.59 ng/dl (nr: 0.7-1.5). During the levothyroxine absorption test, the mean peak of FT4 was 0.80 ng/dl. The average % LT4 absorption was 4.5%. It was < 60% in all patients consistent with the diagnosis of malabsorption. Etiological investigations showed negative celiac disease serology for all patients and a helicobacter pylori gastritis in six patients.
Conclusion
Our results illustrate the interest of the levothyroxine absorption test to confirm the diagnosis of malabsorption and avoid diagnosing wrongly a pseudo-malabsorption.

DOI: 10.1530/endoabs.81.P221

P222

Risk factors for acute kidney injury in patiens with severe hypothyroidism

Adnan Batman[1], M. Masum Canat[2], Emre Sedar Saygili[3], Ender Besler[4], Duygu Yildiz[5], Feyza Yener Ozturk[2] & Yuksel Altuntas[2]
[1]Koc University, Endocrinology and Metabolism, Istanbul, Turkey; [2]University of Health Sciences Turkey, Sisli Etfal Training and Research Hospital, Endocrinology and Metabolism, Istanbul, Turkey; [3]Canakkale 18 Mart University, Endocrinology and Metabolism, Istanbul, Turkey; [4]University of Health Sciences Turkey, Sisli Etfal Training and Research Hospital, Department of Internal Medicine, Istanbul, Turkey; [5]Siirt Training and Research Hospital, Endocrinology and Metabolism, Siirt, Turkey

Objective
This study aims to investigate the factors affecting development of acute kidney injury (AKI) due to severe hypothyroidism.
Methods
This retrospective observational study involved patients with primary hypothyroidism and thyroid stimulating hormone (TSH) levels of more than 50 mIU/l at their review in the endocrinology outpatient clinic, between January 2015 and April 2021. Factors affecting the development of AKI were examined by logistic regression analysis.
Results
A total of 100 patients, 20 (11 male (M), 9 female (F)) in the AKI (case) group and 80 (23 M, 57 F) patients in control group, were included in our study. The median age of the case group (56 years, interquartile range (IQR) 44.3−68.5) was significantly higher than the control group (49 years, IQR 32.3−60; $P=0.027$), and the ratio of males to females was significantly higher in the case group ($P=0.001$). Multivariate logistic regression analyses showed that hypothyroidism diagnosed after the age of 60 years (odds ratio (OR) 59.674, 95% confidence intervals (CI) 5.955−598.031; $P=0.001$), free triiodothyronine (FT3) $<$ 1.3 pg/ml (OR 17.151, 95% CI 2.491−118.089; $P=0.004$) and creatine kinase (CK) $>$ 1000 U/l (OR 1.522, 95% CI 1.602−82.848; $P=0.015$) were predictors for the development of AKI due to severe hypothyroidism (Table 1).
Conclusion
We recommend close follow-up and monitoring of patients with AKI caused by severe hypothyroidism if aged $>$ 60 years, CK $>$ 1000 U/l or FT3 $<$ 1.3 pg/ml.

DOI: 10.1530/endoabs.81.P222

P223

Assessment of the Quality of life in patients with well-controlled primary hypothyroidism: is there a relationship between quality of life and the TSH level?

Chayma Belhadj Slimane, Ibtissem Oueslati, Amani Terzi, Meriem Yazidi & Melika Chihaoui
La Rabta University Hospital, Department of Endocrinology, Tunis, Tunisia

Introduction
Poorly controlled hypothyroidism is a chronic disease frequently associated with an impaired quality of life (QoL). However, persistent symptoms may be observed in well-controlled hypothyroid patients, impacting their QoL. The aim of our study was to assess the QoL in patients with well-controlled primary hypothyroidism and to evaluate the relationship between the TSH level and the QoL.
Methods
A cross-sectional study was conducted in the outpatient clinic of our department in December 2021. Patients with well-controlled primary hypothyroidism (TSH level between 0.35-4.94 mIU/l), and aged less than 65 years were enrolled in this study. Clinical and paraclinical data were collected from medical records. QoL was assessed using the SF36 questionnaire.
Results
Seventy patients (65 women and 5 men) were enrolled in this study. Their mean age was of 51.2 ± 9.6 years. The mean duration of hypothyroidism was of 8.4 ± 6.7 years. Primary hypothyroidism was secondary to Hashimoto's thyroiditis, thyroidectomy, and radioactive iodine therapy in 58%, 23%, and 14% of cases, respectively. The average dose of levothyroxine was of 97.32µg/day (25-225). Mental health score ($r=$-0.24, $P=0.045$) and social role functioning score ($r=$-0.257, $P=0.032$) were negatively correlated with the TSH level. The QoL was good in 52% of patients and moderate to poor in 48% of patients. The mean TSH level was significantly lower in patients with good QoL than in those with moderate to poor QoL ($P=0.024$). On the other hand, role limitation due to emotional problems score and the SF36 total score were significantly higher in patients with TSH level $<$ 2.5 mIU/l than in those with a TSH level $\geq$2.5 mIU/l. A TSH level $<$ 2.5 mIU/l was significantly associated with a better QoL (Odds Ratio=2.83, $P=0.035$, 95% CI: 1.06-7.58).
Conclusion
In patients with well-controlled primary hypothyroidism, mental health and social role functioning scores were negatively correlated with TSH level. A TSH level $<$ 2.5 mIU/l was positively associated with a better QoL. However, many other factors may impact the QoL of patients with hypothyroidism. Therefore, further studies involving larger sample sizes would be useful to confirm our findings.

DOI: 10.1530/endoabs.81.P223

P224

Diagnosis of subacute thyroiditis (SAT) in 2021, during COVID-19 vaccination: observation in a single private secondary endocrine centre in the Savona district, Liguria, Italy

Massimo Giusti & Marilena Sidoti
Endocrine Unit, Priamar Clinical and Diagnostic Centre, Savona, Italy

SAT due to viral infections is a cause of thyrotoxicosis, neck pain and tenderness on palpation. In the COVID-19 era, SAT seems to be a manifestation of the disease which occurs during SARS-CoV-2 infection. In 2021, some SAT cases were reported after COVID-19 vaccination. We reviewed the incidence of SAT from 2000 to 2021. In the Savona district vaccination of the general population started in February 2021 and progressively involved fragile, healthy elderly, adult and young-adult subjects. By the end of 2021, about 80% of adults in the Savona district had received at least two doses of COVID-19 vaccines. Electronic records from June to December in each year from 2000 to 2020 were searched. From 8115 medical files, 51 diagnoses of SAT were retrieved (35 females). In the corresponding period in 2021, SAT was diagnosed in 7 females after COVID-19 vaccination. From 2020 to 2021, 0.6% of patients in our centre had SAT and SAT occurred at the median age of 45 years (IQR 38-52) with an incidence of 2 cases/year (1-3). The long-term evolution of the disease was known in

Table 1 Univariate and multivariate binary logistic regression analysis

	Univariate binary logistic regression				Multivariate binary logistic regression			
		95% CI				95% CI		
Variable:	OR	Lower	Upper	p	OR	Lower	Upper	p
Gender (male)	0.330	0.121	0.902	0.031*				
Age $>$ 60 years	0.222	0.080	0.621	0.004*				
Age $>$ 60 years at diagnosis of hypothyroidism	0.127	0.035	0.462	0.002*	59.674	5.955	598.031	0.001*
DM	0.156	0.042	0.580	0.006*				
HT	0.074	0.023	0.235	$<$0.001*				
Hyperuricaemia	0.110	0.024	0.503	0.004*				
CK $>$ 1000 U/l	0.246	0.082	0.739	0.012*	11.522	1.602	82.848	0.015*
FT3 $<$ 1.3 pg/ml	0.080	0.019	0.345	0.001*	17.151	2.491	118.089	0.004*
FT4 $<$ 0.2 ng/dl	0.241	0.083	0.700	0.009*				
Statin use	0.120	0.026	0.557	0.007*				

*OR: odds ratio; CI: confidence interval; DM: diabetes mellitus; HT: hypertension; CK: creatine kinase; FT4: free thyroxine; FT3: free triiodothyronine. *Statistically significant ($P<$ 0.05).*

25 cases and full thyroid recovery or chronic thyroiditis/hypothyroidism were observed in 72% and 28% of cases, respectively. From June to December 2021, the percentage of SAT in files was 1.5%. SAT diagnoses increased ($P=0.03$) in 2021 in comparison with the 2000-2020 period. The median age of SAT patients in 2021 (54 years; 50-61) was higher ($P=0.05$) than in the 2000-2020 period. To date, 6 women have been followed up for 2-4 months. In 2 women, a decrease in thyroid volume was noted, while in 4, TSH was suppressed or increased; in the remaining 2, L-T4 was ongoing. Pain, palpitation, fatigue and sweating disappeared after prednisone/NSAIDs discontinuation. To date, 19 cases (91% females; median age 40 years) of SAT after COVID-19 vaccinations have been described in the literature, with sub-clinical, normal or increased thyroid function in about 29%, 53% and 12% of cases, respectively, during follow-up. Our findings and the literature data indicate that SAT after COVID-19 vaccination is more frequent in females and at greater age than that occurs in other virus-related SAT cases. In our experience, thyroid function remains undefined after 2-4 months. Our observation of a local increase in SAT during the 2021 COVID-19 vaccination campaign indicates that physicians should be aware of this infrequent side effect, which must be considered and monitored after COVID-19 vaccination.

DOI: 10.1530/endoabs.81.P224

P225

Comparison in lipid parameters before and after L-thyroxine treatment in subclinical hypothyroidism according to the presence of thyroid peroxidase antibodies

Valentina Velkoska Nakova[1], Brankica Krstevska[2], Katerina Cheshlaroska Markushoska[3], Sasha Jovanovska Mishevska[4] & Tatjana Milenkovic[4]
[1]Clinical Hospital, Faculty of Medical Science, University Goce Delcev, Internal Medicine, Stip, Macedonia; [2] Internal Medical Center "Srce", Skopje, Macedonia; [3] General Hospital "Borka Taleski", Internal Medicine, Prilep, Macedonia; [4] University Clinic of Endocrinology, Diabetes and Metabolic Disorders, Skopje, Macedonia

Objective
Subclinical hypothyroidism (ScH) is a common condition and may be associated with dyslipidemia. We investigated the effect of levothyroxine therapy (L-T4) on lipid parameters in patients with a mild form of subclinical hypothyroidism according to the presence of thyroid peroxidase antibodies (anti-TPO antibodies).
Material and methods
Fifty-seven patients with newly diagnosed ScH (TSH levels between upper reference value and 10 mIU/l with normal FT4 and FT3 values) with indications for L-T4 therapy were included in the study. Lipid parameters and presence of anti-TPO antibodies were evaluated at the moment of diagnosis and after 6 months euthyroid stage.
Results
Average value of TSH was 8.1 $\pm$1.9 mIU/l. Thyroid substitution therapy significantly decreased total cholesterol and LDL-C, and increased HDL-C (5.6$\pm$ 0.9 vs. 5.3$\pm$1.1; 3.4$\pm$1.0 vs. 3.2$\pm$1.1; 1.5$\pm$0.5 vs. 1.6$\pm$0.5 mmol/l, $P<0.05$ respectively). Statistically significant decrease in total cholesterol, total cholesterol/HDL-C, and, LDL-C/HDL-C were observed in patients with positive anti-TPO antibodies after 6 months euthyroid state (5.5$\pm$1.1 vs 5.3$\pm$ 0.9 mmol/l; 3.9$\pm$1.5 vs. 3.5$\pm$1.0; 2.5$\pm$1.2 vs. 2.2$\pm$0.8, $P<0.5$ respectively). There was not statistically significant differences in lipid profile in patients with negative anti-TPO antibodies before and after L-T4 treatment.
Conclusion
The effect of the thyroid substitution therapy on lipid parameters was more pronounced in patients with mild ScH and positive thyroid antibodies. Patients with mild ScH and positive anti-TPO antibodies may benefit of L-T4 treatment even in the lower TSH values.
Key words: subclinical hypothyroidism, thyroid peroxidase antibodies, levothyroxine therapy

DOI: 10.1530/endoabs.81.P225

P226

HDAC inhibition as a therapy approach in autoimmune thyroid disease

Pablo Sacristán-Gómez[1], Ana Serrano-Somavilla[2], Miguel Sampedro-Nuñez[3], Monica Marazuela[3] & Rebeca Martínez-Hernández[2]
[1]IIS Princesa, Endocrinology, Madrid, Spain; [2] IIS Princesa, Universidad Autónoma de Madrid, Endocrinology, Madrid, Spain; [3] Hospital Universitario la Princesa, IIS Princesa, UAM, Endocrinology, Madrid, Spain

Introduction
Autoimmune Thyroid Diseases (AITD) are one of the most prevalent autoimmune diseases in industrialized countries (5% of population). The two main phenotypes of AITD, Hashimoto thyroiditis (HT) and Graves' disease (GD), are both characterized by the presence of circulating thyroid antibodies and infiltration by autoreactive lymphocytes in the thyroid gland and sometimes the orbit. One of the most studied mechanisms underlying AITD is the imbalance between immune activation and immune homeostasis of CD4+CD25- cells or T effector cells (Teff) and CD4+CD25+FOXP3+ regulatory T cells (Treg). Histone deacetylases (HDACs) are enzymes that exert postranslational modifications at protein level. HDAC9 interacts with FOXP3, the master regulator of Tregs, leading to an imbalance in Treg function. We have recently reported an increase expression of HDAC9 in Treg cells from AITD patients.
Objective
To investigate the in vitro effects of HDAC inhibitors (trichostatin A (TsA) a pan-inhibitor, TMP-269 a class IIa inhibitor and the FDA approved pan-inhibitor, suberanilohydroxamic acid (SAHA/Vorinostat)) on human freshly isolated CD4+CD25- T effector cells from AITD patients.
Methods
Toxicity assays were evaluated using LIVE/DEAD Viability-Cytotoxicity Kit on T cell proliferation by each inhibitor. Treg suppression assays were carried out in healthy controls and AITD patients. CD4+CD25+ Tregs were isolated from fresh PBMC using CD4+CD25+ Regulatory T Cell Isolation Kit (Miltenyi Biotec). To evaluate proliferation Teff cells were CFSE-labeled, and added to wells in serial dilutions giving Treg/Teff ratios of 0:1, 1:1, 1:2; 1:4 and 1:8 and in the presence or absence of differing concentrations of HDACi and using DMSO as control.
Results
Toxicity assays revealed us that TMP269 and SAHA demonstrate the same number and viability as control cells. On the contrary, TsA decreased significantly the viability at the minimal concentration used, discarding this inhibitor from our assays. Suppression assays using the TMP269 inhibitor did not showed significantly effects on the proliferation of CD25- T cells. However, SAHA caused a mild to moderate impairment of CD25- division.
Conclusions
Among all the inhibitors assessed, SAHA did not exert a toxic effect in cells and had a significantly decrease on Teff proliferation compared to TMP269. Our study also showed that the impaired proliferation of CD4+CD25-Teff cells by SAHA, was not only by a specific Treg mediated effect, but also by the decrease in the CD4+CD25- cell division rate. These findings suggest that HDAC inhibition by SAHA may serve as a possible treatment of inflammation in AITD.

DOI: 10.1530/endoabs.81.P226

P227

Thyrotoxicosis-associated anemia at baseline and after methimazole treatment

Laura Naglabeala[1], Dan Alexandru Niculescu[1,2], Anda Vladescu[3] & Catalina Poiana[1,2]
[1]C. I. Parhon National Institute of Endocrinology, Pituitary and Neuroendocrine Disorders, Bucharest, Romania; [2] Carol Davila University of Medicine and Pharmacy, Endocrinology, Bucharest, Romania; [3] C. I. Parhon National Institute of Endocrinology, Hematology, Bucharest, Romania

Background
Overt newly diagnosed hyperthyroidism is frequently associated with mild anemia. However, there are limited data on long term evolution under methimazole treatment. Our aim was to study the baseline characteristics and evolution of anemia in the hyperthyroidism setting.
Methods
We retrospectively assessed 58 consecutive patients [46 (79.3%) women] presenting with newly diagnosed overt thyrotoxicosis (43 Graves disease, 9 toxic nodular goiters, 4 toxic adenomas and 2 drug induced hyperthyroidism) in our practice. Of these, 30 were reassessed after 4-6 months of methimazole treatment. No patient had treatment for anemia. We measured thyroid-stimulating hormone, free thyroxine, hemoglobin (Hb), hematocrit, red blood cells, mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration at both baseline and 4-6 months assessments. Anemia was defined by a Hb value <12 g/dl in women and <14 g/dl in men.
Results
At baseline, 19 patients (32.76%) had normochromic normocytic anemia, of whom 14 (73.63%) were women. Mean Hb was 11.5$\pm$0.25 g/dl and 12.4$\pm$0.97

g/dl in women and men respectively. FreeT4 (39.53±20.2 pmol/l) inversely correlated with Hb in women ($r=0.45$, $P=0.05$), but not in men. All patients (25 women, 5 men) that were assessed after 4-6 months of methimazole treatment had normal Hb levels (including 7 women and 1 man with anemia at baseline).
Conclusion
Our study demonstrated that hyperthyroidism is frequently associated with mild normochromic normocytic anemia. 4-6 months of methimazole treatment leads to resolution of anemia.

DOI: 10.1530/endoabs.81.P227

P228

When patients with DTC can be discharged to primary care

Nicolas Amich, Estefanía Chumbiauca & Juan Carlos Galofré
University of Navarra, Endocrinology, Pamplona, Spain

Purpose
To evaluate if patients with low- or intermediate-risk differentiated thyroid cancer (DTC) can be discharged to primary care.
Material and Methods
The clinical records and evolution of 346 patients with DTC who had undergone surgery between 1995 and 2020 with a follow-up after a mean of 7.6 ± 6.1 years were retrospectively reviewed. All had a low or intermediate risk of recurrence as defined under the 2015 ATA risk stratification system and a minimum follow-up of one year. Biochemical (thyroglobulin) and structural (imaging findings) yearly evaluations were used to dynamically classify patients based on their response to treatment as *excellent*, *indeterminate*, *biochemically incomplete* or *structurally incomplete*. Primary outcome was the assessment of disease recurrence (biochemical or structural) as defined under the 2015 ATA guidelines.
Results
Throughout follow-up, 14.7% ($n=51$) patients presented disease recurrence. When classified by initial risk of recurrence (low or intermediate) it was seen that 4.53% (11/243) of low-risk patients and 39.81% (41/103) of intermediate-risk patients presented recurrence. This difference was statistically significant ($P<0.0001$) with no statistically significant difference in follow-up times between the two groups ($P=0.34$). Moreover, when examined in terms of response to treatment, it was seen that only 1% (2/193) of low-risk patients with an excellent response to treatment presented recurrence. The majority of patients presented disease recurrence in the first five years of follow-up, 98% (50/51), the mean time to recurrence being 9.38 ± 18.68 months.
Conclusions
Low- and intermediate-risk DTC patients exhibiting an excellent response to treatment have a minimal recurrence risk that could offer the possibility of discharge to primary care follow-up after a five-, or a more cautious ten-year, follow-up period. The 2015 ATA risk stratification system proves to be an accurate and useful tool for the prediction of recurrence both postoperatively as well as at specific points during follow-up.

DOI: 10.1530/endoabs.81.P228

P229

An innovative synthetic support for cytological and immunocytochemical assessment in cytologically indeterminate thyroid nodules. Feasibility study

Silvia Taccogna[1], Roberto Novizio[2], Martina D'angelo[1], Luca Turrini[1], Agnese Persichetti[3], Alfredo Pontecorvi[2], Enrico Papini[4] & Rinaldo Guglielmi[4]
[1]Regina Apostolorum Hospital, Pathology, Albano Laziale, Italy; [2] Fondazione Universitaria Policlinico A. Gemelli, Catholic University of the Sacred Heart, Endocrinology and Metabolism, Rome, Italy; [3] IRCCS-Regina Elena National Cancer Institute, Service of Pharmacovigilance, Rome, Italy; [4] Regina Apostolorum Hospital, Endocrinology and Metabolism, Albano Laziale, Italy

Background
Fine needle aspiration (FNA) is the diagnostic procedure of choice in the evaluation of thyroid nodules. Nodules with indeterminate cytological categories, Tir3A and Tir3B according to Italian cytological classification, pose diagnostic challenges in clinical practice and are frequently submitted to diagnostic surgery. CytoFoam Core (CF) (Diapath, Martinengo, Italy) uses an absorbent foam device inserted into the needle hub to collect the cytological sample aspirated during FNA. The specimen is formalin-fixed and paraffin-embedded similarly to the microhistological material obtained with core-needle biopsy.
Aim of the study
To assess diagnostic efficacy of CytoFoam core, compared to traditional cytology, in re-evaluating thyroid nodules classified as Tir3A. Post-surgical histology was used as reference standard.
Method
Retrospective study on 89 patients with a first indeterminate cytological report who were referred to the Department of Endocrinology of Regina Apostolorum Hospital (Albano L. Rome, Italy) for a second FNA. FNA was performed after at least one month under ultrasound guidance with a 23G needle according to the established procedure. During the second procedure, both traditional cytological (TC) smears and a single-pass CF specimen were obtained for each patient. On CF samples immunocytochemical staining for Galectin-3, HBME-1, and CK-19 was also performed. Forty-five patients eventually underwent surgery, and their histological diagnoses were compared to the TC and CF reports. Four parameters were blindly and independently compared by two cytopathologists with specific thyroid expertise: inadequacy rate, rate of persistent indeterminate (Tir3A and Tir3B) reports, rate of malignancy in persistently indeterminate nodules, and rate of cancer in lesions cytologically classified as malignant.
Results
Non-diagnostic samples were 8/45 (17.7%) in TC vs 5/45 (11.1%) in CF samples ($P=0.4$). Persistent indeterminate samples were 27/45 (60%) in TC vs 16/45 (35.5%) in CF samples ($P<0.005$). The rate of malignancy in persistently indeterminate nodules was 8/16 (50%) in CF group vs 9/27 (33.3%) in TC group ($P=0.4$). Five/45 (11.0%) samples were classified as benign by TC vs 16/45 (35.0%) samples by CF ($P<0.005$). All these nodules resulted benign at post-surgical evaluation. Five/45 (11.0%) samples were classified as suspicious for malignancy/malignant in TC group against 8/45 (18.0%) samples in CF ($P=0.4$). Post-surgical evaluation confirmed malignancy in all these cases.
Conclsion
CytoFoam core demonstrated greater diagnostic accuracy than TC in repeat FNA assessment of cytologically indeterminate nodules. CF increased the conclusive diagnosis rate and decreased the number of cytologically indeterminate cases. A large prospective study is needed to confirm this pilot study results.

DOI: 10.1530/endoabs.81.P229

P230

Development of a new ultrasound score to predict thyroid nodule malignancy

Ibtissem Oueslati[1], Hiba-Allah Chatti[1], Aymen Azaiez[2], Jihene Marrakchi[2], Seif Boukriba[3], Slim Haouet[4], Meriem Yazidi[1] & Melika Chihaoui[1]
[1]La Rabta University Hospital, Department of Endocrinology, Tunis, Tunisia; [2] La Rabta University Hospital, Department of Oto-Rhino-Laryngology, Tunis, Tunisia; [3] La Rabta University Hospital, Department of Radiology, Tunis, Tunisia; [4] La Rabta University Hospital, Department of Pathology, Tunis, Tunisia

Introduction
Thyroid cancer remains a relatively rare entity. Radiological scoring systems aim to stratify the risk of malignancy based on morphological criteria.The objective of this study was to develop a new score based on ultrasound criteria to predict thyroid nodule malignancy risk.
Patients and methods
This was a retrospective study including 200 thyroid nodules (100 malignant nodules and 100 benign nodules). The report of the thyroid ultrasound and the result of the final histological examination were collected for each nodule. Odds ratios (OR) of ultrasound criteria were calculated. The new score represents the sum of the ORs of the ultrasound criteria for each nodule.
Results
Ultrasound criteria associated with nodule malignancy risk were: solid composition (OR=7.81; $P<10-3$), very hypoechoic character (OR=12.49; $P<10-3$), moderately hypoechoic character (OR=6.2: $P<10-3$), irregular contours (OR=7.47; $P<10-3$), taller-than-wide shape (OR=3.58;$P=0.02$), microcalcifications (OR=3.02;$P=0.006$) and the presence of cervical lymph nodes (OR=5.5; $P<10-3$). The mean ultrasound score was 16.7 ± 7.5 for malignant nodules vs 5.65 ± 6.5 for benign nodules ($P<10-3$). A score ≥ 10

was significantly associated with malignancy (OR = 17.9; $P < 10\text{-}3$). The threshold of 10 had a sensitivity of 85% and a specificity of 76%. A score $\geq$ 25 was predictive of malignancy in 100% of cases. The area under the ROC curve was 0.85 for this new score, 0.81 for the EU-TIRADS classification, and 0.82 for the ACR-TIRADS classification.

Conclusion

Our new ultrasound score seems to be effective in predicting thyroid nodule malignancy risk. However, it needs to be validated by prospective multicenter studies.

DOI: 10.1530/endoabs.81.P230

P231

Congestive heart failure as a first-time presentation of thyrotoxicosis in COVID-19 positive patient

Ellen McKay[1,2], Kalthoom Elhilo Mousa[1], Muhammad Abrar Ul Haq[1,3], Karen Kelly[4], Mohamad Shafi Rummun[4], Sean Fleming[4] & Ma Pyeh Kyithar[1]

[1]Midland Regional Hospital Portlaoise, Diabetes & Endocrinology, Ireland; [2] University College Dublin Intern Network, Ireland; [3] The College of Physicians and Surgeons Pakistan, Pakistan; [4] Midland Regional Hospital Portlaoise, Cardiology, Ireland

Background

The clinical manifestations of thyrotoxicosis do not always correlate with the extent of thyroid biochemical abnormalities. Here, we report the case of a COVID-19 positive patient who presented with congestive heart failure as a first-time presentation of thyrotoxicosis.

Case report

A 40-year-old female presented to Emergency Department with two days history of lower limb oedema and abdominal distension. She denied dyspnoea, chest pain, palpitations, weight loss or heat intolerance. She had history of cervical cancer 3 years prior, treated with oophorectomy and hysterectomy and 10 pack-year smoking. On clinical examination, diffusedly enlarged thyroid gland, irregularly irregular pulse and signs of congestive cardiac failure (raised JVP, gallop rhythm, reduced air entry in lower zones of the lungs, pitting oedema up to hips bilaterally) were observed. ECG showed atrial fibrillation with atrial flutter; chest X-ray showed bilateral moderate pleural effusion. Laboratory work-up revealed deranged liver biochemistry (bilirubin 38 umol/l, ALT 13 U/l, GGT 120 U/l, alkaline phosphatase 339 U/l), normal troponin, elevated d-dimer (1340 ng/ml), markedly elevated pro-BNP (7421 pg/ml), markedly elevated free T4 73 pmol/l (range 8.3-19 pmol/l), free T3 27 pmol/l (range 3.8-6 pmol/l) and suppressed TSH $<$0.01 mIU/l (range 0.38-5.33 mIU/l). She had positive SARS-CoV-2 PCR on surveillance testing but no symptoms of COVID-19 infection. Transthoracic echocardiogram demonstrated left ventricular dysfunction (ejection fraction 35%), impaired right ventricular systolic function, dilated left and right atria. CT pulmonary angiogram/abdomen/pelvis showed no evidence of pulmonary embolism but demonstrated moderate to large bilateral pleural effusion with extensive free intra-abdominal fluid, an enlarged thyroid gland and heterogeneous liver parenchymal enhancement. She was treated with IV metoprolol, IV furosemide and anticoagulation on admission, later commenced on oral carbimazole 20 mg bd, propranolol and IV furosemide infusion (180 mg/24hr) for further diuresis. Heart failure medications were adjusted as per cardiology team. Metolazone, spironolactone, bumetanide, ramipril and dapagliflozin were commenced. TPO and anti-TSH receptor antibodies returned positive, consistent with Graves' hyperthyroidism. She was discharged home 8 days after admission with close follow-ups with Endocrinology and Cardiology teams. Upon discharge, she was euvolaemic (14 kg weight loss) with improved thyroid function (free T4 34.6 pmol/l, free T3 9.9 pmol/l, TSH 0.01 mIU/l) and pro-BNP (2176 pg/ml).

Discussion

Our case highlights that thyrotoxicosis can present with congestive cardiac failure without classical symptoms of hyperthyroidism. Thyrotoxicosis should be considered in cases with a new presentation of heart failure. There is evidence that COVID-19 may be associated with high risk of thyrotoxicosis. It remains unclear if COVID-19 infection was coincidental or precipitated thyrotoxicosis with heart failure in our case.

DOI: 10.1530/endoabs.81.P231

P232

Levothyroxine Replacement Therapy overuse. Factors suggesting treatment discontinuation

Sarantis Livadas[1], Christina Bothou[2], Rodis Paparodis[3], Ioannis Androulakis[1], Nicholas Angelopoulos[1], Anastasios Boniakos[1], Panagiotis Anagnostis[4] & Leonidas Duntas[5]

[1]Athens Medical Centre, Athens, Greece; [2] University Hospital of Zurich, Department of Endocrinology, Diabetology and Clinical Nutrition, Zürich, Switzerland; [3] Center for Diabetes and Endocrine Research, University of Toledo College of Medicine, Toledo, United States; [4] Unit of Reproductive Endocrinology, 1st Department of Obstetrics and Gynecology, Medical School, Aristotle University of Thessaloniki, Thessaloniki, Greece; [5]Evgenidion Hospital, Endocrine Unit, Athens, Greece

Background

Levothyroxine (LT4-Rx) is one of the most prescribed drugs worldwide and the vast majority of patients receive long-term treatment. However, in a recent study of 291 subjects we found that 60% of this cohort were euthyroid two months after LT4-Rx discontinuation[1].

Aim of the study

A prospective clinical cohort follow-up study was carried out. In 688 subjects (82% females) aged 48.01 $\pm$ 15.96 (range 17-84years) with 8.59 $\pm$ 6.98 years on LT4Rx without a solid diagnosis of hypothyroidism, the treatment was abruptly interrupted. The treatment indications and corresponding percentage for LT4-Rx were classified as nodule(s) (33%), indefinite (27%), post-partum (7%) and Hashimoto's (33%). Follow up for a short period of time occurred in 54% of subjects ($\leq$ 4 months, Group A) and long-term follow-up was achieved in the remaining (up to 60 months, Group B). The studied subjects were evaluated at the time LT4-Rx was discontinued, 2-4 months later and at the end of follow-up. At each time point, estimation of TSH, FT4 levels and thyroid ultrasound was performed. A TSH value of $\geq$4.5 IU/ml was considered as underlying hypothyroidism.

Results

Among the entire cohort, $n = 158$ subjects became hypothyroid, while the remaining $n = 530$ remained euthyroid off LT4-Rx (23 vs. 77%, $P < 0.001$). On subgroup analysis, 40% of subjects comprising Group A became hypothyroid, whereas the corresponding value for Group B was 3%. In Group A, the reason for LT4-Rx, LT4 dose, LT4 dose/BMI, TSH levels and the existence of thyroid autoantibodies (ATA) were significantly different in those who became hypothyroid. No difference among any parameter evaluated was disclosed in Group B. Subjects with diagnosis of Hashimoto's, positive ATA, higher TSH values and higher LT4 dose had significantly higher probability to became hypothyroid. Furthermore, in Group A, 15.4% became hypothyroid with baseline TSH $>$ 3 IU/ml vs. 5.4% with baseline TSH $<$ 3 IU/ml ($P < 0.001$); the corresponding values for Group B were 44.4% vs. 10.0%, ($P < 0.001$), respectively.

Conclusions

These findings suggest considerable overuse of thyroxine administration. In cases of uncertainty, the existence of nodules, a low-normal TSH value, a relative small T4 dose and the absence of ATA are strong indicators of euthyroid patients on LT4Rx and accordingly treatment discontinuation is strongly advised. Furthermore, in the case that a subject does not became hypothyroid 2-4 months post treatment discontinuation, then the likelihood to develop hypothyroidism long term is insignificant.

Livadas S, *et al*. Thyroid 2018.

DOI: 10.1530/endoabs.81.P232

P233

A case of severe hypothyroidism causing reversible chronic kidney disease

Veshalee Vernugopan[1] & Nida Chammas[2]

[1]School of Medicine, University of Glasgow, United Kingdom; [2] Cromwell Hospital, United Kingdom

Introduction

Despite hypothyroidism being seen in patients with kidney disease, it is rarely the underlying cause. We present a rare case of chronic kidney disease (CKD) secondary to severe hypothyroidism that was totally reversed on commencement of Levothyroxine. The mechanism is multifactorial, and importantly involves the pre-renal and direct renal effects of thyroid hormones.

Case report

A 37-year-old Caucasian male presented to the endocrine clinic in March 2020 after a GP friend mentioned that he did not look well. The patient did not feel unwell himself, however on direct questioning complained of cold intolerance, fatigue, puffy eyelids, and weight gain over the preceding years. Most notable to the patient was hair loss on the body and scalp which had left him bald. The

patient's history was only significant for gout. Blood tests showed TSH 548.7 (0.27-4.2) and Free T4 undetectable <4 (12-22). The thyroid antibodies were within normal range. He was 89.95 kg with a BMI in the obesity range (31.12). Additionally, the patient had asymptomatic CKD seen by metabolic abnormalities in the blood test: normocytic anaemia with haemoglobin 87 (130-175), urea 9.3 (2.1-8.5), creatinine 150 (65-119) and GFR 46 (>90). On examination, he had puffy eyelids, but no evidence of goitre. Systemic cardiovascular, respiratory, and abdominal examinations were unremarkable. A thyroid ultrasound showed a small thyroid gland with benign changes suggestive of chronic thyroiditis. He was diagnosed with primary hypothyroidism and commenced on 150μg Levothyroxine once daily. Within two months of starting Levothyroxine, kidney function improved to a GFR of 88. At present, patient is taking 100μg of Levothyroxine once a day, with normal thyroid function tests and normal kidney function. The patient has marked regrowth of scalp hair and has had a significant weight loss of 15.75 kg.

Conclsion

Despite being commonly encountered and well understood individually, hypothyroidism is an underappreciated reversible cause of renal impairment and the interaction between thyroid hormones and the kidneys are rarely remembered. Patients can be asymptomatic even with severe hypothyroidism and CKD; the treatment is sufficient replacement with Levothyroxine which can show profound kidney improvement — as with our patient this can happen within only two months. Hence, clinicians should ensure that renal function tests be performed on initial diagnosis of hypothyroidism to ensure that this reversible complication can be adequately managed with Levothyroxine.

DOI: 10.1530/endoabs.81.P233

P234

Subacute thyroiditis following mRNA anti-SARS-CoV-2 vaccination in a patient with solitary kidney- a case report

Dimitrios Askitis
Private Practice for Endocrinology, Alexandroupolis, Greece

Introduction

Massive anti-SARS-CoV-2 vaccination campaigns have been established as the cornerstone of confronting the current COVID-19 pandemic. Subacute thyroiditis (SAT) comprises an inflammatory process in the thyroid gland, mostly due to viral infections of the upper respiratory tract, although it may rarely occur after vaccine administration. To date, a few cases of SAT related to anti-SARS-CoV-2 vaccines have been reported globally. Hereby, we present the case of a patient with solitary kidney who developed SAT, mild thyroid autoimmunity activation and subsequent permanent hypothyroidism after mRNA-based anti-COVID-19 vaccination.

Case report

A 79-year old male patient with solitary kidney due to nephrectomy after drug-induced acute renal failure presented for evaluation in terms of newly detected subclinical hyperthyroidism and neck pain starting 20 days ago. The patient had a known history of mild subclinical hypothyroidism diagnosed 2 years ago without laboratory-confirmed autoimmune etiology (negative thyroid-related autoantibodies) and without levothyroxine supplementation. Neck pain and tenderness as well as low grade fever with intermittent episodes of hypothermia had an onset 10 days after the first dose of the mRNA vaccine Comirnaty and continued after administration of the second dose 2 weeks before the patient's visit. The neck ultrasound revealed a pattern typical of subacute thyroiditis with bilateral volume growth and diffuse hetero-echogenicity and inhomogeneity accompanied by reduced blood flow; the adjunctive laboratory evaluation showed elevation of the inflammatory markers (CRP, ESR) with first documentation of slightly elevated TPO-autoantibodies. As the patient reported remission of his symptoms no anti-inflammatory medication was initiated. One month later the patient reported no SAT-related symptoms but the laboratory evaluation revealed overt hypothyroidism. He was started on levothyroxine 88 μg daily and remained euthyroid under supplementation. Neck ultrasound 4 months after the first visit showed a remission of the inflammatory process with reduction of both the thyroid volume and the hypoechoic inflammatory zones.

Conclusion

The above case presentation comprises the first official report of subacute thyroiditis in adjunction with mRNA COVID-19 vaccination in northern Greece. SAT is a self-limiting process and is rarely reported as a mild complication of the anti-SARS-Cov-2 vaccination with only few documented cases related to all types of available vaccines. Therefore, clinicians should be aware of this rare post-vaccination adverse event. Despite the development of permanent hypothyroidism in the present case the definitive benefits of the anti-COVID-19 vaccination outweigh the rare and mostly mild and transient side-effects which shall not comprise an inhibitory factor against vaccination.

DOI: 10.1530/endoabs.81.P234

P235

Long term prognosis of severe tricuspide regurgitation induced by hypothroidism

Ikram Chamtouri, Asma Ben Abdallah & Faouzi Maatouk
Hôpital Fattouma Bourguiba, Cardiology B, Monastir, Tunisia

Background

Hypothyroidism is associated with multiple heart diseases such as tricuspid regurgitation (TR). We aimed to investigate in the prognosis of TR induced by hypothyroidism.

Methods

We conducted a cohort study included all patients with severe primary TR. Long term prognosis of TR induced by hypothyroidism was compared to the prognosis of other severe primary TR causes.

Results

Among 43 patients with severe primary TR, 19 patients presented hypothroism considered as the only cause of severe TR. Thirteen females patients had hypothyroidism. Hypothyroidism was associated with significantly higher renal failure with no difference in hypertension, diabetes and atrial fibrillation or flutter. At two-years evluation, there were a sgnificantly higher prevalence rehospitalization and mortality a in patients with hypothyroidisme despite the treatment of hypothroidism.

Conclusion

Despite adequat hypothroidism treatment, severe TR induced by hypothyroidism had a long term poor prognosis.

	hypothyroidism	Other causes	p
Right ventricle dysfunction	14 (73.7%)	11 (45.8%)	0.06
Rehospitalization	8 (61.5%)	2 (14.3%)	0.01
Mortality	7 (36.8%)	0	0.001

DOI: 10.1530/endoabs.81.P235

P236

Thyrotoxic periodic paralysis: a case report

Abdul Aziz, Dania Ali & Sarah Nadeem
The Aga Khan University Hospital (AKUH), Karachi, Pakistan

A rare complication of thyrotoxicosis among Asians is Thyrotoxic Periodic Paralysis (TPP), with an incidence of approximately 2% in patients with thyrotoxicosis from any cause. TPP is characterized by sudden onset of hypokalemia and muscle paralysis. Hypokalemia in TPP results from an intracellular shift of potassium induced by the thyroid hormone sensitization of Na^+/K^+ −ATPase rather than depletion of total body potassium. Treatment of TPP includes correcting the underlying hyperthyroid state, prevention of potassium shift by using non-selective beta-blockade, and replacing potassium. TPP is curable once a euthyroid state is achieved. We describe here a rare case of TPP in a young Chinese man who presented with sudden bilateral lower limb weakness. A 23-year-old gentleman of Chinese origin, presented to the outpatient department with complain of bilateral lower limb weakness for one day. Motor examination revealed normal bulk and reflexes bilaterally but power was 2/5 in both the lower limbs. His initial electrolytes showed severe hypokalemia of 1.3 mmol/l (Range: 3.5-5.1 mmol/l). Hypokalemia was rapidly corrected with IV potassium. His symptoms subsequently improved and patient was discharged. At discharge his potassium level was 4.1 mmol/l. Follow up was advised but patient was lost to follow up. Three weeks after the initial presentation, patient again presented to the emergency department with complaints of sudden onset of bilateral lower limb weakness. Motor examination of the lower limb revealed decreased tone and power was 1/5 bilaterally. No goiter, lid lag and lid retraction noted. Rest of the systemic examination was unremarkable. Laboratory findings were significant for a potassium of 1.3 mmol/l). Potassium (K) was replaced intravenously (IV) and when rechecked, the potassium level was 5.2 mmol/l. Patient lower limb weakness also improved clinically. Endocrinology was consulted as laboratory workup revealed a suppressed TSH (<0.010 uIU/ml). We advised checking FT3, FT4 and thyroid receptor antibodies (TRAB). FT4 was markedly elevated at 4.24 ng/dl (Range: 0.89-1.76 ng/dl) and TRAB was positive 8.85 IU/l (Range : 0-1.75 IU/l). Endocrine team recommended initiating anti-thyroid medication, Neomarcazole 15 mg two times a day. He was discharged as soon as K levels normalized. Potassium on discharge was 4.9 mmol/l. It is important to consider TPP as a differential in a patient presenting with low

potassium levels and neurological symptoms as management initially with propranolol and of the underlying thyrotoxicosis is essential in definitive treatment of the recurrent periodic paralysis.

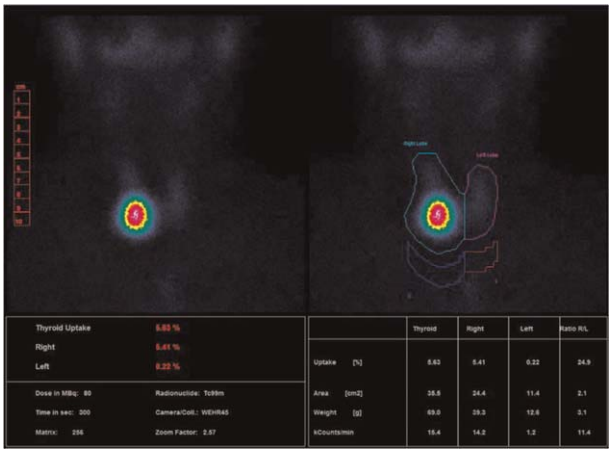
DOI: 10.1530/endoabs.81.P236

P237

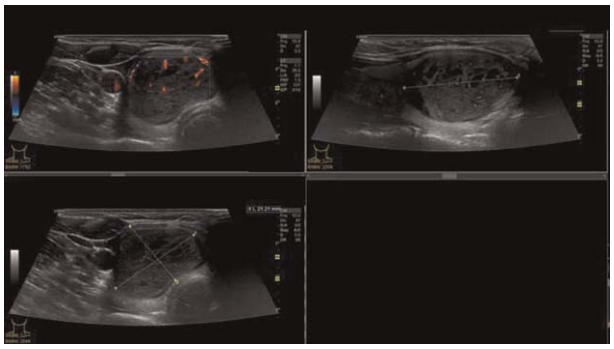
A case of the uncommon Marine-Lenhart syndrome

Maria Mathiopoulou[1] & Ivette Engel-Bicik[2]
[1]University Hospital of Zurich, Thyroid Center, Nuclear Medicine, Zurich, Switzerland; [2] University Hospital of Zurich, Nuclear Medicine, Zurich, Switzerland

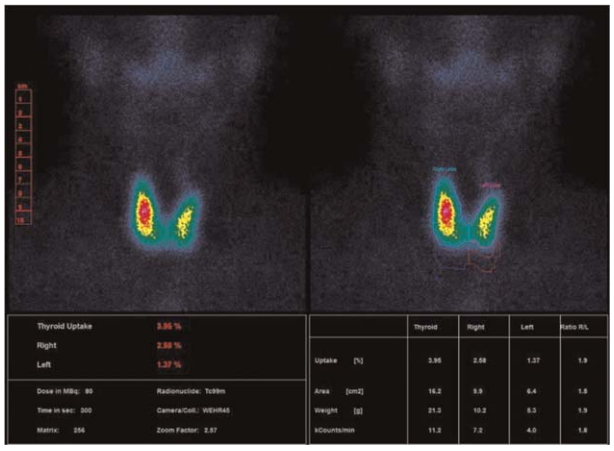
Background
The combination of a toxic adenoma and Graves' disease compose the Marine-Lenhart syndrome. This condition is estimated to occur in 0.8-2.7% of Graves' disease patients and only few cases are reported in the literature.
Patient findings
A 29-year-old female patient was referred to our outpatient clinic due to subclinical hyperthyroidism and a newly discovered thyroid nodule on the right thyroid lobe. She had no thyreotoxic symptoms and the clinical examination was unremarkable. Her initial blood tests were: TSH 0.01 mU/l (reference 0.16-4.25 mU/l), fT3 8.3 pmol/l, (reference 3.6-6.4 pmol/l), fT4 15.6 pmol/l (reference 12.3-20.2 pmol/l) and TSH-Receptor-Ab titers $<$ 0.30 U/l (reference $<$ 1.75 U/l). The thyroid ultrasound and scintigraphy revealed a toxic adenoma in a right sided goiter. Following a radioiodine ablation with 200 MBq 131-I was performed. follow-up ultrasound after six months revealed a 70% volume reduction of the formerly toxic adenoma of (2.6 ml, pre-therapy 8.7 ml). Two months later at the regular after-therapy follow-up, a manifest hyperthyroidism was revealed [TSH 0.004 mU/l, (reference 0.10-4.00 mU/l), fT3 28.1 pmol/l (reference 3.0-9.5 pmol/l) and fT4 21.4 pmol/l (reference 10.0-28.0 pmol/l)] and the TSH-Receptor-Ab titers were elevated [1.85 U/l (reference $<$ 1.75 U/l)]. The patient was still completely asymptomatic. The thyroid scintigraphy was repeated and showed a symmetrical, elevated radionuclide uptake, leading to the diagnosis of Graves' disease. A thyrostatic therapy with carbimazole was initiated and continued for 8 months, until the thyroid function markers in the blood were normalised.
Conclusion
The existence of both a toxic adenoma and a Graves' disease in the same patient has been termed as Marine-Lenhart syndrome. This coexistence may be observed simultaneously or in different stages, according to the bibliography. In cases where radioiodine treatment of a toxic adenoma is indicated, attention is required, because it may trigger the Graves' disease, as shown in this case. Every new presentation of hyperthyroidism should be investigated as a new pathology, as it may reveal a new underlying condition indicating the need for different therapeutical pathways.
Photos
Thyroid scintigraphy 09.06.2020



Thyroid ultrasound 09.06.2020



Thyroid scintigraphy 18.01.2021



DOI: 10.1530/endoabs.81.P237

P238

The use of body composition measured by CUN-BAE as a simple tool to predict the LT4 titration after total thyroidectomy in patients with benign and malignant thyroid disease

Ana María Díaz Abram[1], Estefanía Chumbiauca[2] & Juan Carlos Galofré[2]
[1]Facultad de Medicina, Endocrnología, Pamplona, Spain; [2] Clínica Universidad de Navarra, Endocrinología, Pamplona, Spain

Background
Patients who require levothyroxine (LT4) supplementation after total thyroidectomy often have difficulty achieving target TSH levels. Several studies have attempted to develop a dosing schedule considering different factors such as age, gender, weight, or body mass index (BMI) as potential determinants of the correct dose of LT4. The objective of this study is to determine if a scheme that uses the percentage of body fat (%BF) measured by CUN-BAE is more accurate to correctly predict levothyroxine dose requirements.
Methods
Data from 143 patients who underwent total thyroidectomy for benign and malignant disease at our institution between 1993 and 2021 were retrospectively reviewed. Two new dosing formulas, CUN-BAE Model 1 and CUN-BAE Model 2, were designed using Poisson's regression. These dosing models were applied to our cohort and

compared with other dosing schemes proposed in the literature. The accuracy of each model was established by determining the proportion of correct estimates.
Results
CUN-BAE-1 and CUN-BAE-2 accurately estimated 61.5% and 62.9% of LT4 doses, respectively. These results slightly improve the precision of previous methods such as the Poisson regression proposed by Zaborek *et al* based in several factors including BMI (estimated 60.1%) and the weight-based model (estimated 55.9%) of correct doses.
Conclusion
− The use of %BF calculated by the CUN-BAE formula to adjust the dose of LT4 after total thyroidectomy is a simple and accurate method that improves current formulas based on weight or BMI.

DOI: 10.1530/endoabs.81.P238

P239

Frequency of autoimmune thyroid disease in polycystic ovary syndrome: case-control study

Sawsen Essayeh[1], Radhouan Gharbi[1], Hiba-Allah Chatti[1], Chedi Mhadhbi[1], Sawsen Mnajja[1], Sana Abdelali[2], Hajer Kandara[1] & Ines Kammoun[1]
[1]National Institute of Nutrition and Food Technology of Tunis, Endocrinology, Tunis, Tunisia; [2] National Institute of Nutrition and Food Technology of Tunis, Biochemistry, Tunis, Tunisia

Introduction
Polycystic ovary syndrome (PCOS) is a common endocrine pathology in women with a high prevalence varying between 5 and 20%. Autoimmune thyroid diseases (AITD) are the most prevalent organ-specific autoimmune diseases, particularly in young women. The purpose of our study was to determine the prevalence of AITD in a group of patients with PCOS compared to a control group.
Patients and Methods
103 women were recruited into the study, aged between 18 and 46 years. They were divided into two groups matched for age and body mass index. The first group included 51 women with PCOS and the second group included 52 healthy volunteer women. Serum-free thyroxin (FT4), thyroid-stimulating hormone (TSH), anti-thyroid peroxidase antibody (anti-TPO) levels were evaluated. The diagnosis of Hashimoto's thyroiditis was made when the participant had hypothyroidism coupled with high level of anti-TPO.
Results
The age and the body mass index were comparable between the two groups (29.6± 6.5 vs 29.2 ±6.1 years, $P=0.81$; 30.3±6.5 vs 29.3±8.9 Kg/m^2; $P=0.19$). The TSH, FT4 and ant anti-TPO levels were similar in both groups ($P=0.41$, $P=0.35$, $P=0.41$, respectively). The frequency of Hashimoto's thyroiditis was significantly higher in the PCOS group (21% vs 4%, $P=0.01$). In patients with PCOS and controls, the percentages of positive anti-TPO, subclinical hypothyroidism were similar ($P=0.21$, $P=0.27$, respectively). Graves'disease and subclinical hyperthyroidism were not found in the two groups.
Conclusion
Hashimoto's thyroiditis is a frequent condition in PCOS patients. Therefore, the assessment of TSH and anti-TPO should be considered in patients with PCOS during follow-up even in the absence of overt symptoms.

DOI: 10.1530/endoabs.81.P239

P240

Development of a laboratory alerting system for the early diagnosis of thyroid dysfunction in pregnancy

José Ignacio Martínez Montoro[1], Víctor José Simón Frapolli[1], Andrea Fernández Valero[1], María Molina Vega[1], Andrés Cobos[2], Francisco J. Tinahones[1] & María José Picón César[1]
[1]Hospital Universitario Virgen de la Victoria, Endocrinology and Nutrition, Málaga, Spain; [2] Hospital Universitario Virgen de la Victoria, Clinical Analysis, Málaga, Spain

Introduction
Overt thyroid dysfunction in pregnancy without an early diagnosis and treatment may lead to an increased risk of adverse maternal and fetal outcomes. In this study, our goal was to assess the results of the development of a laboratory alerting system for the diagnosis of thyroid dysfunction in the first trimester of pregnancy.
Material and methods
Observational retrospective study evaluating clinical and biochemical data from pregnant women with overt thyroid dysfunction diagnosed in the first trimester of pregnancy through a laboratory alerting system between October 2020 and August 2021. Overt thyroid dysfunction was defined by overt hypothyroidism (TSH < 4 mcU/ml and low FT4) or overt hyperthyroidism (TSH < 0.1 mcU/ml and high FT4/FT3) in the first trimester of pregnancy. Laboratory alerts were received weekly via e-mail notification and assessed by an Endocrinologist.
Results
A total of 60 laboratory alerts were received. 12 of them did not fulfill the aforementioned criteria and were not considered. Thus, the remaining 48 laboratory alerts from women in the first trimester were evaluated (30.8 ± 7.1 years old, 20.8% presented family history of thyroid disease and 14.5% presented personal history of thyroid disease (6.2% hypothyroidism, 8.3% hyperthyroidism). Considering the 13 laboratory alerts related with overt hypothyroidism, 5 patients presented increased levels of thyroperoxidase antibodies (38.4%), median TSH 7.3 (4.38-617; normal value 0.4-4 μUI/ml), median FT4 10.4 pmol/l (1.98-10.94; normal value: 11-22 pmol/L). 7 women (53.8%) started levothyroxine (median TSH 13.4 μUI/ml), 1 patient was not contacted, and 5 patients presented analytical interferences (normal TSH and slightly decreased FT4) and were not treated. With regard to the 35 laboratory alerts due to overt hyperthyroidism, 3 patients (8.5%) had personal history of transient hyperthyroidism of early pregnancy; 17 (48.6%) presented nausea/vomiting, 1 (2.9%) twin pregnancy and 1 (2.9%) ectopic pregnancy. Positive autoimmunity (TSI) was detected in 5 patients (14-3%), median FT4 22.6 pmol/l (ranging from 22.04 to 55.79), median FT3 7.73 pmol/l (6.88-30.8; normal value 3.1-6.8). 10 patients (28.5%) started treatment with antithyroid drugs, whereas in the rest, the transitory suspension of the iodine supplement was enough for the normalization of biochemical parameters.
Conclsions
A laboratory alerting system for the diagnosis of thyroid dysfunction during pregnancy permitted an early diagnosis and treatment of this pathology in 28.8 % of the received laboratory alerts.

DOI: 10.1530/endoabs.81.P240

P241

Compare the effects of levothyroxine therapy vs liothyronine/levothyroxine combination therapy on cardiac biomarkers in 364 patients with hypothyroidism

Vishal Gupta[1] & Vaishali Teli[2]
[1]VG-ADVANTAGE Diabetes Thyroid and Endocrine Centre, Endocrinology, Mumbai, India; [2] VG-ADVANTAGE Diabetes Thyroid and Endocrine Center, Mumbai, India

Methodology
Between Jan'20 to Jan'21, 364 patients on thyroid replacement therapy were included in the study and analysed retrospectively. They were divided in 2 groups. T4 group (189 on levothyroxine therapy {T4} therapy) & T3 group (175 on levothyroxine/liothyronine combination therapy {T3/T4}. Hypothyroidism was defined as TSH >4.2 mIU/ml on > 2 occasions > 2 weeks apart irrespective of their thyroid antibody (anti-TPO Ab) status or TSH > 4.2 if symptomatic or positive Anti-TPO Ab. Patients were evaluated every 2-3 months for 6 months for CV markers [body mass index-kg/m^2 (BMI), systolic (S) BP, diastolic (D) BP {mm in Hg}, Lipid profile mg/dl (TC, LDL, TG, HDL), Hs-CRP {mg/l}]. Baseline characteristics were analysed using descriptive statistics. Data was analysed using SPSS 26 and represented as mean ± standard error & independent sample t-test was used. P value <0.05 was considered significant (S).
Results
Baseline characters were well matched in both groups except, DBP (mean±SD) (T4 77.72±9.601 Vs T3/T4 81.69±10.87, P-0.00) & LDL (T4 105.121±33.689 Vs T3/T4 114.687±33.9196, P-0.02). T4 group (baseline to 6 months): there was a S reduction in SBP (3.323±0.941, P-0.01), TSH (4.4522±0.7602, P-0.00), TC (14.04274±3.24371, P-0.00), LDL (11.42795±3.03657, P-0.00), TG (16.15090±3.73617, P-0.00). T3/T4 group (baseline to 6 mths): there was S reduction in BMI (0.5160±0.1213, P-0.00), TSH (6.1134406±1.4832301, P-0.00), TC (12.75764±2.80435, P-0.00), LDL (11.63343±2.72702, P-0.00), TG (8.45775±4.38677, P-0.05). Difference between T4 & T3/T4 at 6 mths: There was no difference in hs-CRP mg/l {T4 0.2947±0.3071 vs T3/T4 0.9844±

0.3602, *P*-0.677}, BMI kg/m^2 {T4 0.2361 ± 0.1892 vs T3/T4 0.5160 ± 0.1213, *P*-0.222}, Lipid parameters, SBP & DBP between both groups.
Conclusion
Both T3/T4 combination therapy & T4 are effective in improving lipid parameters. Both T4 & T3/T4 do not impact either hs-CRP or BP.

DOI: 10.1530/endoabs.81.P241

P242

Dyslipidemia in subclinical hypothyroidism : a case control study

Leila Ahmed Ali[1] & Nora Soumaya Fedala[2]
[1]Bab El Oued Universitary Hospital, Department of Endocrinology and Metabolic Diseases, ALGIERS, Algeria; [2] Bab El Oued Universitary Hospital, Department of Endocrinology and Metabolic Diseases, Algiers, Algeria

Subclinical hypothyroidism (SCH) represents a mild or compensated form of primary hypothyroidism. Although the relationship between SH and lipid profile have been reported in several studies, the results are conflicting. The objective of the present study is to assess dyslipidemia among patients with SCH. Our study included 107 patients vs 108 sex matched controls. Clinical information and medical history were obtained through a questionnary from all SCH patients and normal control subjects. Blood samples were collected and analyzed for thyroid-stimulating hormone (TSH), free thyroxine (FT4), total cholesterol (T-Chol), serum triglycerides (STG), low-density lipoprotein-cholesterol (LDL-C), and high-density lipoprotein-cholesterol (HDL-C). Results: average CT and LDL-C were significantly higher in patients respectively: 1.91 ± 0.385 vs 1.77 ± 0.294 (IC 95% 1.84$P = 0.02$), and 1.19-0.341 vs 1.09 -0.258 ($P = 0.01$). The average value of TG was higher in patients 1.23 ± 0.69 Vs 1.14 ± 0.527 (IC 95% 1.10)but the difference was not significant$P = 0.28$. No correlation was found between TSH and lipidic parameters. Our study concluded that SCH is associated with elevated CT and LDL −CT. Therefore the assessment of lipidic parameters is highly recommended in theses patients

DOI: 10.1530/endoabs.81.P242

P243

Resistant Graves' thyrotoxicosis with adverse cardiovascular effects

Scott Williams, Helmine Kejem, Jael Nizza & Upendram Srinivas Shankar
Arrowe Park Hospital, Upton, United Kingdom

A 61-year-old lady presented to her general practitioner in July 2018 with weight loss, loose stools, hair loss, increased anxiety and dry eyes over several weeks. Blood tests revealed Graves' thyrotoxicosis (TSH < 0.10 mU/l, (RR) 0.30-5.50 mU/l; Free T4 (fT4) 26.1 pmol/l, RR 11.5−22.7 pmol/l; Free T3 (fT3) 11.8 pmol/l, RR 0.0-7.0 pmol/l, thyroid receptor antibodies >40.0U/l, RR 0.0-1.8 U/l; thyroid peroxidase antibodies 173.0 iu/ml, RR 0.0-33.9 iu/ml). There was also evidence of mild Grave's orbitopathy. She was commenced on carbimazole 15 mg once daily (od) and propranolol 20 mg three times daily. As thyrotoxicosis worsened, the dose of carbimazole was gradually increased to 60 mg od (December 2019-January 2020). Thyrotoxicosis did not improve (fT4 45.1 pmol/l, fT3 19.2 pmol/l), thus, a month later, aqueous iodine 1 drop three times a day (5 mg) was added first, followed by 1-month course of prednisolone 20 mg per day. No treatment response occurred, so the patient was referred for radioiodine treatment (RAI), that was delayed by the COVID-19 pandemic. In April 2020, the patient suffered an acute inferior ST elevation myocardial infarction (STEMI). This was treated with primary percutaneous coronary intervention, complicated by recurrent stent thrombosis and cardiac arrest. The patient received a 2-day course of Amiodarone to control the ventricular arrhythmias, which interestingly normalised her fT4 and fT3. The patient remained on carbimazole 60 mg od. A surgical thyroidectomy was considered a high operative risk due to the recent STEMI. A month later, the patient was re-admitted with severe congestive cardiac failure. At that time, there was evidence of new hypothyroid (fT4 4.4 pmol/l, TSH 8.10 mU/l). Thus, the dose of carbimazole was reduced to 5 mg once daily. In July 2020, a recurrence of thyrotoxicosis occurred. RAI was administered in July 2020 with 2 weeks of 30 mg per day prednisolone cover for Grave's orbitopathy. Recurrence of thyrotoxicosis occurred as soon as the carbimazole was stopped. Carbimazole 60 mg was restarted and tapered down over the following year, until the carbimazole requirement plateaued at 15 mg/10 mg alternate days. A second radioiodine dose was administered in July 2021 and the carbimazole stopped a month later. By September 2021, the patient had developed profound hypothyroidism (TSH 76.70 mU/l, low fT4 3.8 pmol/l, fT3 < 3.0 pmol/l) and levothyroxine replacement was initiated. This represents a case of Grave's disease which was resistant to treatment with carbimazole, iodine and first dose RAI. Thyrotoxicosis contributed to cardiac complications (STEMI and heart failure). Additionally, the temporary thyroid function suppression following the amiodarone clearly illustrates the Wolff-Chaikoff phenomenon.

DOI: 10.1530/endoabs.81.P243

P244

A case of severe thyrotoxicosis in acute setting presenting with hypercalcemia and deranged liver function test

Kirtanya Ramachandran[1], Gideon Mlawa[2], Hassan Rehmani[3], Writaja Halder[3] & Prateek Prasannan[3]
[1]Queens Hospital, Romford, United Kingdom; [2] Queens Hospital, Acute Medicine, Romford, United Kingdom; [3] Queen's Hospital, London, United Kingdom

Background
Thyroid hormones may affect bone calcium metabolism either by a direct action on osteoclasts or by acting on osteoblasts which mediate osteoclastic bone resorption. Hyperthyroidism induces an accelerated bone loss, causing hypercalcemia and may thereby increase the risk of low energy fractures. Increased IL-6 levels and hyperadrenergic state due to thyrotoxicosis, are also implicated in hypercalcemia.
Case
A 33 year old who is a known case of Graves' thyrotoxicosis presented to the accident and emergency because of poor control of her thyrotoxicosis symptoms and previous history of asthma, for which she is on Propranalol (40 mg BD) and Carbimazole (10 mg OD). Thyroid examination revealed nodular goitre more enlarged on the right side and fine tremors were present in both hands, bilateral pedal oedema. Bloods revealed deranged thyroid and function test and liver function: TSH: <0.01 mU/l, FT4: >100 pmol/l, FT3: 49.4 pmol/l, calcium: 2.84 mmol/l, ALT 36.3 IU/l.
Patient suffered with constant nausea, poor appetite, weakness, myalgia, mood changes and many other symptoms indicative of poor control. So her Carbimazole dosage was stepped up to 30 mg OD and she was put on a short course of Prednisolone to counteract the impending thyroid storm. Her blood tests 6 weeks after this showed: TSH: <0.01 mU/l, FT4: 26.6 pmol/l, FT3: 9.5 pmol/l, with normal calcium: 2.53 mmol/l and normal ALT 17 IU/l.
Discussion
It has been reported that hyperthyroidism is associated with mild to moderate hypercalcemia in approximately 20% of total patients. The serum calcium levels are often increased by mild to moderate range and it rarely exceeds 3.0 mmol/l in hyperthyroidism associated hypercalcemia. The case presented here demonstrates the importance of timely control of calcium level by adequate anti thyroid treatment which was critical. A follow up appointment has also been arranged for her prior to which certain blood tests like Serum PTH and Vitamin D have also been requested in addition to the routine blood tests. However the quick normalisation of calcium level in her blood following optimisation of her anti thyroid treatment points towards thyrotoxicosis as the cause.
Conclusion
Though this is a rare case, clinicians should be aware of the association of hypercalcemia with hyperthyroidism because timely treatment can save the lives of patients and it should not be ignored after ruling out the other causes of hypercalcemia.

DOI: 10.1530/endoabs.81.P244

P458

COVID-19 outbreak and de-escalation of thyroid cancer diagnosis and treatment

Giorgio Grani[1], Valeria Del Gatto[1], Laura Ciotti[1], Teresa Montesano[1], Marco Biffoni[2], Laura Giacomelli[2], Mariaiuisa Sponziello[1], Valeria Pecce[1], Antonella Verrienti[1] & Cosimo Durante[1]

[1]Sapienza University of Rome, Department. of Translational and Precision Medicine, Rome, Italy; [2] Sapienza University of Rome, Department. of Surgical Sciences, Rome, Italy

Background

The COVID-19 outbreak in Italy forced the health system to cancel all non-urgent outpatient activities, to avoid further spreading of the disease inside the healthcare facilities. At our institution, for cancer patients the hospital allowed treatments and consultations: the medical team, however, identified patients whose procedures could be postponed. Even after May 2020, the capacity for non-urgent thyroid surgeries was reduced. These events enhanced our efforts to reduce overdiagnosis and overtreatment of non-threatening thyroid cancers, as was already suggested by current practice guidelines. The aim of this analysis was to describe the features of patients submitted to thyroid surgery with a final diagnosis of cancer before and after the Italian lockdown.

Methods

Single-center, subgroup analysis of a prospective observational study (NCT04031339), approved by the institutional review board. The records on all patients being followed up in our center were analyzed. The cohort was split in two groups: the first one, before the COVID-19 lockdown (March 2019-February 2020, group A), and the second one during and after the lockdown (March 2020-February 2021, group B). The early response to treatment was assessed 6 to 12 months after initial treatment, according to the American Thyroid Association guidelines.

Results

Group A consisted of 58 patients, while group B of 38 patients, due to a reduction of the number of thyroid surgeries. There were no difference in age (group A: 48 years, 36-61; group B: 52 years, 33-61;$P=0.9$), gender distributions (females 74.1% and 65.8%, respectively), and known risk factors (i.e., family history of thyroid cancer, previous neck irradiation). Also, the histotype distribution was similar in the two cohorts ($P=0.46$). However, in the cohort of patients submitted to surgery after COVID-19 outbreak, the median tumor size was higher: 14 mm (IQR 10-25 mm) vs 9 mm (IQR 6-20 mm;$P=0.01$), and the rate of microcarcinomas was lower (12 [31.6%] vs 33 [56.9%], $P=0.02$). Furthermore, the ATA risk stratification distribution was different ($P=0.036$), with less low-risk and more high-risk cancers (19.4% vs 5.5%). This is consistent with a reduction in overtreatment of low-risk diseases. However, the early response to treatment was not affected ($P=0.73$) , as the vast majority of patients had no evidence of persistent disease after treatment (A, 51.7% and B, 57.9%).

Conclsions

The "forced" reduction of thyroid surgeries due to COVID-19 outbreak improved the adherence to international practice guidelines, with decreased overtreatment: the short-term outcomes were not negatively impacted.

DOI: 10.1530/endoabs.81.P458

P459

Staying cool in the heat − the role of thyroid hormone receptor α in thermoregulation

Sarah Sentis, Riccardo Dore & Jens Mittag

Center of Brain, Behavior and Metabolism (CBBM), Institute for Endocrinology and Diabetes, University of Luebeck, Luebeck, Germany

A normal thyroid status is crucial for normal tissue and organ functioning, including temperature homeostasis. The tissue-specific actions of TH on body temperature regulation and thermogenesis are largely modulated via thyroid hormone receptor TRα. Consequently, mice expressing a mutant TRα display bradycardia and a reduced body temperature at 22°C ambient temperature due to excessive heat loss via the tail. To test whether this peripheral heat loss is the sole reason for the hypothermia, we housed TRα-mutants at 30°C, where tail heat loss is minimized. Using infrared thermography, we revealed that the heat loss effect via the tail could be reversed; however, body temperature surprisingly still remains lower during the inactive phase in TRα-mutants. The observed lack of a compensatory brown fat activation suggests that the central regulation of temperature homeostasis may be impaired in TRα-mutants indicating a lower central body temperature set-point, also at 30°C. Whether the expression of mutant TRα in the brain can indeed lower the central body temperature set-point will be tested in future experiments.

DOI: 10.1530/endoabs.81.P459

P460

Thymic hyperplasia associated with Graves' Disease: lessons from the resolution of six individual cases

Lorenzo Scappaticcio[1], Pierpaolo Trimboli[2], Sergio Iorio[1], Alfredo Clemente[3], Francesco Caiazzo[1], Rosa Di Fraia[1], Lucia Digitale Selvaggio[1], Concetta Di Lorenzo[4], Claudia Varro[4], Giuseppe Bellastella[1], Mariaida Maiorino[1] & Katherine Esposito[1]

[1]University of Campania "L. Vanvitelli", Division of Endocrinology and Metabolic Diseases, University Hospital "Luigi Vanvitelli", Naples, Italy; [2] Faculty of Biomedical Sciences, Università della Svizzera Italiana (USI), Lugano, Switzerland, Clinic for Endocrinology and Diabetology, Lugano Regional Hospital, Ente Ospedaliero Cantonale, Lugano, Switzerland; [3] University of Campania "L. Vanvitelli", Naples, Italy, Radiology and Radiotherapy Unit, Department of Precision Medicine, University of Campania "L. Vanvitelli", Naples, Italy; [4] University of Campania "L. Vanvitelli", Naples, Italy

Objective

Since the relationship between thymic hyperplasia (TH) and Graves' Disease (GD) is of paramount importance for diagnostic and therapeutic choices, a wider knowledge of this association is required for endocrinologists in routine clinical practice. Our aim was to assess the prevalence, the clinical features, and the response to treatment of GD-related TH in an Academic referral centre.

Methods

All consecutive cases of GD-related TH at University Hospital "L. Vanvitelli" between January 2019 to December 2021 were retrospectively reviewed. Cases could be included whether: a) TH was initially suspected by symptoms or neck ultrasound (nUS) but confirmed and followed-up also by neck and chest (nc) computed tomography (CT)/magnetic resonance (RM); b) the imaging follow-up time was at least of six months; c) we had complete data at diagnosis of GD and after therapy (i.e., demographic, clinical, laboratory and imaging details).

Results

Among 144 newly diagnosed GD patients, TH was detected in six patients (6/144, 4.2%). Patients with GD-related TH were female with mean age 34.7 years (age range 23-48 years). Typical cardiovascular and neurological symptoms of thyrotoxicosis were the reasons for the consultation, and mild ocular involvement was present in three patients. No other pathologies affected our patients but multiple sclerosis was previously diagnosed in one case. At nUS mean thyroid volume was 25.2 ml (range 14-36 mL). Mean laboratory values were: fT3 12.5 pmol/l (range 11-18 pmol/l), fT4 32.2 pmol/l (range 28-40 pmol/l), thyrotropin receptor antibodies (TRAb) 9 IU/l (range 5-16 IU/l, positive $\geq$ 1.5 IU/l). In all the six cases TH was asymptomatic and initially identified by nUS as a hypoechoic (relative to thyroid tissue) trapezoidal mass with smooth margins and a reticulated pattern located at jugular notch with partial extension in superior mediastinum. In all the six cases confirmation of TH was obtained by the ncRM, which displayed at T2 images a homogeneous well-defined and lobulated soft tissue mass in the mediastinal prevascular space dislocating epiaortic vessels with a mean maximum diameter of 50 mm (range 44-56 mm) that disappeared after therapy. The average time for TH disappearance was nine months (range 6-14 months), and this was obtained after euthyroidism restoration (i.e. two cases by methimazole, three cases by radioiodine and one case by surgery).

Conclusion

Based on our experience, thymic hyperplasia was not infrequent in the GD setting and it was incidentally detected at nUS. TH regressed with the treatment of GD along with euthyroidism restoration.

DOI: 10.1530/endoabs.81.P460

P461

The effect of over- and undertreatment of hypothyroidism on hospitalization outcomes of patients with decompensated heart failure

Dana Kagansky[1], Karen Or[2], Matan Elkan[1], Shlomit Koren[3,4] & Ronit Koren[4,5]

[1]Shamir Medical Center, Department of Internal Medicine A, Israel; [2]Shamir Medical Center, Department of Internal Medicine D, Israel; [3]Shamir Medical Center, Endocrine Institute, Israel; [4]Sackler Faculty of Medicine, Tel-Aviv University, Tel-Aviv, Israel.; [5]Shamir Medical Center, Department of Internal Medicine A, Israel

Background

Hypothyroidism has profound effects on cardiac function, however, the effect of over- and undertreatment of hypothyroidism on hospitalization outcomes of patients with acute exacerbation of heart failure (HF) has not been evaluated yet.

Methods

We conducted retrospective cohort analyses of outcomes among 231 consecutive patients with treated hypothyroidism who were admitted to the internal medicine departments of Shamir Medical Center with HF from 2011 to 2019. Patients were divided into three groups according to their TSH levels – normal (TSH 0.4-4 mIU/l), over-treated groupTSH $<$ 0.4 mIU/l, and undertreated group (TSH $>$ 4 mIU/l). The main outcomes were functional deterioration, in-hospital mortality, and recurrent hospitalization within three months.

Results

Among 231 patients, 106 were euthyroid, 14 were overtreated, and 111 were undertreated. Patients' mean age was 79.8 $\pm$ 9.4 years. Heart failure with reduced ejection fraction was found in 41.1%, hypertension in 91.3%, and COPD in 26.8% of patients. The most common triggers to HF decompensation were anemia, infection, and low compliance for treatment. In-hospital mortality occurred in 4.7% in euthyroid patients, 14.3% in the overtreated group, and 10.7% in the undertreated group ($P = 0.183$). Differences in 30- and 90-days mortality were not significantly different as well. Functional deterioration during hospitalization was found in 9.4% in the euthyroid patients, non in the overtreated group, and 6.3% in the undertreated group ($P = 0.288$). There was no significant difference in recurrent hospitalization within 3 months between the three groups ($P = 0.438$). However, when evaluating patients with extreme values of TSH ($<$ 0.4 mIU/l or $>$ 10 mIU/l), we found higher 90 days mortality (30.4% vs 15.1%, $P = 0.016$), as compared to patients with normal or mildly increased TSH (0.4-10 mIU/l).

Conclsion

Our results show that mild under- or overtreatment of hypothyroidism did not have a significant detrimental effect on mortality, functional deterioration, or rehospitalization of patients with acute decompensated HF. However, significant over- and undertreatment do cause adverse hospitalization outcomes. Larger cohorts are needed to establish the relationship between treatment targets and hospitalization outcomes of patients who are at risk for hospitalization for HF.

DOI: 10.1530/endoabs.81.P461

P462

Impact of COVID-19 vaccination on incidence of graves' disease

Luigi Di Filippo, Fanny Valsecchi, Stefano Frara, Francesca Perticone, Laura Castellino & Andrea Giustina

Institute of Endocrine and Metabolic Sciences, Università Vita-Salute San Raffaele and IRCCS Ospedale San Raffaele, Milan, Italy

Several reports of Graves' disease (GD) onset after COVID-19 vaccination were recently published. The mechanism underlying GD occurrence in these cases could be related to the autoimmune syndrome induced by adjuvants (ASIA), a condition triggered by several vaccine adjuvants and excipients leading to dysfunctional immune response causing different conditions and endocrinopathies in genetically predisposed subjects. In Italy, population campaign for COVID-19 vaccination started in December 2020 and by the end of December 2021 more than 80% of citizens were vaccinated. The aim of our study was to evaluate for the first time the impact of COVID-19 vaccine on incidence of GD in 2021. Of the 33 first-diagnosis of GD in our Center in 2021, in 16 (48.5%) patients, 2 males (12.5%) and 14 (87.5%) females, GD temporally occurred before the vaccination and in 17 patients (51.5%), 5 males (29%) and 12 females (71%), after the first or second vaccine dose. In 14 (83%) patients, GD occurred in the first four weeks after vaccination, in 1 (6%) after 8 weeks and in 2 (11%) after 12 weeks. All 5 male patients with GD after vaccine injection presented symptoms and signs onset and subsequent GD diagnosis in the first four weeks after vaccination. All 33 patients started anti-thyroid treatment. After three months of therapy, TSH was normalized in 7 out of 14 (50%) patients in whom GD occurs after vaccine administration, whereas fT4 and fT3 levels were available in 13 and 12 and within the normal reference range in 11 and 11 patients (85% and 92%), respectively. Anti TSH-receptor antibodies were negative in 2 out of 6 patients (33.3%) with post-vaccine GD. Possibly COVID-19 vaccine-related GD (within 4 weeks after vaccine administration) accounted for more than 50% of the cases observed in our 2021 monocentric experience. Moreover, since one third of post-vaccine GD were males, our observation strengthens the hypothesis of a causal vaccine-GD relationship since males are usually less affected by GD. In conclusion, for the first time we report a remarkable impact of COVID-19 vaccination in GD diagnosis in a single-center experience. Our report can improve awareness of thyrotoxicosis diagnosis by primary-care physicians and endocrinologists, particularly in patients with marked and persistent symptoms, such as fever, palpitations and asthenia, occurring after vaccination.

DOI: 10.1530/endoabs.81.P462

P463

Management of suspicious neck lymph nodes in patients with differentiated thyroid carcinoma

Simone de Leo[1], Matteo Trevisan[2], Carla Colombo[3], Luca Persani[2], Leonardo Vicentini[4] & Laura Fugazzola[3]

[1]Istituto Auxologico Italiano, Division of Endocrine and Metabolic Diseases, Milano, Italy; [2]University of Milan, Department of Medical Biotechnology and Translational Medicine, Italy; [3]University of Milan, Department of Pathophysiology and Transplantation, Italy; [4]Istituto Auxologico Italiano, Endocrine Surgery Unit, Italy

The management of loco-regional metastases in patients with differentiated thyroid carcinoma is still debated. Current American Thyroid Association guidelines state that in this context the main goal is to differentiate between low-volume metastatic disease that will progress and that remaining stable over time. Aim of our study was to evaluate the behavior of suspicious or cytologically confirmed lymph node metastases, detected after initial treatment (i.e. thyroidectomy with or without cervical lymphadenectomy and radioiodine treatment), in patients with differentiated thyroid carcinoma. Secondary endpoints were the analysis of predictive factors useful to precociously recognize the lesions with a more aggressive behavior. We retrospectively evaluated 95 patients, who were followed-up with serum tumor biomarker evaluation and neck ultrasound every 6-12 months, who had a persistent finding of suspicious neck lymph nodes and a minimum follow-up of 12 months. The lymph-nodal disease was considered aggressive when (a) there was a growth of at least 5 mm in the longest diameter at ultrasound, (b) appearance of at least one new suspicious lymph node, (c) at least one lymph-node was PET-FDG avid. After a mean follow-up of 9 years, 75/95 (79%) patients had a stable disease, while 20/95 (21%) had progressive loco-regional disease. Patients with a more aggressive disease were more frequently male (50% vs 25.3%, $P = 0.03$), older (mean age was 54.3 vs 38 years old, $P = 0.0003$), and with a larger primary tumor (31.8 vs 20 mm, $P = 0.005$). We did not find significant differences regarding TNM, histology, papillary thyroid cancer variant, extrathyroidal extension, ablative radioiodine dose, stimulated thyroglobulin at first radioactive iodine, positive thyroglobulin antibodies after initial treatment, finding of distant metastases at the end of follow-up. At the end of follow-up, 16/20 patients with progressive loco-regional disease had a structural disease despite further treatments (i.e. lymphadenectomy, external beam radiotherapy, radioiodine treatment, tyrosine kinase inhibitors). Our study reports that a high majority of patients with cervical lymph node metastases can be safely followed-up with serial neck ultrasound and serum tumor biomarker evaluation. In case of suspicion, a PET-FDG scan may be necessary. The remaining 20% of patients, in particular male, older patients, and with a larger tumor size at surgery, may have lymph node metastases with an aggressive behavior requiring additional treatments.

DOI: 10.1530/endoabs.81.P463

P464

Steroid treatment in the management of destructive thyrotoxicosis induced by PD1 blockade

Alessandro Brancatella[1], Laura Pierotti[1], Isabella Lupi[1], Lucia Montanelli[1], Nicola Viola[1], Daniele Sgrò[1], Chiara Sardella[1], Lucia Antonangeli[1], Sandra Brogioni[1], Chiara Cremolini[1], Claudio Marcocci[1], Ferruccio Santini[1] & Francesco Latrofa[2]

[1]Endocrinology Unit, Department of Clinical and Experimental Medicine, University Hospital of Pisa, Pisa, Italy; [2]Oncology Unit, Oncology Unit, Department of Translational Research and New Technologies in Medicine and Surgery, University of Pisa, Pisa, Italy

Objective
Destructive thyroiditis is the most common endocrine immune related adverse event (iRAEs) in patients treated with anti-PD1/PD-L1 agents. Given its self-limited course, current guidelines recommend no treatment for this iRAE. Nevertheless in patients with enlarged thyroid volume and a poor performance status, thyrotoxicosis may be particularly severe and harmful. Aim of the study is to evaluate if steroid treatment might be useful in improving thyrotoxicosis in subjects with a poor performance status.
Methods
We conducted a case-control study, comparing the course of thyrotoxicosis of 6 patients treated with oral prednisone at the dosage of 25 mg/d (tapered to discontinuation in three weeks) and an enlarged thyroid volume to that of 12 patients with similar thyroid volume who were left untreated.
Results
The levels of thyroid hormones were lower in subjects treated with prednisone compared to those untreated at time 7, 14, 21, 28, 35, 42, 60 and 90 days ($P<0.05$ at each time). The median time to remission of thyrotoxicosis was 24 days in patients treated with steroids and 92 days in untreated patients ($P<0.001$). At 6 months, the rate of evolution to hypothyroidism was similar in the 2 groups (5/6 in steroid group vs 9/12 in untreated group, $P=0.74$) and no difference was found in tumor progression ($P=0.89$).
Conclsions
A short period of prednisone therapy is useful to restore more quickly euthyroidism in patients with a poor performance status and a severe destructive thyrotoxicosis induced by PD-1 blockade. This treatment does not impair the efficacy of immunotherapy.

DOI: 10.1530/endoabs.81.P464

P465

Change in body fat distribution after total thyroidectomy in euthyroid patients and its relationship with serum adiponectin and leptin levels

Mustafa Unal[1], Nese Cinar[2], Iffet Dağdelen Duran[3] & Duygu Yazgan Aksoy[4]
[1]Istanbul Haseki State Hospital, Department of Endocrinology and Metabolism, Istanbul, Turkey; [2]Mugla Sitki Kocman University Faculty of Medicine, Department of Endocrinology and Metabolism, MUĞLA, Turkey; [3]Denizli State Hospital, Department of Endocrinology and Metabolism, Turkey; [4]Acıbadem University Faculty of Medicine, Department of Endocrinology and Metabolism, Ankara, Turkey

Objective
Euthyroid patients undergoing thyroidectomy were reported to gain weight than their matched counterparts. The etiology is still unknown. Serum adiponectin and leptin levels are related to fat mass and thyroid hormones. We aimed to evaluate the influence of thyroidectomy on body composition, serum adiponectin, leptin levels in euthyroid obese and non-obese patients who underwent total thyroidectomy for goiter.
Methods
We conducted a prospective observational study in a training hospital. Twenty-one euthyroid normal-weight patients (16F/5 M, mean age 43.5 ± 8.4 y), 19 obese patients (17F/2 M, mean age 44.3 ± 8.7 y) and 22 healthy controls (21F/1 M mean age 40.4 ± 10.2) were included in the study. Main anthropometric measures, body fat distribution by bioelectrical impedance analysis, preperitoneal fat thickness, plasma glucose (FPG), insulin, lipids, thyroid hormones, leptin, and adiponectin levels were evaluated before and after surgery. L-thyroxine treatment was started immediately. All patients were maintained in a euthyroid status throughout the study, and patients were re-evaluated three months after the achievement of euthyroidism.
Results
At baseline, obese patients had significantly higher BMI, waist circumference (WC), total fat mass, lean body mass, and SC fat thickness than normal-weight subjects and healthy controls ($P<0.001$ for all). Obese patients had higher visceral fat mass than normal-weight patients at a *P*level of 0.051 ($11.0\pm4.5\%$ vs. $8.4\pm3.9\%$). Serum fasting insulin and leptin levels and HOMA-IR values were significantly higher in obese patients ($P<0.05$ for all). In contrast, all groups had comparable FPG and adiponectin levels ($P>0.05$ for both). Mean TSH and free T4 levels were also similar. Although BMI and WC remain unchanged ($P>0.05$), the visceral fat mass increased significantly after surgery (8.4 ± 3.9 vs. 10.0 ± 4.1 in normal-weight; 11.0 ± 4.5 vs. 15.5 ± 6.0 in obese; $P<0.05$). Despite a significant increase in TSH levels, the values remained normal in both groups. Both groups did not show any significant change in serum FPG, insulin, leptin, and adiponectin levels ($P>0.05$ for all).
Conclusions
Total thyroidectomy caused increased visceral fat mass despite no change in clinical anthropometric measures in patients who had a thyroidectomy due to goitre. This change was unrelated to serum adiponectin and leptin levels.

DOI: 10.1530/endoabs.81.P465

P466

Predictive factors of success of radiometabolic therapy in Graves' disease

Daniela Gallo[1,2], Anna Mercuriali[1], Fabio Tanzi[3], Giovanni Veronesi[4], Adriana Lai[1], Silvia Ippolito[1], Jessica Sabatino[1], Bohdan Patera[1], Silvia Lepanto[1], Nicola Lanzo[1], Gaia Fazzino[1], Federica Bianchi[1], Ilaria Clementi[1], Francesca Manzella[1], Maria Laura Tanda[1,5] & Eliana Piantanida[1,5]
[1]ASST Sette Laghi, Endocrine Unit, Varese, Italy; [1] ASST Sette Laghi, Endocrine Unit, Varese, Italy; [3]ASST Sette Laghi, Health Physics Service, Varese, Italy; [4]University of Insubria, EPIMED Centre, Varese, Italy; [5]University of Insubria, Medicine and Surgery, Varese, Italy

Aim of the study
recurrence or persistence of hyperthyroidism occur in 15-25% of cases after radioiodine therapy (RAI) in Graves' disease (GD). Our study aimed to establish prognostic factors affecting RAI outcome and to investigate if a tailored dosimetric approach based on the application of the "effective biological dose" (BED) offered a higher chance of success.
Materials and methods
our cohort comprised 365 GD patients (280 women and 85 men; age 49 ±14 years) treated with RAI in the period 2001-2021. Patients were allocated into two groups: "failure group" in case of persistence of hyperthyroidism for more than six months post-RAI or hyperthyroidism relapse; "success group" in case persistent euthyroidism or hypothyroidism were achieved after treatment. A multivariate analysis was performed to construct a predictive model of success; a BED threshold value was derived using a ROC curve.
Results
success was achieved in 80% of cases. No significant differences emerged between the two groups when analyzing demographic data (age, sex), smoking habit, GD duration and ongoing medical therapies, presence/severity of orbitopathy, RAI uptake and the applied formula for dosimetry calculation. Negative predictive factors for success were higher thyroid volume, nodules (presence and volume) and disease severity at diagnosis, and a higher effective half-life of radioiodine. The success group had higher FT4 levels immediately before the caption curve (within/slightly above the upper limit of the normal range), a higher difference between the administered activity and the calculated one, a higher BED. Thyroid volume was the most predictive variable in the multivariate analysis, but no single factor was able to predict the outcome. A BED of 369 Gy emerged in the ROC curve as a cut-off value (AUC 0.60, $P=0.01$).
Conclusions
Our study suggests that the outcome of RAI is influenced by clinical, biochemical, ultrasound and dosimetric factors, which interact with each other in a complex way. It is a delicate balance, in which no factor, considering individually, can predict the treatment approach. A multidisciplinary approach is necessary, to better understand the different interactions and confounding factors.

DOI: 10.1530/endoabs.81.P466

P467

Vitamin D levels in patients with graves orbitopathy

Georgios Boutzios, Sofia Chatzi, Areti Mina, Eleni Koukoulioti & Athanasios Tzioufas
School of Medicine, National and Kapodistrian University of Athens, Pathophysiology, Athens, Greece

Introduction
Graves' disease (GD) is an autoimmune thyroiditis frequently associated with development of Graves' orbitopathy (GO). GD patients have lower vitamin D

levels compared to the general population. Whether low vitamin D levels are associated with GO is still controversial. The aim of our study was to assess the vitamin D levels in patients with GO and the clinical outcome.
Methods
This is a single-center observational study in an outpatient clinic of autoimmune endocrinopathies at a Tertiary, General, University Hospital. Patients with GO and increased levels of thyroid-stimulating immunoglobulin (*TSI > 1.75 IU/l)* were included in the study. Clinical activity score (CAS) was evaluated according to the European Consensus Report. Patients were divided in two groups according to CAS (inactive CAS <3 and active CAS $\geq$ 3). Laboratory tests for TSH, T3, FT4, TSI, TgAbs, TPOAbs, complete blood count, liver enzymes and 25OHvitamin D levels were performed in all patients.
Results
A total of 78 patients (71.8 % females) with a mean age of 53.9 ± 13.33 years were analyzed. The mean follow-up was 3 ± 9.04 years. The median TSI levels were 5.65 IU/l and the mean CAS was 3 ± 1.42. 47% (37/67) and 26.9% (21/70) of the patients had positive anti-TPO and anti-Tg antibodies, respectively. 23.1% (18/78) of the patients had undergone total thyroidectomy, 10.3% (8/78) had thyroid cancer, 29.5% (23/78) had other autoimmunities, and 69.2% (54/78) had smoking history. Overall, mean 25OHVitamin D levels were 21.98 ± 1.38 ng/ml. When analyzed based on disease activity, mean 25OHVitamin D levels were 21.05 ± 7.8 ng/ml in patients with inactive GO (CAS <3) and 22.51 $\pm$ 10.72 ng/ml in patients with active GO (CAS ≥ 3). Overall, CAS was significantly associated with TSI levels, diplopia and years of the disease ($P=0.011$, $P=0.025$ and$P=0.035$, respectively). 25OHvitamin D levels were significantly associated with anti-TPO and the disease duration in patients with active GO ($P=0.05$).
Conclsion
In our study, we found a correlation of vitamin D levels with anti-TPO and disease duration in patients with active GO. However, further prospective studies are needed to confirm whether there is a correlation between GO activity and vitamin D levels.

DOI: 10.1530/endoabs.81.P467

P468

From hyper to hypothyroidism: pitfalls in graves' disease following DRESS syndrome

Maria Inês Alexandre[1], Catarina Queirós[2] & Ana Gomes[1]
[1]Hospital de Santa Maria, Endocrinology, Diabetes and Metabolism Department, Lisboa, Portugal; [2]Hospital Santa Maria, Dermatology Department, Lisboa, Portugal

Background
Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome is an uncommon severe systemic hypersensitivity drug reaction. Several studies have described the occurrence of newly developed endocrine autoimmune diseases following DRESS syndrome resolution. However, little attention has been paid by endocrinologists to this disorder. Here, we report a case of a patient with Graves' disease following DRESS syndrome.
Clinical case
A 70-year-old man with urinary tract infection was treated with co-trimoxazole. Two weeks later, he presented to the dermatology outpatient clinic with a pruritic dermatosis, fever and peripheral lymphadenopathy. Physical examination revealed erythematous maculopapular lesions affecting his trunk and limbs and laboratory tests showed leukocytosis, eosinophilia and thrombocytopenia. Diagnosis of DRESS syndrome was made by the dermatologist, and treatment with glucocorticoids was initiated and allowed a gradual recovery. One year later, he presented is his follow-up appointment with fatigue, heat intolerance and palpitations. The blood tests revealed a Graves' hyperthyroidism with suppressed TSH (<0.01 uU/ml), elevated free T4 (2.07 ng/dl; N:0.85-1.7 ng/dl) and positive TSH receptor antibodies (TRAbs) (137 U/l; N: <1.22). He was referred to the endocrinology outpatient clinic, with a suspected newly onset Graves' disease succeeding DRESS syndrome resolution. By the time of his first endocrinology appointment, two months later, the laboratory evaluation revealed hypothyroidism (TSH 33.1 uU/ml; free T4 0.67 ng/dl) with persistent positive TRAbs (128 U/l). The patient started levothyroxine and, to this date, he remains euthyroid under 100 mg per day.
Discussion
There are several reports of newly developed Hashimoto's thyroiditis as sequelae of DRESS syndrome. What is original about this case is the association between Graves' disease and DRESS syndrome, a more uncommon association, and also the coexistence of stimulating and inhibiting TRAbs, leading to a rapid shift from hyperthyroidism to hypothyroidism, a rare condition in Graves' disease. We believe that endocrinologists should be aware of this association and that involvement of endocrine glands should be monitored in patients with a history of DRESS syndrome.

DOI: 10.1530/endoabs.81.P468

P469

Graves' disease and polymorphisms in proinflammatory cytokines genes

Celestino Neves[1,2,3], Joao Sergio Neves[1,4], Juliana Gonçalves[1], Paula Soares[2,3,5], José Luís Medina[2] & Davide Carvalho[1,2,3]
[1]Department of Endocrinology, Diabetes and Metabolism, São João University Hospital Center, Porto, Portugal; [2]Faculty of Medicine of University of Porto, Porto, Portugal; [3]Institute for Research and Innovation in Health (i3S), University of Porto, Porto, Portugal; [4]Department of Surgery and Physiology, Faculty of Medicine of University of Porto, Porto, Portugal; [5]IPATIMUP-Instituto de Patologia e Imunologia Molecular da Universidade do Porto, Porto, Portugal

Background
Graves' Disease (GD) is one of the most common organ specific autoimmune disorders, being characterized by an abnormal production of stimulating autoantibodies to the thyrotropin receptor (TSHR). Some studies demonstrated that genetic polymorphisms in certain cytokines, namely interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α), interleukin-1β (IL-1β), are associated with a greater susceptibility of developing GD. Our aim was to evaluate if these single nucleotide polymorphisms (SNP) also contribute to metabolic disturbances in GD patients.
Methods
Glycemic and lipid profiles were assessed in a case-control study comprising 97 Graves' disease patients. Genetic variants in IL6-174 G/C (rs1800795), TNFA-308 G/A (rs1800629), IL1B-511 C/T (rs16944), and IFNGR1-56 T/C (rs2234711) were discriminated by real-time PCR using TaqMan SNP genotyping assays. To evaluate the associations of SNP genotypes with glycemic and lipid profiles we used independent t test and Kruskal-Wallis test. We also performed linear and logistic regression models adjusted for age and sex.
Results
Within our sample of 97 patients with GD, 91.8% (89 subjects) were females, with a mean age of 44.4 ± 15.1 years. The mean TSH level of our population was 0.4 (0.0-1.3) µUI/l, while the mean levels of FT3 and FT4 were 3.0 (2.6-3.5) ng/ml and 1.1 (0.9-1.4) µg/ml, respectively. The allele T in IL1B-511 C/T was significantly associated with a higher prevalence of diabetes ($P=0.029$). The A allele in TNFA-308 G/A was associated with significant lower levels of HDL cholesterol ($P=0.037$), and with higher levels of fasting insulin ($P=0.042$) along with HOMA-β higher levels in both analyses ($P=0.027$;$P=0.020$). The T allele in IFNGR1-56 T/C polymorphism was associated with significantly higher mean values of fasting glucose in the adjusted analysis ($P=0.047$), as well as higher levels of C peptide ($P=0.026$). In addition, the analysis of the insulin-resistance indexes showed that HOMA-IR was significantly higher in the T allele group ($P=0.035$), while the QUICKI's mean was lower when the T allele was present ($P=0.035$).
Conclusions
Our study demonstrated that SNP in some pro-inflammatory cytokines may affect lipid and glycemic profiles in GD patients. TNF-α-308 A allele might be responsible for lower levels of HDL cholesterol along with increased beta cell function in patients with GD. IL1β-511 T allele may be linked with a higher prevalence of diabetes among GD patients, and IFNGR1-56 T allele is associated with insulin resistance. More studies are needed to evaluate the clinical relevance of these findings.

DOI: 10.1530/endoabs.81.P469

P470

McCune-Albright syndrome diagnosed in adulthood with GNAS mutation-related hyperthyroidism and elevated anti-TPO antibodies. Case report.

Katerina Zajickova, Vlasta Sykorova, Karolina Mastnikova & Josef Vcelak
Institute of Endocrinology, Prague, Czech Republic

McCune-Albright syndrome (MAS) is a rare mosaic disorder caused by a postzygotic activating mutation in the GNAS gene encoding the G protein alpha subunit. Although clinical manifestations may be heterogeneous, MAS is often

characterized by the triad of fibrous dysplasia, café-au-lait skin pigmentations and hyperfunctioning endocrinopathy. We report here a 58-year old woman who presented for evaluation of hyperthyroidism, associated with nodular thyroid disease and elevated anti-TPO antibodies. She had been treated with a small dose of methimazole for 16 years but the remission of hyperthyroidism had not been attained. Neck ultrasound revealed a thyroid gland of normal volume with nodules in both lobes. The largest nodules (both hypervascularized and with microcalcifications) were evaluated by fine needle aspiration biopsy (FNAB) and were found to be benign. TSH-receptor antibodies (TRAb) were not elevated. The presence of anti-TPO antibodies led to a misdiagnosis of TRAb negative Graves' disease. Over the course of her disease, and since childhood, the patient exhibited skeletal deformities and fragility fractures that were erroneously diagnosed as atypical osteogenesis imperfecta or familial expansile osteolysis. The presence of skin pigmentation on her right arm raised the suspicion of MAS. The GNAS activating mutation R201H was found in DNA derived from the thyroid nodule by FNAB. Furthermore, the R201H variant was also found in breast cancer tissue of the patient who had recently undergone right mastectomy. Hyperthyroidism is the second most common endocrinopathy in MAS after precocious puberty. The presumption of autoimmune thyroid disease and the incorrect skeletal diagnosis delayed the recognition of MAS in a patient with a classical combination of polyostotic fibrous dysplasia, hyperthyroidism and café-au-lait skin pigmentations. The GNAS genetic testing finally confirmed the diagnosis. Moreover, identification of the R201H mutation in the breast cancer specimen supports the oncogenic role of activating GNAS mutations in multiple tissues. Supported by MH CZ - DRO (Institute of Endocrinology - EÚ, 00023761) and AZV NU21-01-00448.

DOI: 10.1530/endoabs.81.P470

P471

Hyperpigmentation in Graves' disease

Wiem Saafi[1], Hamza Elfekih[1,2], Asma Ben Abdelkarim[1,2], Sinda Allegue[1], Yosra Hasni[1,2], Amel Maaroufi[1,2], Maha Kacem[1,2], Molka Chadli Chaieb[1,2] & Koussay Ach[1,2]
[1]Farhat-Hached University Hospital, Endocrinology-Diabetology Department, Sousse, Tunisia; [2]Faculty of Medicine Ibn El Jazzar, University of Sousse, Sousse, Tunisia

Introduction
Hyperpigmentation is a clinical sign that can be associated with different endocrine disorders. It is commonly seen in Addison's disease and has rarely been reported in Graves' disease. The exact physio pathological mechanism of this sign is not well established in hyperthyroidism. We describe two cases of Graves' disease accompanied by diffuse hyperpigmentation.
Case report
Case 1 was a 63-year-old female admitted to the endocrinology department for the management of a thyroid crisis. The physical examination didn't find signs of thyroid eye disease or goiter, we instead noted diffuse hyperpigmentation. Laboratory investigations confirmed the diagnosis of hyperthyroidism showing a 6-fold elevation of FT4 (7.7; normal: 0.9-1.7 ng/dl) and low serum thyroid-stimulating hormone (TSH <0.001 mIU/l) with positive anti-TSH receptor antibodies. Hepatic function tests revealed cytolysis and cholestasis. Addison's disease and autoimmune hepatic diseases were eliminated. The patient received radioiodine treatment after preparation with antithyroid drugs. She regained euthyroidism with normalization of her liver function tests, but hyperpigmentation persisted.
Case 2 is a 52-year-old male patient who presented to our department with Graves' disease. He had clinical signs of hyperthyroidism a few months before admission with a concomitant change of his skin color. On physical exam, we noted irregular tachycardia with goiter. The patient had diffuse hyperpigmentation. Hyperthyroidism was biologically confirmed; high serum free T4 (10.3 ng/dl) with low serum thyroid-stimulating hormone (TSH <0.001 mIU/l). Anti-TSH receptor antibodies were positive. The rest of the explorations revealed cholestasis with normal transaminase levels. The patient was treated with radioiodine with clinical and biological amelioration. However, hyperpigmentation remained.
Discussion
Hyperpigmentation is rarely described as a clinical sign of hyperthyroidism. Its physiopathological mechanism is not well elucidated. It has been hypostasized that thyrotoxicosis is associated with an increased ACTH release causing overproduction of melanin and that melanocytes express TSH receptors resulting in their proliferation when stimulated with TRAb**.** More studies are needed to understand the relationship between skin color modification and thyroid function status.

DOI: 10.1530/endoabs.81.P471

P472

Cervical lymph nodes metastases in differentiated thyroid cancer: impact on clinical outcome

Carla Gambale, Antonio Matrone, Lea Contartese, Alessandro Prete, David Viola, Laura Agate, Eleonora Molinaro & Rossella Elisei
Endocrine Unit, Department of Clinical and Experimental Medicine, University Hospital of Pisa, Pisa, Italy

Background
Cervical lymph node metastases at histology are common findings in differentiated thyroid cancer (DTC); however, their impact on clinical outcome is debated.
Material and method
1332 DTC patients, performed the first ^{131}I treatment between January 2010 and September 2012 and were divided into 2 groups: absence (Nx/N0) or presence (N1) of lymph node metastases at histology. The latter group was further split in central compartment (N1a) or latero-cervical compartment (N1b) metastases. Clinical outcome, according to 2015 ATA guidelines, was defined at: post-operative and post-^{131}I (median time from surgery: 6 months), first evaluation after ^{131}I (median time from ^{131}I: 8 months) and at last evaluation (median time since ^{131}I: 83 months).
Results
1064 (79.9%) patients were in the Nx/N0 group and 268 (20.1%) in the N1 group. N1 patients were more frequently males (35.8 vs 27.3%, $P<0.01$) and younger (median age 40 vs 47, $P<0.01$). Several pathological features were prevalent ($P<0.01$) in the N1 group: multifocality (63.4 vs 46.8%), mETE (67.9 vs 24.6%), vascular invasion (28 vs 8.9%) and intermediate ATA risk (94.8 vs 36.5%). The incomplete structural response rate was higher in N1 group, in all times of follow-up ($P<0.01$), despite N1 patients significantly experienced higher ^{131}I activities and more neck re-operation. N1b ($n=142$, 53%) patients, compared to N1a ($n=126$, 47%), had higher prevalence of mETE (74.6 vs 59.5%, $P<0.01$) and vascular invasion (33.1 vs 22.2%, $P<0.05$) and lower histological thyroiditis (21.1% vs 35.7, $P<0.01$). Regarding treatment, N1b patients experienced higher ^{131}I activities and more neck re-operation. Structural incomplete response rate was significantly higher at post-operative (16.2% vs 6.3%), post-^{131}I (26.1 vs 8.7%) and at first assessment after ^{131}I (24.3% vs 9.6%). Conversely, at the last evaluation, significance was not reached (17.9% vs 10.4%, $P=0.09$).
Conclusions
Cervical lymph node metastases at histology are associated with more aggressive features in DTC. Despite the higher activity of the ^{131}I administered and the more frequent surgery on neck, the N1 patients showed a higher structural incomplete response rate at each time of the follow-up. N1b patients, compared to N1a, experienced more frequent and aggressive treatments during the follow-up with higher incomplete structural response rate.

DOI: 10.1530/endoabs.81.P472

P473

Comparison of serum calcitonin and neck ultrasound sensitivities in identifying medullary thyroid carcinoma

Antonio Matrone, Carla Gambale, Alessandro Prete, Virginia Cappagli, Loredana Lorusso, Valeria Bottici, Paolo Vitti & Rossella Elisei
Endocrine Unit, Department of Clinical and Experimental Medicine, University Hospital of Pisa, Pisa, Italy

Background
Serum calcitonin (CT) is a very sensitive test for the diagnosis of medullary thyroid carcinoma (MTC). However, its routine dosage in patients with nodular thyroid disease is not recommended by all scientific societies. In addition, to optimize costs, it is only suggested in the case of suspicious nodules on ultrasound, indeterminate nodules at cytology or nodular goiter before surgery. The aim of the study is to evaluate the serum CT in a series of consecutive MTC divided according to the pre-operative ultrasound risk.
Materials
We evaluated the pre-operative features of 152 consecutive patients surgically treated for MTC (2014-2020). Based on the EU-TIRADS, ATA, AACE/ACE-

AME, ACR-TIRADS, and K-TIRADS ultrasound risk stratification systems, we defined 2 groups: Group A (72 pts - 47.4%) with high ultrasound suspicion and Group B (80 pts - 52.6 %) with intermediate-low ultrasound suspicion of malignancy.
Results
The 2 groups did not differ in any epidemiological and clinical features. Pre-operative CT was significantly higher in Group A [369.5 pg/ml (IQR: 84-1718.8)] than Group B [115.5 pg/ml (IQR: 41.5-555)] ($P=0.01$). Despite this difference CT values were suggestive of MTC in both groups. Moreover, CT values directly correlated with nodule size in both groups. To note, in microcarcinomas, also if not clearly diagnostic of MTC, CT value was above the normal range. FNAC was suggestive for MTC only in 43.3% of Group A and 56.5% of Group B, without significant differences.
Conclusions
Increased pre-operative CT values are confirmed to be highly suggestive of MTC, regardless of the ultrasound suspicion of malignancy, the size of the nodule, and the cytological result.

DOI: 10.1530/endoabs.81.P473

P474

Potential risk factors for post-treatment recurrence in patients with intermediate-risk differentiated thyroid carcinoma

Mattia Rossi[1], Chiara Mele[2], Ruth Rossetto Giaccherino[1], Denise Brero[3], Giulia Marsan[4], Gianluca Aimaretti[2], Ezio Ghigo[1] & Loredana Pagano[1]
[1]Endocrinology, Diabetes and Metabolism, Department of Medical Sciences, University of Turin, Turin, Italy; [2]Endocrinology, Department of Translational Medicine, Università del Piemonte Orientale, Novara, Italy; [3]University of Turin, Turin, Italy; [4]Università del Piemonte Orientale, Novara, Italy

Introduction
The recurrence rate of intermediate-risk differentiated thyroid carcinoma (DTC) ranges between 5% and 20% and the therapeutic strategy requires further evaluations.
Aim
We therefore investigated the potential risk factors for post-treatment recurrence of intermediate-risk DTC at 1 and 3 years from diagnosis.
Methods
This retrospective observational study included 121 patients who underwent thyroidectomy for intermediate-risk DTC between January 2017 and December 2020 in two Italian centres (Endocrinology, Diabetology and Metabolism - Department of Medical Sciences, Turin and Endocrinology - Department of Translational Medicine, Novara). For each patient, demographic, biochemical and histopathological features of DTC were evaluated. Moreover, data about radioiodine (RAI) treatment were recorded and rate of tumour recurrence at 1 and 3 years from diagnosis was assessed. Multivariate logistic regression models were used to identify risk factors for tumour recurrence.
Results
Most of patients were females (M/F:1/3) with an age at diagnosis >55 years in 69.4% of cases. Overall, 92 patients (76.0%) underwent RAI treatment. This subgroup had a higher prevalence of microscopic extrathyroidal extension (mETE) of the tumour (53.3% vs 31.0%, $P=0.03$) and clinical lymph node metastasis at diagnosis (74.4% vs 45.0%, $P=0.01$), as well as higher number (5.5 $\pm$ 4.5 vs 1.8 $\pm$ 0.7, $P=0.02$) and dimensions (12.2 $\pm$ 8.4 vs 0.6 $\pm$ 0.7, $P=0.01$) of metastatic lymph nodes than patients who did not undergo RAI. Tumour relapse was observed in 18.1% and 20.7% of cases at 1 and 3 years from diagnosis, respectively, without significant differences between subgroups. Multivariate logistic regression analysis did not show any significant association between the presence of tumour relapse and DTC histopathological phenotype. The presence of clinical lymph node metastasis and radioiodine dose, a higher stimulated Tg levels in patients undergoing RAI (OR = 1.02, 95%CI 1.00-1.03, $P=0.04$) and a lower age at diagnosis (OR = 0.93, 95%CI 0.87-0.99, $P=0.03$) emerged as the only independent risk factors for 1 year-tumour relapse. Instead, the 3-year-tumour relapse was independently predicted only by the presence of 1 year-tumour relapse (OR = 15.41, 95%CI 1.12-212.10, $P=0.04$).
Discussion
In our study, mETE and clinical lymph node metastasis represent the main indicators for referring patients to RAI. Stimulated thyroglobulin levels in patients undergoing RAI, and the age at diagnosis are the only factors that independently influence the risk of recurrences in patients with intermediate-risk DTC.

DOI: 10.1530/endoabs.81.P474

P475

Repeating thyroid FNAC: inter-observer agreement among high- and low-volume thyroid services in Naples metropolitan area and correlation with the EU-TIRADS

Lorenzo Scappaticcio[1], Pierpaolo Trimboli[2], Sergio Iorio[4], Stefania Arena[5], Nicole Di Martino[5], Annarita Palmieri[5], Katherine Esposito[4] & Giuseppe Bellastella[4]
[1]University of Campania "L. Vanvitelli", Division of Endocrinology and Metabolic Diseases, University Hospital "Luigi Vanvitelli", Naples, Italy; [2]Faculty of Biomedical Sciences, Università della Svizzera Italiana (USI), Clinic for Endocrinology and Diabetology, Lugano Regional Hospital, Ente Ospedaliero Cantonale, Lugano, Switzerland; [4]University of Campania "L. Vanvitelli", Division of Endocrinology and Metabolic Diseases, University Hospital "Luigi Vanvitelli", Naples, Italy; [5]University of Campania "L. Vanvitelli", Naples, Italy

Objective
Our institution (University Hospital "L. Vanvitelli" - Naples, Italy) is a high-volume (HV) center in Naples metropolitan area and many patients are referred there to repeat thyroid fine-needle aspiration cytology (FNAC) after initial FNAC performed in low-volume institutions (LV). The aims of the study were to 1) to examine the inter-observer agreement between HV and LV institutions according to the Italian thyroid cytology system, and 2) explore how the discordant FNAC reports were distributed among the European Thyroid Imaging and Reporting Data System (EU-TIRADS) categories.
Methods
All consecutive cases of repeated FNAC performed at University Hospital "L. Vanvitelli" from January 2016 to December 2021 were retrospectively reviewed. Cases could be included whether: a) the second FNAC diagnosis was achieved by HV cytologists blind of the previous LV report; b) HV FNAC sample was independently evaluated by two observers; c) nodule could be classified according to the EU-TIRADS by two endocrinologists reviewing ultrasound (US) blind of FNAC reports. Fleiss' kappa (κ) was used to assess the inter-observer agreement, and categorical variables were compared by chi-square testing. $P < 0.05$ was considered statistically significant.
Results
A total of 124 nodules from 124 adults (mean age 49 years; mean maximum diameter 19 mm) were evaluated. Initial FNAC reports at LV were: 4 (3.2%) TIR1c, 64 (51.6%) TIR2, 48 (38.7%) TIR3A, 8 (6.5%) TIR3B, 0 TIR4, 0 TIR5. At repeated FNAC, cytological diagnosis was unchanged in 64 (51.6%) cases including TIR2 and TIR3A results. A downgraded FNAC diagnosis (i.e., TIR2 vs TIR3A, TIR2 vs TIR3B) was observed in 36 (29%) nodules. An upgraded FNAC diagnosis (i.e., TIR3B vs TIR2, TIR3B vs TIR3A, TIR4 vs TIR3A, TIR5 vs TIR2) was recorded in 24 (19.4%) nodules. The overall FNAC reports were significantly different between the LV and HV institutions. The inter-observer agreement between LV and HV institutions was poor ($\kappa=0.13$). Changed FNAC results were significantly ($P=0.0023$) more frequent in nodules at intermediate/high-risk (i.e., EU-TIRADS 4/5) than in those at no/low risk (EU-TIRADS 2/3) [i.e., 32/48 (66.7%) and 28/76 (36.8%), respectively]. Downgraded FNAC results were significantly more frequent in EU-TIRADS 2/3 ($P=0.001$) while upgraded FNAC were present only in EU-TIRADS 4/5 (24/24, 100.0%).
Conclusion
The inter-observer agreement among LV and HV thyroid services was poor. The EU-TIRADS 4 and 5 categories included all the nodules with FNA results reclassified as higher risk (i.e., TIR3B-TIR4-TIR5) by the high-volume cytology service.

DOI: 10.1530/endoabs.81.P475

P476

Levothyroxine dose adjustment after total thyroidectomy using an artificial intelligence methodology

Hadi Tabesh[1] & Hamid Bazrafshan[2]
[1]Department of Life Science Engineering, Faculty of New Sciences and Technologies, University of Tehran, Tehran, Iran; [2]LMU Klinikum, Ludwig Maximilian University of Munich, Munich, Germany

Introduction
Finding the optimal levothyroxine (LT4) dose regime to ameliorate the abnormally low levels of natural thyroid hormones, especially for thyroidectomized patients, is still challenging. Many researchers have studied various LT4 dosage regimen clinically; and ultimately, they proposed multiple variables affecting LT4 requirements including age, gender, body weight, body mass index (BMI), and body surface area (BSA). However, prescribing the most appropriate LT4 dose regime for different patients remains ambiguous.

Method
We attempt to adjust an appropriate LT4 dose regime for a total thyroidectomized virtual-patient by means of fuzzy logic system (FLS) methodology, an applicable artificial intelligence technique. THYROSIM 3.0© a free web application developed by UCLA Biocybernetics Laboratory, was utilized as a model of feedback control of hypothalamus-pituitary-thyroid axis. In order to evaluate patient responses to LT4 monotherapy, we simulated our total thyroidectomized virtual-patient by setting T3 and T4 secretion parameters at 1% while receiving dynamic oral LT4 dosages post-surgery. In addition, with an assumption that no supplement was administrated, the absorption rate of oral LT4 was set to 88%. Fuzzy logic controller was developed using MATLAB software ver. 2019. The discrepancies of TSH value at day n and one-step time back TSH value (at day n-1) in regard with the TSH set point were considered as the controlled variables while LT4 daily dosage was considered as the manipulated variable.
Results
According to our proposed algorithm, our developed FLS recommends a LT4 monotherapy dose regime for the assumed total thyroidectomized virtual-patient on a daily basis as presented in the following table. The resulting doses provided by FLS are indicated as "Precise FLS LT4 dose" while available doses are presented by rounding the precise dose considering 25 μg intervals in respect with the smallest increment between LT4 dosing strengths.
Conclusion
The FLS method could precisely predict the appropriate LT4 daily doses for our total thyroidectomized virtual-patient. This proposed method would dramatically declines the numbers of days in which our virtual-patient experiences thyroid hormone levels out of normal ranges while eliminating the rigorous fluctuations of the plasma levels of thyroid hormones.

Day	Recommended FLS LT4 dose (μg)	Available LT4 dose (at 25 μg intervals)	TSH error (mU/l) (calculated by FLS)
1	377.87	375	50.05
2	307.86	300	20.82
3	241.83	250	12.35
4	207.31	200	8.29
5	180.45	175	5.81
6	166.31	175	4.30
>6	ca. 159.66	150	ca. 3.38

DOI: 10.1530/endoabs.81.P476

P477

The effects of aging on thyroid C-cells in male rats

Branko Filipović[1], Vladimir Ajdžanović[2], Jasmina Živanović[1], Milica Manojlović-Stojanoski[1], Svetlana Trifunovć[1], Nataša Nestorović[1] & Branka Šošić-Jurjević[1]
[1]Institute for Biological Research "Siniša Stanković" - National Institute of Republic of Serbia, University of Belgrade, Citology, Beograd, Serbia;
[2]Institute for Biological Research "Siniša Stanković" - National Institute of Republic of Serbia, University of Belgrade, Citology, Beograd, Serbia

Thyroid C-cells, as a second type of endocrine cell population within thyroid, produce and secrete peptide hormone calcitonin (CT). This hypocalcemic hormone acts as an inhibitor of bone resorption. The aging is a complex process that alters various cellular functions. Therefore, the aim of this study was to examine the aging-related changes in the structure and function of CT-producing thyroid C-cells in male Wistar rats, using histomorphometric, ultrastructural and biochemical analysis. The investigation was performed on three groups of male rats: adult (3-months old), middle-aged (16-months old) and old (24-months old). The peroxidase-antiperoxidase method was applied for localization of CT in the C-cells. Stereological analysis was performed using Olimpus microscope (BX-51), equipped with a microcator, a motorised stage and a CCD video camera, and controlled by the newCAST stereological software package. Blood serum samples were analyzed for determination of CT, testosterone (T), calcium (Ca^{2+}) and phosphorus (P) concentrations. We found a significant increase in the volume density (Vv) of thyroid C-cells in both middle-aged and old rats, all compared to adult animals. The percentage of smaller volume range C-cells (<500 μm^3) increases, while the proportion of greater volume rang C-cells (both 500-1000 μm^3 and >1000 μm^3) markedly decreases with aging. By ultrastructural analysis we found that the average number of secretory granules *per* C-cell was significantly increased in both middle-aged and aged rats, all compared to adults. Unlike the C-cells of adult rats, these granules in older, especially in old animals, had a content of fairly low density. By the biochemical analysis, we detected a significant increase in serum CT levels, while serum T was markedly reduced in both middle aged and old rats, all in comparison with adults. Serum Ca^{2+} concentration significantly decreased in middle-aged rats compared to adults, while concentration of serum *P* was lower in both middle-aged and old rats, all related to adult group. Our findings show that aging process increases the Vv of thyroid C-cells, with a simultaneous change in percentage of cells with larger and smaller volume rang, and an increase in the number of both cell types. These changes, accompanied by modulation of the cellular ultrastructure and an increase in serum CT levels, reflect the structure and function of CT-producing thyroid C-cells in our aging model.

DOI: 10.1530/endoabs.81.P477

P478

Thyroid nodules and glucose metabolism derangements: does sex matter?

Irene Gagliardi[1], Alberto Gobbo[1], ROBERTA ROSSI[2], Martina Rossi[2], Maria Rosaria Ambrosio[1] & Maria Chiara Zatelli[1]
[1]University of Ferrara, Dept of Medical Sciences, FERRARA, Italy;
[2]Endocrine Unit, Department of Oncology & Specialty Medicines, Ferrara, Italy

Background
Glucose metabolism derangements (GMD) and thyroid nodules (TN) are the most frequent endocrine disorders. A relationship between these conditions has been suggested, but data are still controversial and no evidence was reported regarding sex differences.
Aim
To evaluate the distribution of impaired fasting glucose (IFG), normal glucose tolerance (NGT), impaired glucose tolerance (IGT), type 2 diabetes (T2DM) and TN according to sex.
Methods
Retrospective analysis of 342 patients who underwent both an oral glucose tolerance test and a thyroid ultrasound at our Institution. Only patients with normal TSH levels, with or without replacement therapy (RT), were included.
Results
Most patients were females (78%) and were ≥50 years old. No mean age differences were found among sexes in the whole group and among the different GMD categories. IGT/T2DM rate was higher among patients ≥ 50 years old as compared to younger patients in both sexes (males 66.7% vs. 34.5%, $P<0.01$; females 43.2% vs. 20.8%, $P<0.001$). Males presented IGT/T2DM more frequently than females (54% vs. 33%, $P< 0.01$) even when considering only the 193 patients ≥50 years old (67% vs. 43%, $P< 0.01$). No differences between sexes were found concerning IFG nor insulin resistance. Total TN prevalence was 61%, with no differences between the sexes. TN prevalence assessed in GMD classes did not show any significant difference. However, within the female group, TN prevalence was significantly higher in ≥ 50 years old subjects as compared to younger females (72% vs. 51%, $P<0.01$) and in IFG group as compared to no-IFG group (79% vs. 57%, $P<0.01$). When considering only ≥50 years old females, we confirmed that TN prevalence was higher in the IFG group as compared to no-IFG group (87% vs. 63%, $P<0.01$). Median thyroid volume (TV) was found significantly higher in males as compared to females (13 vs. 10 ml, $P<0.01$) in the whole group and among the different GMD categories, except for the IFG group.
Conclusions
Age was confirmed as a risk factor for TN occurrence and GMD. In males, IGT/T2DM prevalence is higher, but no relationship was found with TN occurrence. Furthermore, they showed higher TV in most of GMD categories. Older females present more frequently TNs that occurred more often in patients with IFG. More studies are needed to further explore the relationship between TN and glucose metabolism disorders in order to identify higher-risk population sub-groups.
*The first two Authors equally contributed to the study

DOI: 10.1530/endoabs.81.P478

P479

Role of irisin as modulator of antioxidants in two models of non-thyroidal illness syndrome

Carmine Bruno[1], Edoardo Vergani[1], Emmanuele Capobianco[1], Maria Anna Nicolazzi[4], Angela Maria Rita Favuzzi[2], Andrea Silvestrini[3], Elisabeta Meucci[3], Nicola Panocchia[1] & Antonio Mancini[1]

[1]Università Cattolica del Sacro Cuore, Medicina e Chirurgia Traslazionale, Rome, Italy; [2]Fondazione Policlinico Universitario A. Gemelli IRCCS, Scienze Cardiovascolari, Rome, Italy; [3]Università Cattolica del Sacro Cuore, Scienze Biotecnologiche di Base, Cliniche Intensivologiche e Perioperatorie, Rome, Italy

Non-thyroidal-illness syndrome (NTIS) is present in chronic diseases and considered an adaptive mechanism. However oxidative stress is linked to NTIS in a vicious circle, due to deiodinases alteration and negative effects of low T3 on antioxidant levels or activity. Moreover there is a tissue-specific thyroid hormone transport, receptor binding and hormone metabolism. Muscle is one of the main targets of thyroid hormone; on the other hand, Irisin is a novel discovered myokine firstly identified for its ability to induce browning of white adipose tissue, increase energy expenditure and finally protect against insulin resistance. Unconclusive data have been reported about the role of Irisin in chronic diseases such as chronic heart and renal failure; moreover, no correlation between Irisin and antioxidant status has been investigated. Therefore, we performed a case-control study with the primary end-point to evaluate Irisin levels in two models of NTIS, such as chronic heart failure and chronic kidney disease during haemodialytic treatment; the secondary end-point was the correlation with total antioxidant capacity in order to establish a possible role of Irisin in the modulation of antioxidant systems. Two groups of patients were selected. Group A included Chronic heart failure patients ($n=18$; Aged 70.22 $\pm$ 2.78 ys; BMI $\pm$ 27.75 $\pm$ 1.28 Kg/m^2); Group B included Chronic Kideny Disease patients ($n=29$; Aged 67.03 $\pm$ 2.64; BMI 24.53 $\pm$ 1.01); Finally, 11 normal subjects have been assumed as controls. Irisin has been evaluated by ELISA method and Total Antioxidant (TAC) capacity by spectrophotometric method. Irisin was significantly higher in Group B vs A and controls (Mean $\pm$ SEM: 20.18 $\pm$ 0.61 ng/ml vs 2.77 $\pm$ 0.77 and 13.06 $\pm$ 0.56, respectively; $P<0.05$); a significant correlation between Irisin and TAC was observed only in group B.
These preliminary data suggest a possible role of Irisin in modulation of antioxidant systems in two chronic syndromes characterized by low T3 syndrome, but with differential pattern in the two models studied. Further studies are needed to confirm these preliminary observations. That can be the basis for a longitudinal investigation, to assess a prognostic role of Irisin evaluation and possible therapeutical implications

DOI: 10.1530/endoabs.81.P479

P480

Radioactive iodine treatment in thyrotoxicosis- audit, Southampton general hospital

Mohammed Salloum, Ma'en Al-Mrayat, Francis Sundram, Jana Bujonova, Ziauddin Saad, Nemia Pilobello, Diane Bray, Alicja Knysak & Philip Newland-Jones
University Hospital Southampton, Department of Endocrinology and Department of Nuclear Medicine, Southampton, United Kingdom

Hyperthyroidism is common and in iodine-sufficient parts of the world the prevalence of overt hyperthyroidism is estimated to be 0.2% to 1.3%. The treatment options include antithyroid medication (ATD), thyroid surgery, or Radioactive iodine (RAI). The latter is increasingly used as a first line definitive treatment for hyperthyroidism. We reviewed the outcomes of patients who received RAI at our tertiary nuclear medicine department over a 4-year period (May 2015 to Dec 2019) and who are under the care of our unit to ensure we have relevant follow up data. We identified 146 Patients who received RAI: 119 Female (82%), 27 Male (18%) with a mean age of 51.3 years. 45.9 % of patients had Grave's Disease, 11.7% had single toxic adenoma (STA), 40.4% had Toxic Multinodular Goitre (MNG) and 2% had mixed disease (MNG & Graves). Outcome post-RAI: 129 patients (88.3%) achieved remission from thyrotoxicosis after a single dose. 7.5% (5 patients with Graves' disease -GD, and 6 patients with MNG) needed 2 doses of RAI to achieve remission. 5 patients (3.4%; 3 with MNG, one patient with mixed disease, and one with GD) did not respond after 2 doses of RAI and were still on ATD. The remission rates after the first dose per diagnosis were: 91 % for GD, 83 % for MNG, 66% for mixed disease, and 100% for STA. 74.6% of the treated patients developed permanent hypothyroidism after responding to RAI. The risk of developing hypothyroidism was higher in GD patients who responded to treatment, of who 95.5% developed hypothyroidism, followed by patients who had STA (82.3%) with only 47.5 % of patients with MNG developing subsequent hypothyroidism. The average time to develop hypothyroidism after RAI was 3.6 months, however, this tended to be longer with patients who had MNG. In conclusion, RAI is an effective treatment for thyrotoxicosis, which is associated with a high rate of hypothyroidism and a small rate of failure. Our Patients were closely followed up post-treatment as per standard recommendations.

DOI: 10.1530/endoabs.81.P480

P481

Unexpected alterations in thyroid status: a case of alemtuzumab-induced Graves' disease with fluctuating course

Bárbara Filipa Araújo[1], Mariana Lavrador[1], Cátia Araújo[1], Ana Ribeiro[1], Sandra Paiva[1] & Isabel Paiva[1]
[1]Centro Hospitalar e Universitário de Coimbra, Endocrinology Department, Coimbra, Portugal

Introduction
Alemtuzumab is a humanized anti-CD52 monoclonal antibody approved for the treatment of relapsing−remitting multiple sclerosis (RRMS). Through an immune reconstitution mechanism, it leads to thyroid autoimmunity in 35% of cases, with Graves' disease (GD) being the most common presentation. Alemtuzumab-induced GD exhibits distinctive clinical and immunological features, with rarely reported cases of fluctuating thyroid status with documented both blocking (TBAb) and stimulating (TSAb) TRAb.
Case description
A 48-year-old woman, diagnosed with RRMS at the age of 33, underwent the first and second cycle of alemtuzumab in 2019 and 2020, respectively. Neither the patient nor her relatives had history of thyroid disease. Clinical and medication history were otherwise unremarkable. Almost 12 months after treatment, she complained about exacerbated fatigue, and was referred to the endocrinology appointment for altered function tests. Clinical examination revealed a non-pulsatile goiter, with no evident signs of orbitopathy (Clinical Activity Score 0). Laboratory workup showed TSH 0.004 mUI/ml (0.4-4), fT4 2.2 ng/dl (0.7-1.5), fT3 5.1 pg/ml (1.8-4.2), TRAb 110 U/l (<1.0) TSAb 40 U/l (<0.1) and anti-TPO 916 UI/ml (<5.6). Thyroid ultrasound excluded nodules. She started treatment with methimazole (MMI) 5 mg/day. Two months after, analytical follow-up revealed TSH 0.29 mUI/ml, fT3 2.1 pg/ml, fT4 0.60 ng/dl and was told to stop MMI. The patient was reevaluated in 2 months, under no therapy, with worsening of fatigue and palpebral oedema, with TSH 93 mUI/ml, fT4 <0.40 ng/dl, fT3 $<$ 1.0 pg/ml, TRAb 98 U/l, TSAb 7.3 U/l. At this point she started levothyroxine (LT4) with progressive doses up to 75 micrograms/day. Six months later, TSH was <0.004 mUI/ml, fT4 1.4 ng/ml, TRAbs 3.1 U/l, TSAb 2.7 U/l and LT4 was stopped. Thereafter, thyroid function kept switching unexpectedly between hyper and hypothyroidism, and was finally proposed to treatment with radioiodine (RAI). Six weeks after RAI, with no other therapy, TSH was 68 mUI/ml, fT4 $<$ 0.40 ng/dl, TRAbs 10 U/l, TSAb 7.3 U/l, and LT4 was re-started in progressive doses.
Conclusion
We present a case of alemtuzumab-induced GD with unexpected fluctuations from hyperthyroidism to hypothyroidism, not explained by omission or changes in therapy. There was evidence of periods were TRAb level were rising but TSAb levels were decreasing, which may be explained by the presence of TBAb in circulation. Our case report emphasizes the need for close monitoring of thyroid function in patients with alemtuzumab-induced GD, as maintaining euthyroidism in these patients may represent a challenge.

DOI: 10.1530/endoabs.81.P481

P482

Thyroid incidentalomas: which features in internal medicine?

Asma Tekaya, Asma Kefi, Khaoula Ben Abdelghani, Mounira El Euch, Cyrine Sassi, Sami Turki & Ezzedine Abderrahim
Charles Nicolle Hospital, Department of Internal Medicine A, Tunis, Tunisia

Background
Thyroid nodules (TN) are common. Their prevalence increases with age. A thyroid incidentaloma (TI) is defined as a non-palpable TN detected fortuitously during a radiological investigation performed for reasons unrelated to the thyroid gland. Although they are mostly benign, the risk of malignancy is estimated from 7% to 15% of nodules. The objective of this study is to investigate the characteristics of TI in a cohort of patients admitted in an internal medicine department.

Methods
A descriptive retrospective study identifying 48 records of TN in patients hospitalized in an internal medicine department between 2016 and 2021. Then we studied cases of TI.
Results
Among the 48 cases of TN, 50% were incidentalomas. There was a clear female predominance (gender ratio: 0.17). The mean age was 50.8 years old (ranging between 29 and 73). The patients had a medical history of chronic renal failure in 6 cases, Systemic Lupus in 4 cases, Sjögren syndrome in 3 cases, Crohn disease in 1 case, sarcoidosis in 1 case, myelodysplasic syndrome in 1 case and AL amyloidosis in 1 case. TI were mostly detected by neck ultrasound. Only 12.5% were discovered by chest CT scan. These investigations were performed in order to examine lymph nodes (45.83%), parathyroid glands (33.33%) lung parenchyma (12.5%) or parotid glands (8.33%). Ultrasonography, performed in all patients, showed: a solitary nodule (41.7%), a multinodular goiter (29.2%) and lymphadenopathy (14.6%). According to the European Thyroid Imaging Reporting and Data System (EU-TIRADS), TN were classified as EU-TIRADS 2 (4.17%), EU-TIRADS 3 (75%), EU-TIRADS 4 (12.5%), and EU-TIRADS 5 (8.33%). Thyroid function test was abnormal in 5 cases: 3 cases of hypothyroidism and 2 cases of hyperthyroidism. Fine needle aspiration biopsy, performed in 6 patients, revealed: benign cytology in 3 cases, atypia of undetermined significance (oncocytic tumor) in 1 case, cytology suspicious for malignancy in 1 case, and was unsatisfactory in 1 case. Thyroidectomy was conducted in 9 cases, revealing a malignant origin in 2 patients (papillary carcinoma in both cases). Therapeutic modalities were surgery (29.2%), radioactive iodine (14.6%) and monitoring (54.2%).
Conclsion
In our study, incidentalomas were discovered in 50% of TN cases. Among them, 2 cases were malignant (8.33%). Thus, screening for thyroid nodules, by cervical ultrasound, seems necessary for internal medicine patients, so as not to miss thyroid cancer, mainly at a subclinical stage.

DOI: 10.1530/endoabs.81.P482

P483

Thyroid dysfunction in patients presenting metabolic syndrome

Ajay Sinha[1], Rajeev Ranjan[2] & R K Jha[3]
[1]NMCH, Medicine, PATNA, India; [2]Chest Clinic, Chapra, India; [3]DMCH, Medicine, Darbhanga, India

Introduction
Metabolic syndrome (MetS) consists of a constellation of metabolic abnormalities which include central obesity, hyperglycemia plus insulin resistance, high triglycerides plus low high-density lipoprotein (HDL) cholesterol and hypertension. A developing collection of proof proposes that metabolic condition is related to endocrine problems including thyroid brokenness. Thyroid brokenness in metabolic condition patients might additionally add to cardiovascular illness hazard subsequently expanding mortality. This study was done to survey thyroid capacity in metabolic disorder patients and assess its relationship with the parts of metabolic condition.
Methods
This cross-sectional study was carried out among metabolic syndrome patients at selected hospital in Bihar from June 2020 to March 2021. We selected 346 patients who satisfied National Cholesterol Education Program-Adult treatment Panel III models. Anthropometric estimations (height, weight, waist circumference) and circulatory strain were taken. Fasting blood tests were analysed to gauge glucose, triglyceride (TG), high thickness lipoprotein (HDL) cholesterol and thyroid chemicals. Patients were supposed to be euthyroid assuming all thyroid chemical levels fell inside the reference range [TSH: 0.47-5.0 mIU/l; FT4: 0.71-1.85 ng/dl]. Subclinical hypothyroidism (SCH) was thought of if TSH $>$5.0 mIU/l. Free T4 is inside ordinary reference esteem (0.71-1.85 ng/dl). Unmistakable hypothyroidism was characterized as TSH $>$ 5.0 mIU/l and free T4 $<$ 0.71 ng/dl.
Results
The study population contained 79 males and 267 females, with a mean period of 42.61 $\pm$ 9.13 years. The normal weight file was 26.37 $\pm$ 3.78 kg/m2. The vast majority of the female members were fat, and introduced focal weight. Thyroid brokenness was seen among 162 subjects with a metabolic disorder. The significant thyroid brokenness i.e., subclinical hypothyroidism which was trailed by clear hypothyroidism. Thyroid brokenness was normal among females when contrasted with males however was not measurably critical. HDL cholesterol had uncovered a negative connection with TSH level. Fatty substances uncovered a huge negative relationship with free T4 and a positive connection with TSH levels.
Conclusion
The prevalence of the metabolic condition is expanding everywhere. Thyroid brokenness, unmistakably subclinical hypothyroidism has been noticed more regularly in metabolic condition patients than the general population. The current review distinguishes thyroid brokenness in metabolic condition patients. Subclinical hypothyroidism was the commonest followed by obvious hypothyroidism. Also, thyroid capacity is related to certain parts of metabolic disorder (high thickness lipoprotein cholesterol and triglycerides). Further review is expected to assess the system of this relationship.

DOI: 10.1530/endoabs.81.P483

P484

Assessing cognitive functions among elderly patients with subclinical hypothyroidism

Anand Shankar[1], Shaibal Guha[2], Amit Kr Das[3] & Subhash Kumar[4]
[1]Shankar Diabetes Care And Research, Diabetes, PATNA, India; [2]Positive Health Center, Patna, India; [3]SHMC Muzaffarpur, Muzaffarpur, India; [4]Diabetes and Obesity Care Center, Diabetes, Patna, India

Background
The consequences of overt hypothyroidism on the central nervous system are well known. Interestingly, there is less proof in regards to the impacts of subclinical hypothyroidism (SCH) on the cognitive functions among elderly subjects. Studies from various countries including India have shown a variable association between SCH and cognitive dysfunction. This study planned to survey the event of cognitive impairment among the older Indian subjects who were introducing subclinical hypothyroidism.
Methods
The participants were 126 elderly subjects (age $>$ 60) with SCH and a similar number of age-matched euthyroid controls. Subclinical hypothyroidism was defined as a serum TSH level of more than 4.0 mIU/l with normal FT3 and FT4. Members were met by a solitary onlooker. Cognitive capacity was evaluated by Mini-Mental State Examination (MMSE) and clock drawing test (CDT). MMSE has the most extreme score of 30 and scores $\leq$ 24 are demonstrative of cognitive impairment. For CDT a score of 3 addresses a cognitive shortfall, while a score of 1 or 2 is viewed as typical. Information was dissected by utilizing SPSS and *P*worth of $<$ 0.05 was huge.
Results
The mean age of the patients' group was 66.3 years and BMI 27.0 kg/m^2 which were tantamount to controls who had a mean time of 68.1 years (*P*-0.17) and mean BMI 26.0 kg/m^2 (*P*-0.24). Any remaining benchmark factors including sex proportion, co-morbidities, family background of dementia, smoking, liquor use, schooling and exercise were likewise similar in both the groups. The mean TSH was 7.7 in the understanding group and 2.8 in the control bunch (*P*-$<$0.06). The mean MMSE score was 26.4 in the understanding group and 27.7 in controls (*P*-0.35). The patients had a mean CDT of 2.31 and control 2.41 (*P*-0.67). Cognitive impairment by MMSE (score $\leq$ 23) was seen in 28.2% of patients and 26.55% of controls (*P*-0.65), additionally the cognitive impairment by CDT (score of 3) was available in 31.3% of patients and 29.8% of controls (*P*-0.48).
Conclusion
Hypothyroidism is known to cause a decrease in cognitive capacities. Studies have tended to the relationship of cognitive impairment with subclinical hypothyroidism with variable outcomes exceptionally in old subjects. In the current review, we have observed that the commonness of cognitive impairment in old subjects with SCH is like the age-matched controls. Subsequently, the expected advantage of LT4 treatment, whenever involved with a point of working on cognitive capacities in this vulnerable group, becomes suspicious.

DOI: 10.1530/endoabs.81.P484

P485

Thyroid pyramidal lobe detection by ultrasound in 500 consecutive patients

Emin Mammadov
Reteaua de Sanatate Regina Maria, Outpatient, Bucharest, Romania

Background
The thyroid pyramidal lobe (TPL) represents a normal anatomical variation of the thyroid gland. Intraoperative TPL identification is of paramount significance, taking into account that the remnant TPL leads to higher thyroglobulin, could contain thyroid carcinoma foci and lead to recurrence.
Methods
We conducted a prospective single-center, single-operator study to identify TPL in 500 consecutive patients undergoing thyroid ultrasound for any indication. We extended the standard technique to actively search for TPL. The findings reported

were presence and site of the TPL (right vs left), presence of incidentally discovered nodules in TPL and thyroglossal duct cysts (TGDC). We excluded patients who underwent thyroid surgery or radioiodine therapy.
Results
Of the 500 consecutive patients, TPL was identified in 113 (22.6%), 4 had TGDC, 2 had hemiagenesis of the left thyroid lobe. Fourty-nine patients (43.4%) presented with left-sided TPL, 64 (56.6%) with right-sided. In 4 patients (3.5%), we identified incidental asymptomatic nodular lesions within TPL.
Conclsions
We suggest to routinely screen for thyroglossal duct remnants (TPL or TGDC) during thyroid ultrasound. This may reduce the rate of postoperative remnant TPL, obtain lower postoperative thyroglobulin levels and potentially lead to less frequent radioiodine therapy indication. Incidental discovery of thyroid nodules within TPL could also play important role in patient management. We observed a higher prevalence of the right-sided TPL in our study, which differs from previous reports stating more frequently left-sided TPL.

DOI: 10.1530/endoabs.81.P485

P486

Resistance to methimazole in a patient with Graves' disease

Joao Roque[1], Cristiana Costa[1], Pedro Marques[1] & Dinis Reis[1,2]
[1]Hospital de Santa Maria - Centro Hospitalar Universitário Lisboa Norte, Endocrinology, Diabetes and Metabolism, Lisbon, Portugal; [2]Universidade de Lisboa, Faculty of Medicine, Lisbon, Portugal

Introduction
Graves' disease (GD) is caused by TSH receptor antibodies (TRAbs) which stimulate thyroid activity. Initial treatment usually relies on antithyroid drugs (ATDs), mainly methimazole, carbimazole or propylthiouracil (PTU). These drugs inhibit the enzyme thyroperoxidase, blocking the synthesis of T3 and T4. Definitive therapeutic options include radioactive iodine and total thyroidectomy which are usually reserved for patients who do not tolerate or respond to ATDs, or for those who relapse or do not achieve remission after a course of ATDs. Here, we present a GD patient who suffered from remarkable resistance to ATDs requiring an early definitive therapy in order to solve her thyrotoxicosis.
Clinical case
A 57-year-old female presented with a 1-year history of palpitations, increased sweating, anxiety, insomnia and weight loss. Laboratory work-up confirmed hyperthyroidism: TSH $<$ 0.01 mIU/l, FT4 2.33 ng/dl (0.7-1.9). The titration of TRAbs was 8.55 IU/l ($<$ 2.13) confirming the diagnosis of GD. Methimazole was commenced and progressively titrated up to 70 mg/day (i.e. fourteen 5 mg-tablets) , which the patient has reassured us to be fully compliant with. Nevertheless, she remained in hyperthyroidism, and under methimazole 70 mg/day her thyroid function tests were: TSH $<$ 0.005 mIU/l, FT4 2.56 ng/dl and FT3 9.76 pg/ml (2.0-4.4). This prompted us to consider an early definitive therapy, and the patient was then proposed for total thyroidectomy. Lugol's solution was added to her ATD therapy, and her thyroid function has improved over the following two weeks, with FT4 and FT3 serum levels dropping from 2.00 and 9.76 down to 1.57 and 4.39 ng/dl, respectively. After controlling her thyrotoxicosis, she underwent an uneventful total thyroidectomy.
Discussion
This case highlights the uncommon, but possible, scenario of resistance to high-dose ATD therapy in patients with GD. In these cases, poor compliance to therapy should always be suspect, but other possible explanations include: i) decreased intestinal absorption; ii) impaired thyroid uptake; iii) greater metabolism and excretion of ATDs. High dietary intake of iodine can also impair the action of ATDs, and may further contribute to resistance to high-dose ATDs. Lugol's solution inhibits thyroperoxidase through Wolff-Chaikoff effect, thus blocking the synthesis and release of T4 and T3, as well as it reduces the vascularization of the thyroid gland. Hence, Lugol's solution must be used in GD patients prior to thyroidectomy, particularly in patients unresponsive to ATDs, as illustrated here.

DOI: 10.1530/endoabs.81.P486

P487

Pazopanib-induced hypothyroidism in a patient with adrenal metastasis of renal cell carcinoma

Cristiana Gomes da Costa, João Roque & Dinis Reis
Hospital Santa Maria, Endocrinology, Lisbon, Portugal

Introduction
Pazopanib is a tyrosine kinase inhibitor (TKI) considered to be a first-line treatment in adult patients with metastatic clear cell renal cell carcinoma (ccRCC). Thyroid dysfunction, namely hypothyroidism, is now recognized as being an important but potentially manageable side effect induced by such therapy. With this case we aimed to recall an endocrinological complication that can emerge during treatment with TKIs and highlight the importance of a thorough follow-up.
Case report
A 51-year-old man, whose past history and family history were irrelevant, was diagnosed with stage 1 ccRCC in 2001. A left radical nephrectomy was performed. In 2013 a lesion with 24 mm in diameter was first recognized in his right adrenal. In 2015 he was referred to the endocrinology outpatient clinic due to an increase in the lesion diameter to 51 mm, the CT scan showed a density of $+30.9$ Hounsfield Units. Laboratory findings excluded autonomous hormone secretion. Due to suspicious radiological findings and rapid tumor growth without evidence of hormonal hypersecretion, a biopsy of the adrenal mass was performed, revealing a ccRCC metastasis. The patient was submitted to a right adrenalectomy and started pazopanib 800 mg daily as adjuvant therapy, along with hydrocortisone and fludrocortisone as substitution therapy. He developed primary hypothyroidism 16 months after he started pazopanib. Anti-thyroid antibodies were normal, and the hypothyroidism was interpreted in relation to pazopanib. Furthermore, due to progressive disease pazopanib was substituted by another drug, however the hypothyroidism did not remit, and the patient remains under levothyroxine substitution therapy at the dose of 50 mg daily for 5 years now.
Conclsion
- √ This case highlights the tendency of ccRCC for adrenal metastases. These metastases may appear several years after the initial diagnosis, in our patient 12 years after the initial diagnosis.
- √ Hypothyroidism is a known adverse effect of pazopanib and therefore periodic surveillance of thyroid function is required. Pazopanib-induced hypothyroidism was recorded in most series in less than 12% of renal cell carcinoma patients.
- √ Pazopanib-induced hypothyroidism in this patient seems to be permanent.
- √ Many mechanisms have been appointed as possibly responsible for the hypothyroidism in relation to TKIs, such as thyroid cell atrophy due to the inhibition of vascularization, drug-induced thyroiditis, thyroid atrophy, deficient hormone production due to anti-thyroperoxidase activity, interference in iodine caption or modification in the RET2 gene. More studies are needed to characterize these mechanisms.

DOI: 10.1530/endoabs.81.P487

P488

Autoimmune thyroiditis, quality of life and underlying symptomatology

Miguel Pereira[1], Celestino Neves[1,2,3], Joao Sergio Neves[1,4], Juliana Gonçalves[1,2] & Davide Carvalho[1,2,3]
[1]Department of Endocrinology, Diabetes and Metabolism, São João University Hospital Center, Porto, Portugal; [2]Faculty of Medicine of University of Porto, Porto, Portugal; [3]Institute for Research and Innovation in Health (i3S), University of Porto, Porto, Portugal; [4]Department of Surgery and Physiology, Faculty of Medicine of University of Porto, Porto, Portugal

Introduction
Hypothyroidism caused by autoimmune thyroiditis (AIT) is a disease that can originate physical, psychological and behavioral symptoms. Quality of life (QoL) and psychopathologial symptoms in thyroid diseases and its relation with thyroid function remains unclear. In hypothyroidism there is a discussion about the normal range of TSH and Free T4 values and in which way its fluctuation influences the patient in its daily activities.
Objective
To analyze the QoL and physical and psychological symptomatology of patients with AIT.
Methods
We analyzed a sample of 145 patients with AIT with a mean age of 54.4 $\pm$ 15.3 years, 89.7 % were female and 63.4 % were married. We assessed thyroid function tests, thyroid antibodies, lipid profile, high-sensitivity C-reactive protein, B12vitamin, folic acid and applied several questionnaires, namely: the Thyroid Dependent Quality of Life questionnaire (ThyDQoL), the Thyroid Symptom Rating Questionnaire (ThySRQ), the Thyroid Treatment Satisfaction Questionnaire (ThyTSQ) and the Brief Symptom Inventory (BSI). Statistical analysis was performed with the One-way ANOVA test and Pearson's correlation test. P values $\leq$ 0.05 were considered as statistically significant.
Results
In this sample we found that patients had a mean BMI of 28.4 $\pm$ 5.2 Kg/m^2 and TSH 2.69 $\pm$ 8.48 µUl/ml, FT4 1.15 $\pm$ 0.40 ng/dl. Patients reported a mean QoL

value of -2.11 points (range from -9 to 1). In regard to the ThySRQ, 46.2 % of patients have noticed at least moderately memory problems, 50.4% of patients reported at least being moderately tired and 62.7 % showed some kind of depressed feelings. In concern with ThyTSQ, 83.5 % demonstrated being satisfied with treatment and 82 % believes that treatment is working well. In terms of correlations, we found positive correlations between TSH and weight gain ($r=0.19$;$P=0.02$) and loss of appetite ($r=0.27$;$P=0.001$). Free T3 correlated negatively with depression ($r=-0.22$;$P=0.009$), skin problems ($r=-0.19$;$P=0.01$) and loss of appetite ($r=-0.22$;$P=0.007$). Antithyroglobulin antibodies were negatively correlated with colder body sensation ($r=-0.17$;$P=0.04$) and antiperoxidase antibodies correlate itself with voice problems ($r=-0.22$;$P=0.01$).

Conclusions

In this study we can clearly see that despite the normal range of the TSH this disease negatively influences the QoL in AIT patients. We also noticed that there are certain symptoms that suffer a more direct influence of thyroid function. Further studies are needed to analyze the symptomatology that contributes to worsening of the QoL in these patients.

DOI: 10.1530/endoabs.81.P488

P489

cGMP is not involved in thyroid cancer cell death

Sara D'Alessandro[1,2], Elia Paradiso[1], Clara Lazzaretti[1], Samantha Sperduti[1,3], Lara Baschieri[1,2], Elisa Mascolo[1], Neena Roy[1], Claudia Anzivino[1,3], Sara Righi[1], Daniele Santi[1,4], Giulia Brigante[1,4], Manuela Simoni[1,3,4] & Livio Casarini[1,3]

[1]Unit of Endocrinology, Department of Biomedical, Metabolic and Neural Sciences, University of Modena and Reggio Emilia, Modena, Italy; [2]International PhD School in Clinical and Experimental Medicine (CEM), University of Modena and Reggio Emilia, Modena, Italy; [3]Center for Genomic Research, University of Modena and Reggio Emilia, Modena, Italy; [4]Department of Medical Specialties, Azienda Ospedaliero-Universitaria di Modena, Modena, Italy

Introduction

Type 5 phosphodiesterase (PDE5) inhibitors (PDE5i) lead to intracellular cyclic-guanosine monophosphate (cGMP) increase and are used for clinical treatment of erectile dysfunction. Studies found that cGMP may up/downregulate the growth of certain endocrine tumor cells, suggesting that the use of PDE5i could impact the risk of certain tumors, such as colorectal cancer.

Aim

We evaluated if PDE5i may impact thyroid cancer cell growth *in vitro*.

Materials and methods

We investigated caspase 3 activation by bioluminescence resonance energy transfer (BRET), in malignant (K1) and benign (Nthy-ori 3-1) thyroid cell lines, expressing a specific biosensor. Cells were treated with the PDE5i vardenafil or the cGMP analog 8-br-cGMP (nM-μM range) and reactions stopped at different time-points (0-24 h). The efficacy of vardenafil and 8-br-cGMP in inducing intracellular cGMP increase was evaluated by BRET, using a specific biosensor. The COS7 cell line served as a reference. Cleavage of caspase 3 was further evaluated by Western blotting, as well as phosphorylation of the proliferation-associated extracellularly regulated kinases 1 and 2 (ERK1/2), while nuclear fragmentation was evaluated by DAPI staining. Cell viability was investigated using 3-(4.5-dimethylthiazol-2-yl)-2.5-diphenyltetrazolium bromide (MTT) assay. Positive controls for cell death were set by treating cells with thapsigargin. Experiments were performed in triplicates and results analyzed by Kruskal-Wallis test ($P<0.05$ significance level).

Results

BRET experiments revealed that both vardenafil and 8-br-cGMP effectively induced dose-dependent intracellular cGMP increase ($P<0.05$) in both the K1 and Nthy-ori 3-1 cell lines, as well as in reference COS7 cells. However, no caspase 3 activation occurred between PDE5i-treated vs -untreated cells, at all concentrations and time-points tested ($P\geq0.05$), in contrast to the results obtained using thapsigargin ($P<0.05$). These results match those obtained upon cell treatment with 8-br-cGMP, which failed in inducing caspase 3 clevage in all the cell lines ($P\geq0.05$). Moreover, they reflect the lack of caspase 3 cleavage, evaluated by Western blotting, as well as missing nuclear fragmentation. Interestingly, the modulation of intracellular cGMP levels with vardenafil or the analog did not impact cell viability of both malignant and benign thyroid tumor cell lines, nor the phosphorylation of ERK1/2 ($P\geq0.05$)
.

Conclusions

This study demonstrated that cGMP-mediated signals are not linked to cell viability and death in K1 and Nthy-ori 3-1 cell lines, suggesting that the use of PDE5i could not impact the growth of thyroid cancer cells.

DOI: 10.1530/endoabs.81.P489

P490

Novel central actions of thyroid hormone in the control of body temperature

Julia Maier[1], Mehdi Pedaran[1], Anna Lena Cremer[2], Heiko Backes[2] & Jens Mittag[1]

[1]University of Lübeck, CBBM, Molecular Endocrinology, Lübeck, Germany; [2]Max-Planck-Institute for Metabolism Research, Multimodal Imaging of Brain Metabolism, Köln, Germany

The ability of thyroid hormones to regulate body temperature is well established. While the active hormone T3 can act peripherally to induce thermogenesis in fat and muscle, it also acts centrally in the brain to increase body temperature through the sympathetic nervous system. Most remarkably, recent studies show that T3 treatment in mice causes an elevated body temperature even at 10°C, far below thermoneutrality, suggesting that the T3 effect constitutes pyrexia rather than hyperthermia. Therefore, mice with induced hyperthyroidism seem to have an altered temperature set point in the brain; however, the precise neuroanatomical substrate has remained unknown. The goal of this research project is to identify the brain region where T3 acts to regulate the body temperature setpoint. Using PET/CT scans of mice treated with T3, several candidate regions have been identified. Among these, the Zona Incerta (ZI), has been associated with the control of body temperature previously. To test whether this region constitutes the missing link between the central T3 effect and pyrexia, we studied the ZI using well-established mouse models. Preliminary data show no difference in cell number of dopaminergic neurons in the ZI when comparing offspring of wild-type mice to those of mice with a mutation in thyroid hormone receptor α1, indicating no developmental effect of thyroid hormones on ZI dopaminergic neurons. However, further studies will be needed to illuminate the acute actions of T3 in this enigmatic brain region.

DOI: 10.1530/endoabs.81.P490

P491

Serum neopterin levels in graves' disease

Goknur Yorulmaz[1], Sinem Gurcu[2], Evin Kocaturk[3], Hatice Hamarat[4], Melisa Sahin Tekin[5] & Ozkan Alatas[3]

[1]Eskisehir Osmangazi University, Endocrinology, Turkey; [2]Eskisehir City Hospital, Pharmacy, Turkey; [3]Eskisehir Osmangazi University, Biochemistry, Turkey; [4]Eskisehir City Hospital, Internal Medicine, Turkey; [5]Eskisehir Osmangazi University, Internal Medicine, Turkey

Aim

Neopterin has been found to be associated with disease activity in various infectious, inflammatory, and autoimmune diseases. It is an indicator of immune response as it is released after activation of monocytes and macrophages by IFN-γ. It was aimed to measure neopterin levels in Graves' disease, which is a T cell-mediated autoimmune disease of the thyroid gland.

Materials and Methods

Twelve healthy individuals (6 women, 6 men), 13 Graves' disease patients (7 women, 6 men) who applied to the endocrinology outpatient clinic and followed up were included in the study. Serum neopterin concentrations were analyzed with commercial enzyme-linked immunosorbent assay (ELISA) kits (Human Neopterin Assay Kit, Bioassay Techonology Laboratory, China) according to manufacturer's instructions.

Results

The mean age of healthy individuals was 42.17 ± 11.52 years, and the mean age of Graves' patients was 41.31 ± 9.85 years. TSH levels were found to be lower and free T3 and free T4 levels were found to be higher in Graves' patients compared to controls ($P<0.05$). Likewise, serum neopterin levels were high (9.299 ± 6.271 nmol/l: Graves', 1.432 ± 1.304 nmol/l: control, $P<0.05$, respectively).

Conclusion

In our study, serum neopterin levels of Graves' disease patients were found higher than the control group. There is generally a significant relationship between neopterin and IFN-γ concentrations. It has been observed that neopterin increases

in body fluids, especially during the activation periods of diseases in which cellular immunity plays a major role in the pathogenesis. The most potent stimulator of neopterin synthesis is IFN-γ, which is a Th1 cytokine, and it has been suggested that serum neopterin levels are a sensitive marker of endogenous IFN-γ release. In our study, a similar result with the literature was found, such as the detection of high neopterin levels in immune system-related diseases.
Keywords: *neopterin, graves, hyperthyroidism.*

DOI: 10.1530/endoabs.81.P491

P492

Simulation of the plasma level of thyroid hormones for a total thyroidectomized virtual-patient treated by BMI and BSA-based LT4 monotherapy dose regimen

Hadi Tabesh[1], Mostafa Hemmati[1] & Hamid Bazrafshan[2]
[1]Department of Life Science Engineering, Faculty of New Sciences and Technologies, University of Tehran, Tehran, Iran; [2]LMU Klinikum, Ludwig Maximilian University of Munich, Munich, Germany

Introduction
Several levothyroxine (LT4) monotherapy dose regimen have been already proposed by different medical scientists which may result in various daily LT4 doses. Comparing the consequences of such dose regimen are rather difficult since they have to be applied on either the same patient or a large study groups. Therefore, a straight forward method would be to simulate the plasma level of thyroid hormones of virtual-patients treated by various dose regimen.
Method
In this study, the resulting plasma levels of thyroid hormones were compared for a total thyroidectomized virtual-patient treated by BMI and BSA-based LT4 monotherapy dose regimen adopted from Elfenbein *et al*., 2016 and Al-Dhahri *et al*., 2019 respectively. Our virtual-patient was considered as a 37 years old male with 72 kg weight and 170 cm height. The BMI of this patient would be 24.9 kg/m^2 while the calculated BSA based on DuBois & DuBois method is 1.83 m^2. In order to evaluate patient responses to LT4 monotherapy dose regimen, we simulated our total thyroidectomized virtual-patient by setting T3 and T4 secretion parameters at 1% using THYROSIM 3.0 while receiving static oral LT4 dosages post-surgery. In addition, with an assumption that no supplement was administrated, the absorption rate of oral LT4 was set to 88%.
Results
Considering the proposed dose regimen by BMI and BSA our virtual-patient should receive static LT4 dose of 1.9 and 1.4 μ g/kg respectively. Parameters to compare these two dose regimen for a period of 30-days are presented in the following table.
Conclusion
the BMI dose regime shows some superiority over BSA method especially in terms of lower time to reach normal TSH level and the discrepancy between TSH at day 30 and normal TSH. At the end of 30-days treatment period our virtual patient experiences a plasma T4 level of 86.56 and 68.26 μg/l if administering LT4 doses based on BMI and BSA methods.

Parameter	BMI	BSA
Time to reach normal TSH level (days)	15	30
Time to reach normal T3 level (days)	3	4
Time to reach normal T4 level (days)	4	5
TSH out of normal range (days)	14	30
T3 out of normal range (days)	2	3
T4 out of normal range (days)	3	4
Discrepancy between TSH at day 30 and normal TSH (=1.93)	1.93	7.11
Discrepancy between T3 at day 30 and normal T3 (=1.35)	-0.51	-0.59
Discrepancy between T4 at day 30 and normal T4 (=78.21)	8.35	-9.95

DOI: 10.1530/endoabs.81.P492

P493

Rare presentation of thyrotoxicosis post CoVID-19 vaccination in acute setting

Megha Mohan[1], Bashir Mahamud[2], Janessa Bell[2], Khash Nikookam[2], Belayet Hossain[2], Hassan Rehmani[2] & Gideon Mlawa[2]
[1]Queen's Hospital, Acute Medicine, London, United Kingdom; [2]Queen's Hospital, London, United Kingdom

Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 has led to unparalleled burden on national and global healthcare systems. Vaccines were viewed as way of combating Covid 19 pandemic. This led to development and implementation of vaccination programmes worldwide. Several vaccines have been approved for use in worldwide including Pfizer-BioNTech, Oxford-AstraZeneca vaccine and Moderna vaccine. Disturbingly, the speed at which these vaccines been approved suggest limited studies regarding their efficacy and possible side effects were carried out. Following their widespread use in general public, a problematic trend of post Covid-19 vaccine manifestations are become more apparent and are being reported with increasing frequency. One such manifestation of post Covid -19 vaccination is new onset of autoimmune diseases such as immune thrombotic thrombocytopenia, IgA nephropathy, rheumatoid arthritis and rarely thyroid dysfunction.
Case series
1- A 49-year-old male presented with shortness of breath and palpitations 2 weeks after AstraZeneca vaccine. The patient also reported significant weight loss. On examination, the patient was tachycardic and palpable thyroid nodules. Blood test results can be seen in table 1. Ultrasounds scan of thyroid gland which demonstrated bilateral thyroid nodules with peripheral vasculature. The patient was subsequently diagnosed with Graves' disease and started on treatment with iv hydrocortisone, propranolol, carbimazole. With endocrine team follow up scheduled. 2- A 53-year-old female referred by her GP with deranged thyroid function tests. Patient reported significant weight loss, lethargy, hair loss and ongoing spikes in temperature at night with associated night sweats. The patient indicated her symptoms started 2 weeks after administration of AstraZeneca vaccine. On examination she was found to be tachycardic and visible anterior neck swelling suggestive of goitre. Further to this she underwent Ultrasound scan of Thyroid gland which demonstrated atrophic thyroid gland with right thyroid nodule. The patient was treated with steroids, propranolol, carbimazole.
Discussion/Conclusion
Thyroid dysfunction after vaccination is a rare phenomenon. However, clinicians should be aware that thyroiditis might be an underreported adverse effect of COVID-19 vaccines. Further research is needed to investigate the prevalence and the mechanisms of thyroiditis after COVID-19 vaccination. Based on the finding of these cases we recommend performing Thyroid function test post Covid-19 vaccination to monitor for thyroid dysfunction.

	Patient 1	Patient 2
TSH	<0.01	0.01
T4	>100	61.5
CRP	1	70
TSH RECEPTOR AB	9.56	0.31
TPO AB	<4	Not performed

DOI: 10.1530/endoabs.81.P493

P494

Female papillary thyroid cancer survivors are at increased risk of hyperproliferative pathology of the reproductive system

Tetiana Tatarchuk[1], Mykola Tronko[2], Panagiotis Anagnostis[3], Liudmyla Kalugina[1], Natalia Pedachenko[4], Anna Danylova[4] & Tetiana Kuchmenko[2]
[1]State Institution "Institute of Pediatrics, Obstetrics and Gynecology of NAMS of Ukraine", Kiev, Greece; [2]State Institution "V.P. Komisarenko Institute of Endocrinology and Metabolism", Kiev, Ukraine; [3]Aristotle University of Thessaloniki, Unit of Reproductive Endocrinology, 1st Department of Obstetrics and Gynecology, Thessaloniki, Greece; [4]Shupik National Healthcare University of Ukraine, Obstetrics, Gynecology and Gynecology Department, Kiev, Ukraine

Purpose
Thyroid cancer (TC) is the most common endocrine cancer worldwide, affecting mainly women of the reproductive age. However, no data exist with regard to its association with endometrial or uterine disorders. The aim of this study was to assess the risk of hyperproliferative pathology of the reproductive system in female TC survivors.
Methods
This was a cross-sectional study in female patients, aged 20-45 years, diagnosed with papillary TC (PTC) during the period 1994-2018. Age-matched females with normal thyroid structure served as controls.
Results
One-hundred and sixteen patients (mean age 36.7 ± 61 years) and 90 age-matched controls were included. PTC survivors demonstrated an increased risk for adenomyosis [odds ratio (OR) 2.5, 95% confidence interval (CI) 1.3-4.8] and endometrial hyperplasia (OR 3.9, 95% CI 1.1-14.3), compared with controls. The risk for adenomyosis was higher after the ten post-operative years (OR 5.3, 95% CI 2.29- 12.05) than during the first 5-10 years (OR 2.3, 95% CI 1.02-5.10) and increased with the number of RAI courses and the degree of TSH suppression. The risk of endometrial hyperplasia was most evident during the first five years post-thyroidectomy (OR 6.0, 95% CI 1.4-25.5), especially in patients with TSH <0.1 mU/l (OR 6.8, 95% CI 1.4-33.28) No difference in uterine leiomyomas or endometrial polyps was found between PTC survivors and controls.
Conclusions
Female PTC survivors are at increased risk of endometrial hyperplasia and adenomyosis compared with those with normal thyroid structure.

DOI: 10.1530/endoabs.81.P494

P495

A rare case of a non-secretory medullary thyroid carcinoma

Ana Rita Elvas, Joana Couto, Raquel G. Martins, Jacinta Santos, Teresa Martins & Fernando Rodrigues
Portuguese Oncology Institute of Coimbra, Department of Endocrinology, Coimbra, Portugal

Introduction
Medullary thyroid carcinoma (MTC) is a rare neuroendocrine tumor (1-2% of all thyroid carcinomas), which arises from calcitonin-producing C cells. Calcitonin (CT) and carcinoembryonic antigen (CEA) are used as tumor markers in the follow-up of patients with MTC. Non-secretory forms of MTC are very rare, accounting for less than 1% of the cases.
Case Report
A 53-year-old man underwent left thyroid lobectomy for a 1.1 cm thyroid nodule subjected to fine-needle aspiration twice, which cytology revealed a "follicular lesion of undetermined significance. Histological examination showed a multifocal MTC (1.2 cm and 0.4 cm) and C-cell hyperplasia. Immunohistochemistry revealed cytoplasmic positivity for CT, chromogranin and synaptophysin, and nuclear positivity for TTF1. Totalization of thyroidectomy and lymph node dissection of the central compartment were performed. Histopathological analysis revealed C-cell hyperplasia and absence of lymph node metastasis in 26 lymph nodes. Preoperatively, there was no elevation of CT or CEA [CT 2.84 pg/ml (NR: 0.40-18.90) and CEA 2.4 ng/ml (NR: <5.0)]. A dilution test for CT was performed and showed no evidence of interference caused by heterophile antibodies. The measurement of fractionated 24-h urinary metanephrines and phospho-calcium metabolism did not show any changes. The search for mutations in the RET gene was negative. In the postoperative study, CT and CEA measurements remained within the normal range. 18F-DOPA positron emission tomography (PET) was requested, which revealed a moderate uptake located in the topography of the duodenal arch. The patient was referred to the Gastroenterology outpatient clinic. He underwent endoscopic ultrasound and abdominal computerized-tomography scan. No duodenal or locoregional lesions were observed. The patient is currently under surveillance, with no clinical, analytical or imaging evidence of recurrent disease.
Conclusion
The reported cases of non-secretory MTC are rare and present a heterogeneous clinical course, which makes it difficult to predict its behavior. It is not clear what is the best way to monitor these patients, as the use of tumor markers is limited. Alternative methods for monitoring are needed to optimize the follow-up of these patients.

DOI: 10.1530/endoabs.81.P495

P496

Outcomes of low-risk differentiated thyroid cancer submitted to radioactive iodine ablation - a comparative analysis in a single tertiary centre

Catarina Ivo[1], Sara Amaral[2], Nuno Raposo[3], Joana Maciel[4], Joana Simões Pereira[4], Helena Vilar[4] & Valeriano Leite[4]
[1]Armed Forces Hospital, Endocrinology Department, Lisboa, Portugal; [2]Centro Hospitalar Lisboa Central, Endocrinology, Diabetes and Metabolism department, Lisbon, Portugal; [3]Hospital Cuf, Endocrinology Department, Lisboa, Portugal; [4]Instituto Português Oncologia de Lisboa Francisco Gentil - IPOLFG, Endocrinology Department, Lisboa, Portugal

Introduction
The update of 2015 American Thyroid Association (ATA) guidelines recommend that radioactive iodine (RAI) ablation therapy should be used in line with patients' risk stratification. However, there is no consensus on benefits of post-operative RAI ablation in patients with low risk differentiated thyroid cancer (DTC). The aim of this study is to compare the outcomes of patients with low risk DCT submitted to RAI ablation with those who were not.
Methods
This is a retrospective study of patients with low risk DTC followed in a tertiary cancer centre between 2016-2019. Clinicopathological features were collected. Clinical outcomes of patients submitted to RAI ablation were compared to a group control. The risk factors considered for recurrence were: multifocality, minimal extrathyroidal extension (ETE), N1 micrometastases (≤ 5 nodes with $<$ 0.2 cm in largest dimension), suspicious or non-specific findings on post-operative ultrasound (US), positive non-stimulated serum thyroglobulin (Tg) and positive Tg antibodies (ATG) levels. Remission was defined as no evidence of disease /indeterminate response and disease recurrence as biochemical or structural evidence of disease, at last follow-up, based on ATA criteria.
Results
739 patients were included (77.9% female) with a mean age of 53.7 ± 15.9 years-old and a mean follow-up of 3.6 ± 1.2 years. RAI ablation was performed in 45%($n=331$). Recurrence was observed in 4.2% ($n=14$) of the patients submitted to RAI ablation and in 2.9% ($n=12$) of the cases that underwent surveillance ($P=0.342$). Multivariate analysis showed that only post-op Tg - Tg >1 ng/ml [$P<0.001$; hazard ratio (HR): 9.5; 95% confidence interval (95%CI):3.0-30.0), Tg between 0.2-1 ng/ml ($P=0.008$;HR: 5.3; 95%CI: 1.6-18.1)- and suspicious findings on post-op US ($P<0.001$;HR: 8.7; 95%CI: 2.8-27.8) were independent risk factors for recurrence.
Conclusions
Our results demonstrated no differences in clinical outcomes between RAI ablation and surveillance after surgery in low-risk DTC patients, reinforcing that these patients do not benefit from RAI ablation. Positive non-stimulated serum Tg levels and suspicious findings on post-operative ultrasound were the only factors associated with recurrence.

DOI: 10.1530/endoabs.81.P496

P497

Impact of 2015 ATA guidelines in 131I prescription in low-risk DTC

Sara Amaral[1], Catarina Ivo[2], Nuno Cordeiro Raposo[3], Joana Maciel[4], Joana Simões-Pereira[4], Helena Vilar[4] & Valeriano Leite[4]
[1]Centro Hospitalar Universitário Lisboa Central, Endocrinology, Diabetes and Metabolism Department, Lisboa, Portugal; [2]Armed Forces Hospital Lisbon, Endocrinology Department, Lisbon, Portugal; [3]Hospital CUF, Lisbon, Lisbon, Portugal; [4]Instituto Português de Oncologia de Lisboa Francisco Gentil, Endocrinology Department, Lisbon, Portugal

Background
To minimize potential harm from overtreatment of low-risk thyroid cancers, the 2015 American Thyroid Association (ATA) Guidelines recommend that radioactive iodine (RAI) ablation should not be routinely used in low-risk differentiated thyroid carcinoma (DTC). The present study aims to evaluate trends in RAI therapy in a tertiary center after the update of these Guidelines.
Methods
Data from patients followed in a tertiary center with low-risk DTC between 2016 e 2019 were analyzed. Risk stratification was based on 2015 ATA stating criteria. Multifocality, minimal extrathyroidal extension, ≤ 5 pathologic N1 micrometastases (<0.2 cm in largest dimension), non-specific findings or suspicious lymph nodes on post-operative ultrasound (US), non-stimulated serum thyroglobulin (Tg) >1 ng/ml and positive anti-Tg were considered potential risk factors for recurrence.

Results
A total of 739 low-risk DTC patients were included (77.9% female) with a mean age of 53.7±15.9 years-old. All patients underwent RAI therapy after recombinant human TSH. The number of RAI therapies in low-risk DTC reduced from 53.9% (2016) to 27.8% (2019). All risk factors for recurrence were significant for RAI ablation decision: multifocality (59.5%; $P<0.001$); non-specific findings on post-op US (35.6%; $P<0.001$); minimal extrathyroidal extension (23.1%; $P<0.001$); non-stimulated serum Tg >1 ng/ml (20.8%;$P=0.002$); suspicious lymph nodes on post-op US (11.5%; $P<0.001$); N1 micro-metastases (5.1%; $P<0.001$) and positive anti-Tg (4.8%;$P=0.008$). RAI activity on overall years was 52.7±32.0 mCi and a decrease was observed between 2016 and 2109 (52.8±31.4 to 40.6±24.1 mCi). Higher activities of RAI were observed in patients with N1 micro-metastases ($P=0.004$) and extrathyroidal extension ($P=0.054$).
Conclsions
Our data demonstrates that the number of RAI treatments of low-risk DTC decreased substantially since the update of ATA recommendations. All considered risk factors were significant for RAI treatment decision. The presence of micro-metastases and extrathyroidal extension were associated with higher activities of RAI.

DOI: 10.1530/endoabs.81.P497

P498

Tocilizumab: an effective and low-cost treatment for recent-onset active moderate to severe graves orbitopathy. a case report

Georgios Boutzios[1], Sofia Chatzi[1], Athina Karampela[1], Andreas Goules[1], Gerasimos Tsourouflis[2] & Athanasios Tzioufas[1]
[1]School of Medicine, National and Kapodistrian University of Athens, Pathophysiology, Athens, Greece; [2]School of Medicine, National and Kapodistrian University of Athens, Second Department of Propedeutic Surgery, Athens, Greece

Introduction
Graves orbitopathy (GO) is an inflammatory condition of the orbital fat and muscles and affect 30-50% of patients with Graves' disease. The first-line treatment of moderate to severe GO according to EUGOGO is intravenous glucocorticoids, but 20-30% of the cases appear to be corticosteroid resistant or refractory. Promising results have been described with Tocilizumab (TCZ) as a second-line moderate to severe GO treatment.
Case presentation
We report a case of a 33-year-old female presented in our hospital with severe bilateral proptosis and spontaneous retrobulbar pain, lower eyelid retraction, periorbital edema, chemosis without diplopia. She was a former smoker, diagnosed with GO one year before and treated with intravenous methylprednisolone (cumulative dose 4.5gr) with only partial response. After glucocorticoid cessation, the disease relapsed with clinical signs of dysthyroid optic neuropathy and the patient underwent orbital radiotherapy (20Gy). At presentation patient was in thyrotoxic state with TSH=<0.008μIU/ml (n.v.: 0.27-4.2), T3=7.2 nmol/l (n.v.: 0.9-2.8), T4=265 nmol/l (n.v.: 58-140) and markedly increased TSI=19.30 IU/l (n.v <1.75). She was treated with methimazole. CAS score was calculated at 5/7, and protrusion was measured with Hertel exophthalmometer at 30 mm for the right and 31 mm for the left eye, respectively. Upon ophthalmologic evaluation, she was diagnosed with severe keratopathy due to cornel exposure. Orbital MRI was performed, which revealed inflammation of all orbital muscles, predominantly the inferior, medial and lateral rectus binocular. Due to the severity and the progression of the disease despite the corticosteroid treatment and radiotherapy, the patient initiates therapy with TCZ (RoActemra), a monoclonal antibody that inhibits the IL-6 receptor. She received 4 intravenous doses (8 mg/kg) every 28 days, according to Perez-Moreiras RCT. On follow up, symptoms were improved impressively, and CAS score regressed to 1/7. On exophthalmometry, proptosis was 21 for the right, 22 for the left eye, and TSI were within normal values. Moreover, a significant radiological improvement on MRI was established, with decreased size of all affected muscles.
Conclsion
We present this case to raise awareness for the effectiveness of the IL-6 receptor inhibitor (Tocilizumab), to the management of moderate to severe, corticosteroid resistant or refractory GO, of recent-onset, with lower cost compared to other novel therapies such as teprotumumab.

DOI: 10.1530/endoabs.81.P498

P499

Variation of anti-TSH receptor antibodies after iodine-131 therapy

Inês Vieira[1], Martim Monteiro[2], Paula Soeiro[3], Dírcea Rodrigues[1], Gracinda Costa[2] & Isabel Paiva[1]
[1]Coimbra Hospital and University Center, Endocrinology, Diabetes and Metabolism, Portugal; [2]Coimbra Hospital and University Center, Nuclear Medicine, Portugal; [3]São João Universitary Hospital Center, Nuclear Medicine, Portugal

Introduction
Graves' disease (GD) is a systemic autoimmune disease characterized by lymphocyte activation and synthesis of anti-TSH receptor antibodies (TRABs). Higher values of TRABs are associated with a higher risk of Graves' ophthalmopathy and dermatopathy. Iodine-131 therapy (RAI) is one of the well-established options in GD, but it can cause a transient increase in TRABs.
Objectives
To evaluate the evolution of TRABs after RAI; to identify factors associated with a more marked increase in TRABs.
Material and methods
Retrospective analysis of a sample of patients with GD undergoing RAI. Information on demographic data, antithyroid drug therapy (ATD), TRAB values over time (pre-RAI and at 1, 3, 6 and 12 months after RAI) and response to RAI were collected.
Results
We analyzed 86 episodes of RAI, involving 75 patients, mostly female (80.0%), 84.9% corresponded to 1st therapies and 15.1% to subsequent therapies. Age at RAI administration was 40.9±17.2 years, mean 3.0±3.0 years after diagnosis, and 82.6% were under ATDs. The pre-therapeutic TRABs had a median value of 8.0±17.5 U/l (reference range < 1U/l) and, compared to the post-therapeutic TRABs: no statistically significant difference was found at 1 M (8.3±18; $P=0.910$), statistically significant increase was found at 3 M (14.5±28, $P=0.000$) and 6 M (17.0±29.0, $P=0.001$); no statistically significant difference was found at 1 year ($P=0.335$). A doubling of TRABs in relation to the median pre-therapy value, at some point in the 1st year post-therapy, occurred in 54.7%. These patients had a longer diagnostic-therapeutic interval (3.0±3.0 vs 1.0±2.0 years, $P=0.020$), higher estimated glandular mass (57.5±32.7 vs 43.0±25, 0 g, $P=0.024$) and were more frequently of the female gender (60.8 vs 29.4%, $P=0.029$). There was no significant difference in administered dose (11.0±4.6 vs 10.0±4 mCi, $P=0.384$). In multivariate analysis, female gender and the estimated glandular mass maintained a statistically significant relationship with the probability of duplication of the TRABs ($P=0.015$ and$P=0.017$, respectively).
Discussion
Most patients registered an elevation of the TRABs post-RAI. Female patients with larger glandular mass may be especially at risk for higher elevations. These data may have implications for the extrathyroidal manifestations of Graves' disease.

DOI: 10.1530/endoabs.81.P499

P500

Immune check point inhibitors- induced thyroid disorders -would you recognise them?

Jegadeshwaran Gandhi[1], Bashir Mahamud[1], Janessa Bell[1], Ghada Ahmed[1], Suhier Elshowaya[1], Hassan Rehmani[1], Khash Nikookam[1] & Gideon Mlawa[2]
[1]Queen's Hospital, London, United Kingdom; [2]Queen's Hospital, Diabetes and Endocrinology/Acute Medicine, London, United Kingdom

Introduction
Development and progression of cancers is multifactorial encompassing several mechanisms that aid its proliferation. One of the hallmarks of cancer progression is inhibition of the immune system. Cancer cells can activate different immune checkpoint are pathways that harbour inhibitory or stimulatory mechanisms that enabled self-tolerance and assist with immune response. Through activation of immune checkpoint pathways cancers can suppress immune response against it. Monoclonal antibodies that target immune checkpoints have garnered immense interest in management of solid tumours. The mechanism of action immune checkpoint inhibitors is that they block inhibitory molecules on T-Cells. However, they also downregulate immunological tolerance to self-antigens, inducing immune related adverse events (IrAES). IrAES have been reported in several organs including the endocrine glands including the thyroid and pituitary glands. Here we present cases of two patients which developed hypothyroidism following immune checkpoint inhibitor therapy for their metastatic carcinoma.
Case presentations
Case-1. An 80-year-old gentleman with a background his of metastatic squamous cell carcinoma of the lung was given pembrolizumab(anti-PD-1) treatment. He subsequently developed transient hyperthyroidism (characterised by TSH -69.10

mU/l, FT4 -0.5 *P*mol/l). Five months post therapy he became hypothyroid, (elevated TSH and low FT4). He was subsequently started on levothyroxine and became euthyroid.

Case-2. A 63-Year-old male with history of metastatic cancer of the colon was started on atezolizumab (anti-PD-L1). Post therapy the patient developed severe hypothyroidism characterised by myopathy and myosititis. Before immunotherapy the patient was euthyroid with normal levels of TSH and FT4. Subsequent blood test post treatment showed high levels of TSH >150 mU/l and FT4 6 *P*mol/l. He was treated with high dose of levothyroxine to get him back to his baseline.

Discussion/Conclusion

Thyroid toxicity post immune checkpoint inhibitor therapy is being reported with increasing frequency, based on literature this complication irreversible with patients requiring continuous therapeutic management and follow up which can put increased pressure on patients, who are often under increased mental strain in dealing with their cancer treatment. Based on the case reported here we recommend baseline thyroid function test should be done at initiation of therapy, periodically after immunotherapy and during each cycle of infusion.

DOI: 10.1530/endoabs.81.P500

P501

Thyroid involvement in the context of sars-cov-2 infection

Kostoglou Athanasiou Ifigenia[1], Lambros Athanassiou[2], Sofia Nikolakopoulou[3], Alexandra Konstantinou[3], Olga Mascha[4], Ioannis Bliziotis[3], Charilaos Samaras[3] & Panagiotis Athanassiou[5]
[1]Asclepeion Hospital, Voula, Department of Endocrinology, Athens, Greece; [2]Asclepeion Hospital, Voula, Department of Rheumatology, Athens, Greece; [3]Asclepeion Hospital, Voula, Covid-19 Department, Athens, Greece; [4]Asclepeion Hospital, Voula, Department of Biochemistry, Athens, Greece; [5]St. Paul's Hospital, Department of Rheumatology, Thessaloniki, Greece

Introduction

The SARS-CoV-2 virus has severely affected humanity. The disease causes pneumonia which may be severe. In many cases, patients, especially if there are comorbidities, may have a fatal outcome. The disease affects all organs and the variability of its manifestations has attracted intense scientific interest.

Aim

The aim of the study was to describe the case of a patient who developed subacute thyroiditis after infection with the SARS-CoV-2 virus.

Case description

A patient, female, aged 52 years, developed signs of respiratory infection with a mild clinical picture and fatigue. Hospitalization was not necessary. Sixty days later, she developed signs of subacute thyroiditis with pain in the area of the thyroid gland radiating to the ears, hyperidrosis, tachycardia and intense fatigue. Laboratory investigations revealed IgG Ab COVID-19 31.9 (normal values <1) (ELISA), IgM Ab COVID-19 0.6 (normal values <1) (ELISA), CRP 4.27 mg/dl (normal values <0.5 mg/dl), ESR 85 mm/h and TSH 0.03 μIU/ml. A thyroid ultrasonogram was performed which revealed hypoechoic areas. Non-steroidal-anti-inflammatory drugs were administered which led to pain relief. A month later the patient presented with tachycardia, pain in the area of the thyroid and fatigue. Methylprednisolone was administered 16 mgx2 daily and propranolol 20 mgx2 daily and the patient improved. However, a month later the patient presented with disease relapse. Methylprednisolone 16 mgx2 was administered and the patient improved and is now asymptomatic.

Conclusions

The disease caused by the SARS-CoV-2 virus affects all organ systems. The virus enters cells by attaching to the ACE2 (angiotensin converting enzyme 2) which acts as a receptor for the virus. It has been observed that thyroid cells express the ACE2. It appears that the SARS-CoV-2 virus infects thyroid cells via the ACE2. Cases of subacute thyroiditis, a post-inflammatory disease, have been described mainly in female patients after SARS-CoV-2 infection. In conclusion, it appears that the SARS-CoV-2 virus may affect the thyroid gland.

DOI: 10.1530/endoabs.81.P501

P502

Comparing non-diagnostic FNA results in thyroid nodules

A K Chandra[1], Vijay Kumar[2], Manish Kumar[3] & R K Jha[4]
[4]Kurji Holy Family Hospital, Medicine, Patna, India; [2]Diabetes Clinic, Patna, India; [3]Chikitsa Clinic, Patna, India [4] DMCH, Medicine, Darbhanga, India

Introduction

Multiple specialities teach and perform ultrasound-guided fine-needle aspiration biopsy (USG-FNA) of thyroid nodules, including Radiology, Endocrinology, and Pathology. Contrasts in cytopathology results might connect with various USG-FNA procedures just as contrasts in the knobs assessed. This study planned to play out a nitty-gritty investigation of USG-FNA results among these different showing administrations at a solitary scholarly clinical focus.

Methods

We performed a review outline survey of patients who went through USG-FNA of a thyroid knob at a solitary scholarly clinical focus from 2015-to 2017, barring patients with hyperthyroidism. Cytopathology results were arranged by the Bethesda framework and separated by the performing strength (Radiology, Endocrinology, and Pathology). Segment, clinical, and ultrasound factors were likewise analysed to additionally research contrasts between the performing specialities.

Results

Of the 356 total thyroid nodules examined by USG-FNA, 167 nodules were biopsied by Radiology, 119 by Endocrinology, and 70 by Pathology. Onsite cytopathology assessment was accessible to Radiology and Pathology, but not to Endocrinology during this period. The appropriation of Bethesda results was different between the three performing administrations ($P < 0.05$). The pace of a Bethesda I (non-indicative) cytopathology result was 3.6% for Radiology, 10.1% for Endocrinology, and 11.4% for Pathology ($P < 0.05$). Contrasts between the pace of harmless (Bethesda II), uncertain (Bethesda III-IV), or high-hazard (Bethesda V-VI) results were not measurably critical. The Radiology-performed USG-FNA group included 58.9% knobs found unexpectedly contrasted with 43.9% and 32.8% for Endocrinology and Pathology, separately ($P^1/_4 0.001$). A larger part of knobs was somewhat or dominatingly cystic in the Radiology (53.4%) and Pathology (55.5%) gatherings, however not in the Endocrinology group (34.6%), which just arrived at a measurable pattern ($P^1/_4 0.07$). No other huge contrasts

DOI: 10.1530/endoabs.81.P502

P716

Antenatal thyroid hormone therapy and antithyroid drug use in Norway from 2004 to 2018

Kjersti Bakken[1], Kristina Nermo[2], Bjørn Gunnar Nedrebø[3], Tim IM Korevaar[4] & Tor A. Strand[5]
[1]Innlandet Hospital, Women's Clinic, Lillehammer, Norway; [2]Innlandet Hospital, Department of Microbiology, Lillehammer, Norway; [3]Haugesund Hospital, Department of Medicine, Haugesund, Norway; [4]Erasmus University Medical Center, Academic Center for Thyroid Diseases, Rotterdam, Netherlands; [5]Innlandet Hospital, Department of Research, Lillehammer, Norway

Thyroid disease during pregnancy is associated with adverse pregnancy outcomes and suboptimal fetal development. During the last decades, guidelines for diagnosing thyroid disease during pregnancy have changed considerably, and there has been increased awareness. This study aimed to describe the prevalence of thyroid disease treatment over time among pregnant women in Norway. We combined historical data from the Medical Birth Registry of Norway and the Norwegian Prescription Database, identifying pregnant women using thyroid therapy before, during and after pregnancy from 2004 to 2018. A total of 855.067 pregnancies were included in the analyses. The proportion of women using thyroid hormone replacement therapy during pregnancy increased from 1.46% ($n=800$) in 2004 to 3.57% ($n=1940$) in 2018. The proportion of women using antithyroid medications also increased from 0.04% ($n=20$) in 2004 to 0.10% ($n=56$). During these 15 years, the mean maternal age increased by 0.9 years. When adjusting for age, the risk for being on thyroid hormone replacement therapy during pregnancy increased by an average of 5% per year (odds ratio 1.05, 95% confidence interval 1.05−1.05). The reasons behind the increased use of thyroid therapy could be many. Firstly, an enhanced focus on better diagnostics lead to an increased prevalence of thyroid disease, which is evident by the results of a repeated population-based cross-sectional study in Norway. However, one of the key clinical issues in this field is the definition of gestational thyroid disease. A second reason could be the increase in inadequate iodine intake among the pregnant population. Recent study from Norway found that pregnant and postpartum women with mild-to moderate iodine deficiency had altered thyroid. Furthermore, experimental and epidemiological studies have shown that a wide spectrum of environmental contaminants have the potential to adversely affect the hypothalamic-pituitary-thyroid axis, resulting in reduced maternal thyroid hormone synthesis affecting fetal neurodevelopment. Another possible contributor to the increased use of thyroid therapy could be that euthyroid women, with thyroid autoantibodies, use thyroid hormone treatment. The proportion of

babies born after assisted reproductive therapy has increased by 2.2% during the studied period. During the recent 15 years, there has been a substantial increase in the use of thyroid hormone therapy in Norwegian pregnant women. We speculate that this could be due to an increased awareness in combination with overdiagnosis because of inappropriate diagnostic criteria. To truly understand the possible causes and consequences of this development, further research is warranted.

DOI: 10.1530/endoabs.81.P716

P717

DICER1 mutations in pediatric thyroid nodules

Karolina Mastnikova[1], Barbora Pekova[1], Vlasta Sykorova[1], Jitka Moravcova[1], Eliska Vaclavikova[1], Petr Vlcek[2], Rami Katra[3], Daniela Kodetova[4], Josef Vcelak[1] & Bela Bendlova[1]
[1]Institute of Endocrinology, Department of Molecular Endocrinology, Prague, Czech Republic; [2]2 nd Faculty of Medicine, Charles University in Prague and Motol University Hospital, Department of Nuclear Medicine and Endocrinology, Prague 5, Czech Republic; [3]2 nd Faculty of Medicine, Charles University in Prague and Motol University Hospital, Department of Ear, Nose and Throat, Prague 5, Czech Republic; [4]2 nd Faculty of Medicine, Charles University in Prague and Motol University Hospital, Department of Pathology and Molecular Medicine, Prague 5, Czech Republic

Objectives
Mutations in the *DICER1* gene represent driver events in development of pediatric thyroid nodules, malignant as well as benign. The occurrence of these mutations has been reported in differentiated thyroid carcinomas, poorly differentiated thyroid carcinomas, non-invasive follicular thyroid neoplasms with papillary-like nuclear features (NIFTPs), multinodular goiters and follicular adenomas. The aim of this study was to detect mutations in *DICER1* gene in a large cohort of pediatric thyroid nodules and correlate found mutations with clinicopathological data with a focus on prognosis of disease in patients with papillary thyroid carcinoma (PTC).
Methods
The study consisted of 132 thyroid nodule samples from 124 pediatric patients (age 6-20 years). The cohort included 110 PTCs, 2 NIFTPs and 20 benign nodules. DNA was isolated from fresh frozen thyroid tissues using the Allprep DNA/RNA/miRNA Universal kit and the QIAcube Connect Extraction System (Qiagen, Germany). DNA was used for next-generation sequencing on MiSeq sequencer (Illumina, USA) using the Nextera XT DNA Library Prep Kit (Illumina). Mutations in the *DICER1* gene were visualized in Integrative Genomics Viewer (Broad Institute, USA) and evaluated by VarSome platform (Saphetor SA, Switzerland).
Results
Pathogenic *DICER1* hotspot mutations (E1705K, D1709 N, E1813D) in 7 of 132 (5.3 %) pediatric thyroid samples were detected. Six of them were PTCs (follicular variant), from which 5 were encapsulated. Five PTC patients received only one dose (100 mCi) of radioiodine treatment and are in remission. Only in one case, the patient received three doses of radioiodine (2× 100 mCi, 1× 120 mCi). This patient had a 60-mm carcinoma and angioinvasion was described only in this patient. The *DICER1* alteration was also found in one NIFTP case. All *DICER1*-mutated tumors did not possess other driver mutations (in the *BRAF* gene, *RAS* genes, fusion genes).
Conclusion
In summary, *DICER1* mutations are important molecular markers in pediatric thyroid nodules. Almost all our *DICER1*-mutated carcinomas represented low-risk malignancies and patients had an excellent response to the treatment. However, one patient had an incomplete response to treatment due to the advanced stage at the time of diagnosis. In conclusion, *DICER1*-mutated tumors appear to be indolent, but should not be underestimated.
Supported by AZV NU21-01-00448 and MH CR RVO 00023761.

DOI: 10.1530/endoabs.81.P717

P718

Clinical presentation and significance of thyroid dysfunctions secondary to PD-1/PD-L1 blockade cancer immunotherapy

Giulia Di Dalmazi[1], Sofia Elena Sorbo[1], Andrea Dudiez[1], Beatrice Ciappini[1], Ilaria Cipolloni[1], Gianluca Russo[2], Dimitri Luisi[2], Giorgio Napolitano[1] & Ines Bucci[1]
[1]University "G.d'Annunzio" of Chieti-Pescara, Department of Medicine and Aging Sciences, Chieti, Italy; [2]Pescara General Hospital, Medical Oncology Unit, Pescara, Italy

Background
Thyroid dysfunctions are among the most common immune-related adverse events (irAEs) following the administration of immune checkpoint inhibitors (ICIs) for malignancies. The pathogenesis of thyroid irAEs remains unclear and the clinical course can be multifaceted.
Aim
Aims of this study were a) to describe the incidence and the clinical course of thyroid irAEs b) to determine the association between thyroid irAEs and overall survival (OS).
Methods
We performed a single-center retrospective study of cancer patients treated with anti-PD-1/PD-L1 from January 2018 to December 2020. Demographic data, thyroid function tests (serum thyrotropin, TSH; free thyroxine FT4; free triiodothyronine, FT3) and thyroid ultrasonographic findings (if available) were retrieved at baseline and at regular intervals after starting ICIs. Patients were excluded if a) they had abnormal thyroid function at baseline b) were on anti-thyroid drugs or levothyroxine (LT4) replacement c) had missing data.
Results
One hundred sixty-six cancer patients were considered for potential enrollment, and after assessment of inclusion and exclusion criteria, 112 were enrolled. The mean age was 67.9 (10.6) years, and 82 patients (73.2%) were males. Lung cancer accounted for 65.8% of all cancers, followed by melanoma (16.2%), squamous cell carcinoma (9.9%), genitourinary cancers (6.3%) and other cancers (1.8%). Among all patients, 97 (86.6%) were treated with a PD-1 blockade, whereas 15 (14.4 %) received a PD-L1 inhibitor. Previous treatments had been performed in 72 patients (79.1%). During the study period, 25 patients (22.3%) developed thyroid irAEs with a median time to onset of 5.1 months (iqr 6.7). Two of them (8%) initially presented with thyrotoxicosis and 23 (92%) with hypothyroidism. Patients with thyrotoxicosis had an earlier median time to onset compared to those who had hypothyroidism (1.3 vs 5.2 months, $P=0.045$). Overall, 19 patients (76%) required LT4 replacement. Systemic steroids were not required in all cases. Thyroid ultrasonography, performed in 19 patients at thyroid irAEs onset, revealed a slightly increased thyroid volume in patients with thyrotoxicosis and a reduced volume in hypothyroid patients (18.1 vs 8.4 mL, $P=0.01$). Multivariable Cox regression analysis revealed that the occurrence of thyroid irAEs was independently associated with better OS (H.R. 0.3, CI 95% 0.1- 0.7, $P=0.006$).
Conclsion
This study confirms that thyroid irAEs occur with a high frequency in routine clinical practice and with heterogenous clinical presentation. It also supports that thyroid irAEs may represent a predictive biomarker of better response to ICIs.

DOI: 10.1530/endoabs.81.P718

P719

Serum FT3 levels and FT3/FT4 ratio as predictors for poor prognosis in hospitalized COVID-19 patients

Marica Milo[1], Giulia Di Dalmazi[1], Fabrizio Febo[2], Sara Coluzzi[2], Federica Carrieri[1], Marco Terrenzio[1], Giovanna Ferrandu[3], Antonella Spacone[4], Giorgio Napolitano[1] & Giustino Parruti[5]
[1]University "G.d'Annunzio" of Chieti-Pescara, Department of Medicine and Aging Sciences, Chieti, Italy; [2]Pescara General Hospital, Endocrinology and Metabolism Unit, Pescara, Italy; [3]Pescara General Hospital, Internal Medicine Unit, Pescara, Italy; [4]Pescara General Hospital, Respiratory Medicine Unit, Pescara, Italy; [5]Pescara General Hospital, Infectious Diseases Unit, Pescara, Italy

Background
The coronavirus disease 2019 (COVID-19) can involve multiple organs and systems, including the endocrine system. In particular, thyroid dysfunctions are frequently seen in COVID-19 patients. The aim of this study was to evaluate thyroid function in hospitalized COVID-19 patients and to correlate thyroid function with inflammatory status, blood count parameters and mortality.
Materials and methods
Data of COVID-19 patients admitted to the hospital of Pescara between October 2020 and March 2021 were retrospectively evaluated. Serum thyrotropin (TSH), free thyroxine (FT4), free triiodothyronine (FT3), FT3/FT4 ratio, thyroid antibodies (TgAb, TPOAb), inflammatory and blood count parameters (C-reactive protein, CRP; interleukin-6, IL-6; red blood cell, RBC; white blood cells, WBC; platelets, PLT; neutrophil to lymphocytic ratio, NLR) were analyzed and compared between survivors and non-survivors.

Results
Three hundred thirty-four adult COVID-19 patients were considered for potential enrollment, and after assessment of inclusion and exclusion criteria, 264 were enrolled. The median age was 74.4 (20.6) years, and 167 patients (63.5%) were males. The average hospital stay was 9 days. Of the 264 enrolled patients, 101 (38.2 %) died of COVID-19 complications. The characteristics of survivors and non-survivors are shown in table 1. Serum FT3 levels and FT3/FT4 ratio were significantly lower in non-survivors compared to survivors. Instead, inflammatory and blood count parameters, except for RBC, were significantly higher in survivors. Notably, FT3 levels and FT3/FT4 ratio negatively correlated with CRP and NLR (r=-0.2, $P<0.05$). In Kaplan-Meier and Cox regression analyses, low FT3 levels (FT3 less than 2.5 pg/ml) were independently associated with mortality (H.R. 1.7, CI 95 % 1.01- 2.96, $P=0.042$).
Conclusions
FT3 levels and FT3/FT4 ratio correlate negatively with inflammatory markers and may be predictive for poor prognosis in hospitalized COVID-19 patients.

	***Survivors* (*N*=163)**	***Non-survivors* (*N*=101)**	***P* value**
Age, years	68.5 (18.8)	83.5 (12.7)	<0.001
Sex M, N %	104 (63.8%)	64 (63%)	ns
Hospital stay, days	10 (8)	9 (11)	ns
TSH (μUI/ml)	0.7 (0.9)	0.7 (0.9)	ns
FT4 (ng/dl)	1.1 (0.3)	1.1 (0.4)	ns
FT3 (pg/ml)	2.5 (0.4)	2 (0.6)	<0.001
FT3/FT4 ratio	2.3 (0.9)	1.9 (0.7)	<0.001
TPOAb (IU/ml)	0.5 (0.9)	0.5 (1.2)	*ns*
TgAb (IU/ml)	0 (0.2)	0 (0.2)	*ns*
IL-6 (pg/ml)	38.9 (109.9)	58 (80.9)	*<0.05*
CRP (pg/ml)	45.1 (65.5)	98.1 (87.9)	*<0.001*
WBC (*10^3 /μL)	6.4 (4.4)	8.2 (5.6)	*<0.001*
RBC (*10^6 /μL)	4.4 (0.8)	4.1 (1.0)	*<0.001*
PLT (*10^3 /μL)	165 (123)	193 (111)	*<0.05*
NLR	5.3 (6.5)	11.2 (19.8)	*<0.001*

DOI: 10.1530/endoabs.81.P719

P720

Diagnostic accuracy of ultrasonographic features in detecting thyroid cancer in the transition age: a meta-analysis from the TALENT group

Alessia Cozzolino[1], Tiziana Filardi[1], Ilaria Simonelli[2,3], Giorgio Grani[4], Camilla Virili[3], Ilaria Stramazzo[5], Maria Giulia Santaguida[5], Pietro Locantore[6], Massimo Maurici[3], Daniele Gianfrilli[1], Andrea M Isidori[1], Cosimo Durante[4] & Carlotta Pozza[1]
[1]Sapienza University of Rome, Experimental Medicine, Rome, Italy; [2]Service of Medical Statistics and Information Technology, Fatebenefratelli Foundation for Health Research and Education, Rome, Italy, Rome, Italy; [3]Università degli Studi di Roma "Tor Vergata", Biomedicina e Prevenzione, Rome, Italy; [4]Sapienza University of Rome, Translational and Precision Medicine, Italy; [5]"Sapienza" University of Rome, Latina, Medico-Surgical Sciences and Biotechnologies, Italy; [6]Università Cattolica del Sacro Cuore, Rome, Endocrinology Unit, Fondazione Policlinico Universitario Agostino Gemelli-IRCCS, Italy

Context
Significant uncertainty exists about the diagnostic accuracy of ultrasonographic (US) features used to predict the risk of thyroid cancer in the pediatric population. Moreover, there are not specific indications for thyroid nodule evaluation in patients during the transition age.
Objective
The meta-analysis aimed to address the following question: which thyroid nodule US features have the highest accuracy in predicting malignancy in the transition age.
Methods
We performed a meta-analysis of observational/cohort/diagnostic accuracy studies dealing with thyroid nodule sonography, reporting US features, and using histology as reference standard for the diagnosis of malignancy and histology or cytology for the diagnosis of benignity in the transition age (mean/median age 12-21 years).
Results
The inclusion criteria were met by 14 studies, published between 2009 and 2020, including 1306 thyroid nodules (mean size 17.9 mm). The frequency of thyroid cancer was 36.6%. The US features with the highest diagnostic odds ratio for malignancy were the presence of suspicious lymph nodes [DOR: 56.0 (95% CI: 26.0-119.0)], a "taller than wide" shape of the nodule [6.0 (95% CI: 2.0-16.0)], the presence of microcalcifications [13.0 (95% CI: 6.0-29.0)] and irregular margins [9.0 (95% CI: 5.0-17.0)]. Heterogeneity among the studies was substantial.
Conclusions
Following the diagnosis of a thyroid nodule in transition age, a thorough US examination of the neck is warranted. The detection of suspicious lymph nodes and/or thyroid nodules with a "taller than wide" shape, microcalcifications and irregular margins is associated with the highest risk of malignancy in the selection of nodules candidates to biopsy.

DOI: 10.1530/endoabs.81.P720

P721

Does the risk of new metabolic changes among thyroid cancer survivors depend upon thyroid function?

Elena Izkhakov[1,2], Yacov Shacham[2,3], Tomer Ziv-Baran[4], Iris Yaish[1,2], Gilad Horowitz[2,5], Anton Warshavsky[2,5], Nidal Muhanna[2,5], Narin Nard Carmel-Neidermann[2,5], Karen Tordjman[1,2] & Yona Greenman[1,2]
[1]Tel Aviv Sourasky Medical Center, Institute of Endocrinology, Diabetes, Metabolism and Hypertension, Tel Aviv-Yafo, Israel; [2]Tel Aviv University, Tel Aviv-Yafo, Israel; [3]Tel Aviv Sourasky Medical Center, Department of Cardiology, Tel Aviv-Yafo, Israel; [4]Tel Aviv University, School of Public Health, Sackler Faculty of Medicine, Tel Aviv-Yafo, Israel; [5]Tel Aviv Sourasky Medical Center, Department of Otolaryngology, Head & Neck and Maxillofacial Surgery, Tel Aviv-Yafo, Israel

Background
Various components of metabolic syndrome (MS) significantly increase the risk of thyroid cancer (TC). Moreover, thyroid cancer survivors (TCS) are at increased risk of new components of MS (MSC). The role of thyroid function in this context has not yet been determined. We investigated changes in selected MSC and their association with thyroid function during a two-year follow-up among TCS.
Materials and Methods
This retrospective, nested case-control study used data from a single academic hospital. The one-hundred and fifteen participants had undergone total thyroidectomy, radioactive iodine treatment and thyroid-stimulating hormone-suppressive L-thyroxine therapy for two years due to differentiated TC.
Results
The numbers of MSC in the entire cohort at baseline compared to those after a two-year follow-up were as follows: none in 58.3% patients vs 30.4% patients, respectively, 1 in 20.9% vs 35.7%; 2 in 11.3% vs 16.5%; 3 in 7.8% vs 13.9%; 4 in 1.7% vs 1.7%; and 5 in 0% vs 1.7%. The incidence of MSC increased during the two-year follow-up period in 51 TCS (cases), while none of the 64 TCS (controls) developed any new MSC. The multivariable logistic regression analysis showed that TCS with a FT3/FT4 ratio greater than 0.22 (lower tertile) had a significantly increased risk of a new MSC (odds ratio 2.73, 95% confidence interval 1.14−6.57, $P=0.025$).
Conclusions
Our study demonstrated that an FT3/FT4 ratio greater than 0.22 is correlated with detrimental metabolic changes among TCS.

DOI: 10.1530/endoabs.81.P721

P722

Clinicopathological characteristics and response to therapy in patients with tall cell variant papillary thyroiid carcinoma in an institution: analysis of 109 cases

Hernan Tala[1], Josefina Razmilic[1] & Jeannie Slater[2]
[1]Clínica Alemana de Santiago, Facultad de Medicina Clínica Alemana/Universidad del Desarrollo, Internal Medicine (Endocrinology Unit), Chile; [2]Clínica Alemana de Santiago, Facultad de Medicina Clínica Alemana/Universidad del Desarrollo, Pathology Department, Chile

Objectives
1.-Characterization of patients with tall cell variant papillary thyroid carcinoma (TCV-PTC) at diagnosis (Dx) compared to patients with classic papillary thyroid carcinoma (c-PTC);

2.-Evaluation of response to therapy (RT) in the (TCV-PTC) cohort
Experimental design: Retrospective observational study
Materials and methods
Patients submitted to surgery for PTC in our institution since 2010 were evaluated. Clinicopathological characteristics at dx. were compared between TCV-PTC y c-PTC. Subsequently, the RT in the TCV-PTC cohort was evaluated. Continuous variables (v) are described with median and range and categorical variables as proportions. ANOVA was used to compare continuous variables and chi square or Fisher in categorical variable. Logistic regression was used for multivariate analysis.
Results
From 1475 patients with PTC, 1040 (70%) correspond to c-PTC and 109 (7%) to TCV-PTC. Table 1 compares the clinicopathological characteristics most relevant at Dg. In multivariate analysis, TCV-PTC was independently associated with a higher probability of ETE and LNF-Inv in the pathology report. RAI was given to 86% of patients. Of the 68 patients in whom it was possible to evaluate RT (median follow-up 21 months), 66% presented excellent RT, 16% indeterminate RT and 7% structural incomplete RT. RT was significantly better in patients with tumors $\leq$2 cm without lymph node metastases (LNM) at Dg (Table2).

Table 1 Clinicopathological characteristics at diagnosis

	TCV-PTC	c-PTC	p
	n=109	*n*=1040	
Age (Median, range)	46 (19-77)	42 (6-86)	< 0.05
Female	83%	76%	0.10
Tumoral size ≥10 mm	43%	29%	< 0.05
Extra-thyroidal extensión (ETE+)	47%	23%	< 0.05
Linfovascular invasión (LNF-Inv) (+)	46%	23%	< 0.05
Necrosis (+)	5%	1.4%	< 0.05
pT (AJCC 2017)			
pT1a	55%	70%	*P*< 0.05
pT1b	28%	21%	
pT2	5%	7%	
pT3a	0	0.4%	
pT3b	8%	0.9%	
pT4	4%	0.7%	
pN0/Nx	67%	66%	0.7
pN1a	24%	22%	
pN1b	9%	12%	

Table 2: RT according to AJCC-2017

	pT1a/pT1b-N0/Nx	Otros	P
Excelent RT	31/38 (82%)	14/30 (46%)	< 0.05
Indeterminate RT	7/38 (18%)	9/30 (30%)	
Structural incomplete RT	0	7/30 (23%)	

Conclusions
At diagnosis, TCV-PTC has a higher probability of ETE, LNF-Inv, necrosis and larger tumor size. Despite that, RT seems to be good in patients with tumors $\leq$2 cm without LNM. Studies with longer follow-up and larger number of patients are needed to confirm these observations.

DOI: 10.1530/endoabs.81.P722

P723

Metastatic papillary thyroid carcinoma without identifiable primary tumor in a patient with IgG4-related thyroiditis: challenging diagnosis and management of a rare case

Kasiani Papadimitriou, Melpomeni′ Moustaki, Anastasios Tsitsimpis, Nektaria Papanikola, Alexandros Dermentzoglou, Loukia Spanou & Andromahi Vryonidou

Red Cross Hospital, Endocrinology, Diabetes, and Metabolism Department, Athens, Greece

Introduction
IgG4-related thyroiditis (IgG4-RTD) is a rare fibroinflammatory disorder. It is characterized by dense lymphocyte infiltration (mainly IgG4+ plasma cells), enlargement and dysfunction of the thyroid gland. IgG4-RTD includes mostly cases of Hashimoto's (HT) but also of Riedel's and Graves' thyroiditis. Diagnosis is set according to imaging and histopathological criteria. Papillary thyroid carcinoma (PTC) is the most common form of thyroid cancer (~90%). Co-occurrence of HT and PTC is found in 23-30% and the presence of HT is considered a favorable prognostic factor. The association between PTC and IgG4-RTD remains unclear. Metastatic PTC without an identifiable primary tumor is also a very rare phenomenon.
Case presentation
A 48-year-old woman attended our outpatient clinic presenting with progressive painless cervical enlargement and HT. The patient was euthyroid under levothyroxine treatment. Clinical examination revealed a diffusely enlarged, moderately hard thyroid and palpable, painless, mobile cervical lymph nodes. Neck ultrasonography showed diffuse thyroid enlargement with inhomogeneous, hypoechoic, hypovascular echostructure and several enlarged lymph nodes of the central and lateral cervical compartment. Cytological examination after fine needle aspiration of two suspicious nodes of the central compartment was suggestive of non-specific reactive lymphadenitis. Later, the patient presented further thyroid enlargement with marked stiffness, dysphagia and hoarseness. Thyroid core needle biopsy provided findings of the fibrosing variant of HT and IgG4-RTD. Serum IgG4 levels were also elevated. Computed tomography of chest, abdomen and retroperitoneum returned no findings of systemic IgG4-related disease. She was treated with methylprednisolone 16 mg/d and presented progressive clinical and imaging improvement. After surgical review, total thyroidectomy was carried out. Pathology report revealed HT with extended fibrosis at thyroid specimens and metastatic infiltration of follicular variant of PTC in two cervical lymph nodes. Post-op the patient received 50 mCi of I-131 for remnant ablation. Negative post-ablation whole body scan in conjunction with undetectable thyroglobulin levels and negative anti-thyroglobulin antibodies title were compatible with disease remission.
Discussion
IgG4-RTD, though an unusual clinical entity, should be considered in the differential diagnosis of thyroid enlargement. The management of a patient with IgG4-RTD and metastatic thyroid carcinoma without an identifiable primary tumor is rather challenging, as the impact of IgG4-RTD on cancer prognosis is still ambiguous. Failure in identifying primary tumor may be attributed to the small size (<3 mm) and/or the extended fibrosis of thyroid.

DOI: 10.1530/endoabs.81.P723

P724

Congenital central hypothyroidism diagnosed in-utero

Michal Yacobi Bach[1,2], Yonit Marcus[1] & Yona Greenman[1]
[1]Tel Aviv Medical Center, Endocrinology Institute, Tel Aviv, Israel; [2]Tel Aviv Medical Center, Genetics Institute, Tel Aviv, Israel

Introduction
Congenital central hypothyroidism (CH), is characterized by low levels of thyroid hormones and TSH. It is not possible to diagnose this condition by neonatal screening programs based on TSH measurements, hence it is often missed. The assumption that CH is usually a mild condition has been refuted, and more than 50% of all newborns with CH have moderate to severe disease. Early diagnosis and treatment lead to better neurodevelopmental outcomes. Isolated CH is a rare condition with an estimated prevalence of 1:13000. More than 90% of cases are due to pathogenic mutations in five known genes: *thyroid releasing hormone receptor* (*TRHR*), *thyroid stimulating hormone beta subunit* (*TSHB*), *immunoglobulin superfamily member 1* (*IGSF1*), *transducin (beta)-like 1X-linked* (*TBL1X*) and in *insulin receptor substrate 4* (*IRS4*) genes. Mutations in both *IGSF1* and *TBL1X* can lead to X-linked isolated CH. *IGSF*1 mutations are also associated with low PRL, variable GH deficiency, metabolic syndrome, and postpubertal macroorchidism.
Case description
A 40-year-old pregnant woman with a past medical history of hemithyroidectomy due to goiter, was diagnosed with CH at the age of 20 years. Prolactin levels were low, adrenal function was preserved and pituitary imaging was normal. She reported having had lactation problems after her first pregnancy. The family history was unremarkable and there is no known consanguinity. Genetic evaluation: A prenatal CMA (chromosomal microarray) revealed a normal

male karyotype 46XY with a 250kb deletion on chromosome X :arr (hg19) Xq26.1- Xq26.2 (130.181.100-130.431.733)*0. This deletion encompasses two omim genes*: ARHGAP36, IGSF1 and* was later confirmed to be inherited from the patient. Central congenital hypothyroidism was diagnosed clinically in the newborn baby, and treatment with thyroid hormone replacement was initiated, there was no need for steroid replacement therapy.
Discussion
X linked *IGSF1* deficiency syndrome is the main etiology for Congenital CH. As far as we know, this is the first described case of a molecular diagnosis made in utero. Such early diagnosis enables focused surveillance of the fetus, regarding thyroid size, bone age and heart rate. Hypocortisolism was described in 20% of neonates with CH. Prenatal diagnosis enables early treatment with thyroid hormones and steroids if needed, and reduces the risk of neurodevelopmental problems.

DOI: 10.1530/endoabs.81.P724

P725

TIRADS system: what does clinical practice tell us?

Catarina Ivo, Vitória Duarte, David Veríssimo, Ana Cláudia Martins, João Silva, Luís Lopes, Dolores Passos, João Jácome Castro & Mafalda Marcelino
Armed Forces Hospital - Lisbon, Endocrinology Department, Lisboa, Portugal

Introduction
Thyroid nodules have a high prevalence in the adult population (20-76%). In 2018, the American College of Radiology proposed an ultrasound classification score of thyroid nodules - Thyroid Imaging Reporting and Data System-TIRADS, with 88% of sensitivity and 49% of specificity to predict malignancy. Since then, several studies report sensitivity values of 70.6-97% and specificity of 30-98%. We pretend to compared TIRADS score with cytologic results based on Bethesda classification.
Methods
This is a retrospective study of patients with thyroid nodules submitted to fine-needle aspiration (FNA) in an endocrinology department, during 16 months. Cytologic results (Bethesda classification) and TIRADS score (TR) were evaluated. TR score was calculated at the time ultrasound-guided FNA was performed. All Bethesda I (non-diagnostic) results were excluded.
Results
A total of 143 FNA of thyroid nodules were analysed, from 123 patients (57.7 % female) with a mean age of 64 $\pm$ 14.3 years-old. The nodules' mean dimension was 24.6 $\pm$9 mm. 61.5% of nodules were classified as TR 4, 27% TR3, 7% TR5, 2.1% TR1 and 1.4% TR2. 90.2% of FNA were Bethesda II (benign) and 9.8% were Bethesda III (follicular lesion of undetermined significance). No results of Bethesda IV-VI were diagnosed (malignancy). Analysing all TR1 and TR2 nodules, 80% were Bethesda II and 20% were Bethesda III. From nodules of TR3 to TR5, Bethesda II results were obtained in 92.3% of TR3, in 92% of TR4 and 72.7% of TR5, and Bethesda III were obtained in 7.7% of TR3, 8% of TR4 and 27.3% of TR5. No statistically significant difference was verified between categories ($P=0.392$). A 91.9% specificity was achieved for TIRADS score to identify benign thyroid nodules.
Conclusion
Our data demonstrated an elevated TIRADs score specificity that is in line with that reported in the published literature. Our results showed that TIRADs score seems to be particularly useful in identifying benign thyroid nodules. Higher risk TIRADS categories did not reflect higher risk for malignancy in cytologic diagnosis. More studies with greater samples are needed.

DOI: 10.1530/endoabs.81.P725

P726

Graves' eye disease associated with SARS-CoV2 infection

Jane Noble[1], Brian Carthy[1] & Siobhan McQuaid[1,2]
[1]Mater Misericordiae University Hospital (MMUH), Endocrinology Department, Dublin 7, Ireland; [2]University College Dublin, Dublin 4, Ireland

Introduction
SARS-CoV2 infection or vaccination against SARS-CoV2 has been linked to the onset or recurrence of Autoimmune and subacute thyroiditis resulting in thyroid dysfunction.
Case
We describe a case of Thyroid eye disease temporally associated with SARS-CoV 2 infection in a 48 year old female with a one-year history of subclinical hypothyroidism without interval thyroid hormone replacement or SARS-CoV2 vaccination. Two months following PCR confirmed SARS-CoV 2 infection, the patient presented with eye irritation and oedema. Direct ophthalmological assessment led to a diagnosis of thyroid eye disease. CT orbit confirmed bilateral proptosis with increased intraorbital fat. TSH was 0.01 mIU/l (0.27-4.2) and FT4 18 pmol/l (12-20). Carbimazole 10 mg BD was commenced as she complained of palpitations, heat intolerance and tremor. TFTs three months later indicated T3-thyrotoxicosis (TSH <0.01 mIU/l (0.35-4.94), FT4 14.3 pmol/l (9.0-20.0) Free T3 6.3 pmol/l (2.6-4.9)) with elevated TSH Receptor Antibody 3.5 U/l (0-0.4) in keeping with a diagnosis of Grave's Disease. The patient was referred to Endocrinology for clinical assessment. At that assessment, nine months following eye symptom onset, the patient was clinically and biochemically euthyroid on Carbimazole 5 mg BD (TSH 3.24 mIU/l (0.35-4.94), FT4 11.8 pmol/l (9.0-20.0), Free T3 3.9 pmol/l (2.6-4.9), Anti TPO 108.1 IU/ml (<5.6)). She was an ex-smoker of 2 years with no family history of autoimmunity. Of note the patient reported L-thyroxine replacement until 4 years prior to presentation. Review of available TFTs one year prior, off L-thyroxine, showed TSH 8.7 mIU (0.27-4.2), T4 13.4 pmol/l (12-22), thyroid antibodies unavailable. Mild non-tender goitre was evident on exam with palpebral oedema and conjunctival injection without exophthalmos or lid retraction. Carbimazole was stopped. Although still troubled by eye irritation the patient remains clinically and biochemically euthyroid on review 12 months following onset of eye symptoms (TSH 2.85 mIU/l (0.35-4.94), FT4 12.8 pmol/l (9.0-20.0), Free T3 4.5 pmol/l (2.6-4.9) with reducing titres of TSH Receptor Antibody 1.2 U/l ((0-0.4)).
Conclusion
There have been numerous published cases of new or recurrent Graves' disease and Subacute thyroiditis following SARS-CoV2 infection. In our case, the rapid response to antithyroidal medications and predominant ophthalmic symptoms perhaps point to a dual diagnosis of acute thyroiditis and Graves' Eye Disease. The case is also interesting in that she had a history of sub-clinical hypothyroidism. Should she become hyperthyroid again, thyroid scintigraphy would be beneficial. Clinicians should remain cognisant of the effect of SARS-CoV2 infection on thyroid dysfunction.

DOI: 10.1530/endoabs.81.P726

P727

Alemtuzumab induced thyroid disease: a Danish cohort study

Juliana Frohnert Hansen[1], Melinda Magyari[2], Åse Krogh Rasmussen[3], Finn Sellebjerg[2] & Ulla Feldt-Rasmussen[3]
[1]Amager Hospital, Department of Internal Medicine, Copenhagen S, Denmark; [2]Copenhagen University Hospital, Rigshospitalet, Glostrup, Danish Multiple Sclerosis Center, Department of Neurology, Copenhagen, Denmark; [3]Copenhagen University Hospital, Rigshospitalet, Department of Endocrinology, Copenhagen, Denmark

Objectives
Alemtuzumab, a monoclonal antibody against CD52, is used in the treatment of multiple sclerosis. A side effect to the treatment is development of autoimmune thyroid disease. The aim was to evaluate the rate, type and course of thyroid disease in Danish patients with multiple sclerosis (MS) previously treated with Alemtuzumab.
Methods
The study was a retrospective cohort study of patients treated with first series of alemtuzumab for multiple sclerosis (MS) in the Capital and Zealand regions (population: 2.6 million) of Denmark between 2014 and 2018 ($n=60$). The following data was collected from patient records: known previous thyroid disease, date of first series of alemtuzumab, onset date of thyroid dysfunction, blood sample result of thyroid hormones and thyroid antibodies and thyroid scintigraphy and ultrasound to determine type of thyroid disease, type of treatment, duration and course of thyroid dysfunction.
Results
The follow-up period was median 58.5 months (31-83, range). Thyroid disease occurred in 24 of the 60 patients (40 %), with a median onset at 24 months after the first alemtuzumab treatment (1-63, range). Graves' disease (GD) occurred in 18 of 60 patients (30 %) and three of these also had silent or postpartum thyroiditis with undetectable thyroid receptor antibodies (TRAB) before onset or after remission of GD. Isolated silent or subacute thyroiditis occurred in two of 60 patients (3 %), unclassified hyperthyroidism (due to lack of information) in two of 60 patients (3%) and toxic multinodular goitre also in two of 60 patients (3%).
An unusual or unpredictable course of GD was observed in 12 patients, with a rapid change in serum hormone concentrations unrelated to changes in

medication, e.g. sudden changes from hyperthyroidism to hypothyroidism, being the most common. Some of these patients were treated with antithyroid hormone or thyroxine titration regimen, while others were switched to block and replace treatment. Full remission of GD, defined as undetectable TRAB, was at the time of data collection only seen in four patients.
Conclusion
Data from this Danish population was in accordance with recent published studies and supports previous observations of both unusual, long-lasting and unpredictable courses of GD in a subgroup of patients. Hypothetically, some of these may benefit from block and replace treatment, to stabilize an otherwise clinically inappropriate fluctuating GD.

DOI: 10.1530/endoabs.81.P727

P728

A rare etiology for thyrotoxicosis − case report

Teodor Dumitras[1], Gheorghita Patriciu Zubascu[1], Marius Lucian Mitrache[1], Adrian Miron[2,5], Cornelia Nitipir[2,4], Dana Terzea[5] & Simona Fica[1,2]
[1]Elias University Emergency Hospital, Endocrinology, Bucharest, Romania; [2]"Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania; [3]Elias University Emergency Hospital, General Surgery, Bucharest, Romania; [4]Elias University Emergency Hospital, Oncology, Bucharest, Romania; [5]C.I. Parhon National Institute of Endocrinology, Bucharest, Romania

Introduction
Hyperthyroidism and thyrotoxicosis can have multiple etiologies, varying from the most frequent described in clinical practice (Graves disease, toxic nodular goiter, thyroiditis) to very rare causes such as anaplastic thyroid cancer, thyroid lymphoma, amyloidosis or even secondary malignancy of the thyroid gland.
Case report
A 53 year old man presented to our department for progressive goiter enlargement in the last two months which was accompanied by dysphagia and dysphonia. The patient had a history of smoking for almost 40 years and also mentioned that in the last two weeks he lost in weight approximately 3 kg. The clinical exam was in normal limits, with the exception of multiple laterocervical adenopathies and the enlarged, firm thyroid gland which was painful and presented local inflammatory signs. The paraclinical investigations showed an acute inflammatory syndrome (ESR 42 mm/h, CRP 85.2 mg/l, Fibrinogen 606 mg/dl) with thyrotoxicosis (TSH - 0.01 mIU/ml, freeT4 - 4.13 ng/dl and total T3 - 278 ng/dl) and negative autoimmunity. The thyroid ultrasound showed a pseudonodular heterogenous aspect with decreased blood flow and multiple non-inflammatory laterocervical adenopathies, largest one being almost 2 cm. In addition, thyroid scintigraphy showed no hyperfunctioning areas while the computed tomography of the neck and thorax discovered a right apical pulmonary nodule of 35/36/46 mm. During his hospital stay he received anti-inflammatory treatment with dexamethasone and ibuprofen. His largest right laterocervical adenopathy was surgically removed and sent to the anatomical pathology department who described a ganglionar metastasis of pulmonary carcinoma with clear large cells. The patient underwent total thyroidectomy and the result confirmed a thyroid metastasis of pulmonary carcinoma. He received replacement therapy with levothyroxine and oncologic treatment with pembrolizumab, pemetrexed and carboplatin. During his last examination, after eight months of treatment, the patient was stable, presenting euthyroidism while the right apical pulmonary nodule had a dimensional regression. Unfortunately, he presented multiple cervical adenopathies for which he will undergo palliative radiotherapy.
Conclusions
This was a rare case of thyrotoxicosis which required a proffesional multidisciplinary team in order to offer an appropriate diagnosis and treatment. Secondary malignancy of the thyroid gland is quite rare, and especially in the form of thyrotoxicosis which probably was caused by a destructive invasion of thyroid tissue with malignant cells, similar to a "thyroiditis".
Key words: thyrotoxicosis, secondary malignancy, pulmonary carcinoma

DOI: 10.1530/endoabs.81.P728

P729

Hyperthyroidism and ischemic stroke in a young adult

Yosra Hasni[1,2], Hamza Elfekih[1,2], Ghada SAAD[1,2], Wiem Saafi[1], Oumayma Zarrouk[1], Amel Maaroufi[1,2], Maha Kacem[1,2], Molka Chadli Chaieb[1,2] & Koussay Ach[1,2]
[1]Farhat-Hached University Hospital, Endocrinology-Diabetology Department, Sousse, Tunisia; [2]Faculty of Medicine Ibn El Jazzar, University of Sousse, Sousse, Tunisia

Introduction
Moyamoya disease is a rare angiopathy characterized by a progressive stenosis of the intracranial internal carotid arteries (ICA). First described in 1957, its pathophysiological mechanisms are still not well understood. Its association with various systemic diseases is termed moyamoya syndrome
Observation
A 21-year-old female patient, with a family history of hypothyroidism, was admitted initially with stroke. The clinical examination revealed hemiparesis of the right hemisphere and dysarthria, in addition to a moderate goiter and tachycardia. Cerebral CT scan with contrast showed bilateral stenosis of the intracranial ICA with 78% in the left and 30% in the right ICA, confirming the diagnosis of moyamoya angiopathy. Biological analysis on admission and prior to the imaging procedure revealed suppressed TSH level and 10-fold increase in serum FT4. The diagnosis of Graves' disease was made upon the presence of anti-TSH receptor antibodies: 5 IU/l (< 2 IU/l) and high thyroidal technetium-99 m pertechnetate uptake. Thyroid peroxidase antibodies were also positive and 32-fold elevated (1600 IU/ml). The patient received 30 mg qd of thiamazole in addition to rehabilitative management with improvement of its poststroke hemiparesis.
Discussion
Moyamoya syndrome represents one-third of moyamoya angiopathy and is associated with well-recognized conditions like neurofibromatosis type 1, Down syndrome, sickle cell disease but also autoimmune diseases. Autoimmune thyroiditis are increasingly reported in the literature in patients with moyamoya angiopathy suggesting a possible role of the immune process in the pathogenesis of this disease.

DOI: 10.1530/endoabs.81.P729

P730

Effect of levothyroxine replacement therapy on testosterone, LH, FSH levels in men with overt hypothyroidism

Abhishek Shrivastav[1] & Bharat Saboo[2]
[1]R&R hormone clinic, endocrinology, jabalpur, India; [2]Prayas Diabetes Centre, Diabetes, Indore, India

Introduction
The prevalence of hypothyroidism overtly ranges from 5% to 11%. Though Hypothyroidism is less common in males as compared to females but deficiency of thyroid hormone affects almost all metabolic organs of the body, which includes changes in growth hormone, steroid metabolism, sexual function, antioxidative function.
Aim
− The aim of our study was to assess the levels of total testosterone LH, FSH levels in males with overt hypothyroidism pre and post levothyroxine therapy. In our study we included 51 patients with overt hypothyroidism, with mean age 40.2 years(32-56 years). 50% of patients had low testosterone level at baseline, low testosterone level associated with hypothyroidism has not been well documented in several studies with varying prevalances. In our study only 5 patients had low LH level at baseline while FSH level of all the patients was normal at baseline, semen analysis could not be done due to non consent of patients. In our study after attainment of euthyroidism or after 4 months of replacement of levothyroxine therapy 70% of hypogonadic patients had their testosterone level normal, more than 80% of patients with low ADAMS score showed improvement in their parameters.
Conclusion
Thyroid hormone deficiency affects all tissues of the body, including multiple endocrine changes that alter growth hormone, corticotrophin, glucocorticoids, and gonadal function. Primary hypothyroidism is associated with hypogonadotropic hypogonadism, which is reversible with thyroid hormone replacement therapy. The same has been seen in our study also that after levothyroxine replacement there was significant improvement in free testosterone level, significant improvement in ADAMS score, although predominance of hypogondotropic hypogonadism was not that significant but still some degree of relevance was observed. So according to the results we concluded that overt hypothyroidism can induce hypogonadism or low testosterone levels in men that is reversible with thyroxine replacement therapy. Importantly, some of the clinical manifestations of primary hypothyroidism in men may be due in part to a reduction in free testosterone. Further evaluation of this potential clinical interaction would require a controlled trial of androgen replacement in the hypothyroid state. However, hypogonadotrophic hypogonadism with thyroxine replacement is reversible with full restoration of normal thyroid function.

DOI: 10.1530/endoabs.81.P730

P731

Epidemiological, clinic-pathological, evolutionary profile of differentiated thyroid carcinoma in adolescents and young adults:About 161cases

Hajar Khouchaf[1], nassim essabah haraj[2], Siham El aziz[1] & Asma Chadli[2]
[1]Ibn Rochd University Hospital, Endocrinology, Diabetology, Nutrition and Metabolic Diseases Department, Casablanca, Morocco; [2]Ibn Rochd University Hospital, Endocrinology, Diabetology, Nutrition and MetabolicDiseases Department, Casablanca, Morocco

Introduction
Adolescent and young adult differentiated thyroid cancers are frequently under diagnosed forms. They would be characterized by their aggressiveness and the presence of particular histological forms. The aim of the study was to describe the characteristics of thyroid carcinoma in adolescents and young adults by analyzing the clinical, histological, therapeutic and evolutionary characteristics.
Materials and methods
We conducted a retrospective study in Endocrinology and Diabetology department of Ibn Rochd University Hospital of Casablanca between 1986-January 2022, including 161 cases of thyroid cancer in young adults under 30 years among all thyroid differentiated cancers (927 patients). This group of patients was compared to a second one aged between 30 and 45 years (386patients). The statistical analysis was performed by the software SPSS version 25.0
Results
Mean age at diagnosis was 22.7years (10-29), with a clear female predominance (91.3%). Familial thyroid neoplasia was found in 11.8% of patients. Predominant mode of discovery was multinodular goiter suspected in 62.1% of cases and lymph node metastases in 9.3% of cases. All patients underwent total thyroidectomy associated with lymph node dissection in 21.1% of cases. Papillary carcinoma was the predominant histological type in 95% of cases. Recurrences were found in 6.1% of cases: locoregional recurrence (4.3%) and pulmonary metastases (1.8 %). The analytical study had shown that the following prognostic factors including multifocality, capsular invasion and bilaterality were significantly higher in the group of young patients compared to the older one ($P <$ 0.001), and that the occurrence of metastases were earlier
Conclusion
Differentiated cancers of the young subject are becoming more and more frequent and invasive. The precocity and frequency of local and distant metastases reflect particularly aggressive forms as reported in the literature.

DOI: 10.1530/endoabs.81.P731

P732

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) in advanced thyroid cancer (TC) patients; single-center experience

George Simeakis, Stavroula A. Paschou, Maria Alevizaki & Katerina Saltiki
National Kapodistrian University of Athens, Dept of Clinical Therapeutics, Athens, Greece

Objectives
Patients suffering from pulmonary or/and neoplastic disease are at higher risk of developing serious illness from SARS-CoV-2. TC patients with lung metastases are classified as high-risk for severe CoV-2 disease. Aim of this study was to investigate SARS-CoV-2 prevalence and severity in this particular subgroup of patients.
Methods
Out of 28 patients with metastatic Differentiated Thyroid Cancer (**DTC**) and 21 patients with metastatic Medullary Thyroid Cancer (**MTC**) followed-up in our Dept, 12 and 11 respectively, present lung metastases and they are under Tyrosine Kinase Inhibitors (TKIs) treatment. During a follow-up period of 18 months (from April-2020) SARS-CoV-2 infections (PCR-confirmed) as well as clinical course of TC patients with lung metastases were recorded.
Results
$n = 4/12$ (33.3 %) **DTC-**patients were diagnosed with SARS-CoV-2. **Two patients**, a 68-year-old-female and a 50-year-old-male, with mediastinal lymph nodes/lung metastases, partial structural response to, Sorafenib-800 mg and Lenvatinib-14 mg respectively, experienced mild symptoms and further hospitalization was not required for them. The **third patient**, a 63-year-old-female, with mediastinal lymph nodes/lung/bone metastases, disease stabilization under Sorafenib-800 mg, required further hospitalization- for a total period of 20 days -with administration of Dexamethasone and Remdesivir; Sorafenib was discontinued during this period. The **fourth patient**, a 52-year-old-male, with lung/liver/bone metastases and disease progression under third line TKI Cabozantinib, succumbed to the disease during his hospitalization. $n = 3/11$ (27.3 %) **MTC**-patients were diagnosed with SARS-CoV-2. **Two patients**, a 52-year-old-female and a 47-year-old-male, (sporadic MTCs), with lung metastases and disease stabilization under Vandetanib-300 mg, experienced mild symptoms and further hospitalization was not required for them. The **third patient**, a 34-year-old-female, (MEN2B), with lung/liver metastases and disease stabilization under Vandetanib-300 mg, suffering with concomitant Multiple-Sclerosis under immunomodulatory treatment, required further hospitalization- for a total period of 10 days -with administration of Dexamethasone and Remdesivir; Vandetanib discontinuation was not requisite. All six patients, during a follow-up period of at least two months, stay healthy with neither residual symptoms nor progression of the neoplastic disease to have been recorded. All but one (MEN2B patient) had undergone SARS-CoV-2 vaccination(BNT162b2).
Conclusions
TC patients with lung metastases, under TKIs treatment, are at high-risk of severe CoV-2 disease. Disease stabilization under TKIs as well as lower metastatic burden seem to be favourable prognostic factors regarding SARS-CoV-2 clinical course. TKIs discontinuation, when questioned, has to be performed under a multidisciplinary team (MDT) approach, with a cost-effectiveness analysis, balancing possible risks of neoplastic disease progression.

DOI: 10.1530/endoabs.81.P732

P733

Increased incidence of primary hyperparathyroidism in patients with papillary thyroid cancer. Just a coincidence or a new syndrome. I have problems defining the rationale of the study Why PHP and thyroidectomy were performed at the same time

Nektaria Papadopoulou-Marketou[1,2], George Chrousos[1], Panagiotis Tsiamyrtzis[3] & Evaggelos Karvounis[4]
[1]National Kapodistrian University of Athens, University Research Institute of Maternal and Child Health and Precision Medicine, Athens, Greece; [2]National Kapodistrian University of Athens, Endocrinology Unit, 1st Department of Propaedeutic and Internal Medicine, School of Medicine, Athens, Greece; [3]Department of Mechanical Engineering, Politecnico di Milano, Milan, Italy; [4]Euroclinic Hospital, Department of Endocrine Surgery, Center of Excellence, Greece

Presence of primary hyperparathyroidism (PHPT) in patients with thyroid disease has been previously reported. However, co-existence of PTHPT and papillary thyroid cancer (PTC) has been reported very rarely, mainly in the form of isolated case reports. Since the pathophysiological mechanisms of the two diseases are theoretically quite different, no causal relation between these diseases has been inferred. The aim of this study was to investigate the presence of PHTP in individuals who underwent thyroidectomy for suspected thyroid cancer or large nodular goiter.
Patients and Methods
A retrospective observational study involving 3230 patients (24% men, mean age 49.8 years, and 76% women, mean age 47.7 years) who underwent total thyroidectomy in the Department of Endocrine Surgery, Euroclinic Hospital, Athens, Greece, over a period of 13 years (2005-2018). The patient groups were categorized according to histopathological criteria of the parathyroid and thyroid glands.
Results
1945 patients (64%) had large benign nodular goiter, while 978 (32%) had papillary thyroid carcinoma. Among patients with benign nodules and those with papillary carcinoma respectively 16 (11 women/5 men) and 38 (33 women/5 men) had PHPT. The relative risk for coexistence of PHPT and PTC was 2.0 (95% CI 1.7 to 2.4, $P <$ 0.0001). The age groups between 30 and 60 years were associated with the highest relative incidence (82%) of PHTP, while there was sexual dimorphism, with a ratio of 4.4:1 in women *vs.* men.
Conclusions
Our study found that coexistence of PHPT and PTC is relatively common. As primary hyperparathyroidism is a chronic disease that is associated with many complications and requires early diagnosis and treatment, this co-morbidity should be considered in all patients requiring thyroidectomy for cancer. Further investigation of the possibly shared pathogenetic mechanisms between primary hyperparathyroidism and papillary thyroid carcinoma and is warranted.

DOI: 10.1530/endoabs.81.P733

P734

Short and long-term efficacy of image-guided laser and radiofrequency ablation therapies: a prospective monocentric and single-operator study

Maria Francesca Birtolo[1], Simone Antonini[1], Tiziana Ierace[2], Giacomo Cristofolini[1], Giulia Maida[1], Gherardo Mazziotti[1,3], Andrea Lania[1,3] & Luigi Solbiati[2,3]
[1]IRCCS Humanitas Research Hospital, Endocrinology, Diabetology and Andrology Unit, Rozzano, Italy; [2]IRCCS Humanitas Research Hospital, Department of Radiology, Rozzano, Italy; [3]Humanitas University, Department of Biomedical Sciences, Pieve Emanuele, Italy

Background
In the last decades mini-invasive techniques have been proposed to reduce costs and complications of emithyroidectomy and thyroidectomy, both for benign nodular goiter and thyroid microcarcinoma, and image-guided laser and radiofrequency ablation are the most used.
Purpose
To investigate short and long-term efficacy of image-guided laser and radiofrequency ablation as therapy options for benign nodular goiter.
Methods
For this prospective monocentric, single-operator study 41 consecutive patients who underwent either ultrasound-guided laser (USG-L) (25 cases) or radio-frequency (USG-RF) (16 cases) ablation were enrolled. All patients had large, predominantly solid nodules with previous benign, THY2 cytological diagnosis. Subsequently, they underwent follow-up assessment with B-mode, color-Doppler and contrast-enhanced sonography at 1-2 months (first follow-up) and 1-, 2- and 3 years after ablation, with evaluation of the volume reduction ratio (VRR).
Results
The median volume (MV) of the nodules undergone USG-L was 15.7 ml (range 0.75–91.58 ml). At the first follow-up the MV was 10.08 ml, with a median VRR of 44.06% ($P < 0.05$: 34.17-53.94%), while at the 3-year follow-up the MV was 4.08 ml and the median VRR 88.09% ($P < 0.05$: 80.83-95.36%), with positive correlation between patients' age and 3-year VRR ($\theta = 0.43$, $P = 0.031$). In the cohort treated with USG-RF, the MV of nodules was 28.65 ml (range 9.81-109.89 ml) before ablation, and 13.89 ml at the first follow-up, with median VRR of 46.80% ($P < 0.05$; 38.44-55.17%). At 3-year follow-up the MV was 5.17 ml, and the median VRR 80.84% ($P < 0.05$: 73.60-88.08%). The difference in number of cases and pre-ablation size between the two groups do not allow to perform statistically significant comparisons. No immediate or late complications occurred, apart from a moderate local discomfort immediately at the end of the procedure, lasting 24-48 h, in almost all patients. No nodular regrowth was detected and no replacement therapy had to be administered to any patient during the 3-year follow-up.
Conclusion
In accordance with the literature, our study confirms that both USG-L and USG-RF can safely achieve significant and long-lasting size reduction of large benign thyroid nodules. Further studies are needed to evaluate if specific features, such as nodular volume and shape, can affect the procedure outcomes and to compare the effectiveness of the two modalities of treatment.

DOI: 10.1530/endoabs.81.P734

P735

Comparison of virtual 3D-modelling assisted teaching vs traditional lecture-based teaching for first-year medical students to understand the anatomy of various endocrine organs during the COVID-19 pandemic

Kashish Goyal[1], Kashish Malhotra[1], Rohin Kansal[1], Shubam Trehan[1], Mahima Marwah[1], Harry Goyal[2] & Sakshi Malhotra[3]
[1]Dayanand Medical College and Hospital, Ludhiana, India; [2]All India Institute of Medical Sciences, New Delhi, India; [3]Pandit BD Sharma PGIMS, Rohtak, India

Background
3D-modelling is a computer-generated simulation technique that allows the users to interact with a three-dimensional environment and provide an immersive experience to understand minuscule details which becomes especially important when understanding the anatomical relations of endocrinology organs. During the COVID-19 pandemic, medical lectures were shifted to online mode which diminished the opportunity of cadaveric-based teaching that is routinely done for first-year medical students. This study aims to assess the effectiveness of virtual 3D-modelling assisted teaching for first-year medical students and its comparability to online one-way teaching.
Methods
Various three-dimensional models of endocrine organs including thyroid, adrenal, pancreas, and pituitary were used and first-year medical students of Punjab, India were invited to our week-long online 3D-modelled training to teach anatomy of endocrinology organs. A pre-session and a post-session test was done using multiple-choice questions and short answer questions to assess the effectiveness of the session. Perspectives of medical students' were ascertained using a five-point Likert scale questionnaire along with open-ended questions. The data was analyzed using SPSS statistics v26.0.
Results
Amongst 38 respondents, a significantly higher improvement ($P < 0.001$) was seen in the post-session scores with the majority of students (84.2%) strongly preferring/preferring teaching via 3D models rather than online one-way teaching. Majority of the students had never learned previously (92.1%) via 3D-modelling and strongly agreed/agreed (73.7%) that 3D-modelling shall be included more routinely in teaching to teach complex anatomical relations.
Conclusion
The results indicate that 3D-modelling assisted teaching may be used as an adjunct/alternate to the current online one-way teaching. Besides using this technology to learn about the fundamental sciences like anatomy, it may also be used to get hands-on experience in performing endocrine surgeries in the future after further advancements.

DOI: 10.1530/endoabs.81.P735

P736

Thyroid hormones and platelet activation in COVID-19 patients

Elena Colonnello[1], Mariaignazia Curreli[1], Rossella Tozzi[2], Anna Criniti[1], Emiliano Lorusso[1], Lucio Gnessi[1], Orietta Gandini[2] & Carla Lubrano[1]
[1]Department of Experimental Medicine, Section of Medical Pathophysiology, Food Science and Endocrinology, Sapienza University of Rome, Rome, Italy; [2]Rome, Department of Molecular Medicine, Sapienza University of Rome, Rome, Italy

Background
The relationships between thyroid hormones (TH) and platelets (PLT) have not been fully established. Physiological concentrations of L-thyroxine (T4) activate human PLT resulting in ATP release and aggregation. On the other hand, subclinical hypothyroidism has been frequently associated with hypercoagulability, in particular mean platelet volume (MPV), a marker of platelet activation, has been found higher in patients with subclinical hypothyroidism. A possible prothrombotic action of TSH has also been hypothesized. COVID-19 is a pleiotropic virus known to exert its effects in many endocrine glands, including the thyroid. In fact, both direct and indirect mechanisms of Sars-CoV2 infection can render the thyroid dysfunctional. In COVID-19 patients hyperactivated platelets, with an increased MPV, and a low T3 syndrome have been described.
Aim
The aim of this study is to evaluate the relationships among TSH, FT3, FT4 and FT3/FT4 ratio and the MPV in 104 patients affected by COVID-19 on admission to the emergency room.
Methods
104 patients (46 males, 58 females) with real-time polymerase chain reaction testing-confirmed COVID-19 admitted to the Policlinico Umberto I hospital of Rome were included in the analysis. Patients without a history of thyroid disease who had a thyroid function test at admission, before starting any treatment, were enrolled.
Results
The mean age of the patients was 75.2 $\pm$ 11.6 years. The mean MPV was 9.03 $\pm$ 1.36 fL. The mean levels of TSH, FT3 and FT4 were, respectively 1.69 $\pm$ 1.14 μU/ml; 2.48 $\pm$ 0.64 pg/ml; 1.43 $\pm$ 0.53 ng/ml. FT3 showed a trend of negative correlation with MPV (r =-,1195P = 0.351), not statistically significant. FT4 was positively correlated with MPV (r = .2951, P = 0.019). Both TSH and FT3/FT4 ratio had a statistically significant inverse correlation with MPV (respectively, r =-,3848;P =,001 for TSH, r =-,2437, P =,05 for FT3/FT4). All the linear regression were adjusted for age, sex and BMI.
Discussion
In this cohort of COVID-19 patients the relationship between TSH and MPV showed an opposite behavior with respect to that reported in non-sick subjects, suggesting that different mechanisms of interaction of TH with PLT may exist in the setting of acute COVID-19 infection that may be protective against platelet activation.

DOI: 10.1530/endoabs.81.P736

P737

Correlation between painful subacute thyroiditis and COVID-19

Tamar Maghradze, Elena Shelestova & Ramaz Kurashvili
National Center for Diabetes Research, Endocrinology, Tbilisi, Georgia

Background
Subacute thyroiditis is an inflammatory condition of the thyroid with characteristic presentations and clinical course. Patients with the classic, painful (DeQuervain′s; Granulomatous) thyroiditis, (PFSAT) typically present with painful swelling of the thyroid. At times, the pain begins and may be confined to the one lobe, but usually spreads rapidly to involve the rest of the gland. Pain may radiate to the jaw or the ears. Malaise, fatigue, myalgia and arthralgia are common. A mild to moderate fever is expected, and at times a high fever of 104°F (40.0°C) may occur. It is suggested that the etiology of the disease is mainly viral, in addition, subacute thyroiditis often develops after infection of the upper respiratory tract, influenza, measles. COVID 19 is a potentially severe, primarily respiratory illness caused by a coronavirus and characterized by fever, coughing, and shortness of breath. In some people, the disease also damages major organs.
Aim
This study attempts to review the correlation of PFSAT and COVID 19
Method
Within months after the onset of the Covid pandemic, the number of patients referring to the National Center for Diabetes Research and diagnosed with of PFSAT has increased dramatically. Anamnesis showed that the vast majority had suffered Covid-19. Observations were made on 12 patients (8 females/4 males, mean age 22–51 years,) who had a history of Csovid-19 within past 2-3 months.
Discussion
The following studies were performed: test for Covid 19 antibodies and thyroid function tests (TSH and elevation of total T4 and T3 levels consistent with the thyrotoxic state). T3 (ng/dl) to T4 (mg/dl) ratio was less than 20. ESR (>50), CRP and thyroglobulin were all elevated; TPO-ab, Tg-ab and TSHR-ab were negative; RAIU/Scan-thyroid gland was "low or not" visible; ultrasound echogeneity was hypoechoic and vascularity was decreased. Classical treatment of subacute thyroiditis was started initially with non-steroidal anti-inflammatory agents, but the majority of patients (91%) required treatment with prednisone (20-40 mg daily). Beta blocking agents were prescribed in the majority of patients (76%). Most patients recovered in 6-8 weeks.
Conclsion
Data of our small research have shown that Covid 19 can cause sub-acute thyroiditis, though its course does not differ from the classical sub-acute thyroiditis. Data of new large-scale studiesare needed. We plan to continue our observations and increase the number of patients involved.

DOI: 10.1530/endoabs.81.P737

P738

Predictors of associated autoimmune diseases in patients with Hashimoto′s thyroiditis.

Rosaria Ruggeri[1,2], Francesca Trunfio[1,2], Giuseppe Giuffrida[1,3], Francesco Trimarchi[2], Alfredo Campenni[4] & Salvatore Cannavò[1,3]
[1]Endocrine Unit at University Hospital of Messina, Italy; [2]Department of Clinical and Experimental Medicine, University of Messina, Italy; [3]Department of Human Pathology DETEV, University of Messina, Italy; [4]Department of Biomedical and Dental Sciences and Morpho-Functional Images, University of Messina, Italy

Background
Increased rates of autoimmune diseases (ADs) have been reported in association with Hashimoto′s thyroiditis (HT); however, the risk factors for coexisting ADs in HT patients have been poorly investigated.
Objective
To evaluate the prevalence and factors associated with AD comorbidities in patients with HT.
Materials and Methods
We recruited 687 patients (626 F and 61 M, mean age at diagnosis 39 ± 14.06 yr, F: M = 10.2: 1) diagnosed with HT in 2019-2021. Clinical, biochemical and demographic data of subjects with and without concomitant ADs were statistically compared.
Results
Among the 687 patients with TH, comorbid ADs were found in 322 (47%; $n=292$ F, mean age 39.5 ± 14.8 yr), of whom 86 (12.5%) suffered from more than one associated ADs. Rheumatic diseases exhibited the highest frequency ($n=226$, 33%, including in order of frequency fibromyalgia, rheumatoid arthritis, Siogren syndrome, to mention a few,), followed by cutaneous ($n=71$, 10%, including vitiligo, psoriasis, alopecia, ….) and gastroenteric ($n=62$, 9% coeliac disease, atrophic gastritis, IBD, …) disorders. HT patients with and without comorbidities did not differ in gender and age at diagnosis ($P>0.005$). However, stratifying patients by age, the prevalence of comorbidities increased with increasing age. The two groups did not differ regarding exposure to the main environmental factors (including cigarette smoking, residence in urban areas or with high industrial density compared to small towns/countryside, eating habits, iodine nutrition and vitamin D). However, a family history of either thyroid or non-thyroid autoimmune diseases was significantly more frequent ($P<0.0001$) in patients with associated comorbidities than in those without. Logistic regression analyses revealed that female sex (odds ratio [OR] = 2.45, 95% confidence interval [CI] = 1.24-4.82; $P=0.011$), age (OR = 1.61, 95% CI = 1.18-4.27; $P=0.04$) and family history of ADs (OR = 5.18, IC 95% = 2.217–12.105; $P=0.001$) were predictors of associated ADs.
Conclsions
Female HT patients with increasing age and a family history of ADs have increased rates of AD comorbidities. These data suggest a preponderant role of genetic background, of which familiarity can be considered a surrogate marker, in determining the risk of developing autoimmune comorbidities in HT patients.

DOI: 10.1530/endoabs.81.P738

P739

The impact of insulin resistance on thyroid function in pregnancy

Andrzej Nowak[1], Grzegorz Sokolowski[2], Alicja Hubalewska-Dydejczyk[2] & Malgorzata Trofimiuk-Muldner[2]
[1]Medical University of Warsaw, Department of Gynecological Endocrinology, Warszawa, Poland; [2]Jagiellonian University Medical College, Chair and Department of Endocrinology, Kraków, Poland

Background
The influence of hyperinsulinemia and insulin resistance on thyroid function is debatable. Insulin, as an anabolic hormone, may also play a role in thyroid hypertrophy and nodular goitre development. Some recent reports focus on the possible interplay between thyroid function and glucose status in pregnancy, including gestational diabetes mellitus.
Aim
The study aimed to assess the relationship between insulin resistance indices and thyroid function in pregnancy.
Material and methods
The study included 1069 pregnant women (median age 29 years, IQR-6 years). Serum TSH, FT4, FT3, and aTPO were measured in each patient. Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) index was assessed based on fasting glucose and insulin concentrations. In each pregnant woman, a thyroid ultrasound was also performed.
Results
The study participants were stratified into three groups based on HOMA-IR. Group 1 included 324 women with HOMA-IR <1; group 2 – 570 women with HOMA-IR between 1 and <2.5, and group 3 – 175 women with HOMA-IR <2.5. Group 1 and 2 differed significantly in TSH (1.66 mIU/l vs. 1.84 mIU/l, $P=0.0205$), and FT3 concentrations (5.12 mIU/l vs. 4.76 mIU/l, $P=0.002$). No difference was found in FT4 concentrations (12.91 pmol/l vs. 12.65 pmol/l, $P=0.1153$). Group 1 and 3 differed significantly in TSH (1.66 mIU/l vs. 1.96 mIU/l, $P=0.0023$), FT4 (12.91 pmol/l vs. 11.47 pmol/l, $P=0.0000$), and FT3 concentrations (5.12 pmol/l vs. 4.66 pmol/l, $P=0.0000$). The significant difference between group 2 and 3 was only found for fT4 concentrations ($P=0.000$) (P values for difference in TSH and FT3 concentrations were 0.1958 and 0.2593 respectively). The groups did not differ in aTPO concentrations. aTPO-positivity was not related to HOMA-IR values (mean HOMA-IR in aTPO-positive and aTPO-negative women was 1.63 and 1.80 respectively, $P=0.32$). Fasting insulin >10 mIU/ml was found in 27.53% of pregnant women (286 out of 1039) with thyroid volume <25 mL, in contrast to 36.67% women (11 out of 30) with thyroid volume <25 mL.
Conclusions
our results indicate that insulin resistance may impact thyroid function in pregnancy independently of thyroid autoimmunity, with higher TSH and lower thyroid free hormone concentrations in pregnant women with higher HOMA-IR indices.

DOI: 10.1530/endoabs.81.P739

P740

Sub acute thyroiditis following COVID-19 vaccination – case report and International survey

William Bennet, Aisha Elamin & John Newell-Price
Sheffield Teaching Hospitals, Endocrine Department, Sheffield, United Kingdom

Case report
A 52-year-old woman developed painful anterior neck swelling seven days after receiving the first COVID-19 vaccine AstraZeneca (AZ). Investigations showed TSH 0.14 mIU/l, CRP 34 mg/l and TRAb 0.3 IU/l. A neck Doppler ultrasound scan on day 15 showed features of thyroiditis. On day 21, she was hyperthyroid with TSH <0.02 mIU/l and free T4 70.3 pmol/l. COVID-19 test was negative, and she was advised to start Carbimazole and propranolol but took only the beta-blocker. She felt well seven weeks after vaccination, and her TSH was spontaneously normalised. Later, she remained asymptomatic but was biochemically mildly hypothyroid with TSH 11 mIU/l and free T4 9 pmol/l, and by week 18, her TSH had spontaneously normalised again. The diagnosis was subacute thyroiditis. She had no prior history of thyroid disease; she was otherwise well and took no regular medication. She was concerned that the COVID-19 vaccination had triggered her subacute thyroiditis.
Survey results
In light of this case report, we conducted an email survey via the Society for Endocrinology UK, about subacute thyroiditis arising within 28 days of administration of a COVID-19 vaccine. Seventeen cases were reported to us: seven were from the UK, 14 were from physicians, and three were from patients. Eleven cases followed Pfizer-BioNTech mRNA vaccine, five followed AZ ChAdOx1 S recombinant vaccine, and one occurred after Moderna mRNA vaccine. Nine cases developed after the first dose of vaccine and eight after a second dose, with symptom onset a mean of 14.5 days after vaccination, ranging from self-limiting to a more severe illness requiring glucocorticoid therapy.
Discussion
There was a temporal association between COVID-19 vaccination and the onset of subacute thyroiditis. It appears likely that COVID-19 vaccines can trigger subacute thyroiditis due to an autoimmune/inflammatory (ASIA) syndrome. Case reports and small case series of subacute thyroiditis following COVID-19 vaccination have recently been described. Endocrinologists should be aware of potential vaccine sequalae when managing thyrotoxic patients, including the heightened risk that thyrotoxicosis following COVID-19 vaccination will result from a potentially self-limiting subacute thyroiditis. It has also been reported that Graves′ disease can develop shortly following COVID-19 vaccination. With over 7 billion COVID-19 vaccine doses administered to date, and a background subacute thyroiditis incidence of 4.9 per 100.000, there remains a caveat that the cases reported here may have arisen by chance.

DOI: 10.1530/endoabs.81.P740

P741

Efficacy of radioactive iodine treatment in Graves Disease using a calculated 131I dose and predictive factors of success in a Portuguese cohort

Sara Franco[1], Rita Teixeira Ferreira[2], Inês Cardoso Ferreira[2], Ana Quítalo[1], David Barbosa[1], Maria Manuel Costa[1], Henrique Vara Luiz[1], Luisa Raimundo[1] & Ana Isabel Santos[2]
[1]Hospital Garcia de Orta, Endocrinology, Portugal; [2]Hospital Garcia de Orta, Nuclear Medicine, Portugal

Aim
Dose corrected for thyroid gland size is one of the methods used to determine radioactive iodine (RAI) activity for patients with Graves disease (GD). This study was aimed to investigate the real-world success rate of this method and the predictors of success after first treatment.
Methods
This is a retrospective study of 80 patients with GD treated between 2014 and 2020 in a tertiary referral hospital in Almada, Portugal. The successful group was defined as maintained Eu- or hypothyroid for at least 12 months after RAI therapy. We used SPSS and Excel to analyze the data.
Results
A total of 80 patients (67 females; mean age: 48 years (SD 13)) were selected and enrolled. The mean estimated thyroid gland size was 59.6 (SD 25) g. Out of 80 patients, 63 (79%) were successfully (Group 1) and 17 (21%) were unsuccessfully (Group 2) treated with the first dose of RAI. In Group 1, one year after the first dose of radioactive iodine therapy, 65% of patients were hypothyroid and 14% were euthyroid. The mean overall dose was 11.6 mCi (SD 4). Univariate analysis showed a significant association between shorter disease duration ($P=0.031$), lower T3 levels ($P=0.017$) and treatment success, but no significant association between sex, age, TRAb titres, RAIU, thyroid gland size, and previous anti-thyroid treatment. Multivariate logistic regression analysis failed to demonstrate a single independent factor capable of predicting RAI effectiveness, although some variables showed a tendency toward a statistical significance: shorter disease duration since the diagnosis ($P=0.056$) smaller RAI dose ($P=0.05$), and non-smoking ($P=0.057$). Nevertheless, we must consider these are only preliminary results, based on a relatively small sample. Further studies with larger samples are needed to confirm the results.
Conclusion
First RAI therapy using dose corrected for thyroid gland size had a success rate of 79% in patients with Graves disease, which is in line with previous studies. We found that shorter disease duration and lower T3 levels were strongly associated with treatment efficacy in the univariate analysis.

DOI: 10.1530/endoabs.81.P741

P742

Curcumin attenuates the pro-inflammatory response induced by hyaluronan oligosaccharides in human thyroid fibroblasts and thyrocytes

Rosaria Ruggeri[1,2], Aurelio Minuti[2,3], Federica Aliquò[3], Alfredo Campennì[3], Angela Avenoso[3], Fiorenza Gianì[4], Roberta Masto[4], Salvatore Cannavò[2,5] & Angela D'Ascola[1]
[1]University of Messina, Dep Clinical and Experimental Medicine, Messina, Italy; [2]Endocrine Unit at University Hospital, Messina, Italy; [3]University of Messina, Department of Biomedical Sciences and Morphological and Functional Images, Messina, Italy; [4]University of Catania, Dept Clinical and Experimental Medicine, Catania, Italy; [5]University of Messina, Dep Human Pathology of Adulthood and Childhood "G. Barresi", Messina, Italy

Background
Lymphocytic infiltration and inflammation in autoimmune thyroid diseases (AITDs) results in accumulation of HA, contributing to the pathogenesis of both thyroidal and extra-thyroidal (ophthalmopathy, pretibial dermopathy and mixedema) manifestations of AITDs. HA fragments, originating from native HA during tissue inflammation and injury, in turn promote the expression of different mediators of oxidative stress and inflammation, by interacting with the Toll-like receptor 2 (TLR-2) and 4 (TLR-4) and CD44, via nuclear factor kappa-B (NF-kB). Curcumin (diferuloylmethane) is a phytochemical with anti-inflammatory properties. It has been reported to have suppressive effect on NF-kB signaling pathway in various cell types. This study was aimed at investigating the effects of curcumin treatment in cultured primary human thyrocytes and fibroblasts after exposure to 6-mer HA oligosaccharides (6-mer HA).
Methods
Cultured cells were treated with increasing concentrations of curcumin (5 and 10 μg/ml), with and without 6-mer HA (50 μg/ml). mRNA and proteins expression for TLR-2, TLR-4, inducible nitric oxide synthases (iNOS), interleukin-1beta (IL-1beta), IL-6, matrix metalloproteinase 9 (MMP-9), and thyroid-specific genes [thyroglobulin (Tg) and sodium iodide symporter (NIS)] were evaluated by real-time PCR and Western Blot, respectively. Protein quantification was assessed by densitometry analysis. NF-kB (p65) activation was determined in nuclear extracts by DNA binding activity assay. The pro-inflammatory cytokines IL-1 beta and IL-6 levels were measured by ELISA. Levels of NO were measured in culture medium by a fluorometric assay.
Results
In both cell lines 6-mer HA treatment induced the increase in mRNA and protein of TLR-2, TLR-4, CD44, as well as the activation of NF-kB, that in turn increased iNOS, IL-1beta, IL-6 and MMP-9 expression and NO levels. The addition of curcumin at increasing concentrations (5 and 10 μg/ml) decreased NF-κB activation and significantly reduced, iNOS, IL-1beta, IL-6, MMP-9, and NO levels in a dose-dependent manner ($P<0.01$ and $P<0.001$ respectively). Furthermore, in thyrocytes curcumin significantly restored the mRNA expression of Tg and NIS, decreased after exposure to 6-mer HA. Curcumin only slightly reduced CD44 expression ($P<0.05$) and did not change TLRs levels, suggesting that its anti-inflammatory effect mainlly depends on the inhibitory effect on NF-kB activation.
Conclusions
Curcumin attenuates the pro-inflammatory effects of HA oligosaccharides in both thyrocytes and fibroblasts. Since HA fragments might contribute to inflammation in both thyroidal and extra-thyroidal (i.e. dermal and orbital) tissues in the course of AITDs, curcumin could be beneficial in these disorders as a suitable adjunct to conventional pharmaceutical therapy.

DOI: 10.1530/endoabs.81.P742

P743

Concomitant Graves' disease with COVID-19 infection

Raluca Trifanescu[1,2], Iustin-Daniel Toma[2], Maria - Alexandra Mohora[2], Marioara Cristina Corneci[2], Ileana Nitu[2], Nicoleta Baloseanu[2], Suzana Vladoiu[3], Sorina Schipor[3], Anda Dumitrascu[4] & Catalina Poiana[1,2]
[1]"Carol Davila" University of Medicine and Pharmacy, Endocrinology, Bucharest, Romania; [2]"C.I. Parhon" National Institute of Endocrinology, Pituitary and Neuroendocrine Disorders, Bucharest, Romania; [3]"C.I. Parhon" National Institute of Endocrinology, Scientific Research Laboratory, Bucharest, Romania; [4]"C.I. Parhon" National Institute of Endocrinology, Radiology Department, Bucharest, Romania

Background
Subacute thyroiditis, autoimmune thyroiditis and an atypical form of thyroiditis due to primary injury of the thyroid gland by SARS Cov2 itself are complications of COVID-19. Angiotensin-converting enzyme 2 is also expressed in the thyroid gland. On the other hand, both untreated thyrotoxicosis and COVID-19 affects heart, generating cardiac complications.
Case report
A 36-year-old woman resident in an iodine sufficient area, heavy smoker, presented for palpitations, resting dyspnea, pedal edema, 40 kg weight loss in the past 2 months, tremor and asthenia. She denies cough, sore throat, rhinorrhea, smell or taste loss, myalgias or diarrhea. Physical examination reveals resting dyspnea, SaO2-95-96%, atrial fibrillation with arrhythmic HR = 200/min, severe heart failure with right pleural effusion and pedal edema, small goiter, tremor, low fever, agitation. Biochemical assessment revealed autoimmune thyrotoxicosis (TSH = 0.0007 mIU/l; FT4 = 40.06 pmol/l, total T3 = 309.88 ng/dl, increased TRAb (160 UI/l) and TPO Abs (209.7 IU/ml), anemia, leukopenia (3680/mm3) with lymphopenia. ESR, fibrinogen, C-reactive protein, procalcitonin were normal. Liver enzymes are elevated, hyperbilirubinemia was present (total bilirubin = 2.6 mg/dl, direct bilirubin = 1.9 mg/dl), alkaline phosphatase (180 U/l) and GGT were also increased. From cardiac point of view, D-Dimers were increased (403.925 ng/ml), CK MB was slightly increased (32 UI/l), troponin was normal, but NTproBNP was significantly increased (6112 pg/ml). RT PCR for SARS Cov2 was positive, IgM Abs against SARSCov 2 were slightly elevated, Ig G Abs were negative. A native CT scan confirmed right massive pleural effusion, without significant pulmonary involvement. Thyroid diffuse enlargement and markedly increased color flow Doppler signal with diffuse homogeneous distribution were present on thyroid ultrasound.
Treatment
During the hospitalization, antithyroid drugs were initiated, well tolerated, with significant decrease of FT4 within 3 days from 40.6 pmol/l to 23.64 pmol/l. High dose beta blockers, digoxin, double diuretic medication and anticoagulation with NOAC were administered for controlling heart rate and severe heart failure.
Follow-up
Despite having initially an increased score for thyroid storm (85), this patient with concomitant Graves disease and COVID-19 infection had a significant improvement within 4 weeks: weight gain, atrial fibrillation converted to sinus rhythm, FT4 was low-normal (8.43 pmol/l), NTproBNP significantly decrease (1007 pg/ml). No pleural effusion was described on her chest X-Ray; Her RT-PCR test was still positive for SARS-CoV-2 and Ig G Abs were increased (43IU/ml).
Conclusion
concomitant Graves disease and COVID-19 infection may be a cause of atrial fibrillation and severe heart failure during SARS Cov2 pandemic.

DOI: 10.1530/endoabs.81.P743

P744

Echocardiogram findings in patients with hyperthyroidism

Wiem Madhi[1], Khaled Ezzaouia[2], Meriem Yazidi[1], Fatma Chaker[1] & Mélika Chihaoui[1]
[1]Rabta Hospital of Tunis, Endocrinology - Diabetology, Tunisia; [2]Rabta Hospital of Tunis, Cardiology, Tunisia

Introduction
Thyroid hormones have an impact on the function and structure of the cardiac muscle.
Aim
Investigate the prevalence and risk factors of structural and functional cardiac complications in patients with hyperthyroidism.
Methods
We conducted a cross-sectional study on 30 patients with uncontrolled hyperthyroidism. Clinical, biological and therapeutic data were collected. A trans-thoracic echocardiography (TTE) and lung ultrasound has been performed to all patients.
Results
Eight patients presented with left heart failure (HF) signs/symptoms, two presented with right HF signs/symptoms. TTE was abnormal in 12 patients (40%) (Table); all of whom presented pulmonary hypertension (PH). Echocardigraphic signs of HF were present in eight patients: seven patients met the definition of HF with preserved ejection fraction and one had HF with reduced ejection fraction. Clinical signs/symptoms of HF, lower TSH levels, elevated LVFP and a higher E/E′ were associated to PH, $P = 0.013$, $P = 0.004$, $P = 0.003$, $P = 0.002$. HF and PH were associated to the presence of tachycardia in the 24-h Rhythmic Holter monitoring$P = 0.039$, $P = 0.011$, they were also associated to a higher number of premature atrial contraction$P = 0.007$, $P = 0.007$.
Conclusion
Hyperthyroidism can modify the cardiovascular hemodynamic leading to congestive heart failure and pulmonary hypertension.

Table 1 Echocardiographic parameters in patients with hyperthyroidism

Echocardiography parameter	
Pulmonary hypertension, *n (%)*	12 (40)
Elevated filling pressure, *n (%)*	8 (27)
Dilated left atria, *n (%)*	7 (23)
Dilated right atria, *n (%)*	4 (13)
Pulmonary B-lines, *n (%)*	3 (10)
Mitral insufficiency, *n (%)*	5 (17)
Mild	4
Moderate	1
Dysfunction the right ventricle, *n (%)*	2 (7)
Right ventricle hypertrophy, *n (%)*	2 (7)
Right ventricle dilation, *n (%)*	2 (7)
Reduced LV ejection fraction (<50%), *n (%)*	1 (3)
E/E′, m ± SD (extremes)	7.84 ± 5.7 (4 – 35)
LV end-diastolic diameter (mm), m ± SD (extremes)	45.3 ± 4.8 (39 – 62)
Cardiac output (l/min), m ± SD (extremes)	6.79 ± 2.29 (2.57 – 11.36)

LV left ventricle, m mean, SD standard deviation

DOI: 10.1530/endoabs.81.P744

P745

Myxedema coma of both primary and secondary origin, with non-classic presentation and elevated creatine kinase

Mihai Lucian Pavel[1], Anca Elena Sirbu[1,2], Miruna Maria Popa[1,2], Irina Bargaoanu[1] & Simona Fica[1,2]
[1]University Hospital of Emergency Elias, Endocrinology, Bucharest, Romania; [2]Carol Davila University of Medicine and Pharmacy, Bucharest, Romania

Introduction
Myxedema coma is the end stage of untreated or inadequately treated hypothyroidism. It has an estimated incidence of 0.22 per million per year. The clinical picture is often that of an elderly obese female, presenting in midwinter with increased lethargy, somnolence and confusion. The presentation is one of severe hypothyroidism, with or without coma.
Such cases are predominantly based on a primary thyroid disorder such as Hashimoto's thyroiditis. However, the underlying cause in approximately 5% of myxedema cases is hypothalamic or pituitary disease, where the patient usually lacks multiple anterior pituitary hormones, including thyroid-stimulating hormones (TSH).
Case study
A 69 years old male presents to the ER with dizziness, headache, postural instability, bradylalia and bradypsyhia symptoms that appeared 1 week prior. A stroke diagnosis was suspected and a cerebral CT scan was made showing a 22/21/38 mm pituitary adenoma with suprasellar extension. Laboratory tests showed high creatine kinase (4459 U/l) and LDH (591 U/l) and low natrium (122 mmol/l). He was then transferred to our clinic.
General examination revealed bradylalia, bradypsyhia, dry, coarse skin, hoarse voice, thin scalp and eyebrow hair with little to no body hair. Laboratory tests showed low values for FT4 (<0.3 ng/dl), TT3 (<40 ng/dl) low values for IGF1 (43.92 ng/ml), FSH (0.683 mIU/ml), LH (<0.1 mIU/ml), morning cortisol (1.06 microg/dl), ACTH

not available and high prolactin (1772 ng/ml) but high thyroglobulin antibodies (> 4000 IU/ml), and less than predicted high TSH (41.8 microUI/ml), TPO antibodies not available. The patient had prolonged QT interval on ECG and minimal pericardial effusion and minimal ventricular dyskinesia on cardiac ultrasonography. We started treatment with L-thyroxine, corticotherapy and cabergoline with clinical improvement.
Conclusion
A male patient diagnosed with myxedema coma of both primary (Hashimoto′s thyroiditis) and secondary origin (macroprolactinoma with associated panhypopituarism) with high creatin kinase and non-classical presentation is treated with hormonal replacement therapy and dopamine receptor agonist with favorable evolution.
Key words: myxedema coma, primary and secondary origin, prolactinoma

DOI: 10.1530/endoabs.81.P745

P746

Lenvatinib-induced hypocalcaemia due to transient hypoparathyroidism: a case-report

Matteo Trevisan[1], Carla Colombo[2], Noemi Giancola[1], Luca Persani[1,3], Laura Fugazzola[2,3] & Simone De Leo[3]
[1]Department of Medical Biotechnology and Translational Medicine, University of Milan, Milan, Italy; [2]Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy; [3]Division of Endocrine and Metabolic Diseases, Istituto Auxologico Italiano IRCCS, Milan, Italy

Radioiodine refractory differentiated thyroid cancer can be effectively treated with multi-tyrosine-kinase inhibitors (mTKI). Due to their pleiotropic mechanism of action, these drugs may cause different side effects. Hypocalcaemia has been reported in up to 35% of patients treated with mTKI, but little is known about its pathophysiology and clinical relevance. We report the case of a 78 years old woman treated for a multifocal papillary thyroid cancer, infiltrating perithyroidal tissues, striated muscles, oesophagus, blood and lymphatic vessels. Due to the tumour extension and infiltration to contiguous structures, the extent of surgery was limited to hemithyroidectomy and radioactive-iodine treatment could not be performed. The patient was therefore started on lenvatinib 10 mg per day. During the first months of treatment, the patient experienced grade I-II anorexia, fatigue, diarrhoea, nausea and hypertension, according to CTCAE, with no significant alteration at blood exams. Serum thyroglobulin (Tg) decreased from 6825 µg/l to a minimum of 49.6 µg/l, with negative anti-Tg antibodies. After four months of therapy, the patient accessed the E.R. for sudden dyspnoea, muscular cramps and spasms in the upper and lower limbs. Blood exams revealed a grade III hypocalcaemia (corrected serum calcium: 6.6 mg/dl), due to primary hypoparathyroidism (serum PTH: 12.6 pg/ml; serum phosphorus: 4.7 mg/dl). The patient was treated with intravenous calcium infusions and oral vitamin D supplementation. After discharge, the oral dose of carbonate calcium was of 6 g per day. Lenvatinib was discontinued for the duration of hospitalization and restarted three days after discharge, when serum calcium levels were effectively stabilized by oral supplementation (corrected serum calcium: 8.8 mg/dl). Calcium intake was titrated according to blood exams performed every 3-5 days. Two weeks after discharge, while taking calcium 3 g per day, the patient complained worsening of anorexia and stupor. Grade II hypercalcemia (serum calcium: 11.7 mg/dl) was demonstrated. She was treated with an intravenous infusion of physiological solution and calcium supplementation was interrupted. During the following follow up, the patient remained and still is eucalcemic without calcium supplementation. Though hypocalcaemia has already been described as potential side effect, this is the first report of a lenvatinib-induced primary hypoparathyroidism. This case is of particular interest since the patient was submitted to hemithyroidectomy and the hypoparathyroidism was thus definitely not-related to surgery. Further studies are needed to clarify pathogenesis and relevance of this life-threatening adverse event.

DOI: 10.1530/endoabs.81.P746

P747

Outcomes of incidental thyroid nodules identified during imaging for primary hyperparathyroidism: a retrospective observational clinical study

Quratulain Yousuf[1], Paul Wilson[2] & Laks Varadhan[1]
[1]University Hospitals of North Midlands, Diabetes and Endocrine, Stoke on Trent, United Kingdom; [2]University Hospitals of North Midlands, ENT, United Kingdom

Introduction
Pre-operative localization of parathyroid adenoma is generally done by two localization studies: ultrasonography (US) and parathyroid scintigraphy using 99 m-techentium sestamibi SPECT with CT (Tc-MIBI SPECT/CT), which also report on Incidental thyroid nodules. The aim of our retrospective study was to determine the incidence, characteristics and outcomes of these incidental thyroid findings during parathyroid imaging.
Method
A database of all patients who underwent parathyroid surgery over 2 years (2017-2019) was derived from ENT department. As per local clinical practice, all patients had pre-operative localization with US and Tc-MIBI SPECT/CT. Patients with tertiary hyperparathyroidism were excluded. Clinical details including thyroid function status, outcomes of imaging, referral for further investigations such as FNA and their outcomes were collected. Suspicious thyroid nodules were investigated as per standard clinical practice and local thyroid MDT decisions.
Results
A total of 111 patients were included for analysis. The anatomical outcomes were: Normal gland 52, ectopic thyroid gland 2, unclassified nodules including multinodular goitre 14, benign thyroid nodule not requiring further investigation (graded as U2 on US) 31 and nodules requiring further investigation (graded U3 or above on US). FNA of these 12 patients showed: thyroid carcinoma 7(4 papillary and 3 follicular variant), benign intra-thyroid parathyroid adenoma 3, hyperplastic nodule 1 and lymphocytic thyroiditis 1. All patients with thyroid carcinoma proceeded to total thyroidectomy as per MDT outcome.
On the Tc-MIBI SPECT/CT, 8 patients showed heterogeneous or reduced thyroid uptake, including 3 out of 7 thyroid carcinoma patients proceeding for biopsy and 1 lymphocytic thyroiditis all these patients were on thyroxine replacement. One patient with hyperplastic nodule showed persistent intense uptake while rest 102 patients showed homogenous and symmetrical uptake and were biochemically euthyroid.
Conclusion
A significant number of incidental thyroid findings are identified during parathyroid localization imaging. Our study showed 11% that required further investigations with incidental diagnosis of thyroid cancer.

DOI: 10.1530/endoabs.81.P747

P748

Oncocytic carcinoma of the thyroid: epidemiological, clinical and anatomopathological characteristics

Nezha Raki, Nassim Essabah Haraj, Siham El Aziz & Asma Chadli
UHC IBN Rochd, Endocrinology and Metabolic Disorders, Casablanca, Morocco

Introduction
Oncocytic thyroid carcinoma is rare. It is an aggressive tumor, with high nodal and distant metastatic potential.
Purpose of the study
to describe the epidemiological, clinical and anatomopathological particularities of oncocytic carcinomas of the thyroid.
Method
Descriptive retrospective study, including patients followed in thyroid carcinoma consultation at the Endocrinology Department of the CHU Ibn Rochd in Casablanca from 1986 to 2021.
Results
we collected 12 cases of oncocytic carcinomas of the thyroid. The average age of the patients was 53.4 years with a female predominance (11women/1 man). The circumstance of discovery was a multiheteronodular goiter in 67% of the cases, a thyroid nodule in 25% and a toxic multinodular goiter in 8% of the cases. In our series, the majority of patients (67%) had nodules on ultrasound classified EU-TIRADS4. Treatment consisted of total thyroidectomy in 100% of patients, associated with cervical lymph node dissection in 17% of patients. The average size on the anatomopathological examination of these carcinomas was 4.4 cm; the multifocal character was objectified in 25% of the cases with an extrathyroid microscopic extension in 41.6% of the cases. All our patients subsequently benefited from radioactive iodine therapy.
Conclusion
Oncocytic carcinomas of the thyroid constituting a particular anatomo-clinical entity. The diagnosis is based on a range of clinical (size of the nodule, age over

50 years) and histological (capsular rupture, multifocality, angioinvasion) arguments. The surgery must be wide in front of the resistance to radioactive iodine therapy.

DOI: 10.1530/endoabs.81.P748

P749

Sonographic and cytological characteristics of non invasive thyroid follicular neoplasm with papillary nuclear features vs papillary carcinomas

Nezha Raki, Nassim Essabah Haraj, Siham El Aziz & Asma Chadli
UHC IBN Rochd, Endocrinology and Metabolic Disorders, Casablanca, Morocco

Introduction
NIFTP (non invasive follicular neoplasm of the thyroid with papillary-like nuclear features, formerly noninvasive encapsulated follicular variant of papillary thyroid carcinoma) has been removed from the carcinoma category due to its indolent nature and its good prognosis. The purpose of our study was to identify preoperative ultrasound and cytological differences between NIFTP and papillary thyroid carcinoma (PTC).
Materials and methods
retrospective study including patients followed in the endocrinology department of the CHU Ibn Rochd in Casablanca, from 2017 to 2021, with histological diagnosis of PTC or NIFTP
Results
A total of 113 cases, including 27 NIFTPs, 86 papillary carcinomas, were observed. The 14 NIFTPs involved 24 women and 3 men, with an average age of 51.9 years, 2 patients had a history of familial thyroid carcinoma. The majority of patients ($n=24$) were euthyroid, 3 were hyperthyroid. Preoperative cytological data were available for 11 cases. Compared to papillary carcinomas, nodules corresponding to NIFTPs are more isoechogenic (59.3% vs 8.1%; $P\leq0.001$), have regular contours (85.2% vs 52.3%; $P\leq0.01$) and have a TIRADS score 3 (48.1% vs 8.1%; $P\leq0.001$), TIRADS 4 (40.7% vs 43%) or TIRADS 5 (7.4% vs 48.8%). Cytologically, NIFTPs are preferentially distributed in categories III (18% vs. 3.8%), IV (9% vs. 11.5%) and V (36.3% vs. 38.4%) of the Bethesda classification without significant difference compared to papillary carcinoma ($P\leq 0.9$).
Conclusion
NIFTPs appear mostly non-suspicious on preoperative ultrasound and of indeterminate significance on cytology. These differences compared to papillary carcinomas can make it possible to suspect the diagnosis preoperatively and to better adapt the surgical management.

DOI: 10.1530/endoabs.81.P749

P750

BRAFV600E, NRAS, TERT promoter mutations and correlations with clinicopathological features and distant metastasis in Turkish patients with papillary thyroid carcinoma

Ezgi Yılmaz[1], Yesim Gaye Guler Tezel[2], Olcay Kurtulan[2], Jale Karkaya[3], Murat Tuncel[4] & Alper Gurlek[5]
[1]Hacettepe University, Internal Medicine, Ankara, Turkey; [2]Hacettepe University, Pathology, Ankara, Turkey; [3]Hacettepe University, Biostatistics, Ankara, Turkey; [4]Hacettepe University, Nuclear Medicine, Ankara, Turkey; [5]Hacettepe University, Endocrinology and Metabolism, Ankara, Turkey

Background
Various molecular mechanisms play a role in the pathogenesis of papillary thyroid cancer(PTC). Understanding the underlying pathogenesis and genetic changes is needed to improve clinical outcomes in PTC. In this study, it was aimed to determine the frequency of, *BRAF* ^{V600E} *TERT promoter* and *NRAS* mutations in Turkish patients with papillary thyroid cancer, the relationship of mutations between clinicopathological features and distant metastasis and the prognostic and predictive value of mutations.
Methods
In the study, mutations were detected by PCR and direct sequencing method from the paraffin-embedded tumor tissues of 42 PTC patients over 18 years of age who were followed up in Hacettepe University Hospital and archived in the Department of Pathology between 2004-2021, with 16 distant metastasis and 26 without distant metastasis patients and their relationship with clinicopathological features was determined. Pearson′s, chi-square and Mann-Whitney U tests were used for statistical analysis. A value of $P<0.005$ was considered statistically significant.
Results
The overall frequency of *BRAF* ^{V600E} mutation was 64.3% (27/42), *BRAF* positivity was found in %22.2 (6/15) of patients with distant metastasis and 77.8% (21/25) in those without ($P=0.006$). There was no statistically significant difference between *BRAF*^{V600E} mutation and age at diagnosis, gender, tumor size, histological variant, extrathyroidal invasion, multifocality, lymphovascular invasion, capsule invasion, lymph node metastasis, recurrens and distant metastasis. The survival rate was found to be lower in *BRAF*^{V600E} positive cases (3.7%) than in negative cases (96.3%) ($P=0.03$). The frequency of *TERT promoter* mutation was found to be 9.5% (4/42). These mutations were all mutations at position C228T. No statistically significant difference between *TERT promoter* mutation and age at diagnosis, gender, tumor size, histological variant, extrathyroidal invasion, multifocality, lymphovascular invasion, capsule invasion, lymph node metastasis, recurrens and distant metastasis. There was no statistically significant difference for clinicopathological features and distant metastasis in cases with *BRAF* ^{V600E} and *TERT promoter* mutations and in cases with both.
Conclusions
In contrast with the observations in other populations, *BRAF* ^{V600E} was found to be higher in Turkish PTC cases without distant metastasis compared to ones with distant metastasis. The combination of *BRAF* ^{V600E} and TERT promoter mutations in PTC is not prognostic or predicitive for distant metastasis.

DOI: 10.1530/endoabs.81.P750

P751

Postoperative thyroglobulin (Tg) as a predictor of long-term recurrence in differentiated thyroid carcinoma (DTC)

Nerea Utrilla Uriarte[1], Miren Badiola Molinuevo[1], Virginia Urquijo Mateos[1], Pedro Gonzalez Fernandez[1], José Genollá Subirats[2] & Javier Santamaría Sandi[1]
[1]Cruces University Hospital, Endocrinology, Spain; [2]Cruces University Hospital, Nuclear Medicine, Spain

Introduction
To determine the risk of recurrence in DTC, different clinical factors have been used (presence of adenopathies, extrathyroid extension, histology...). The objective was to examine whether the value of early postoperative Tg concentration may also predict long-term recurrence of DTC.
Material and Methods
The study included 249 consecutive patients (78.3% women, mean age 50.72 $\pm$ 14.26 years) with DTC who were initially treated by total thyroidectomy $\pm$ lymphadenectomy between 2000 and 2016. Serum Tg level was measured 6-8 weeks after surgery using the Immulite 2000 Siemens method, with a sensitivity of 0.5 ng/ml. The patients have been followed-up for a minimum of 5 years (mean 7.27 $\pm$ 2.7 years) or until recurrence was detected. At the end of follow-up, their clinical situation was analyzed according to dynamic risk stratification. Patients with positive anti-Tg antibodies were excluded.
Results
The results obtained are shown in Table 1.

Tg:	$n=249$	Disease recurrence	Excellent response*
<0.5 ng/ml	175	6 (3.4%)	152 (86.9%)
0.5-2 ng/ml	41	6 (14.6%)	25 (61%)
>2 ng/ml	33	17 (51.5%)	12 (36.4%)

*Excellent response was defined as Tg<0.2 ng/ml and no structural disease in neck sonogram.The mean time to recurrence was 35.9 months in patients with Tg<2 ng/dl and 26.4 months in those with Tg<2 ng/ml ($P=$ ns).

Conclsions
Postoperative Tg helps to predict the risk of DTC recurrence, so it should be used routinely in the postoperative evaluation of these patients. 2. In our series, Tg >2 ng/ml predicts a high risk of long-term recurrence, so therapeutic measures and surveillance should be intensified.

DOI: 10.1530/endoabs.81.P751

P752

Thyroid Cystic Papillary Carcinomas - What's visible is not always seen

Catarina Roque, Ricardo Fonseca & Ana Sofia Osório
Hospital Professor Doutor Fernando Fonseca, Endocrinology, Lisbon, Portugal

The vast majority of thyroid cancers are solid. Predominantly cystic tumors occur in <3% cases. Guidelines report as US characteristics consistently associated with a higher risk of malignancy eccentric position of the solid component, acute angle interface and microcalcifications and as less robustly associated lobulated margins and increased vascularity of the solid portion. We reviewed the US characteristics of predominantly cystic papillary carcinomas confirmed on histological analysis diagnosed at our institution in 2021. The patients had no identifiable clinical risk factor for malignancy. Ultrasound evaluation: Patient 1, 49 y.o. female: predominantly cystic 15 mm nodule with a 5 mm eccentric mixed isoechoic and hypoechoic solid component with irregular margins and hyperechogenic foci, on the isthmus. Histology confirmed 12 mm PTC, pT1b(s)NxMx. Patient 2, 30 y.o. male: predominantly cystic nodule with 61 mm on the right lobe, with an isoechoic solid component with irregular margins and an area of thick wall with hyperechoic foci. Histology confirmed the rare macrofollicular encapsulated variant of the PTC with 50 mm, pT3 NxMx. Patient 3, 42 y.o. male: A solid hypoechoic nodule with lobulated margins and hyperechoic foci with 29 mm on the isthmus and a predominantly cystic nodule with a solid lobulated hypoechoic component with hyperechoic foci that showed increased sign on color-doppler on left lobe. Histology confirmed a 25 mm PTC, pT2(s)N1aR2. All patients had a single mixed supra-centimetric nodule. Margin irregularity or lobulation, microcalcifications and eccentric position of the solid component were present in all three. In all cases the nodules had more than one suspicious feature on US, but not all were described in the US report. US image review is crucial in thyroid nodule evaluation as it alerts the clinician and enables identification of at risk patients to be selected for timely and proper treatments.

DOI: 10.1530/endoabs.81.P752

P753

Somatostatin analog therapy in advanced sporadic medullary thyroid carcinoma: a case report

Roxana Dumitriu[1,2], Calin Cristiana[1,2], Iulia Florentina Burcea[1,2], Anda Dumitrascu[2] & Catalina Poiana[1,2]
[1]Carol Davila University of Medicine and Pharmacy, Bucharest, Romania, Endocrinology, Bucharest, Romania; [2]C. I. Parhon National Institute of Endocrinology, Pituitary and Neuroendocrine Disorders, Bucharest, Romania

Introduction
Medullary thyroid carcinoma (MTC) is an aggressive neuroendocrine tumor derived from C cells that is responsible for approximately 5% of the gland malignancies, most of them occuring sporadically. Lymph node metastasis may occur early in disease pathogenesis and is one of the most important negative prognostic factor. Surgery is the only curative therapy while other chemotherapeutic options are limited. Neuroendocrine differentiated C cells may express somatostatin receptors (SSTR) and somatostatin analogs have been used with variable therapeutic success in cases of advanced MTC.
Case description
We present the case of a 56-year-old male patient who underwent total thyroidectomy for MTC. He was admitted in our clinic for a anterior neck mass. Thyroid ultrasonographic examination demonstrated a hypoechogenic 25/23/37.5 mm sized nodule invading the left thyroid lobe with microcalcifications. Laboratory work-up revealed an elevated calcitonin, greater than 2000 pg/ml (normal range < 14.3), carcinoembryonic antigen (CEA) of 139.79 ng/ml (normal range: 0-2.5) and normal thyroid function. Our patient underwent a total thyroidectomy with total neck disection. Histological and immunohistochemical studies diagnosed the presence of multifocal MTC (pT2 mN1b) and papillary thyroid microcarcinoma (pT1aN0). The lymph nodes specimen showed metastases from the first lesion (six lymph nodes). The Ki-67 index was <1% and at the investigation for multiple endocrine neoplasia (MEN), RET protooncogene mutation was negative. Since CEA and calcitonin levels were high during follow-up period, neck ultrasonography was performed, with no evidence of pathologic lymphadenopathy, Cervical CT scan revealed a paratracheal left mass. Immunohistochemistry showed positive expression of somatostatin receptors (SSTR) 2 and 5 and the therapy with Octreotide LAR 30 mg every 4 weeks was initiated. An octreotide scan was performed with no detection of metastatic lesions. Six months later, under therapy with octreotide, calcitonins, CEA, serotonin, neuron specific enolase were within the normal range. The therapy was well tolerated with no side-effects recorded.
Conclusions
MTC can be a rare source of carcinoid syndrome. Some studies have shown that long-term octreotide and octreotide-LAR treatment offer a subjective and biological partial remission in one third and in one fourth of the MTC patients, respectively, but it does not improve the natural course of the tumor.
References
Vainas I *et al*, Somatostatin receptor expression *in vivo* and response to somatostatin analog therapy with or without other antineoplastic treatments in advanced medullary thyroid carcinoma. J Exp Clin Cancer Res. 2004 Dec;23(4) :549-59. PMID: 15743023.

DOI: 10.1530/endoabs.81.P753

P754

Graves' disease and neutropenia: Diagnostic trap

Hajar Khouchaf, Nassim Essabah Haraj, Siham El Aziz & Asma Chadli
Ibn Rochd University Hospital, Endocrinology, Diabetology, Nutrition and Metabolic Diseases, Casablanca, Morocco

Introduction
Hematologic abnormalities are frequently observed during hyperthyroidism and are related to complex multifactorial pathogenic mechanisms that are still poorly understood and may affect the three hematopoietic lineages in isolation or in combination. These abnormalities are exceptionally revealing and are usually subclinical. For the endocrinologist, they raise the problem of the risk of their aggravation under the hematotoxic effect of synthetic antithyroid drugs (ATS). However, certain abnormalities such as leuko-neutropenia are sometimes simply the expression of a physiological phenomenon of margination of white blood cells which falsely underestimates the count of this lineage and which must be detected.
Observation
Patient aged 45 years, followed for hyperthyroidism on Graves' disease initially put on CTC 60 mg with adjuvant treatment, presented a cardiac complication such as of an AFib put on Sintrom and b-blockers, with a past history of angina put, diabetic since 5 years on insulin, at the clinical examination, patient in good general condition, FC: 89 bpm, homogeneous grade 2 goiter without palpable nodul with bilateral inactive exophthalmos, the biological test objectified a TSHus: 0. 001 µIU/ml, T4L: 48.4 pg/ml (6-12), T3L: 13.2 pg/ml (2.6-5.7), TRAK: 19. 8 IU/l, associated with haematological disturbances such as neutropenia controlled on several occasions: WBC: 5320/mm3, PNN: 850/mm3, before the start of the antithyroid treatment, a control of the blood count formula after 2 h of physical activity, objectified a re-ascension to normal PNN levels at 2780/mm3. This was in fact a physiological margination of the PNN on the blood vessel wall, which was unmasked by the effort, a situation aggravated by the hyperthyroidism but which did not contraindicate the introduction of synthetic antithyroid.
Conclusion
Faced with the coexistence of hyperthyroidism and leukocyte lineage disturbances, a simple stress test should be rapidly performed to unmask false neutropenia, thus avoiding unnecessary transfer to the hospital.

DOI: 10.1530/endoabs.81.P754

P755

Graves' disease and unilateral gynecomastia - An uncommon initial presentation of a common disease

Daniela Dias, Ana Carolina Neves & Inês Sapinho
Hospital CUF Descobertas, Endocrinology, Lisbon, Portugal

Most cases of gynecomastia are idiopathic. Among the most frequently identified etiologies are: persistent pubertal gynecomastia, hypogonadism, anabolic steroids and other pharmaceutical drugs use. In the literature, ginecomastia is a well-recognized manifestation of thyrotoxicosis in male patients (in the range of 10% to 40%). However, it is extremely rare in clinical practice as the initial presentation of thyrotoxicosis. The two main factors that contribute to gynecomastia in thyrotoxicosis are: increase of SHBG production in the liver

(which leads to a reduction in free testosterone); and increased peripheral aromatization of androgens. We report a case of a 41-year-old white male who applied to our clinic with a 2 weeks history of right-sided breast enlargement. He did not report reduced libido. No past medical history or drug intake were reported. On examination he was normotensive and had normal-weight. Glandular tissue could be palpated on the right breast, underneath the nipple area. Galactorrhoea was not observed. Cervical palpation was normal. The testicles had a normal size and no palpable abnormalities were found. Laboratory data showed testosterone level of 1116 ng/dl (241-827), free testosterone level of 24 pg/ml (8.69-54.69), estradiol level of 51 pg/ml (<32), SHBG of 107 nmol/l (10-57), LH 7.46 mUI/ml (1.5-9.3), FSH 7.68 mUI/ml (1.4-18), TSH <0.01 mUI/l (0.35–5.5), free T4 (FT4) 2.16 ng/dl (0.8–1.76) and free T3 (FT3) 7.52 pg/ml (2.3-4.2). Anti-TSH receptor antibodies values were 2.47 UI/l (<1). Levels of prolactin, alpha-fetoprotein, human chorionic gonadotropin, dehydroepiandrosterone sulfate were normal. An ultrasound examination revealed a thyroid gland diffusely heterogeneous, without nodularity. The diagnosis of Graves' disease was made. He was treated with thiamazole 15 mg daily. After 1 month from the start of treatment, gynecomastia had resolved. The monthly follow-up laboratory findings showed normalization of FT3 and FT4. SHBG and total testosterone levels decreased significantly after 2 months and free testosterone increased. GD may present with atypical symptoms and the classic symptoms of thyrotoxicosis may not always be in the foreground. In case of gynecomastia, thyrotoxicosis should be kept in mind. An attentive diagnosis may identify a potentially treatable cause of gynecomastia.

DOI: 10.1530/endoabs.81.P755

P756

Radiofrequency and ethanol ablation for benign thyroid nodules: case series

Pedro Jimenez Torrecilla, Paloma González Lázaro, Antonio Moreno Tirado, Cristina Montalban Méndez, Maria Zhao Montero Benítez, Florentino del Val Zaballos & Ines Gomez García
Hospital General La Mancha Centro, Alcázar de San Juan, Spain

Introduction
Thyroid nodule is a frequent condition, being diagnosed in up to 70% of subjects who had undergone thyroid ultrasound. Around 90-95% of them became being benign and, if the do not cause compressive symptoms or esthetical problems, they do not need specific therapy, only clinical follow up. Traditionally, thyroidectomy has been the main therapeutic option in these cases. Radiofrequency and ethanol ablations are recently introduced non-invasive therapies that permit avoid surgery and its related possible complications. Many studies have already evaluated the effectiveness of radiofrequency and ethanol ablation therapies in the reduction of benign thyroid nodule volume. The aim of this study has been to evaluate its efficacy in reducing the volume of benign thyroid nodules.
Material and Methods
This study is a series of 5 patients with a benign thyroid nodule, verified by FNA. All of them were woman between x and x years old, three radiofrequency ablation and two ethanol ablations. We have determinate the hormonal levels and the measures of the nodule before the ablation, 1 month, 2 months and 6 months after of the intervention. We also asked patients about their initial symptoms and the degree of satisfaction with this procedure.
Results
5 subjects (100% woman) were analysed with an average age of 53.2 ± 12 years old with diagnosis of benign thyroid nodule. Initially, measures average was 20.4 x 24.20 x 33 cm (APxTxS), thyroid function was normal in all the patients, and 80% of the cases noticed compressive symptoms. One month after the intervention, nodules size decreased to 14x19x27.3 cm on average and compressive symptomatology disappeared total or partially. Even six months later nodules continued decreasing to 11.2 x 11.7 x 20.6 cm. Along this time, thyroid hormones were at range. All the patients are so satisfied and would repeat it if were necessary.
Conclusions
As we have found (and many other studies), radiofrequency and ethanol ablations permit reduce nodules size and solve compressive symptoms caused by them. Both techniques have few complications and patients feel so satisfied. Considering all this points, they are demonstrating being excellent alternatives to hemithyroidectomy in the treatment of benign thyroid nodules.

DOI: 10.1530/endoabs.81.P756

P757

Clinical presentation of patients with primary hypothyroidism in rural India

Aniket Inamdar
Samarpan Clinic, Internal Medicine, Omerga, India

Background
Hypothyroidism is a clinical state resulting from underproduction of the thyroid hormones thyroxine (T4) and triiodothyronine (T3). Most cases are due to primary hypothyroidism, a failure of the thyroid gland to produce thyroid hormones. Primary hypothyroidism is defined as thyroid-stimulating hormone (TSH) concentrations above the reference range and free thyroxine concentrations below the reference range. Patients with hypothyroidism usually present with puffy eyes, cold intolerance, coarse hair, constipation, poor memory, slow thinking, muscle cramps, weak muscles, depression, dry skin, and hypersomnolence.
Aim
To study the clinical presentation of patients with primary hypothyroidism in rural India.
Materials and methods
This cross-sectional study was conducted in a hospital in rural India from March 2021 to December 2021. TSH, free T3 and free T4 levels were measured using venous blood in all patients with presented with signs-symptoms of hypothyroidism. Patients having biochemically confirmed primary hypothyroidism (elevated TSH, low free T3 and low free T4) were selected for the study. Proper history was taken from patients and their relatives to obtain the demographic and clinical data including hypothyroidism symptoms.
Results
87 patients with primary hypothyroidism were included in the study among whom 75% were female, 45% aged between 25 to 50 years, 90% lived in rural and suburban areas. Hypertension was the most common (45%) co-morbid condition followed by obesity (29%), diabetes (23%), obstructive sleep apnoea (19%) and ischemic heart disease (15%). 31% patients presented with TSH more than 100. Puffiness of face was most common (65%) symptom followed by dry skin (52%), cold intolerance (42%), constipation (29%), muscle cramps (23%) and hypersomnolence (19%).
Conclusions
Primary hypothyroidism is one of most common and easily treatable endocrine disorder. Despite being potentially manageable, primary hypothyroidism is often undiagnosed and untreated. Timely diagnosis of primary hypothyroidism is utmost important. The medical and family history can be very helpful in identifying patients in whom thyroid dysfunction should be assessed. Gender, age, family or personal history of thyroid diseases, recent pregnancy, presence of autoimmune diseases, medications and radiation history should all be noted. Hypothyroidism is far more common in women, and the prevalence of mild hypothyroidism increases in the elderly. Patient education regarding signs and symptoms of hypothyroidism, regular screening with TSH, free T3 and free T4 are very crucial to diagnose this easily manageable endocrine disorder.

DOI: 10.1530/endoabs.81.P757

P758

Prevalence and factors associated with arrythmia in patients with hyperthyroidism

Wiem Madhi[1], Khaled Ezzaouia[2], Meriem Yazidi[1], Ibtissem Oueslati[1] & Mélika Chihaoui[1]
[1]Rabta Hospital of Tunis, Endocrinology - Diabetology, Tunisia; [2]Rabta Hospital of Tunis, Cardiology, Tunisia

Introduction
Thyroid hormones represent a biomarker of heart rhythm disorders and pathophysiological origins remain unknown. Some of these disorders like atrial fibrillation (AF) are major issues particularly in asymptomatic patients with in Hyperthyroidism and cause of thromboembolic complications.
Aim
Taking into account the uncertainty of prevalence of cardiac rhythm disorders, we aimed to investigate the prevalence of rhythmic cardiac complications and its risk factors in patients with hyperthyroidism.
Methods
We conducted a cross-sectional study on 30 patients with uncontrolled hyperthyroidism. Clinical, biological and therapeutic data were collected. A 24-h Rhythmic Holter monitoring has been performed to all patients.
Results
The patients were seven male and 23 female, mean age was 44.8 ± 14.4 years. Twenty three patients (77%) had palpitation. The mean heart rate was 95 ± 14

(66 – 124) and 16 patients (53%) had tachycardia. Electrocardiogram showed ventricular premature complexes in one patient (3%). Atrial fibrillation was present in two patients (7%). The 24-h Rhythmic Holter monitoring revealed tachycardia in 16 patients (53%), supra-ventricular premature contraction in 16 patients (53%). Thirteen patients (43%) had ventricular premature complexes. Atrial fibrillation was present in three patients (10%), it was permanent in one patient (3%) and paroxysmal in two (7%). The study of risk factors showed that age > 50 years, the presence of nodules (palpable and on ultrasound) and negativity of TSH receptor antibodies were associated to atrial fibrillation$P=0.041$, $P=0.020$, $P=0.029$, $P=0.008$. Toxic nodular goiter was associated to atrial fibrillation$P=0.004$.

Conclusion

Hyperthyroidism increases heart rate and may cause arrhythmia, mainly atrial fibrillation. This complication is more frequent in older patients with toxic nodular goiter.

DOI: 10.1530/endoabs.81.P758

P759

Autoimmune polyglandular syndrome Type 2 presenting with autoimmune thyroid disease, diabetes mellitus Type 1 and addison's disease

Angelie Rose Barjose, Jerome Barrera, Daniel Mark Yumol & Ivan Rommel Caluscusin
Zamboanga City Medical Center, Internal Medicine, Zamboanga, Philippines

A. Background/Significance

Autoimmune polyglandular syndrome Type II (APS-II) is a rare polyendocrinopathy with a prevalence of 1 to 2 in 100.000, instigated by immune-mediated destruction of several organs. Knowledge of APS-II is crucial, especially in the early detection of polyglandular disorder among patients with endocrine autoimmunity.

B. Case

This case is of a 40-year-old male who initially presented with Grave′s disease after showing signs and symptoms of hyperthyroidism, as supported by low thyrotropin (< 0.05 uIU/ml; nv: 0.35-4.94) and high free thyroxine levels (2.05 ng/dl, nv: 0.71-1.85). He was maintained on methimazole. Five months following diagnosis, he developed symptoms of Diabetes Mellitus Type 1 (T1DM) as confirmed by high capillary blood glucose, undetectable C-peptide, and positive anti-Glutamic acid decarboxylase. Insulin and rosuvastatin were added on his maintenance medications. Ten months later, he discontinued methimazole and became lost to follow-up. One month after discontinuation, he sought consult again after experiencing symptoms of fatigue, muscle cramps, cold intolerance, forgetfulness, abdominal pain, diarrhea, and episodes of hypoglycemia at home. On examination, he was noted to have hypotension of 80/60 mmHg and skin hyperpigmentation. His random blood sugar was 408 mg/dl. High thyrotropin (57.8777 uIU/ml, nv: 0.35-4.94), low free thyroxine (0.57 ng/dl, nv: 0.71-1.85), and positive antithyroid peroxidase antibody levels revealed Hashimoto′s thyroiditis. Low fasting 8 am serum cortisol (81 nmol/l, nv: 138-635) and low serum cortisol 30 mins (403.85 nmol/l) and 1 h (542.31 nmol/l, normal response: >550 nmol/l) after adrenocorticotropic hormone stimulation test in addition to the clinical manifestations, supported the diagnosis of Addison′s disease. With the combination of Addison′s disease, Autoimmune thyroid disease, and T1DM, a diagnosis of APS Type II was made. Management included insulin, prednisone, and levothyroxine. These resulted in significant improvement in the patient′s symptoms. He is now clinically well and compliant to regular follow-up.

C. Learning Points/Conclusion

It is crucial in APS-II management to identify and manage the associated autoimmune disorders to prevent significant morbidity and mortality. Therefore, in the presence of any autoimmune disorder, a high index of suspicion for APS-II is essential. There should be regular follow-up and observation of patients with autoimmune endocrine disorders to ensure early detection of APS-II. Patient health education must include identifying symptoms of the disorders for which they are at high risk.

DOI: 10.1530/endoabs.81.P759

P760

Added value for Graves' orbitopathy management in a tertiary center – report of four cases

Inês Manique[1], Sara Amaral[2], Luísa Cortez[3], Ana Palha[2], Ana Duarte[4] & José Silva-Nunes[2]
[1]Centro Hospitalar Universitário Lisboa Central, Endocrinologia, Diabetes e Metabolismo, Lisboa, Portugal; [1] Centro Hospitalar Universitário Lisboa Central, Endocrinologia, Diabetes e Metabolismo, Lisboa, Portugal; [3]Centro Hospitalar Universitário Lisboa Central, Endocrinologia, Diabetes e

Table 1

		Case 1	Case 2	Case 3	Case 4
Age (years old)		39	42	44	47
Gender:		Female	Male	Female	Male
Nationality:		Guinea-Bissau	Guinea-Bissau	Portugal	Portugal
DG diagnosis		2012	2016	2016	2018
Hyperthyroidism (Clinical/Biochemical)		Yes	Yes	Yes	Yes
Initial TRAb (positive >1.5)		2.8 U/l	40 U/l	21.6 U/l	6.5 U/l
GO:	**Activity**	Inactive	Active	Active	Active
	Severity	Moderate/Severe	Moderate/Severe	Moderate/severe	Severe/sight-threatening (dysthyroid optic neuropathy)
GD Medical therapy	**Treatment**	Thiamazole (Evacuated to Portugal in 2017 without therapy)	Thiamazole (Evacuated to Portugal in 2016 under thiamazole)	Thiamazole	Propylthiouracil
	Maximum dose	20 mg/day	45 mg/day	60 mg/day	300 mg/day
	Duration	2.5 years	3 years	1 year and 4 months	3.5 years
Total thyroidectomy (histology)		Yes (9 mm papillary microcarcinoma)	Yes (8 mm medullary carcinoma)*	Yes (Follicular hyperplasia)	Waiting
OG Medical therapy	**Treatment**	- Local treatment (artificial tears)	- Local treatment (artificial tears) Iv MPDN (4.5 g)	- Local treatment (artificial tears) Iv MPDN (4.5 g)	- Local treatment (artificial tears, botulinum toxin injection) - Iv MPDN (8 g) Radiotherapy Tocilizumab
OG Surgical treatment (inactive phase)	**Treatment**	(2019) - Bilateral orbital decompression - Correction of eyelid retraction	(2020) - Bilateral orbital decompression - Correction of upper eyelids retraction	(2018) - Bilateral orbital decompression - Correction of upper eyelids retraction	(2020) - Bilateral orbital decompression

ivMPDN – intravenous methylprednisolone
* negative for RET mutations, maintained cure criteria

Metabolismo, Portugal; [4]Centro Hospitalar Universitário Lisboa Central, Oftalmologia, Lisboa, Portugal

Introduction
Graves orbitopathy is the major extrathyroidal manifestation of Graves Disease (GD). The approach depends on its clinical activity and severity. Treatment and referral to specialized centers, with Endocrinology and Ophthalmology, has a strong impact on the prognosis of Graves' Disease (GD) and GO.
Cases report
We report four cases of DG with OG. Their characteristics and clinical evolution are shown in Table 1.
Conclusion
In these four cases a definitive therapy (surgery) was needed to treat GD, suggesting the presence of a more severe disease. GO can progress into severe forms and this evolution is often unpredictable. These 4 clinical reports are illustrative of the importance of a multidisciplinary approach (Endocrinology and Ophthalmology) in specialized centers for patients with GD and GO.

DOI: 10.1530/endoabs.81.P760

P761

Role of corticosteroids in the treatment of refractory hypothyroidism : a case report

Yousra Settai, Nassim Essabah Haraj, Siham El Aziz & Asma CHADLI
UHC IBN ROCHD, Endocrinology and Metabolic Disorders, Casablanca, Morocco

Introduction
Refractory hypothyroidism is known as the persistence of clinical and biological signs of hypothyroidism after 6 weeks of treatment or therapeutic adjustment, despite a dose exceeding 1.9µg/Kg/d of Levothyroxine. Several etiologies may be incriminated.
Observation
A 36-year-old patient, followed for Gougerot-sjogren syndrome, having benefited from a thyroidectomy in 2015 in a context of biological hyperthyroidism, on Levothyroxine (LT4) 200µg/d and Liothyronine sodium (LT3) 25µg/d with persistence of refractory hypothyroidism. The clinical examination revealed a slightly slowed down patient, presenting a mucocutaneous infiltration, a hoarse voice, a bilateral galactorrhea evolving since 1 year, and a chronic constipation. All this in a context of generalized asthenia. At the workup, TSHus was 500µUI/l, free T4 $<$0.4 ng/dl (0.7-1.5), hypertriglyceridemia at 12.9g/l put on fenofibrate 160 mg/d. Brain MRI showed a pituitary bulge with no other detectable abnormality. After elimination of poor compliance and possible drug interactions, the diagnosis of refractory hypothyroidism was retained. Parasitological examinations of the stools showed Giardiasis and the patient was put on metronidazole. The Helicobacter Pylori serology came back positive with a pangastritis aspect at the oeso-gastro-duodenal fibroscopy, put under eradication treatment. As hypothyroidism persisted, the patient was put on Dexamethasone 1 mg/d for one week, then tapered to 0.5 mg/d, reduction of levothyroxine dose to 175µg/d and maintenance of Liothyronine sodium at 25µg/d, with clinical improvement of hypothyroidism signs. The thyroid check-up showed a TSHus of 4.63µUI/ml, and a free T4 of 19.86 pmol/l (10.6-19.4)
Conclusion
High-dose glucocorticoids may be considered in some cases of hypothyroidism, especially in patients requiring high doses of thyroid hormones when even the LT4 + LT3 combination is insufficient to achieve euthyroidism.

DOI: 10.1530/endoabs.81.P761

Late Breaking

P245

Recalculating renin and aldosterone to improve specificity in the diagnosis of primary aldosteronism

Luc Doyle[1], Julie Okiro[1], Aysha Sarwani[1], Michael Troy[2], Yousef Ansari[1], Darragh O'Donoghue[1], David Lappin[3], John Mcevoy[4], Paula O'Shea[2,5], John Ferguson[6] & Michael Conall Dennedy[7]
[1]University Hospital Galway, Centre for Diabetes, Endocrinology and Metabolism, Galway, Ireland; [2]School of Medicine, National University of Ireland Galway (NUIG); [3]University Hospital Galway, Department of Nephrology, Galway, Ireland; [4]National University of Ireland Galway (NUIG), School of Medicine, Galway, Ireland; [5]University Hospital Galway, Department of Clinical Biochemistry, Saolta University Health Care Group (SUHCG), Galway, Ireland; [6]National University of Ireland Galway (NUIG), Biostatistics Unit, HRB Clinical Research Facility, NUI Galway, Galway, Ireland; [7]National University of Ireland Galway (NUIG), Discipline of Pharmacology and Therapeutics, Lambe Institute for Translational Research, NUI Galway, Galway, Ireland

Rationale
The Aldosterone:Renin ratio (ARR) is commonly used for patients fulfilling screening criteria for primary hyperaldosteronism (PA), followed by confirmatory testing. Reference intervals for interpretation of the ARR vary in accordance with local population and assay 1. While ARR provides high sensitivity for PA, this is compromised by low specificity, further compounded by medication interference. However, additional variables may improve the specificity of ARR as a diagnostic test, potentially mitigating the need for confirmatory testing in all patients. In the current study, we investigated the relationship between aldosterone and renin as single diagnostic measure for PA.
Methodology
A population-based study of individuals attending a specialist hypertension clinic was performed. PA was screened using the ARR, and confirmed using the saline infusion test. 82 patients with matched ARR and Saline Infusion Tests were investigated. Logistic Regression was used to estimate the relationships between renin, aldosterone, ARR, clinical variables and the probability of a diagnosis of PA. Predictive capacity of each model was measured using Area Under the Curve using "*leave one out*" cross validation to avoid overfitting.
Results
The AUC for the model using ARR on its own was estimated to be 0.68. The model, excluding ARR, but including renin, aldosterone and their interaction on the log-scale: log(Renin) + log(Aldosterone) + log(Renin)*log(Aldosterone), improved the AUC to 0.73. Using this log-structure, as opposed to including aldosterone and renin as linear effects in a logistic model, makes sense since the model involving ARR alone is nested within the log-structure model, which would not be true under the linear model. Covariates including eGFR, serum potassium and the presence of an adrenal nodule were then individually tested for statistical significance, conditional on the choice of this log-scale interactive model. The model Log(Renin) + log(Aldosterone) + log(Renin)*log(Aldosterone) + Adrenal_Nodule provided the highest performance with an AUC of 0.782. For the ARR and the log-model, at a sensitivity of 80%, specificity was 37.5% and 64% respectively, and for a sensitivity of 98%, specificity was 12.5% and 24% respectively.
Conclusion
This log model incorporating the adrenal nodule as a variable improved the AUC from 0.68 (model with ARR alone) to 0.782. This study highlights the importance of statistically re-visiting well-established calculations to better inform clinical practice. Ongoing validation of our findings is proceeding in other clinical samples.

DOI: 10.1530/endoabs.81.P245

P246

Pituitary -adrenal axis insufficiency among hemodialysis patients

Anat Bel-Ange[1], Daniel Fux[1], Dana Zelnik Yovel[1], Ronit Koren[1], Ilia Beberashvili[1], Carlos Benbassat[1] & Shlomit Koren[1,2]
[1]Shamir Medical Center (Assaf Harofeh), Be'er Ya'akov, Israel; [2]Tel Aviv University, Tel Aviv-Yafo, Israel

Background
The diagnosis of hypocortisolism is challenging in hemodialysis (HD) patients due to shared clinical features between renal failure and cortisol deficiency. We hypothesize that in a significant percentage of HD patients we miss cortisol deficiency.
Methods
A prospective cohort of 56 end stage kidney disease patients on maintenance HD treatment (mean age 65.3$\pm$13.1, females 80 %) was studied. Low dose (1 mg) adrenocorticotropic hormone (ACTH) test was performed on all patients and blood tests for cortisol, ACTH, insulin like growth factor 1 (IGF-1), triiodothyronine (TSH), free thyroxine (FT4), renin and aldosterone, were obtained before hemodialysis session. Adrenal insufficiency was defined as a peak serum cortisol level of $<$500 nmol/l at 30 or 60 min after stimulation.
Results
14 patients (25%) out of the study population had an abnormal low dose ACTH test. Mean systolic blood pressure in the group with abnormal ACTH test was 135.2$\pm$22.0 mm Hg with no difference in blood pressure in multivariable models between the groups of HD patients with abnormal and normal ACTH test. Neither differences were observed in electrolyte levels, nor in renin/aldosterone levels between these groups. Baseline ACTH level predicted an abnormal ACTH test in the study population in both, univariate and multivariate analyses. For each pg/ml increase in baseline ACTH concentration the odds for abnormal ACTH test was

1.15 (95% CI: 1.03 to 1.29). In addition, IGF-SDS (standard deviation score) higher than -0.04 significantly decreased odds for hypocortisolism (OR 0.14, 95% CI: 0.02 to 0.81) in multivariable logistic regression models.
Conclusions
We offer routine testing of hypophyseal-adrenal axis function to detect adrenal insufficiency in HD patients even in the absence of markers characteristic of hypocortisolism.

DOI: 10.1530/endoabs.81.P246

P247

Long-term mortality and excess mortality after hip fracture in the main urban area of Romania

Ramona Dobre, Ioana Ruzandra Poiana, Dan Alexandru Niculescu, Catalin Cirstoiu, Gheorghe Popescu & Catalina Poiana
Carol Davila University of Medicine and Pharmacy, Bucureşti, Romania

Background
Excess mortality after hip fracture remains a problem of public health concern. Until present, for Romania no data is available regarding long term mortality rate and excess mortality after hip fracture. We aimed to evaluate the mortality rate 3 years after hip fracture and also standardized mortality rates of osteoporotic hip fracture in the capital city of Romania and suburban area.
Methods
we collected data from over 98 % of fractures admitted during 12 months (09/01/2017 - 08/31/2018) in Orthopedic Surgery Departments in the area of interest. Patients were selected using the hip fracture codes (S72.0, 1, 2, 3, 7, 8, 9), age >40 years old and low-trauma mechanism (fall from a standing height or less). We used the 2018 estimations for stable population in the area selected. We calculated the mortality rate (MR) 3 years after the event and standardized mortality rates (SMR) of hip fracture.
Results
we included a total of 1977 patients with fragility hip fracture (86.5% in the capital city and 13.5 % in the suburban area). MR after 3 years was 46.42% in all patients with a mean age of 81 years old, 69% women. Almost a quarter of patients were not surgically treated. Advanced age, male sex, extracapsular fracture and especially conservative management were associated with increased mortality. SMR after 1st 2nd and 3rd year and cumulative for the whole 3-year period in all patients were 13.69, 5.45, 5.94 and 26.06 respectively. As expected, SMR decreased with advancing age, but remained higher even in patients >85 years old (2.79 for 1st year, 2.34 for 3-year period). Notable differences were observed in SMR between sexes, 29.18 for women and 19.6 for men, 3 years after the fracture.
Conclusion
this is the first study to describe the long-term mortality rate and excess mortality after osteoporotic hip fracture in Romania. Hip fracture has the highest impact on short-time mortality, the risk in the 2nd and 3rd year being significantly smaller compared to 1st year. Even after 3 years, excess mortality for hip fracture patients can be still observed.

DOI: 10.1530/endoabs.81.P247

P248

The differences between normocalcemic and hypercalcemic primary hyperparathyroidism: a tertiary center's experience

Nikolaos Kalogeris, Nektaria Papanikola, Eleni Herolidi, Eleni Palioura, Vasiliki Papanikolaou, Vasiliki Loi & Andromahi Vryonidou
General Hospital Korgialenio-Benakio, Hellenic Red Cross, Department of Endocrinology & Metabolism – Diabetes Center, Athens, Greece

Introduction
Normocalcemic Primary Hyperparathyroidism is today considered a variant of Primary Hyperparathyroidism. It is characterized by persistently normal calcium levels and increased levels of parathyroid hormone, after the exclusion of other causes of secondary hyperparathyroidism. We aimed to compare clinical, biochemical and imaging data from patients with normocalcemic and hypercalcemic primary hyperparathyroidism.
Methods
This is a retrospective study from the archives of our Department that included 161 patients (38 men and 123 women), who were monitored from 2010 to 2021, 68 with Normocalcemic Primary Hyperparathyroidism (NPHPT) and 93 with Hypercalcemic Primary Hyperparathyroidism (HPHT). The biochemical tests included calcium, total and adjusted for albumin, phosphorus, magnesium, parathyroid hormone and 25OHD3 levels and 24-h urinary calcium. The imaging tests included thyroid ultrasound, scintigraphy with Tc99 m Sestamibi, kidney ultrasound and bone density measurement. We also, accessed the eligibility for surgical treatment of the disease, according to the criteria of the Fourth International Workshop for the Management of Asymptomatic Primary Hyperparathyroidism.
Results
No differences between the two groups were found regarding, age of diagnosis, body mass index (BMI), serum magnesium and 25OHD3 levels and 24-h urine calcium concentration ($P>0.05$). Patients with HPHPT had significantly higher levels of corrected calcium (11.3 ± 0.57 vs 9.8 ± 0.44 mg/dl, $P<0.001$) and PTH (219.2 ± 209.8 vs 111.8 ± 35.5 pg/ml, $P<0.001$) and lower phosphorus levels (2.7 ± 0.54 vs 2.9 ± 0.43 mg/dl, $P<0.01$) compared to patients with NPHPT. No differences were found in the prevalence of osteopenia/osteoporosis, fragility fractures and the need to receive anti-osteoporotic treatment ($P>0.05$). Patients with HPHPT had significantly higher prevalence of nephrolithiasis clinically (history of renal colic: 40.3% vs 25.8%, $P<0.05$) and discovered by imaging (renal ultrasound: 54.3% vs 34.7%, $P<0.03$). Patients with HPHPT more often met the criteria for surgical treatment (54.3% vs 34.7%, $P<0.001$).
Conclusions
Patients with NPHPT often have disease complications, especially osteoporosis, fragility fractures and nephrolithiasis both clinically and through imaging. Until more data on the pathophysiology and natural course of NPHPT are provided, patients with this form of primary hyperparathyroidism should be managed as patients with HPHPT.

DOI: 10.1530/endoabs.81.P248

P249

Glycogen hepatopathy - a case series

Bhavna Sharma, Rohit Baslas, Amar Sharif & Elaine Hui
Northwick Park Hospital, United Kingdom

Glycogen Hepatopathy (GH) was initially described in 1930 by Pierre Mauriac. 90 years later, GH remains underrecognized in adults. The clinical or radiological characterization of GH is difficult, further compounded by lack of widespread literature. We present two cases of GH characterized by recurrent lactatemia and transient liver function and radiological abnormalities.

- 19 years old male with Type 1 diabetes admitted with nausea and vomiting. pH 6.9, glucose 33 mmols/l and lactate 7.7 mmol/l (normal 0.5-2 mmol/l). He was started on intravenous (IV) fixed rate insulin. Lactate initially improved however was noted to be rising 8 h into being started on insulin peaking at 9.2 mmol/l. On admission, bilirubin 10 umol/l (normal range 0-21 umol/l), ALP 80 IU/l (normal range 0-390 IU/l) ALT 162 IU/l (normal 10-50 IU/l) Albumin 44 gm/l (normal 35-50 gm/l). ALT worsened during admission peaking at 790 IU/l corresponding to lactate. Liver screen including hepatitis, HIV, EBV, CMV, alpha 1 antitrypsin, caeruloplasmin, anti-smooth muscle antibodies, anti-liver kidney microsomal antibodies and ANA were negative. Liver ultrasound revealed smooth gross hepatomegaly with increased liver reflectivity. Liver function started resolving at Day 5 and ALT came down to 442 IU/l on Day 8. Repeat liver function 2 months later was normal. MRI liver three months later revealed normal sized liver with no abnormal enhancement with a smooth surface and no fatty infiltration or cirrhosis.
- 21 years old female, first presentation of Type 1 diabetes with diabetic ketoacidosis (DKA). pH 7.2 on admission, glucose 20 mmol/l and lactate 7 mmol/l. Lactate initially improved with fluids however at 24 h peaked at 8.6 mmol/l. Liver ultrasound showed echogenic enlarged liver. Liver function on admission was normal (ALT 31 IU/l) but worsened after starting IV insulin to 578 IU/l and peaked to 752 IU/l at Day 4. Liver function normalized after 3 months. GH was first reported when short acting insulin was introduced. Supraphysiologic rapid acting insulin dosages during DKA management may be a potential cause to drive glycogen storage in rapid hypo- and hyper-glycaemia cycle. A dual peak of lactate may signify a change from Type 1 (impaired perfusion) to Type 2 lactatemia (impaired gluconeogenesis). Further work is needed to characterize patients at risk of GH in re-attendances and potential plans to give lower dose of rapid acting and higher dose of long-acting insulin in acute phase may be explored.

DOI: 10.1530/endoabs.81.P249

P250

Metabolic parameters in type 2 diabetic patients with positive Candida cultures

Danijela Radojkovic[1], Saša Radenković[1], Vojislav Ćirić[1], Milan Radojkovic[2], Jana Pesic Stankovic[3], Sanja Curkovic[1] & Sonja Kostic[1]

[1]University Clinical Center Nis, Clinic of Endocrinology, Diabetes and Metabolic Disorders, Nis, Serbia; [2]University Clinical Center Nis, Surgical Clinic, Nis, Serbia; [3]Institute of Public Health, Nis, Serbia

Introduction
The gut microbiota plays an important role in host metabolism, immunity, digestibility and even a behavior. *Candida spec*. is common resident of the gastrointestinal tract and integral part of the microbiota. Number of 10^1 to 10^3 fungal cells per g stool are considered as normal range. However, when mucosal surface is disrupted or host immunity is compromised, life-threatening invasive infection can ensue.
Objective
The aim of the study was to evaluate if positive *Candida* cultures in the stool, influence metabolic parameters in type 2DM patients.
Patients and methods
The study included 46 patients with type 2 DM (20 women and 26 men), 30 -77 years old, with oral antidiabetic treatment (metformin and glimepiride or gliclazide). Beside medical history and clinical examination, all patients were tested for coproculture, fasting glycaemia (FPG), HbA1C, total cholesterol (Hol) triglycerides (Tg), high density lipoproteins (HDL) and low density lipoproteins (LDL).
Results
All patients were divided into following groups: study group (S = 18 patients with positive *Candida sp*. cultures in stool; 39.13%) and control group (C = remaining 28 patients; 60.87%). Comparing the average age in S and C group (68.21 ± 10.4 vs. 66.97 ± 9.7 years), no statistical significance was obtained. Study group patients had a higher BMI compared to the control group (31.41 ± 5.29 vs. 25.18 ± 3.58; $P < 0.001$). Higher values of Tg (2.03 ± 1.13 vs 1.80 ± 0.58), Hol (5.23 ± 1.23 vs 4.73 ± 0.92), LDL (3.27 ± 0.75 vs 2.86 ± 0.83) and HDL (1.63 ± 0.25 vs 1.08 ± 0.44) were verified in study group, compared to the control group, but without statistical significance. HbA1C values were significantly higher in study group patients (9.8 % ± 1.74 vs 6.9% ± 1.89; $P < 0.05$) as well as FPG (10.87 ± 1.35 vs 7.47 ± 1.03; $P < 0.01$).
Conclsion
Type 2DM patients with positive *Candida sp*. have higher FPG, HbA1C and BMI. Uncontroled glycoregulation is one of the host condition which favors candida colonization and subsequent infection. This may be related to the decrease in commensal bacteria-probably the result of yeast-bacterial competition. On the other hand, we have to keep in mind, that a significantly increased number of *Candida* colonies can affect the rate of digestion and absorption of carbohydrates and consequently increase the level of glycaemia in patients with diabetes.

DOI: 10.1530/endoabs.81.P250

P251

Polyglandular autoimmune syndrome in the elderly: a case report

Sindhuja Suresh[1], Felicity Kaplan[1] & Alastair Cruickshank[2]
[1]East & North Hertfordshire NHS Trust, United Kingdom; [2]Regal Chambers Surgery, United Kingdom

Polyglandular autoimmune syndrome (PAS) is characterised by the coexistence of two or more autoimmune mediated disorders. While the pathophysiology remains poorly understood, environmental triggers and genetic susceptibility are thought to contribute to the dysregulated immune response. PAS has been classified into three main subgroups: Type 1 is seen in the paediatric population while types 2 and 3 are found in adults with autoimmune thyroid disease and insulin-requiring diabetes, are differentiated by the presence or absence of Addison′s disease, and most commonly present in the third decade. There are very few studies looking at the presentation of type 3 PAS in the elderly. Thyroid dysfunction commonly presents in the elderly, but newly diagnosed antibody positive type 1 diabetes is rare in this group. Coeliac disease is prevalent in nearly a quarter of patients with thyroid disease and 10% of those with type 1 diabetes but also rarely presents late in life. We present a rare case of a 76 year old female with features of type 3 PAS. She had a history of hypertension and dyslipidaemia but no personal or family history of autoimmune conditions. The patient was referred to the endocrinology department for further investigation of diabetes and mild hypercalcaemia in the context of weight loss and thirst. Given her age and mildly elevated HbA1c, she had been diagnosed with type 2 diabetes but on further investigation, was found to be GAD and IA-2 antibody positive and started on treatment for type 1 diabetes. Further evaluation also identified TPO antibody positive hypothyroidism and anti -TTG positive coeliac disease. She had normal vitamin B12 levels showing no evidence of pernicious anaemia, no history of vitiligo and normal cortisol, antinuclear antibody and serum angiotensin converting enzyme levels. She is currently under investigation for probable hyperparathyroidism. This is a unique case of type 3 PAS presenting atypically in an elderly patient. Not only is the age of presentation unexpected, but the lack of pernicious anaemia and other autoimmune features typically seen in type 3 PAS make this very distinctive. It highlights the need for further epidemiological research into this presentation, particularly in the elderly, to allow for early detection of a possible autoimmune syndrome. With an ageing population, further understanding is needed on how to manage these complex autoimmune conditions in this vulnerable group.

DOI: 10.1530/endoabs.81.P251

P252

Immunotherapy induced hypopituitarism including hypogonadism in patient with previous PCOS: call for early detection and endocrine work-up

Gesa Tiemeier, Bhavna Sharma, Mushtaqur Rahman, Asjid Qureshi & Ranjna Garg
Northwick Park Hospital, United Kingdom

Background
Immune checkpoint inhibitors are now commonly used in melanoma, renal cell carcinoma and non-small cell lung cancers. Patients on immune check point inhibitors experience at least one type of immune related adverse event(irAEs) which can occur even after discontinuation of therapy. Endocrine toxicities are commonly reported irAE′s and tend to be irreversible. The most frequently recognized endocrine complications include thyroid dysfunction (30%) hypophysitis (5.6-11%), type-1diabetes (0.2-2%) and adrenal insufficiency (0.7%) Literature is limited on potential impact on gonadal axis.
Case presentation
We report a 50-year-old Caucasian female with metastatic renal cell carcinoma, who was treated with a nephrectomy followed by immune checkpoint blockade with ipilimumab plus nivolumab. After 4 months of treatment she presented with fatigue, generalized pains and being emotional. She was switched to single agent nivolumab, however her symptoms persisted. Investigations revealed hypocortisolism(cortisol 50 nmol/l [range 160-550 nmol/l], hypogonadism(testosterone < 0.7 nmol/l [range 0-2.8 nmol/l], estradiol 280 pmol/l [range 45-1461 pmol/l], FSH10.9 IU/l [normal 25.8-134.8 IU/l]) and hypothyroidism (TSH 0.15 mIU/l [0.27-4.20 mIU/l]), IGF-1 levels were noted to be 20.7 nmol/l (range7.5-35 nmol/l). Patient had been started on prednisolone 10 mg/day, prior to referral to endocrine therefore ACTH was uninterpretable. She was switched to physiological dose hydrocortisone(10 mg/5 mg/5 mg) Retrospective evaluation revealed a background of previous hyperandrogenism related to polycystic ovarian syndrome one year prior to starting immunomodulators. However gradual drop in testosterone was noted from 4.8 nmol/l to undetectable levels (rangel 0-2.8 nmol/l) after starting immunotherapy. Prolactin was also noted to fall from normal values (158 mIU/l) pre-immunotherapy to undetectable level(< 20 mIU/l)(range 102-496 mIU/l). PET Scan did not reveal any abnormalities in pituitary/adrenal gland.
Conclusion
Our case demonstrates gradual onset hypopituitarismwith recognition of only cortisol deficiency. Hypogonaidsm was not identified.
Discussion
Thyroid function and Cortisol are commonly checked hormones. All components of the endocrine axis should be assessed and considerations for correcting each part of pituitary-target axis is needed. Further research is needed on potential impacts on sexual function, fertility in both males and females and bone health. Sexual dysfunction are not reported early on or be taken as part of ongoing treatment or underlying disease, being aware of endocrine dysfunction can improve patients well being as weel as timely counselling of the patinets. Most European guidelines emphasize that hypophysitis is not a contraindication for immunotherapy, we therefore recommend that all patients undergoing immunotherapy with nivolumab and ipilimumab should have a pre-treatment endocrine profile with periodical monitoring and timely endocrinology input to ensure early recognition and appropriate treatment of endocrine dyscrasias.

DOI: 10.1530/endoabs.81.P252

P253

Central diabetes insipidus from a patients′ perspective – from management to psychological co-morbidities and re-naming of the condition

Cihan Atila[1,2], Ben Loughrey[3,4], Aoife Garrahy[5], Bettina Winzeler[1,2], Julie Refardt[1,2], Patricia Gildroy[6], Aparna Pal[5], Malak Hamza[7], Chris Thompson[8,9], Joseph Verbalis[10], Steven Hunter[3], Mark Sherlock[8,9],

Miles J Levy[7], Niki Karavitaki[11,12], John Newell-Price[13], John Wass[5] & Mirjam Christ-Crain[1,2]
[1]Department of Endocrinology, Diabetology and Metabolism, University Hospital Basel, Switzerland; [2]University Hospital Basel, Department of Clinical Research, Switzerland; [3]Royal Victoria Hospital, Regional Centre for Endocrinology and Diabetes, Ireland; [4]Queen's University Belfast, Patrick G Johnston Centre for Cancer Research, Ireland; [5]Churchill Hospital, Oxford Centre for Diabetes, Endocrinology and Metabolism, United Kingdom; [6]Administrator and Patient Advocate for the Facebook Group: Got Diabetes Insipidus?, United States; [7]University Hospitals of Leicester, Department of Endocrinology, United Kingdom; [8]Royal College of Surgeons in Ireland, Ireland; [9]Beaumont Hospital Dublin, Department of Endocrinology, Ireland; [10]Georgetown University Medical Center, United States; [11]University of Birmingham, Institute of Metabolism and Systems Research, United Kingdom; [12]Birmingham Health Partners, Centre for Endocrinology, Diabetes and Metabolism, United Kingdom; [13]University of Sheffield, Deptartment of Oncology and Metabolism, United Kingdom

Background
Central diabetes insipidus (cDI), a rare neuroendocrine condition affecting 1 in 25.000, is characterized by deficiency of arginine vasopressin. Data about treatment-related side effects, psychological co-morbidities, and incidence of wrong management due to confusion with *diabetes mellitus* are scarce and limited to small studies or case series. Furthermore, increasing interest has arisen on a potential need for re-naming the condition.
Methods
A web-based anonymous survey was developed by an international team of endocrinologists and patient representatives covering issues from management of the condition and quality-of-life to lack of awareness amongst medical professionals. Patients were provided with the link to the online survey either via their physician during routine check-ups or the homepages of the *UK Pituitary Foundation*, *Pituitary World News*, *Facebook* group *Got Diabetes Insipidus?*, and *Pituitary Society*.
Results
Worldwide, 1034 patients with cDI, 47%($n=488$) with isolated posterior and 53%($n=546$) with combined anterior/posterior pituitary dysfunction, participated. Median[IQR] age was 42[32, 53], 77%($n=794$) were female. Duration of cDI was 9.0[3.0, 19.0] years and its aetiologies were idiopathic 30%($n=315$), pituitary tumors/cysts (pre-surgical 21%($n=217$), post-surgical 25%($n=254$)), inflammatory/autoimmune 6%($n=61$), infiltrative diseases 6%($n=59$), genetic/familial 4%($n=44$), head trauma 3%($n=34$), and other causes 5%($n=50$). Ninety-six percent ($n=994$) were on desmopressin therapy - oral tablets 56%($n=575$), nasal spray 23%($n=233$), and sub-lingual tablets 12%($n=126$). Among these patients, 26%($n=273$) experienced hyponatremia (self-reported) at least once whilst on desmopressin. Patients who routinely omitted desmopressin (up to several times a week) to allow aquaresis had significantly lower risk of hyponatremia compared to those who did not follow this approach (OR 0.4, 95%CI 0.3-0.7, $P<0.01$). Sixty-four percent($n=660$) reported low quality of life indicated with 6[IQR 4-7] out of 10 points. Thirty-six percent($n=369$, equally prevalent in isolated posterior and combined pituitary dysfunction) experienced psychological problems after the diagnosis, of whom 70%($n=258$) reported higher anxiety levels, 71%($n=263$) sleep disturbances, and 65%($n=239$) depressed mood. Eighty percent($n=823$) encountered a situation where medical professionals, friends or family members confused the diagnosis with "diabetes mellitus", of these 88%($n=637$) indicated that this confusion affected the management of their cDI. In total, 85%($n=884$) would prefer a re-naming of the condition; amongst those, the most common suggestion was "vasopressin deficiency".
Conclusion
This is the so far largest survey conducted in patients with cDI using a web-based method and patient involvement in the survey development. We show a high percentage of treatment-related hyponatremia, a high prevalence of psychological co-morbidities and a clear need for re-naming of the condition from patients' perspective.

DOI: 10.1530/endoabs.81.P253

P254

Facial phenotype changes and its impact in Quality of Life of acromegaly patients

Laura Ferrer[1], Maria Antonia Martínez-Momblán[2], Montse Marqués-Pamies[1,3], Federico vazquez[1], Berta Soldevila[1], Raquel Ciriza[4], Elena Valassi[1] & Manel Puig-Domingo[1]
[1]Germans Trias i Pujol Hospital, Badalona, Spain; [2]Universitat Autònoma de Barcelona, Bellaterra, Spain; [3]Hospital Municipal Badalona, Badalona, Spain; [4]Spanish Association of Acromegaly People

Acromegaly is a rare disease usually diagnosed late in disease evolution. It implies for skeletal changes of most flat bones including those of the skull. Consequently, a progressive facial disfiguration occurs at slow velocity of irreversible nature. Even after curation most of these changes stay for the whole life of the patient.
Aim
to study the potential relationship between disfiguring facial modifications and psychosocial and Quality of Life (QoL) impact in a group of acromegaly patients.
Patients and methods
Thirty patients accepted to participate in this study (13 women and 17 men); mean age was 61.1 ± 15.8 and 56.3 ± 12.4 years, respectively. Variables studied included: a) Anxiety level, measured through the State-Trait Anxiety Questionnaire (STAI); b) Quality of life evaluation by AcroQoL; c) Self-esteem status through the Rosemberg Self-Esteem Scale and d) Facial acromegaly phenotypic changes evaluated from face photographs and scored by 8 trained endocrinologists. Results: There were gender differences in anxiety levels, with higher values in women than in men (trait: 6.1±2.2 and 5.0±2.0 ($P=0.025$); state: 8.2±1.1 and 3.1±2.1 ($P=0.004$), respectively. Also, there were differences in the Global AcroQoL score: 69.3 ± 17.7 for males and 51.1 ± 21.8 for females ($P=0.004$) and this was reflected in all dimensions. Self-esteem was similar in both groups. There were lower scoring values for the face appearance in women at pre-diagnostic phase compoared to men (3.4±1.3 vs. 4.75±1.5). A negative correlation between self-esteem and changes in facial scores at the pre-diagnostic and diagnostic periods ($r_s=-0.559$, $P=0.074$) was found, consistent with a high impact of facial changes in the psychologic status of the patients. Conclusion: acromegaly facial changes negatively impact the psychosocial condition of these patients with maximal deleterious effects at the time of diagnosis; these disturbances persist over time despite cure or hormonal control and are of higher intensity in women.

DOI: 10.1530/endoabs.81.P254

P255

Cushing syndrome in older women: age-related differences in disease origin and clinical manifestations

Amit Akirov[1,2], Ilan Shimon[1,2], Manisterski Yosi[3], Nirit Aviran-Barak[3], Varda Nadler[4], Sandra Alboim[4], Gloria Tsvetov[1,2,3] & Dania Hirsch[1,2,3]
[1]Tel Aviv University, Sackler School of Medicine, Tel Aviv-Yafo, Israel; [2]Beilinson Medical Center, Petah Tikva, Israel; [3]Maccabi Health Services, Tel Aviv-Yafo, Israel; [4]Maccabi Healthcare Services, Rehovot, Israel

Background
Adrenocorticotropic hormone (ACTH)-producing pituitary adenoma is the most common cause of endogenous Cushing syndrome (CS), but the relative proportion of adrenal causes of CS is rising. Limited data are available on the clinical manifestations and cause of CS in older women.
Objective
Determine the clinical presentation, biochemical profile, and cause of CS in women 65 years of age and older, compared with younger patients with CS.
Methods
Retrospective charts review of women with pituitary or adrenal CS, treated at Rabin Medical Center between 2000 and 2017, or at Maccabi Healthcare Services in Israel between 2005 and 2017. Patients were classified into 3 groups, according to age at diagnosis: ≤45 (young), 46-64 (middle-age), or <65 (elderly) years.
Results
The cohort included 142 women (mean age, 46.0 ± 15.1 years), including 81 (57.0%) with ACTH-producing pituitary adenoma, and 61 patients (43.0%) with adrenal CS: 68 young, 55 middle-aged, and 19 elderly women. Pituitary source for CS was more common among young patients (48 patients, 70.6%), compared with middle-aged (27 patients, 49.1%) or elderly women (6 patients, 31.6%) ($P<0.05$). Weight gain was evident in 57.4% of young women (60.0% pituitary, 56.3% adrenal), compared with 15.8% of elderly women (50% pituitary, 0% adrenal) ($P=0.011$). Cushingoid features were more common among young vs. elderly patients, but the difference was not significant (40.0% vs. 22.1%, respectively; $P=0.15$). Among patients with adrenal CS, diagnosis of hypercortisolism was established following an incidental finding of an adrenal mass in 3 of 20 (15.0%) young women vs. 7 of 13 (53.8%) elderly women ($P<0.001$). Mean urinary free cortisol levels were highest for young women (5.03±3.6xULN), followed by middle-aged (4.80±6.0xULN) and elderly (3.5±2.6xULN) women ($P<0.001$), while no difference was recorded for serum cortisol levels following low-dose dexamethasone. Adrenal or pituitary tumor size was not different between groups. While in young patients with CS, urinary free cortisol levels were higher for those with adrenal vs. pituitary CS (6.61±3.2xULN vs. 4.36±3.6xULN), in middle aged (3.42±3.4xULN vs. 6.24±7.7xULN) and elderly (2.62±1.9xULN vs. 5.33±2.9xULN) patients, pituitary CS was associated with higher urinary free cortisol levels than adrenal CS.

Conclusions
Older patients with CS have distinct disease cause and presentation, as pituitary source is less common than adrenal CS, the latter is associated with milder hypercortisoluria and is frequently diagnosed incidentally. Weight gain was prevalent in young women, and uncommon in older women.

DOI: 10.1530/endoabs.81.P255

P256

Hobnail variant of papillary thyroid carcinoma, a systematic review and meta-analysis

Ariadni Spyroglou[1], George Kostopoulos[2], Konstantinos Bramis[1], Sofia Tseleni[3], Konstantinos Toulis[2], George Mastorakos[1], Manousos Konstadoulakis[1], Kyriakos Vamvakidis[4] & Krystallenia Alexandraki[1]
[1]National and Kapodistrian University of Athens, 2 nd Department of Surgery, Aretaieion Hospital, Athens, Greece; [2]424 General Military Hospital, Department of Endocrinology, Thessaloniki, Greece; [3]National and Kapodistrian University of Athens, Department of Pathology, Athens, Greece; [4]"Henry Dunant" Hospital Center, Department of Endocrine Surgery, Athens, Greece

Background
Although papillary thyroid carcinoma (PTC) is considered to have an excellent prognosis, some more aggressive variants have been identified that show reduced overall survival rates. Besides from the diffuse sclerosing, tall cell, columnar cell, and solid variant, the hobnail variant was newly recognized as one of these aggressive forms, affecting recurrence, metastasis, and overall survival rates.
Methods
We performed a systematic review and meta-analysis of studies including cases or case series with patients with hobnail variant of PTC. Furthermore, we included our own case series consisting of six patients.
Results
The pooled mortality rate in the cohort consisting of 191 patients was 3.43 (95% CI 1.72-6.82) per 1000 person/months. No sex differences could be observed concerning mortality ($P=0.52$) but older age and tumor size significantly affected mortality ($P=0.03$ and$P=0.02$, respectively). The percentage of hobnail variant did not affect mortality ($P=0.29$), neither did the presence of BRAF mutations. Classical characteristics as the presence of extrathyroidal extension ($P=0.001$), distant metastases ($P<0.001$) and lymph node metastases ($P<0.001$) all had a significant impact on mortality.
Conclusions
Hobnail variant correlates with worse overall survival and all PTC cases should be carefully assessed for this variant.

DOI: 10.1530/endoabs.81.P256

P257

Retrospective assessment of malignant thyroid nodules in a group of children and adolescents according to BTA U classification and ACR TI-RADS ultrasound-based risk stratification system in combination with elastography

Artur Bossowski, Hanna Borysewicz-Sanczyk, Beata Sawicka, Filip Bossowski, Agata Karny, Aleksandra Rusak & Janusz Dzieciol
Medical University in Bialystok, Dep of Pediatric Endocrinology and Diabetes, with a Cardiology Division., Białystok, Poland

The risk of malignancy in thyroid nodules correlates with the presence of ultrasound features. In adults, ultrasound risk-classification systems have been proposed to indicate the need for further invasive diagnosis. Furthermore, elastography has been shown to support differential diagnosis of thyroid nodules. The purpose of our study was to assess the application of the American Thyroid Association (ATA) and British Thyroid Association (BTA) ultrasound risk-classification systems as well as strain elastography in the management of thyroid nodules in children and adolescents. Seventeen nodules with Bethesda III, IV, V and VI were selected from 165 focal lesions in children. All patients underwent ultrasonography and elastography followed by fine needle aspiration biopsy. Ultrasound the ATA and BTA stratification systems were assessed retrospectively. The strain ratio in the group of thyroid nodules diagnosed as malignant was significantly higher than in benign nodules (6.07 vs. 3.09, $P=0.036$). According to the ATA guidelines, 100% of malignant nodules were classified as high suspicion and 73% of benign nodules were assessed as low suspicion. Using the BTA U-score classification, 80% of malignant nodules were classified as cancerous (U5) and 20% as suspicious for malignancy (U4). Among benign nodules, 82% were classified as indeterminate or equivocal (U3) and 9% as benign (U2). Our results suggest that application of the ATA or BTA stratification system together with elastography may improve differential diagnosis and help make a clinical decision about the need for further invasive diagnosis of thyroid nodules in children.

DOI: 10.1530/endoabs.81.P257

P258

Discordant thyroid function tests following Ibrutinib therapy

Alwyn Yung Zhuang Choo & Jayamalee Jayaweera
West Suffolk Hospital, Endocrinology and Diabetes, Bury St. Edmunds, United Kingdom

Background
Tyrosine kinase inhibitors (TKI) are a chemotherapeutic group which include drugs known to cause thyroid dysfunction such as axitinib, imatinib, pazopanib, sorafenib, and sunitinib. However, reports of TKI-Ibrutinib causing thyroid dysfunction are scarce. Although several hypotheses have been proposed to explain TKI-associated thyroid dysfunction there is no clear guidance on how to manage this situation.
Case
86-year-old lady was referred to the endocrinology clinic for evaluation of abnormal thyroid function tests. Her relevant medical histories included stage IV mantle cell lymphoma, hypothyroidism, stage III chronic kidney disease, hypertension, and diverticular disease. She was diagnosed with hypothyroidism in 2003 and has been on Levothyroxine dose of 100 mg and 75 mg on alternate days for many years. She was diagnosed with stage IV mantle cell lymphoma and was commenced on Ibrutinib in June 2020. Her first recorded thyroid function test in 2012 showed hypothyroidism, following that remained relatively stable with the same dose of Levothyroxine. Following introduction of Ibrutinib in June 2020, there was a concurrent rise in thyroid-stimulating hormone (TSH) and free thyroxine (FT4) with mildly decreased free triiodothyronine (FT3). She was fully compliant with Levothyroxine and confirmed taking the tablet well apart from her meals and other tablets. Other relevant blood tests showed stable chronic kidney disease, normal liver function test. Assay interference results were unremarkable. Serial thyroid functions showed rise in TSH (9.4;11.4;8.34;4.39;5.91;11.1) with concurrent rise in FT4 (19.5;23;26;26.9;23;23.1) and low FT3 levels (2.4;2.2;2.5) following Ibrutinib. Thyroxine dose was increased to 100 mg daily as TSH had risen to 11.1 and she complained of excessive tiredness.
Discussion
Suggested mechanism for this pattern is the induction of type 3 deiodinase (D3) pathway which converts FT4 to rT3 and inhibition of type 2 deiodinase (D2) which converts FT4 to FT3, with the balance towards D2 inhibition. Thyroid-binding globulin was not elevated hence it could not account for the raised TT4. Non thyroidal illness causing this picture is unlikely given raised TSH. Induction of uridine diphosphate-glucuronosyltransferases is a plausible cause, which enhances clearance of T4 and T3 (as suggested for another TKI-Imatinib) resulting in hypothyroidism in patients receiving Levothyroxine replacement, however T4 levels were not reduced.
Conclsion
This case highlights the importance of thyroid function testing prior to starting Ibrutinib and the value of close monitoring of thyroid status throughout. Clinicians who prescribe Ibrutinib should be aware of this potential thyroid function dysfunction, and to seek endocrinology advice as appropriate.

DOI: 10.1530/endoabs.81.P258

P503

Salivary free cortisol and serum DHEA-sulfate measurements with cosyntropin stimulation improve accuracy of secondary adrenal insufficiency diagnosis in pregnancy

Ashley B Humrickhouse & Maya Y Peltsverger
Novant Health New Hanover Regional Medical Center, Wilmington, United States

Background
Diagnosis of secondary adrenal insufficiency (SAI) during pregnancy is challenging due to physiological adaptations and progressive increase of cortisol level throughout the pregnancy (1). The 250-mg standard ACTH stimulation test

(CST) is recommended for evaluation of adrenal hypofunction in pregnancy however, measurement of serum cortisol (SC) maybe misleading in patients with partial SAI. Furthermore, utility of salivary free cortisol (SaFC) (2) and serum DHEA-sulfate (DHEA-S) measurements has been proposed to improve the accuracy of SAI diagnosis (3).

Case

We report the case of a 33-year old female with history of hypopituitarism secondary to Langerhans cell histiocytosis treated with pituitary irradiation during pre-teen years subsequently leading to Diabetes Insipidus, hypogonadism, and growth hormone deficiency. Prior to pregnancy, her thyroid function and ACTH stimulation tests were normal. She presented at 25 weeks of gestation with complaints of profound fatigue and weight loss. Pregnancy was conceived via in vitro fertilization. Morning serum ACTH and SC were 14.9 pg/ml (7.2-63.3 pg/ml) and 14.95 mg/dl (6.2-19.4 mg/dl), respectively. Serum DHEA-S was 39.5 mg/dl (84.8-378.0 mg/dl). During pregnancy SC levels increase 2-to-3-folds higher than in non-pregnant women and DHEA-S levels usually increase by 2nd trimester (4). Thus, secondary adrenal insufficiency was suspected. Patient underwent 250-mg ACTH stimulation test with measurements of SC, DHEA-S, and SaFC concentration before, 30, and 60 min after cosyntropin stimulation. SC increased from 14.76 mg/dl to 25.67 mg/dl and 29.69 mg/dl at 30 and 60 min, respectively. Baseline SaFC was 0.128 mg/dl (0.36 +/-0.17 mg/dl) and minimally increased to 0.276 mg/dl and 0.412 mg/dl at 30 and 60 min, respectively. Baseline DHEA-S was 17.1 mg/dl and minimally increased to 19.1 mg/dl and 21 mg/dl at 30 and 60 min, respectively.

Discussion

Previous studies have reported that SaFC and serum DHEA-S measurements can improve the accuracy of SAI diagnosis. Suri *et al*. proposed that SaFC is superior for assessing adrenal response to ACTH stimulation with cutoff for second trimester being 0.36 +/-0.17 mg/dl at baseline and 2.37+/-0.99 mg/dl after cosyntropin stimulation. Patient in this case report had normal SC peak response to CST however, SaFC levels did not reach expected range after stimulation. Serum DHEA-S is a sensitive indicator of impaired ACTH secretion in patients with SAI (5). Patient in this report had DHEA-S levels that were low throughout the pregnancy. Collectively, the patient′s findings reported here suggest SAI. Initiation of hydrocortisone therapy significantly improve patient′s symptoms.

DOI: 10.1530/endoabs.81.P503

P504

Adrenal incidentaloma, single center clinical experience

Beril Turan Erdogan[1], Berna Evranos Ogmen[2], Caglar Keskin[1], Sevgul FAKI[1], Cevdet Aydin[2], Oya Topaloglu[2], Reyhan Ersoy[2] & Bekir Cakir[2]

[1]Ankara City Hospital, Department of Endocrinology and Metabolism, Ankara, Turkey; [2]Yildirim Beyazit University Faculty of Medicine, Ankara City Hospital, Department of Endocrinology and Metabolism, Ankara, Turkey

Backgorund

Adrenal incidentalomas (AI) are lesions discovered incidentally on imaging without clinical symptoms or examination findings. AI can produce hormones in 5-30% of cases. Autonomic cortisol secretion (ACS) is the most common of these. Although ACS is asymptomatic, it increases the risk of metabolic disorders.

Methods

Patients aged < 18 years with adrenal adenoma and upper abdominal MRI who presented and were examined in the endocrinology outpatient clinic, had their data retrospectively documented. Comorbidities, examinations and hormonal tests and results of these patients were evaluated. Those who failed dexamethasone suppression tests (cortisol > 1.8 g/dl) and did not have Cushing's syndrome were classified as ACS.

Results

Among the 223 patients, 138 (61.9%) were women with a median age of 56 (18-80). Of the patients, 26.9% had diabetes mellitus (DM), 54.3% had hypertension (HT), 17.9% had hyperlipidemia (HL), 12.1% had coronary artery disease (CAD), 1.3% had heart failure (HF). Hormone testing revealed that 6 (2.6%) of the patients had primary aldosteronism, 5 (2.2%) had pheochromocytoma, and 35 (15.6%) had ACS. Patients with and without ACS were compared for the presence of other additional diseases and adenoma size (Table-1). DM, HT and HL were higher in the ACS group ($P < 0.05$, for each). Adenoma size was larger in the ACS group ($P < 0.05$). Both groups had comparable age and sex distribution ($P > 0.05$).

Conclusion

İndividuals with large adenomas are more likely to have ACS. Large adrenal adenomas should be monitored for ACS and associated cardiometabolic risks, as well as necessary treatments.

Table 1 Comparison of patient characteristics with and without autonomic cortisol secretion

Autonomic cortisol secretion	Yes	No	P
Sex, Woman/Man	2.18	1.54	0.45
Age (years), median (min-max)	59 (36-80)	55 (18-74)	0.071
Size of adenoma (mm)	25 (10-54)	18 (10-60)	0.001
T2DM	17 (48.6%)	43 (22.9%)	0.002
HT	25 (71.4%)	96 (51.1%)	0.028
HL	13 (37.1%)	27 (14.4%)	0.003
CAD	7 (20%)	20 (10.6%)	0.154
HF	1 (2.9%)	2 (1.1%)	0.402
Osteoporosis or osteopenia	6 (30%)	13 (56.5%)	0.125

T2DM type 2 diabetes mellitus, HT hypertension, HL hyperlipidemia, CAD coronary artery disease, HF heart failure

DOI: 10.1530/endoabs.81.P504

P505

Primary hyperparathyroidism, familial hypocalciuric hypercalcaemia or both?

Ashutosh Kapoor[1], Bhavna Sharma[1], Danujan Sriranganathan[1], Neil Tolley[2], Aimee Dimarco[2] & Mushtaqur Rahman[1]

[1]London North West University Healthcare NHS Trust, United Kingdom; [2]Imperial College Healthcare NHS Trust, United Kingdom

Introduction

Primary hyperparathyroidism (PHPT) is an endocrine condition in which autonomous excessive secretion of parathyroid hormone (PTH) results in hypercalcaemia. In approximately 80% of cases the aetiology is due to a single parathyroid adenoma, the remainder are due to hyperplasia of more than one gland. Familial Hypocalciuric Hypercalcaemia (FHH) is an autosomal dominant, inactivating mutation of the calcium-sensing receptor, causing a right-shift in the concentration-response curve, and producing biochemistry similar to PHPT.[1] Although usually benign, it can cause pancreatitis. More than 75% of cases are due to the following genotypes, in descending order of incidence, CASR, AP2S1, GNA11: FHH 1, 3, and 2, respectively.

Case details

We report the case of a 53-year South Asian male, referred with hypercalcaemia. Serum adjusted calcium was 2.71 mmol/l, PTH 4.5 pmol/l, FE_{Ca} 0.014, and 24h urine calcium 6.08 mmol; a previous 24h urine calcium was 8.76 mmol (normal 2.5-7.5). The patient had a history of renal stones, enough to cause hydro-ureteronephrosis. Therefore, despite the equivocal biochemistry, it was felt that this was in keeping with PHPT. Dual-modality imaging did not reveal a discrete adenoma and so 4-gland exploration was undertaken with the removal of three glands, which had features of hyperplasia and was in keeping with the negative results of imaging; peak pre-operative PTH was 13.2, dropping to 4.4 pomol/l after surgery. Due to recurrence of hypercalcaemia and the equivocal FE_{Ca}, genetic testing was undertaken and showed the patient to be heterozygote FHH2 (GNA11).

Discussion

PHPT and FHH occurring in the same patient is rare, but has been reported.[2] A FE_{Ca} < 0.02 should prompt consideration of FHH, but this patient presented with renal stone disease, more in keeping with primary hyperparathyroidism. Therefore, an operative approach was valid and there may have been reduced penetrance of the pathological variant of FHH. Where these conditions co-exist, surgery can reduce the level of hypercalcaemia and treatment choice should be based on presence of end-organ effects[2]; an alternative approach is to use cinacalcet, a calcimetic agent.[1]

References

1. Lee JY, Shoback DM. Familial hypocalciuric hypercalcemia and related disorders. Best Pract Res Clin Endocrinol Metab. 2018 Oct; 32(5): 609-619.
2. Frank-Raue K *et al*. Inactivating calcium-sensing receptor mutations in patients with primary hyperparathyroidism. Clin Endocrinol (Oxf). 2011 Jul; 75(1): 50-5.

DOI: 10.1530/endoabs.81.P505

P506

Initial results and patient satisfaction with the new oral formulation of semaglutide

Francisco Javier Martinez Martin[1,2], Agnieszka Kuzior[1,2], Claudia Arnas-Leon[1,2], Paula Fernandez-Trujillo-Comenge[1], Sara Quintana-Arroyo[3], Carmen Acosta-Calero[4], Ana Delia Santana-Suarez[1], Paula Gonzalez-Diaz[5], Alba Hernandez-Lazaro[1] & Ricardo de Leon-Durango[1]
[1]University Hospital of Gran Canaria Dr. Negrin, Endocrinology & Nutrition, Las Palmas de Gran Canaria, Spain; [2]Hospitales San Roque, Endocrinology & Nutrition, Las Palmas de Gran Canaria, Spain; [3]Hospital Insular de Gran Canaria, Endocrinology & Nutrition, Las Palmas de Gran Canaria, Spain; [4]University Hospital of Gran Canaria Dr. Negrin, Cardiology, Las Palmas de Gran Canaria, Spain; [5]University Hospital of Gran Canaria Dr. Negrin, Emergency, Las Palmas de Gran Canaria, Spain

Introduction
Oral semaglutide has been available in the Spanish market since November 2021. This new formulation has broken the self-injection barrier, and may enhance patient satisfaction.
Methods
Retrospective review of the patients′ records and presential or telephonic interviews. All patients expressed their consent for the anonymous processing of their data. Numeric data are given as mean + s.d; paired t-test was used for comparison. Satisfaction was categorically expressed as very poor, poor, fair, good or very good.
Results
36 obese patients with type 2 diabetes who had taken at least one pill of oral semaglutide were included. Their age was 56 + 12 years; 58% were female; diabetes duration was 6 + 2 years. Of them 34 remain on treatment, 1 withdrew due to gastric intolerance and 1 due to difficulty to schedule the medication intake. 9 are still on the lowest dose (3 mg/day), 11 on the medium dose (7 mg/day) and 14 on the full dose (14 mg/day), 5 of which started on this dose because they were transferred from previous parenteral GLP-1RA therapy. 24 patients have a HbA1C measurement after at least 2 months on oral semaglutide and the difference with the previous is -1.2 + 0.5%. ($P=0.013$). 26 patients have a weight measurement after at least 2 months and the difference is -3.2 + 1.3 kg ($P=0.032$). Mild gastrointestinal disturbances were reported by 8 of the patients (22%), and only persist in 3 of them (8%) but in one case epigastric pain, nausea and vomiting caused withdrawal. No severe hypoglycemia has been reported. Five patients were on previous levothyroxine treatment and their dose was maintained but the intake hour was rescheduled; no dosing changes have been required so far. Seven of the patients were diagnosed with non-proliferative diabetic retinopathy but none were in active treatment; no worsening has been reported. One patient (3%) reported very poor satisfaction, 1 (3%) poor, 4 (11%) fair, 11 (31%) good and 19 (53%) very good. All 5 patients who were transferred from parenteral GLP-1AR reported very good satisfaction.
Conclsions
Our initial experience with oral semaglutide is quite satisfactory, with the expected gastrointestinal disturbances which were mild and non-persistent in the large majority of the patients. No additional clinical problems emerged. Glycemic control was significantly improved without serious hypoglycemia, and body weight was significantly decreased. Satisfaction was good or very good in 5 out of 6 patients.

DOI: 10.1530/endoabs.81.P506

P507

Insights into the early use of oral semaglutide in routine clinical practice

Bharat Saboo
Prayas Diabetes Center, Indore, India

Introduction
Oral semaglutide (Rybelsus; Novo Nordisk) is the first glucagon-like peptide-1 receptor agonist (GLP-1 RA) developed for oral administration for the treatment of type 2 diabetes (T2D), and it has been approved by the US Food and Drug Administration and the European Medicines Agency. The efficacy and safety of oral semaglutide were assessed in the (PIONEER) program.
Aim
The purpose of this study was to investigate the initial patterns of routine clinical use of oral semaglutide, as well as the clinical features and glycemic control, and weight of patients.
Method
a retrospective, observational cohort study utilizing retrieved electronic medical records involved database search of 28 patients for the demographic parameters at the index date, as well as baseline co-morbidities, antidiabetic drugs, and HbA1c. Baseline and after 1-month, weight and FBS levels were determined for patients with relevant data. For inclusion, adult patients (aged < 18 years) required a diagnosis of T2D and at least one prescription for oral semaglutide. Patients with type 1 diabetes or gestational diabetes were excluded. The results were analyzed using MS Excel.
Result
Although the medical instructions recommend raising the dose to 7 mg after 30 days, 64.3 percent of patients obtained a prescription solely for the initial 3 mg dose. The mean body mass index was 36.2 kg/m^2 n, and the mean HbA1c level was 9.1%. The mean change in FBS from baseline to about one month after initiating oral semaglutide was 6.3%, with more significant reductions in those with higher baseline FBS. The average weight loss was 2.3 kg, significantly more significant in patients with a higher baseline BMI.
Discussion
Our data demonstrates early trends in the use of oral semaglutide in routine clinical practice. Oral semaglutide initiators have a high prevalence of obesity and other co-morbidities, a varied treatment history, and improved glycemic control following therapy initiation. The relatively high number of patients allocated 3 mg as their maximum dose shows that, in patients who tolerate oral semaglutide well, dose escalation to 7 and 14 mg, as indicated, may result in even more significant glycemic control improvements. These findings emphasize the critical nature of bridging existing treatment and knowledge gaps in order to maximize the potential of oral GLP-1 RA therapy. Further examination of real-world data will give more information on the translation, uptake, and impact of such breakthroughs in standard treatment.

DOI: 10.1530/endoabs.81.P507

P508

In Individuals with obesity, resting energy expenditure does not decrease after weight loss with GLP-1 agonist liraglutide

Mostafa Mohseni[1,2], Mila Welling[1,2], Renate E.H. Meeusen[1,2], Wietske G.C.L.M. Broeders[1,2], Eline van der Valk[1,2] & Elisabeth van Rossum[1,2]
[1]Erasmus MC, University Medical Center Rotterdam, Internal Medicine, Division of Endocrinology, Rotterdam, Netherlands; [2]Erasmus MC, University Medical Center Rotterdam, Obesity Center CGG, Division of Endocrinology, Rotterdam, Netherlands

Background
Obesity (BMI < 30 kg/m^2) is a chronic and progressive disease, that is associated with many co-morbidities such as cardiovascular and psychiatric diseases, cancer, and arthritis. Lifestyle interventions are the cornerstone of obesity treatment, but when ineffective, anti-obesity pharmacotherapy could be added. In recent years, several anti-obesity agents have been approved, such as the glucagon-like peptide-1 (GLP-1) analogue liraglutide. Liraglutide induces weight loss, presumably by suppressing appetite and improving satiety. It is however unclear whether liraglutide also induces weight loss by alterations of the resting energy expenditure (REE).
Methods
In this observational longitudinal study, we evaluated individuals with obesity who were treated with liraglutide 3.0 mg at the Obesity Center CGG, Erasmus MC Rotterdam, The Netherlands. We included 24 individuals (18 women), of whom four had a confirmed genetic obesity, thirteen had clinical features suspective of genetic obesity, and seven had common obesity. At baseline and after 16 weeks of treatment, which included dose escalation over a period of 4 weeks, we measured anthropometric parameters, body composition using bio-electrical impedance (Inbody S10, BioSpace, Seoul, Korea), and REE using indirect calorimetry (Q-NRG®, Cosmed, Roma, Italy). Predicted REE was calculated using the Harris-Benedict formula.
Results
At baseline, mean weight and BMI were 124.1 kg (± 24.1) and 42.7 kg/m^2 (± 7.5), respectively. Their weight decreased significantly (-5.7%, $n=23$) after 12 weeks of treatment. Fat mass and fat-free mass (FFM) decreased significantly (-5.2 kg and -2.7 kg, respectively; $n=18$) and percentage of fat mass decreased from 47.6% to 46.5% ($P=0.096$). REE increased from 1879 kcal/day to 1956 kcal/day ($P=0.150$), and REE per kg FFM increased from 29.7 kcal/kg/day to 32.3 kcal/kg/day ($P=0.023$). Lastly, REE as a percentage of predicted REE increased from 94% to 98% ($P=0.204$).
Conclsion
In patients with obesity, treatment with GLP-1 analogue liraglutide effectively induces weight loss, with improved body composition. Furthermore, despite decreases in fat free mass, of which muscle mass is a major component, resting energy expenditure did not decrease. Our findings suggest that weight loss induced

by liraglutide may not only be facilitated by decreases in caloric intake through the anorexigenic effects of GLP-1 analogues, but also by increasing the resting energy expenditure per kg fat-free mass.

Funding
EFCvR is funded by a Vidi grant from the Netherlands Organization of Scientific Research NWO/ZONMW (grant number: 91716453). EFCvR is financially supported by the Elisabeth Foundation.

DOI: 10.1530/endoabs.81.P508

P509

Neuroprotective properties of GLP-1 receptor agonists and SGLT-2 inhibitors in experimental stroke

Anna Simanenkova[1,2], Natalya Timkina[1,2], Tatiana Karonova[1,2], Polina Tikhomirova[2], Alexandr Gagiev[2], Fedor Radugin[1] & Timur Vlasov[2]
[1]Almazov National Medical Research Centre, Saint-Petersburg, Russian Federation; [2]Pavlov First Saint-Petersburg State Medical University, Saint-Petersburg, Russian Federation

Background and aims
The most outstanding cardioprotective potential has been demonstrated for GLP-1 receptor agonists (GLP-1RA) and SGLT-2 inhibitors (SGLT-2i). But only long-acting GLP-1RA dulaglutide (DULA) and semaglutide decrease stroke incidence, while data concerning the influence of any drug on stroke severity are lack. At the same time, ischemic stroke remains one of the leading causes of death in type 2 diabetes mellitus (DM2). The aim of our study was to investigate neuroprotective actions of liraglutide (LIRA), DULA and empagliflozin (EMPA), in comparison with metformin (MET) in acute rat brain ischemia. We have chosen two GLP-1RA with different action duration to evaluate drug- or class-effect.
Materials and methods
male Wistar rats 200-255 g were treated for 7 days with LIRA 1 mg/kg s.c. once daily ("LIRA", $n=12$), DULA 0.12 mg/kg s.c. every 72 h ("DULA", $n=10$), EMPA 2 mg/kg per os once daily ("EMPA", $n=9$), MET 200 mg/kg kg per os once daily ("MET", $n=8$) or 0.9% NaCl s.c. once daily ("Control", $n=12$). Then all animals were subjected to 30-min filament middle cerebral artery occlusion (MCAO). 48 h after MCAO neurological deficit was evaluated by Garcia scores – healthy animals have 18 points, maximal neurological deficit is characterized by 3 points. Then rats were euthanized, brain slices were incubated with 1% 2,3,5-triphenyltetrazolium chloride for necrosis measurement. Blood glucose level (BGL) was studied every second day.
Results
Brain infarct volume was significantly smaller in "LIRA" and "DULA" (5.50(3.97;5.50)% and 6.65(4.1;11.0)%) comparing with "Control" (16.56(13.33;24.65)% of total brain volume). Stroke volume in "EMPA" (4.91(2.67;14.49)%) was also smaller than in "Control". There was no difference among "LIRA", "DULA" and "EMPA" groups. Treatment with MET also led to brain damage volume decrease (8.67(5.39;30.07)%), comparing with control, but it was larger than in other treatment groups. Rats in groups "LIRA" and "DULA" had less prominent neurological deficit and more points according to Garcia score (14.0(11.5;15.5) and 13.5(8.5;15.0)) comparing with "Control" (12.0(9.0;14.0)), with no difference between LIRA and DULA. Neither EMPA (12.0(9.5;14.0)), nor MET (12.0(6.5;12.5) points) diminished neurological deficit, comparing with "Control". BGL was normal in all groups.
Conclusions
GLP-1RA, SGLT-2i and MET are neuroprotective in rat transient brain ischemia and this effect is not connected with glucose metabolism. Infart-limiting effect of LIRA, DULA and EMPA is similar and is more prominent than that of MET. Only GLP-1RA diminish neurological deficit. Neuroprotective property of GLP-1RA with different action duration is similar, being most probably a class-effect.

DOI: 10.1530/endoabs.81.P509

P510

Suppressor of cytokine signaling-3 in pregnant females with or without hypertension: a case-control study

Huma Ali[1], Mubeen Ali[1], Sabah Farhat[2] & Syeda Sadia Fatima[3]
[1]Aga Khan University, Medical College, Karachi, Pakistan; [2]Aga Khan University, Department of Biological and Biomedical Sciences, Karachi, Pakistan; [2]Aga Khan University, Department of Biological and Biomedical Sciences, Karachi, Pakistan

Suppression of Cytokine Signalling-3 (SOCS-3) modulates the inflammatory pathways responsible for vascular stability by playing a role in inflammatory pathway. It acts by inhibiting the activation of Janus kinase-signal transducer and activating of transcription (JAK-STAT) pathway to transmit their information into the cell nucleus. Therefore, this study aimed to estimate SOCS-3 levels in 2 nd trimester pregnant females and correlate it with blood pressure. A case control study recruiting ($n=111$) females was conducted at the Aga Khan University Hospital, Karachi from January 2017 till February 2018. Pregnant females in their 2 nd trimester (13 to 27 weeks) between the ages of 20-35 years were included in the study. Females with any comorbid such as gestational diabetes, twin pregnancies, chronic cardio metabolic illness or infectious diseases such as HIV, HBV, HCV or females on anti-inflammatory medication, were excluded from the study. Furthermore, females with pre-existing hypertension, and complicated cases were excluded from this study. Recruited females were then classified as pregnancy-induced hypertensives or normotensive as per American College of Obstetricians and Gynecologists Guidelines. Weight, body mass index, lipid profile and blood glucose were recorded while SOCS-3 was measured by ELISA. Results showed that higher SOCS-3 levels were seen in hypertensive group (30 pg/ml) vs normotensive (16 pg/ml). Both systolic & diastolic blood pressure ($r=0.520$; $P<0.001$) ($r=0.490$; $P<0.001$) showed an independent significant positive correlation with SOCS-3 level. Although hypertensive pregnant females were obese and had a higher BMI compared to normotensive females ($P<0.05$), no difference in the lipid profile levels was observed, suggesting that SOCs-3 may act as an independent marker for blood pressure in pregnancy. Higher SOCS-3 levels were seen in hypertensive group (30 pg/ml) vs normotensive (16 pg/ml). Thus, it is safe to suggest that SOCS-3 has an association of causing high blood pressure. However, more research needs to be conducted to establish a mechanism and chronological order to these events in a pregnant female.

DOI: 10.1530/endoabs.81.P510

P511

Silent acromegaly- a case report

Hanaan Ashraf[1] & Idrees Mubarik[2]
[1]Aster DM Healthcare, Internal Medicine, Dubai, United Arab Emirates; [2]Aster DM Healthcare, Endocrinology, Dubai, United Arab Emirates

Background
Mammosomatotroph cell adenoma is rare, accounting for fewer than 2% of all pituitary adenomas and about 8% of tumors associated with acromegaly. A variety of adenomas may present with clinical signs and symptoms of GH hypersecretion including pure GH cell adenomas, mixed GH and prolactin cell adenomas, and monomorphous adenomas with primitive cells able to secrete GH and prolactin including the acidophilic stem cell adenoma and the mammosomatotroph cell adenoma. Here we present a patient with pituitary macroadenoma discovered three years ago with elevated Insulin Growth Factor-1 (IGF-1) but no clinical features of acromegaly.
Clinical presentation
A 35-year-old Caucasian nulliparous woman, known case of pituitary macroadenoma with a recent onset of hypertension presented to the clinic for routine check-up. Her initial presentation was of irregular menstruation, labs revealed high PRL and MRI confirmed pituitary macroadenoma in the year 2019. MRI′s at the time of diagnosis and further follow-ups were compared, despite the use of cabergoline the tumor size did not reduce; Hence she was evaluated for NFPA. Endocrinological workup for our patient revealed Ft4 1.10(1-2 ng/dl), prolactin 18(6 - 29.9 ng/ml), cortisol 10.3(3.7-19.4 mg/dl), OGTT values were 114/144, Hba1c 5.5, serum IGF-1 levels of 721(63.4-223.0 ng/ml), Growth hormone suppression test revealed 1 h GH of 12 ng/ml. Over the three years pituitary MRI′s were done each year and size in first, second and third MRI are 1.2X1.3X1.2 cm,1.2X1.3X 1.1 cm and 1.2X1.1X0.95 cm respectively. There was no reduction in tumor size over the past 3 years. Her serum IGF-1 levels were 3 times the normal upper limit. GH suppression test confirmed somatotroph adenoma with no symptoms of acromegaly. With these results, cabergoline was stopped, patient was advised for pituitary surgery.
Conclusion
In conclusion, the clinical spectrum of acromegaly varies from florid to subtle/no features and the diagnosis may be missed in some patients who are presumed to have clinically nonfunctioning pituitary tumors or no pituitary disorder. IGF-1 and GH should be checked in all patients of pituitary macroadenomas irrespective of initial symptoms as clinical features may take time to evolve. This recognition expands the therapeutic options to include pharmacological treatment and also provides a tumor marker to monitor the efficacy of treatment.

DOI: 10.1530/endoabs.81.P511

P512

Changes in acromegaly presentation and treatment over a three-decade period

Charlotte Aagaard[1], Amanda S Christophersen[1], Susanne Finnerup[1], Christian Rosendal[1], Peter Vestergaard[1,2], Jesper Karmisholt[1], Eigil H Nielsen[1] & Jakob Dal[1]
[1]Aalborg University Hospital, Endocrinology, Aalborg, Denmark; [2]Steno Diabetes Center, North Jutland, Aalborg, Denmark

Objective
To study time-dependent changes in the prevalence and patient characteristics of acromegaly, as well as to access the impact of changes in treatment on disease control.
Methods
A total of 107 patients with acromegaly were identified by healthcare registries and subsequently validated by patient chart review over a three-decade period (1992-2021).
Results
The prevalence of acromegaly significantly increased throughout the study period ($R^2 = 0.94$, $P < 0.001$) and was 122 cases/10^6 in 2021 whereas the annual incidence was constant 4.6 cases/10^6. The age at the first sign of acromegaly and the age at diagnosis significantly increased during the study period, whereas GH and IGF-I decreased. Incidentalomas constituted 32% of all cases diagnosed with acromegaly in the last decade. Primary surgery was used in 93% of all cases, and reoperations decreased from 24% to 10% during the three decades. The use of somatostatin analogues (SSA, 21%-48%) and second-line medical treatment (4%-20%) increased with a concomitant improvement of biochemical disease control (58%-91%).
Conclusion
The prevalence of acromegaly is higher than previously reported and the clinical presentation has shifted towards a milder phenotype. Modern treatment of acromegaly enables individualized treatment and disease control in the majority of patients.

DOI: 10.1530/endoabs.81.P512

P513

The first reported pregnancy and birth by a patient affected by Alström Syndrome: a case report

Luca Marozio[1], Gianluca Bertschy[1], Emilie M. Canuto[1], Pietro Maffei[2], Gabriella Milan[2], Francesca Dassie[2], Stefano Cosma[1] & Chiara Benedetto[1]
[1]Department of Obstetrics and Gynecology, University of Turin, Turin, Italy; [2]Department of Medicine, University of Padua, Padua, Italy

Background
Alström Syndrome (ALMS, OMIM 203800) is an ultra-rare disease caused by autosomal recessive mutations of the *ALMS1* gene (2p13). ALMS is characterized by double sensory impairment and systemic comorbidities, including hyperandrogenism in female patients. Fertility issue and conception have not been systematically studied.
Case
This case report describes the pregnancy and birth by an ALMS patient with mild phenotype, characterized by late onset visual impairment, hypertension and mild cardiac fibrosis at MRI. Patient had no history of hyperphagia, metabolic, hepatic, nephrological comorbidities and auditory disorders. From a gynecological point of view, menarche occured at the age of twelve years and the following menses was regular, she had a Tanner stage of 5 for breast development and 3 for pubic hair representation. The year before her pregnancy her hormonal evaluation on follicular phase showed normal levels of gonadotropin, prolactin, oestradiol, progesterone, testosterone, dehydroepiandrosterone-sulfate, SHBG, TSH, insulin, fasting glucose and increased levels of Dihydrotestosterone (1.33 nmol/l normal values 0.08-1.26) and androstanediol glucuronide (7.70 mg/l normal values 0.34-7.53). She had conceived spontaneously in January 2020. A rigorous clinical follow-up of maternal and fetal conditions was carried out. A weight gain of 10 kg during pregnancy was recorded. The course of pregnancy was normal up to 34 weeks gestation when preeclampsia developed. She was treated with corticosteroid as prophylaxis for respiratory distress syndrome, nifedipine, ursodeoxycholic acid, Alfametildopa and Labetalol. Due to patient's preeclampsia and elevated blood pressure, a cesarean section was performed at 35 weeks plus 3 days of gestation. A healthy male weighing 1.950 g was born. Histological examination of the placenta showed partial signs of flow obstruction, limited abruption areas, congested fetal vessels and villi, and a small single infarcted area.
Conclusion
The present case demonstrates that, although hyperandrogenism and comorbidities, conceiving is possible for ALMS patients. A particular attention can be observed for management of systemic comorbidities.

DOI: 10.1530/endoabs.81.P513

P514

Superior vena cava syndrome associated with graves' disease

Himmet Durmaz[1], Unzile Arifoglu[2], Mustafa Ömer Yazıcıoglu[3], Muhammed Sacıkara[2], Narin Nasıroglu İmga[2], Oya Topaloglu[1], Reyhan Ersoy[1] & Bekir Cakir[1]
[1]Department of Endocrinology and Metabolism, Ankara Yildirim Beyazit University Faculty of Medicine, Ankara Bilkent City Hospital, Ankara, Turkey; [2]Department of Endocrinology and Metabolism, Ankara Bilkent City Hospital, Ankara, Turkey; [3]Department of General Surgery, Ankara Bilkent City Hospital, Ankara, Turkey

Introduction
Goiter means that the thyroid gland is larger than the normal size for the patient's age and gender. Some of the causes of goiter are iodine deficiency, thyroid nodules, Graves' disease(GD). Goiter, hyperthyroidism, ophthalmopathy and dermopathy can be seen in GD. Compression symptoms due to goiter (dyspnea, dysphagia, superior vena cava syndrome) are also seen. Here, we will present a case of GD with superior vena cava syndrome.
Case
A 50-year-old male patient, who had been using methimazole for 6 years due to hyperthyroidism, applied to our outpatient clinic with swelling in the neck. The patient was taking methimazole 10 mg/day. On physical examination, he had goiter, bilateral venous collaterals in the neck, and inactive Graves' ophthalmopathy. Pemberton's sign was positive. In laboratory tests, TSH, fT4, fT3, antiTPO, antiTG, TSH receptor antibody were: <0.008 mU/l, 1.01 ng/dl, 10.6 ng/l, >13000 U/l(<60 negative), 724 IU/ml (<1.3 negative), 34.3 U/l (≤ 1 negative), respectively. In the thyroid ultrasound, the dimensions of the right lobe were 33.9x33.4x73.4 mm, the dimensions of the left lobe were 35.3x50x78.5 mm, the dimension of the isthmus was 20 mm, no thyroid nodule was observed. The thyroid gland showed retrosternal extension. Thyroid scintigraphy was consistent with GD. Computed tomography of the neck and thorax was performed to evaluate the differential diagnosis and cervical region: The dimensions of both thyroid lobes have increased considerably, extending to the paraesophageal, paratracheal, and intrathoracic retrosternal areas, and significant extrinsic compression of the larynx and esophagus was observed. In addition, bilateral subclavian veins were pressed by the thyroid gland, and diffuse dilated venous structures were observed in the skin-subcutaneous part of the anterior of the thyroid. Varicose dilated veins were observed in the anterior mediastinum. (Secondary to subclavian vein compression?). No pathological finding was detected in the lung parenchyma. Bilateral total thyroidectomy was performed. Its pathology was reported as diffuse toxic hyperplasic thyroid gland. Venous collaterals in the neck of the patient disappeared in the postoperative period. Clinical improvement was observed.
Conclusion
The most common cause of hyperthyroidism is GD. Compression symptoms due to diffuse hyperplasia of the thyroid gland may be seen. In particular, the retrosternal extending goiter may cause superior vena cava syndrome by compressing the vascular structures. The most common cause of superior vena cava syndrome is malignancy. GD should also be considered in the differential diagnosis of superior vena cava syndrome. Improvement in this situation is expected with thyroidectomy.

DOI: 10.1530/endoabs.81.P514

P515

Parathormone washout in cytology of Suspicious for Follicular Neoplasm

Himmet Durmaz[1], Burçak Cavnar Helvacı[2], Nagihan Beştepe[2], Ayşegül Aksoy Altınboğa[3], Ahmet Dirikoc[1], Oya Topaloglu[1], Reyhan Ersoy[1] & Bekir Cakir[1]
[1]Department of Endocrinology and Metabolism, Ankara Yildirim Beyazit University Faculty of Medicine, Ankara Bilkent City Hospital, Ankara, Turkey; [2]Department of Endocrinology and Metabolism, Ankara Bilkent City Hospital, Ankara, Turkey; [3]Department of Medical Pathology, Ankara Yildirim Beyazit University Faculty of Medicine, Ankara Bilkent City Hospital, Ankara, Turkey

Introduction
The risk of malignancy in thyroid nodules is reported by the Bethesda system by performing fine needle aspiration biopsy (FNAB). Atypia of undetermined significance(AUS) or follicular lesion of undetermined significance(FLUS)(Bethesda 3) and suspicious for a follicular neoplasm (Bethesda 4) create uncertainty about treatment and follow-up. Molecular tests, ultrasonographic features of the nodules, and calcitonin level help us for this uncertainty. Here, we will present a patient whose FNAB cytology was Bethesda 3 and Bethesda 4.

Case
A 53-year-old female patient was admitted to our outpatient clinic after detecting a thyroid in neck ultrasound. She had familial Mediterranean fever, osteoporosis, and renal transplantation (5 years ago). In addition, the patient stated that she had been operated on the parathyroid gland while she was receiving dialysis treatment. There was no document related to parathyroid surgery. In laboratory tests, thyroid function tests, calcitonin, calcium levels were normal. 25-OH vitamin D, parathormone level, creatinine, eGFR were 14 ng/ml, 152 pg/ml, 1.51 mg/dl, 39 ml/minute respectively. Secondary hyperparathyroidism due to vitamin D deficiency was considered. On thyroid ultrasound, a hypoechoic nodule that containing cystic degeneration areas was observed adjacent to inferior carotid artery in the right lobe. The dimensions of nodüle were 9.7x11.4x13.7 mm. FNAB was reported as Bethesda 3. The second FNAB cytology was also reported as Bethesda 4. Molecular testing could not be performed in our hospital. The microscopy of FNAB revealed "some of the cells were small, round, monotonous nuclei with pale cyanophilic cytoplasm with unclear borders". No uptake suggestive of parathyroid lesion was observed in parathyroid scintigraphy. Third FNAB cytology was nondiagnostic; Parathormone washout was 525 pg/ml. Due to the high suspicion of parathyroid lesion, fourth FNAB and diluted PTH washout were performed. Fourth FNAB cytology was Bethesda 3, diluted parathormone level was 103871 pg/ml. The lesion was evaluated as intrathyroidal lesion (adenoma or parathyroid seeding due to surgery). Follow-up was planned for the patient.
Conclusion
In parathyroid lesions evaluated as thyroid nodules, FNAB cytology and microscopy give us an idea in terms of intrathyroidal parathyroid lesion. Parathyroid scintigraphy also does not always show uptake. In this situation, PTH washout can be done. If the ultrason features, FNAB microscopy and PTH washout are inconsistent, diluted PTH washout may provide accurate results due to possible hook effect. In addition, intrathyroidal parathyroid seeding should also be kept in mind in patients who have undergone parathyroid surgery for tertiary hyperparathyroidism.

DOI: 10.1530/endoabs.81.P515

P516

Myxedema coma: case report and literature review

Renata Cassitas Mendonça[1], Laura Vilas Boas[2], Thielsen Cardoso da Silva[2], Laura Maranho Ribas[1], Tamila Sohn Fagundes[1], Taciane Elizabeth Cesca[2] & Mirnaluci Paulino Ribeiro Gama[1]
[1]Hospital Universitário Evangélico Mackenzie, Brazil; [2]Evangelical Mackenzie Faculty of Parana, Brazil

Introduction
Myxedematous coma is a rare endocrine emergency that settles in the absence of appropriate treatment for hypothyroidism for a long period. The severe and chronic reduction of serum thyroid hormones culminates in the insufficiency of compensatory mechanisms that maintain the physiological homeostasis of the organism. The clinical condition is severe, commonly associated with hypoxemia, hypercapnia, hypothermia, reduced cardiac output, and altered mental status.
Case report
A 60 years old female patient with a previous history of thyroidectomy, was admitted at the Hospital hemodynamically unstable, with bradycardia, hypothermia, sedated with midazolam 10 mL/hr, and fentanyl 10 mL/hr, RASS scale – 2 (Richmond Agitation Sedation Score), and miotic pupils. Blood pressure 115x80 mmHg with noradrenaline 10 mL/hr, heart rate 52 bpm, and oxygen saturation 94% on mechanical ventilation. Due to high suspicion of myxedematous coma, was administered an attack dose of levothyroxine (500 mg/day) via a nasogastric probe in the first three days with hydrocortisone 100 mg every 8 h. Levothyroxine dose was maintained at 250 mg/day by a nasogastric probe, and hydrocortisone 50 mg intravenous every 8 h. Laboratory: amylase (160 UI/l) and lipase (250 UI/k), TSH 26 (0.3 and 4.0 mU/l) and free T4 <0.017 (0.9 to 1.8 ng/dl). Chest tomography: massive pericardial and pleural effusion, as well as parenchymal opacities in the outstanding portions and septal thickening inferring pulmonary edema. X-ray: increase cardiothoracic ratio caused by pericardial effusion. Abdominal computerized tomography: ascites, more evident in the upper abdominal (peri-hepatic) and liquid infiltration of intra and extraperitoneal fat by generalized anasarca. She was unstable during the hospitalization period, presented with progressive hypoxemia and hemodynamic instability. Thus, due to suspicion of pulmonary thromboembolism, in addition to the adjustment of vasoactive drugs, full dose enoxaparin was initiated. Meantime, due to the severe condition of refractory hypotension the measures instituted, the patient progresses to death on his twenty-second day of hospitalization.
Conclusion
Although myxedematous coma has an arduous prognosis, there are still gaps regarding the best medication management. It emphasizes the need for studies for the development of a scientific basis that standardizes the most appropriate pharmacological treatment to be instituted. Since there is no consensus on the best form of monotherapy - T4 or in combination with T3. Furthermore, there is a lack of data in the literature to corroborate the effective dose of levothyroxine orally in a myxedematous coma in places where there is no IV medication, such as the situation of this clinical case.

DOI: 10.1530/endoabs.81.P516

P762

Do polymorphisms of the glucocorticoid and mineralocorticoid receptors play a role in adrenal crises?

Irina Chifu, Freytag Janik, Sabine Herterich, Weber Heike & Stefanie Hahner
University Hospital Würzburg, Würzburg, Germany

Introduction
Polymorphisms of the glucocorticoid (NR3C1) and mineralocorticoid receptor (NR3C2) have been linked to the regulation of HPA-axis and to glucocorticoid sensitivity. We investigated whether NR3C1 and NR3C2 polymorphisms correlate with the occurence of adrenal crises (AC) in patients with primary adrenal insufficiency (PAI).
Material and methods
We investigated 100 patients with PAI (70% women, mean age 51 ± 15 years). DNA was extracted from whole-blood and NR3C1 and NR3C2 polymorphisms were genotyped by PCR and MALDI-TOFF mass spectrometry. Results were correlated with history of AC (number of events since first diagnosis and number of events per patient years), replacement therapy, HbA1c and 24-h blood pressure profile.
Results
Three NR3C1 polymorphisms (rs6198, rs17100289, rs4912911) and one NR3C2 (rs5522) polymorphism were significantly associated with a higher prevalence of AC. For NR3C1 rs6198, AC occured more often in C allele carriers (66% CC/CT vs 44% TT, $P=0.04$, OR 2.5 95% CI 1.0-6.0). For NR3C1 rs17100289, patients with AA genotype experienced more frequent AC (61% AA vs 40% TT/TA, $P=003$, OR 2.4 95% CI 1.0-5.5) and exhibited lower HbA1c levels (5.3 (4.8-8.2) AA vs 5.7 (4.6-8.1) TT/TA, $P=0.03$) and higher degrees of noctural blood pressure dipping (-14% (-26, -5) AA vs -8% (-19, 7) TT/TA, $P=0.02$). For NR3C1 rs4912911, AC occured more often within AA genotype (61% AA vs 38% GA/GG, $P=0.021$, OR 2.6 95% CI 1.1-5.8). For NR3C2 rs5522, AC occured more often in C allele carriers (74% TC/CC vs 44% TT, $P=0.02$, OR 3.5 95%CI 1.2-10.6).
Conclusion
We identified several NR3C1 and NR3C2 polymorphisms that are associated with a higher incidence of AC. The identified NR3C1 polymorphisms have been shown to decrease glucocorticoid sensitivity, whereas NR3C2 rs5522 seems to interfere with the glucocorticoid stress response. Our preliminary data suggests that inter-individual differences in glucocorticoid sensitivity may contribute to increased susceptibility to AC.

DOI: 10.1530/endoabs.81.P762

P763

Actions taken for prevention of adrenal insufficiency in adult patients who are at risk - audit report

Jayamalee Jayaweera, Sara Sheikh, Rakitha Higgoda, Karthayani Kundrapu, Bilal Jajah & Anupam Brahma
West Suffolk Hospital, Bury St Edmunds, United Kingdom

Background
Adrenal insufficiency (AI) is can be often under recognised condition in the clinical practise which can potentially result in adrenal crisis or even death if not treated properly. Identification of patients who are at risk of developing AI is important in order to take appropriate steps in minimising unwanted incidents.
Objectives
Study aims to assess whether we identify patients who are at risk of AI and take recommended precautions.
Method
We performed a single centred retrospective audit at West Suffolk hospital in the United Kingdom using electronic health records to identify 57 adult patients who were on long term steroid therapy. This included oral, inhaled or injected steroids

for a period exceeding 4 weeks, being prescribed by different specialties (respiratory, rheumatology, haematology, renal gastroenterology) and patients who already had the diagnosis of hypopituitarism and Addison′s disease. The records were then searched from 2016 to 2022 and data was collected on demographics, whether appropriate advice had been given and whether they were managed appropriately during inpatient stays.
Results
Over two thirds (64.3%) of patients had no alert on their record to state they were at risk of AI. Only one patient had documentation of having received a steroid emergency card. Just 22.8% of patients were documented as having an emergency intramuscular hydrocortisone pen. Documented 'sick day rules′ advice was not given to almost two thirds of patients (67.9%). In contrast we noted 100% of patients who had the diagnosis of hypopituitarism and being followed up at endocrine clinics had been given sick day rules. Nearly one fifth of our study population comprised patients with a former diagnosis of hypopituitarism and Addison′s disease. Just less than a half of patients who had surgery or invasive procedure had been appropriately managed with pre-operative steroids. Finally, 17.5% of patients had been admitted to hospital in adrenal crisis at least once.
Conclusion
This audit report highlights the importance of raising awareness of AI among clinicians across different subspecialties and making relevant recommendations to prevent any undesired events.

DOI: 10.1530/endoabs.81.P763

P764

Hypertension in Pheochromocytoma and paraganglioma : Characteristics, treatment and outcomes

Nada Derkaoui[1], Achwak ALLA[1], Rania El Amel[1], Rami Imane[1], Siham ROUF[1] & Hanane Latrech[1]
[1]Mohamed VI University Hospital Center Oujda - Faculty of Medicine and Pharmacy Oujda, Endocrinology Diabetology and Nutrition Department, Oujda, Morocco

Introduction
Pheochromocytomas and paraganglioma are neuroendocrine tumors that arise from the chromaffin cells of the adrenal medulla or originate from the autonomic nerve ganglia. Hypertension in patients with PPGL is the most frequent symptom and can be responsible of lethal cardiovascular complications. The aim of our work is to describe the clinical characteristics of hypertension in PPGL, the treatment and the outcomes after surgical treatment.
Materials and methods
Our study is retrospective descriptive, involving 34 patients (29 patients with pheochromocytoma and 5 patients with functional paraganglioma) followed in our Endocrinology-Diabetology and Nutrition Department of Mohammed VI University Hospital Center in Oujda, Morrocco.
Results
The mean age of our patients was 47 ± 17.9 years (15-81) with a sex ratio H/F of 0.4. History of hypertension was present in 58.8% of cases of which (55%) had uncontrolled treated hypertension, and (45%) had well controlled hypertension under antihypertensive medication. Hypertension was diagnosed at the same time as the tumor in 14.3% of cases. Half of our patients (47%) had permanent hypertension, 11.7% had paroxysmal hypertension and 11.7% experienced orthostatic hypertension. 24-h urinary metanephrine level was elevated in 76% of the cases, and 24 h urinary normetanephrine level was elevated in 84% of the cases. Imaging revealed unilateral abdominal PPGL in 73% of cases, bilateral pheochromocytoma in 11.7% of cases and cervical PGL in 6% of cases. The mean size of the tumor was 51.4 mm $\pm$ 29.4. Before surgery, all of our hypertensive patients received α1blockers preparation 15 days before surgery. Peroperatively, only 12% of patients presented hypertensive peaks without further complications. Good blood pressure control was achieved postoperatively and antihypertensive medication was reduced in all of our hypertensive patients with good clinical and biological outcomes.
Discussion–Conclusion
Although rare, PPGL can be dangerous due to the excess of catecholalmines and cardiovascular complications. Treatment of hypertension before, during and after the removal of the tumor is mandatory to avoid complications. The preoperative management of hypertension usually includes treatment with α1blockers at least 10 to 14 days before surgery, with the addition of beta blockers when necessary. Surgical removal of functional PPGL is the main treatment.
PPGL : Pheochromocytoma and paraganglioma

DOI: 10.1530/endoabs.81.P764

P765

Multiple vertebral fractures following ibrutinib therapy in a patient with B-cell chronic lymphocytic leukemia

Jelena Andric[1], Marija Ivic[2], Özren Jaksic[2], Renata Huzjan Korunic[3], Darko Perovic[4] & Vlatka Pandzic Jaksic[1]
[1]Dubrava University Hospital, Department of Endocrinology, Zagreb, Croatia; [2]Dubrava University Hospital, Department of Hematology, Zagreb, Croatia; [3]Dubrava University Hospital, Department of Radiology, Croatia; [4]Dubrava University Hospital, Department od Orthopaedics and Traumatology, Croatia

Some hematologic malignancies might increase the risk of fractures due to intrinsic factors of the disease but also because of the treatment with steroids or chemotherapy. The direct impact of novel targeted agents on the development of osteoporosis in these patients has not been recognized yet. A 64-years old female patient with B-cell chronic lymphocytic leukemia (B-CLL) has been followed for four years with no other comorbidities. In order to measure the burden of the disease consecutive CT scans were performed. Two years ago, she underwent endocrinological evaluation because of incidental adrenal adenoma. Hypercortisolism and other endocrine disorders were excluded. She has never experienced a bone fracture before and no radiographic vertebral fractures were present. According to Fracture Risk Assessment Tool her 10 years probability of fractures with bone mineral density and adjusted for trabecular bone score was 5.2% for major osteoporotic fracture and 0.7% for hip fracture. Her B-CLL progressed with lymph nodes enlargement and first line therapy with ibrutinib – bruton tyrosine kinase (Btk) inhibitor was started. Three months later the patient presented with severe lumbar pain that occurred suddenly without clear precipitating factor. Radiologic examinations were performed and multiple osteoporotic lumbar vertebral fractures were found (Genant′s grade 2 in L2 vertebra and grade 1 in L1, L3 and L4 vertebrae). We repeated endocrinological investigation. Vitamin D was reduced (44 nmol/l) but no evident secondary causes of osteoporosis were revealed. Her bone mineral density was significantly deteriorated. We deferred vertebroplasty and the treatment with teriparatide and cholecalciferol was introduced. Increased risk of axial fractures was already observed in B-CLL patients and infiltration of bone marrow with leukemic cells has been recently shown to impair osteoblastogenesis and promote osteoclastogenesis. Ibrutinib up to now has not been labeled as a drug that could significantly impair bone health. Early experimental studies suggested that it could even inhibit osteoclast differentiation and function. However, recent observations recorded signals of potential increase of fractures with ibrutinib therapy. Although no cause and effect could be claimed, the occurrence of multiple osteoporotic vertebral fractures shortly after the ibrutinib therapy was introduced, suggests that this might play a role in bone damage and warrants further studies.

DOI: 10.1530/endoabs.81.P765

P766

Diagnostic process in a lipodystrophic syndrome suspition, a clinical case

Pablo Ferreira[1], Paula Martínez de la Cruz[2], Ane Miren Azkutia Uribe Echevarría[1], Amir Shabaka Fernández[3], Pablo Lois Chicharro[1], Sandra Carolina Doejo Marciales[1], Solange Fabiola Barra Malig[1], Cristina Garmendia Fernández[2], Francica Almodóvar Ruiz[1] & Juan José Gorgojo Martínez[1]
[1]Hospital Universitario Fundación Alcorcón, Endocrinology, Metabolism and Nutrition, Alcorcón, Spain; [2]Hospital Universitario Fundación Alcorcón, Internal Medicine, Alcorcón, Spain; [3]Hospital Universitario Fundación Alcorcón, Nephrology, Alcorcón, Spain

The lipodystrophic syndromes are a heterogeneous group of congenital or acquired disorders characterized by either complete or partial lack of adipose tissue with the apparent accumulation of fat in other regions of the body. Their prevalence is low and ranges from 1:200000/500000 and they usually suffer metabolic abnormalities associated with the abnormal distributition of fat such as severe insulin resistance with acantosis and diabetes, progressive liver disease along with muscle hipertrophy, internal megaly, hirsutism, developmental delay or proteinuric renal dammage. The diagnosis of these síndromes is thus very complex and demmand multiple studies. We report a case of suspected lipodistrophy that we follow in our center in Alcorcon (Madrid) in the year 2022.
Case Report
36 year old woman, born in Colombia, with unique background of diabetes mellitus cataloged as type 2, diagnosed at age 18 with no familiar history and

treated with insulin along with severe acantosis nigricans and PCOS. Admitted under episode of hyperosmolar hyperglucemic síndrome secondary to poor acces to treatment, extended folliculitis and urinary infection due to K. pneumoniae. Good progress under emergent insulin and antibiotic treatment. We detect a particular phenotype consisting of prominent muscularity and low peripheric adipose tissue, severe acantosis nigricans plates, rough facial traits and hirsutism. There was therefore a suspition of a syndrome that could include all the manifestations depicted, specifically lipodystrophic síndrome. We deepened in the study of diabetes with a 12% HbA1c determination but normal C-Peptide, pancreatic autoinmunity and pancreatic imaging with abdominal tomography that on the other hand revealed several dermic thickening, low subcutaneous celular tissue, gastric and renal lypomas. Greater find of difuse adenopathies in all the abdominal cavity though normal proteinogram without monoclonal pike and normal urine inmunofixation. 24-h urianalsys demonstrated nefrotic proteinuria in context of diabetic nephropaty in a renal biopsy. Negative HIV study. Due to clinical stability the patient is discharged, with presumptive diagnosis of adquired generalized vs partial congenital lipodystrophy, only remaining the leptin determination.
Conclusion
The lipodystrophic syndromes though rare entities, must be suspected when several metabolic disorders combine with phenotipic features i.e lack of peripheral adipose tissue. The proper study of the etiology and the secondary alterations is crutial to assure the good treatmente and prognosis of these patients.

DOI: 10.1530/endoabs.81.P766

P767

Correlation of adiponectin and resistin with atherogenic markers in insulin resistant and non-insulin resistant adolescent women with polycystic ovary syndrome

Aleksandra Atanasova Boshku & Daniela Ivanova Panova
University Clinic of Gynecology and Obstetrics, Faculty of Medicine, Ss. Cyril and Methodius University Skopje, Skopje, North Macedonia

Aim
To evaluate adiponectin and resistin levels and their relationship with various biochemical and metabolic and atherogenic parameters markers, as well as their correlation, and to investigate its contribution in pathogenesis of insulin resistance in cohort women with PCOS and of insulin resistance as well as in non-insulin resistant women with PCOS. Methods: This study was designed as a cross-sectional and involves 80 premenopausal women. Of these patients, 63 females have met the criteria for PCOS (59 insulin resistant, 28 non-insulin resistant). We assessed anthropometric indices of obesity –waist and hip circumference, waist to hip ratio, serum glucose, insulin, total cholesterol, HDL-cholesterol, triglycerides, FSH, LH, E2, testosterone, adiponectin and resistin. Body mass index, waist to hip ratio, HOMA-IR, LDL-cholesterol, and adiponectin to resistin ratio were calculated. Results: Insulin resistant PCOS woman had significantly lower levels of adiponectin compared to non-insulin resistant PCOS women, and controls. Resistin levels were higher in IR-PCOS, but without statistical significance. Adiponectin showed significant positive correlation with LH, HDL-C, and negative correlation with BMI, insulin, HOMA-IR and triglycerides. Resistin correlated positively with BMI and WC. A/R was significantly higher in insulin resistant PCOS women compared to non-insulin resistant and control women. Conclusions: These results suggest that PCOS women were at higher metabolic and atherogenic risk as compared to the healthy women, and also more pronounced in the insulin-resistant group. Correlations of adipokines with insulin resistance suggest their involvement of adipokines in modulation of insulin action in PCOS women.

DOI: 10.1530/endoabs.81.P767

P768

Insulin-Like Growth Factor-I might be a predictor for severe nonalcoholic fatty liver disease in morbidly obese patients

Seda Turgut[1], Didem Acarer Bugün[1], Hakan Seyit[2], Naim Pamuk[1], Hamide Pişkinpaşa[1], Evin Bozkur[1], Mehmet Karabulut[2] & İlkay Çakır[1]
[1]University of Health Science Bakırköy Dr. Sadi Konuk Training and Research Hospital, Endocrinology and Metabolism, Istanbul, Turkey; [2]University of Health Science Bakırköy Dr. Sadi Konuk Training and Research Hospital, General Surgery, Istanbul, Turkey

Aim
To compare the IGF-1, metabolic and clinical parameters among the ultrasonographically classified NAFLD groups, to examine the effect of weight loss on metabolic parameters and determine the factors that may predict the NAFLD severity in morbidly obese patients who underwent bariatric surgery.
Method
This descriptive cross-sectional study was conducted in 316 morbidly obese patients (250 females, 66 males). The data of patients before and 1st year after bariatric surgery were included in the study. According to the NAFLD assessment, patients were classified as normal (Group 1, $n=57$), mild and moderate (Group 2, $n=219$), or severe (Group 3, $n=40$). IGF-1 standard deviation score (SDS) levels were calculated according to age and gender. Preoperative and postop 1st-year clinical and metabolic parameters and factors that could predict the presence and severity of NAFLD were evaluated in all groups.
Results
IGF-1 levels were significantly associated with severe NAFLD compared with the normal group, and the significance remained between the same groups when IGF-1 levels were standardized as SDSIGF1. Moreover, liver diameter explained 50% of severe NAFLD than the normal group and %13 of severe NFLAD compared to mild-moderate NAFLD. FPG, ALT, AST, and GGT were also significant predictors for severe NAFLD compared to the normal and mild-moderate NAFLD groups.
Conclusion
Together with liver diameter, FPG, AST, ALT, and GGT, IGF-1 is among important predictors of NAFLD in bariatric surgery candidate morbidly obese patients. Further studies are needed to validate the clinical utility of IGF-1 in the presence and staging in NAFLD patients.

DOI: 10.1530/endoabs.81.P768

P769

Coexistence of hypopituitarism caused by Sheehan′s syndrome and Hashimoto′s thyroiditis. A case report, review of literature.

Marjeta Kermaj[1], Irsa Zaimi[2], Mirjeta Guni[3], Adela Shkurti[4,5], Thanas Fureraj[1] & Agron Ylli[6]
[1]UHC "Mother Tereza", Endocrinology, Tirana, Albania; [2]Fier Regional Hospital, Endocrinology, Fier, Albania; [3]American3 Hospital, Endocrinology, Tirana, Albania; [4]Vila Maria, Endocrinology, Tirana, Albania; [4]Vila Maria, Endocrinology, Tirana, Albania; [1] UHC "Mother Tereza", Endocrinology, Tirana, Albania

Introduction
Hypopituitarism due to Sheehan′s syndrome is a rare complication and its diagnosis is often overlooked. The vast majority of people with hypothyroidism have primary hypothyroidism, often due to Hashimoto's thyroiditis. Coexistence of hypopituitarism and primary hypothyroidism, may accelerate clinical manifestations, mainly those associated with hypothyroidism. Hashimoto′s Thyroiditis with concomitant hypopituitarism is rare but has been described previously, but there are no reports of Hashimoto′s Thyroiditis occurring with Sheehan′s syndrome.
Case report
In this case study, we report a patient with Hashimoto′s Thyroiditis associated with Sheehan′s syndrome. Our case is a 38 –year-old female patient, presented with generalized fatigue, weakness, pain in the muscles of the lower extremities and other nonspecific complaints which were aggravated in recent months. She was consulted with various doctors but with the medication she received, there was no improvement until she presented in poor condition in emergency unit. She gave birth 7 years ago; after delivery she had a history of prolonged bleeding, amenorrhea and inability to lactate. Her physical examination revealed pale, dry, cold, rough skin, sluggish speech and thick voice, decreased body hair. Her laboratory evaluation showed, low levels of free thyroxin (FT4) and free triiodothyronine (FT3), high normal level of thyrotropin stimulating hormone (TSH). Thyroid antibodies were high level. She had hypogonadotropic hypogonadism, hypoprolactinemia, hypocortizolism with low level of adrenocorticotropic hormone and growth hormone deficiency, normochromic normocytic anemia, high level of LDL-cholesterol. Her magnetic resonance imaging was empty sella. Her thyroid ultrasonography revealed aspect of chronic thyroiditis. Our diagnosis was Hypopituitarism due to Sheehan′s syndrome co-existing with Hashimoto′s Thyroiditis. She was treated with hormone replacement and she was in a good condition 2 months later.
Conclusion
A high index of suspicion is crucial for the early diagnosis of the coexistence of hypopituitarism due to Sheehan′s syndrome and Hashimoto′s thyroiditis that is a rare condition in clinical practice, to prevent long-term morbidity.

DOI: 10.1530/endoabs.81.P769

P770

A patient with acromegalic heart disease

Mehdi Houssein[1], Kubra Turan[1], Ahmet Temizhan[2], Belma Tural Balsak[1], Abbas Ali Tam[1], Oya Topaloglu[1], Reyhan Ersoy[1] & Bekir Cakir[1]
[1]Ankara City Hospital, Department of Endocrine and Metabolic Diseases, Ankara, Turkey; [2]Ankara City Hospital, Department of Cardiology, Ankara, Turkey

A 36 years of old patient was admitted to the intensive care unit of cardiology when he experienced palpitations and orthopnea. The patient's complaints started about 2 years ago as syncope and sudden shortness of breath. Thorax CT showed pleural effusion and increased cardiothoracic index. Findings on ECHO were : Ejection fraction 35%, severe mitral regurgitation and global hypokinesia. Coronary angiogram showed a fibrocalcific plaque noted in in the distal LAD. The patient was started on Furossemide, spironolactone, isosorbide mononitrate. Despite the treatment, the patient's complaints gradually increased and over the course of the next 24 months, the patient was repeatedly hospitalised due to heart failure, and his medication was adjusted several times. Two years later, the patient was admitted to our center with the diagnosis of acute heart failure. A decrease in ejection fraction was detected in the new echocardiography (%10), and no further clinical improvement was seen, the decision was then taken to initiate treatment with levosimendan and noroadrenaline. Dilated cardiomyopathy was observed with cardiac MRI. He was consulted to the endocrine departement because of suspected acromegaly. When he was evaluated, he complained of shortness of breath, arthralgia and increasing shoe size. Physical examination was positive for acral growth, nose widening, and prognathism. GH and IGF-1 levels were increased at diagnosis (table 1), the baseline and peak GH concentrations were 8.74 and 34.4 ng/ml during 75-g OGTT, showing paradoxical increases in GH (table 2). Pituitary MRI showed a non-invasive, intrasellar, macroadenoma (fig1). The diagnosis made was: Acromegaly due to growth hormone secreting pituitary macroadenoma leading to dilated cardiomyopathy. His family history was negative, but due to his young age and aggressive clinical course, the patient was screened for AIP gene mutation; a germline AIP mutation was not identified. TSS was scheduled, and primary medical treatment with sandostatin lar 20 to improve the patient's condition. However, the patient developed cardiogenic shock and unfortunately before surgery and before assessment of response to therapy.

Table 1

Hba1c (%)	6.4
P (mg/dl) (2.4-5.1)	5.3
Cortisol (μg/dl)	10.6
ACTH (pg/ml) (Sabah 07:00-09:00 <46)	50.2
Testosterone (ng/dl) (164-783)	130
FSH (mIU/ml)	6.4
LH (mIU/ml)	5.6
PRL (ng/ml)	17.7
GH (ng/ml) (0.05-3)	25
IGF-1 (ng/ml) (75-212)	359

Table 2

Minute	**0.**	**30.**	**60.**	**90.**	**120.**
Glucose	80	112	162	198	173
GH	8,74	10,4	34,4	20,9	14,3

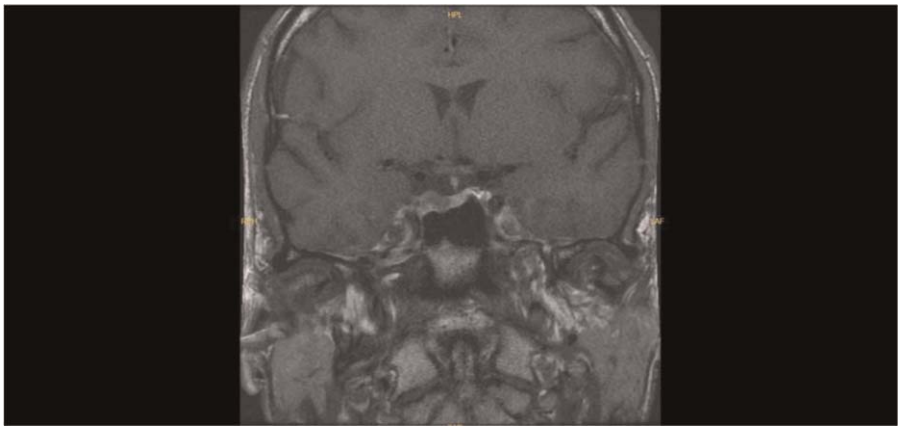
DOI: 10.1530/endoabs.81.P770

P771

SRSF6 (Serine/arginine-Rich Splicing Factor 6) is a novel factor regulating androgen receptor signalling in prostate cancer cells

Antonio J. Montero-Hidalgo[1,2,3,4], Juan Manuel Jimenez-Vacas[1,2,3,4], Ana de la Salud De la Rosa-Herencia[1,2,3,4], Vicente Herrero-Aguayo[1,2,3,4], Enrique Gómez-Gómez[1,3,4,5], Antonio Carlos Fuentes-Fayos[1,2,3,4], Manuel David Gahete-Ortiz[1,2,3,4] & Raul Miguel Luque-Huertas[1,2,3,4]
[1]Maimonides Institute of Biomedical Research of Cordoba (IMIBIC), Córdoba, Spain; [2]University of Cordoba, Department of Cell Biology, Physiology and Immunology, Cordoba, Spain; [3]Reina Sofia University Hospital (HURS), Cordoba, Spain; [4]CIBER Physiopathology of Obesity and Nutrition (CIBERobn), Cordoba, Spain; [5]Reina Sofia University Hospital (HURS), Urology service, Cordoba, Spain

Prostate cancer (PCa) represents the most diagnosed tumour pathology in developed countries among men population. The main pharmacological approach to treat this pathology is based on the blockade of the androgen receptor signalling pathway, commonly known as androgen-deprivation therapy. However, some of the patients does no longer respond to this therapy, therefore developing castration-resistant prostate cancer (CRPC), the most aggressive phenotype of this pathology, which remains lethal nowadays. Therefore, new molecular targets with potential to identify more effective therapeutic strategies are extremely needed. In this sense, alteration of RNA-splicing process has raised as a new hallmark of cancer. Herein, we studied the presence and pathophysiological role of SRSF6, a splicing factor that has been reported to have an oncogenic potential in other tumor-types (e.g., ovarian, lung and colon). To that aim, SRSF6 levels were interrogated by quantitative real-time PCR (mRNA levels) and immunohistochemistry (protein levels), in two well-characterized cohorts: 1) fresh PCa ($n=42$) and control ($n=9$) samples, and 2) formalin-fixed, paraffin-embedded PCa ($n=84$) and non-tumour adjacent tissue ($n=84$) samples. Additionally, functional and mechanistic assays were performed in different cell models [PCa cells (LNCaP, 22Rv1, DU145, and PC-3) and non-tumour prostate cells (PNT2)] in response to SRSF6 silencing (using a specific siRNA). Moreover, the effect of SRSF6 *in vivo* silencing was also tested using a xenograft mouse model. Finally, we also analysed *in vitro* the putative relationship between the expression levels of SRSF6 with the androgen signalling and the resistance to androgen-deprivation therapy. Our results revealed that SRSF6 is upregulated (at mRNA and protein levels) in PCa samples and its levels are directly associated to key clinical and molecular parameters of PCa aggressiveness [e.g., Gleason grade, androgen-receptor (AR) signalling pathway]. Furthermore, the silencing of SRSF6 significantly decreased critical functional aggressiveness parameters in PCa cells (i.e. proliferation and migration rates and tumorsphere formation). Mechanistically, SRSF6 silencing altered the splicing process of AR, by reducing specifically the oncogenic splicing variant AR-V7. Consistently, a preclinical approach showed that the treatment with SRSF6 siRNA reduced the size of 22Rv1-derived tumours, impacting key molecular pathways (e.g., AR signalling). Taken together, our results suggest that SRSF6 impact AR signalling by



dysregulating AR-V7 splicing and that its targeting could represent a novel and promising therapeutic strategy for the treatment of advanced PCa.

DOI: 10.1530/endoabs.81.P771

P772

Thionamides-induced agranulocytosis in a patient with previous hematological disease: a case report

Tamila Sohn Fagundes[1], Laura Vilas Boas[2], Thielsen Cardoso da Silva[2], Laura Maranho Ribas[1], Renata Cassitas Mendonça[1], Letícia Peon Train Nicoluzzi[2], Maria Roberta Bianchini Fernandes[2] & Mirnaluci Paulino Ribeiro Gama[1]
[1]Hospital Universitário Evangélico Mackenzie, Brazil; [2]Evangelical Mackenzie Faculty of Parana, Brazil

Introduction
The treatment of thyroid diseases with thionamides can cause agranulocytosis a potentially fatal side effect. The manifestations resulting from such a condition include, in most cases, infections that, if not treated immediately, have a high risk of septicemia. Therefore, the clinical presentation includes fever of unknown origin and infections such as pneumonia, tonsillitis, and abscesses. Most patients who do not receive immediate medical intervention progress to septicemia, a fact that shows the relevance of early diagnosis and adequate management
Case report
A 38-year-old female patient had Chronic Myeloid Leukemia without follow-up and treatment. She developed severe neutropenia induced by thionamide used to control hyperthyroidism. Laboratory tests performed on admission at the Hospital showed Hb 8.6 g/dl, pancytopenia with worsening leucopenia: leukocytes 720/mm3, absolute segmented count 9 mm3, 0/mm3 (zero) basophils, 0 /mm3 (zero) blasts, and 670/mm3 lymphocytes, TSH 0.029 mU/l (normal 0.4-4.5 mU/l) and free T4 4.93 ng/dl (normal 0.7-1.8 ng/dl). Autoantibodies against TSH receptor (TRAb) were negative The absence of evidence of transformation into accelerated and blastic phases of Chronic Myeloid Leukemia, positive clinical response, resolution of neutropenia 8 days after the suspension of thionamides, and the presence of a 5/1 Myeloid: Erythroid ratio in bone marrow biopsy, suggested the previous destruction of neutrophils, with recovery after drug discontinuation.
Conclusion
The state of severe neutropenia is attributable to drugs in 70 to 90% of cases. The absence of evidence of transformation for the accelerated and blast phases of Chronic Myeloid Leukemia, positive clinical response associated with resolution of neutropenia after thionamide withdrawal and the presence of a 5/1 Myeloid: Erythroid ratio in bone marrow biopsy, suggesting the previous destruction of neutrophils, with recovery after discontinuation of the drug evidence the differential diagnosis of thionamide-induced agranulocytosis overlying the underlying diagnosis of hematological disease. The manifestations resulting from such a condition include, in most cases, infections that have a high risk of progressing to septicemia. After resolution of the condition, which occurs between 3-14 days after the drug is discontinued, definitive treatment for hyperthyroidism should be considered, usually with radioactive iodine or surgery.

DOI: 10.1530/endoabs.81.P772

P773

Thyroglobulin antibodies in women with recurrent pregnancy loss: a systematic review and meta-analysis

Perrine Huisman[1], Jesper Krogh[1], Claus Henrik Nielsen[2], Henriette Svarre Nielsen[3], Ulla Feldt-Rasmussen[1] & Sofie Bliddal[1]
[1]Copenhagen University Hospital, Medical Endocrinology and Metabolism, København, Denmark; [2]Rigshospitalet, Institute for Inflammation Research, Center for Rheumatology and Spine Diseases, København, Denmark; [3]Copenhagen University Hospital (Rigshospitalet), Recurrent Pregnancy Loss Unit, Fertility Clinic 4071, København, Denmark

Background
Thyroid autoimmunity is the most prevalent autoimmune disorder among women of reproductive age and has been linked to pregnancy loss. In recurrent pregnancy loss (RPL), couples suffer several consecutive losses resulting in physical as well as psychological strains. Thyroid autoimmunity has been suggested as a risk factor in RPL, but most studies have focused on thyroid peroxidase antibodies (TPOAbs), not taking into account the presence of thyroglobulin antibodies (TgAbs). The aim of this study was to systematically assess the prevalence of TgAbs in women suffering from RPL, and whether TgAb-presence was associated with a lower live birth rate in the next pregnancy.
Methods
A systematic literature search for studies reporting on TgAbs in women with recurrent pregnancy loss was performed. The primary outcome was TgAb-positivity in RPL women compared to healthy controls, with a secondary outcome of association between TgAb-positivity and live birth in the next pregnancy. Pooled effect estimates were expressed as odd ratios (OR) with 95% confidence intervals (95% CI) using a random-effects approach. Heterogeneity was reported as I^2 statistic. The study was registered with PROSPERO and adhered to PRISMA guidelines.
Results
A total of 518 studies were screened, sixteen of which included a total of 3869 women. The prevalence of TgAb-positivity in women with RPL ranged from 3.6 to 27% compared to 2.3 to 29% in healthy controls. The OR for women with RPL being TgAb-positive was 2.21 (95% CI: 1.54-3.12; $I^2 = 36\%$) compared to healthy controls, while the OR for women with RPL being positive for TgAbs and/or TPOAbs was 2.23 (95% CI: 1.45 to 3.44; $I^2 = 61\%$). Two studies reported on the outcome of the next pregnancy after referral in TgAb-positive women compared to TgAb-negative women and yielded highly heterogenous results. One study reported an almost equal risk of pregnancy loss (OR 0.96), while the other reported an OR of 10.0 for pregnancy loss in women being TgAb-positive. Consequently, a meta-analysis could not be performed.
Conclusion
Women suffering from RPL were significantly more often TgAb-positive than healthy controls - independent of TPOAb-positivity. No conclusion could be drawn on the association of TgAbs and subsequent live birth rate in women with RPL because of high heterogeneity and an overall lack of prospective studies on the topic. Such studies are necessary in order to firmly determine the role of thyroid autoimmunity in RPL.

DOI: 10.1530/endoabs.81.P773

P774

Regulatory B cells involvement in autoimmune phenomena occurring in pediatric graves' disease patients.

Artur Bossowski[1], Kamil Grubczak[2], Aleksandra Starosz[2], Karolina Stożek[3], Filip Bossowski[4] & Marcin Moniuszko[5]
[1]Medical University in Bialystok., Department.of Pediatric Endocrinology and Diabetes, with a Cardiology Unit, Bialystok, Poland; [2]Medical University in Bialystok, Department of Regenerative Medicine and Immune Regulation, Bialystok, Poland; [3]Medical University in Bialystok, Dep. Of Pediatric Endocrinology and Diabetes, with a Cardiology Unit, Bialystok, Poland; [4]Medical University in Bialystok, Dep of Pediatric, Endocrinology and Diabete, with a Cardiology Unit, Bialystok, Poland; [2]Medical University in Bialystok, Department of Regenerative Medicine and Immune Regulation, Bialystok, Poland

Graves's disease is the most common type of autoimmune hyperthyroidism. Numerous studies indicate different factors contributing to the onset of the disease. Despite years of research, the exact pathomechanism of Graves' disease still remains unresolved, especially in the context of immune response. B cells can play a dual role in autoimmune reactions, on the one hand, as a source of autoantibody mainly targeted in the thyroid hormone receptor (TSHR) and, on the other, by suppressing the activity of proinflammatory cells (as regulatory B cells). To date, data on the contribution of Bregs in Graves' pathomechanism, especially in children, are scarce. Here, we investigated the frequencies of Bregs before and during a methimazole therapy approach. We reported higher Foxp3+ and IL-10+ Breg levels with CD38- phenotype and reduced numbers of CD38 + Foxp3 + IL-10+ in pediatric Graves' patients. In addition, selected Breg subsets were found to correlate with TSH and TRAb levels significantly. Noteworthy, certain subpopulations of Bregs were demonstrated as prognostic factors for methimazole therapy outcome. Our data demonstrate the crucial role of Bregs and their potential use as a biomarker in Graves' disease management.

DOI: 10.1530/endoabs.81.P774

Adrenal and Cardiovascular Endocrinology

EP1

Fatty acid binding protein 4 mediates atherosclerosis by disrupting gut microbiota and immunity

Lingling Shu[1,2], Xiaoping Wu[1,3], Leigang Jin[1,2], Laiyee Cheong[1,2], Boya Liao[1,3], Zixuan Zhang[1,3], Ruby L C Hoo[1,3] & Aimin Xu[1,2,3]
[1]The University of Hong Kong, HKU State Key Laboratory of Pharmaceutical Biotechnology, Hong Kong; [2]The University of Hong Kong, Department of Medicine, Hong Kong; [3]The University of Hong Kong, Department of Pharmacology & Pharmacy, Hong Kong.

Introduction
Atherosclerosis is a chronic inflammatory arterial disease and is currently one of the most common causes of cardiovascular morbidity and mortality worldwide. Therefore, there is an urgent need to discover new therapeutic targets for treatment of this fatal chronic disease. Fatty acid binding protein 4 (FABP4), a pro-inflammatory adipokine that links obesity with its related metabolic diseases, has been implicated in the development of atherosclerosis. This study aims to investigate whether FABP4 potentiates atherosclerosis by mediating the crosstalk between gut microbiota and immunity and to explore whether targeting FABP4 is therapeutically effective for treatment of this disease.
Method
$FABP4^{+/+}ApoE^{-/-}$ and $FABP4^{-/-}ApoE^{-/-}$ mice were generated for the study and fed with high fat and high cholesterol diet (HFHC) for 12 weeks. Biochemical, immunological, flow cytometry and denaturing gradient gel electrophoresis (DGGE) analysis were conducted to determine the pathophysiological roles of FABP4 in potentiating diet-induced atherosclerosis by altering gut microbiota and immunity. Fecal microbiota transplantation (FMT) were performed to further investigate the role of FABP4 in atherosclerosis mediated through microbiota. The FABP4 chemical inhibitor BMS309403 was used to evaluate the effects of FABP4 inhibition in alleviating atherosclerosis.
Result
The aortic trees stained with Oil Red exhibited significantly reduced atherosclerosis in $FABP4^{-/-}ApoE^{-/-}$ mice comparing to $FABP4^{+/+}ApoE^{-/-}$ littermates. Likewise, FMT of $FABP4^{-/-}$ feces to $FABP4^{+/+}$ mice significantly attenuated the development of atherosclerosis. DGGE analysis of fecal DNA showed that the pattern of bacterial phyla was obviously changed in $FABP4^{-/-}$ mice comparing to $FABP4^{+/+}$ littermates. These changes in $FABP4^{-/-}$ mice were accompanied by significantly increased expression of zona occuldens protein-1 (ZO-1) and occludin in intestinal villa, suggesting that FABP4 may enhance the intestinal permeability in mice in response to HFHC diet. Furthermore, FABP4 promoted macrophage infiltration and the polarization of macrophage from M0 to pro-inflammatory M1 subtype in the intestine of mice. Treatment with the FABP4 inhibitor BMS309403 dramatically alleviated the inflammatory response in the gut and atherosclerotic plaque formation, and elevated the intestinal expression of ZO1 and occludin in $FABP4^{+/+}$ mice.
Conclusion
FABP4, which is elevated during obesity, alters the composition of gut microbiota and intestinal permeability by creating a pro-inflammatory microenvironment, leading to endotoxinemia and subsequently contributing to the development of atherosclerosis. Targeting FABP4 with small-molecule inhibitors such as BMS303409 is a promising therapeutic strategy for treatment and prevention of atherosclerosis by modulating gut microbiota and intestinal immunity.
Acknowledgement
Hong Kong Health and Medical Research Fund (06172596)

DOI: 10.1530/endoabs.81.EP1

EP2

Limb-girdle muscular dystrophy type 2J: case report

Fatima Zahra Outtaleb[1], Amal Tazzite[2], Bouchaib Gazzaz[2,3] & Hind Dehbi[1,2]
[1]Ibn Rochd University Hospital, Laboratory of Medical Genetics, Casablanca, Morocco; [2]Faculty of Medicine and Pharmacy. Hassan II University, Cellular and Molecular Pathology Laboratory, Casablanca, Morocco; [3]Royal Gendarmerie, Genetics Analysis Institute, Rabat, Morocco.

Limb-girdle muscular dystrophies are a heterogeneous group of disorders regarding both their phenotypes and their underlying genetic causes. One of these defects is limb-girdle muscular dystrophy type 2J (LGMD2J), which has an unknown prevalence. Our aim is to describe clinical features an evolution of a novel case of this rare condition. Our patient is female, aged 29 from a non-consanguine family bearing features of limb-girdle muscular dystrophy. The first signs of this affection appeared around age 13 and gradually worsened, leading this patient to be unable to walk 10 years after onset. Her brother actually displayed a similar symptomatology and her father presented with lower limb muscular weakness that begun at age 30. Genetic analysis revealed the presence of a compound heterozygous *TTN* mutation c.4261C>T and c.65672C>T winch confirms diagnoses of LGMD2J. Family members will be tested for these two mutations in order to confirm the father's diagnosis of tibial muscular dystrophy and to provide appropriate genetic counselling to this family. Disorders caused by pathogenic *TTN* variants are a large and heterogeneous group of muscular dystrophies. Among these are both LGMD2J and tibial muscular dystrophy. Furthermore, *TTN* gene, that codes for protein titin, is one of the main genes involves in dilated cardiomyopathies, which have a prevalence of 17%. Considering that physiopathology of these disorders remains unknown, it seems therefore very important to report such disorders so as to improve their diagnosis and to obtain a better genotype phenotype correlation regarding *TTN* variants.

DOI: 10.1530/endoabs.81.EP2

EP3

Impact of adrenocortical carcinoma and associated adrenal insufficiency on patient wellbeing – a systematic review

Phillip Yeoh[1], Wladyslawa Czuber-Dochan[2], Simon Aylwin[3] & Jackie Sturt[1]
[1]KING'S COLLEGE LONDON, Florence Nightingale Faculty of Nursing, Midwifery & Palliative Care, London, United Kingdom; [2]King's College London Waterloo Campus, United Kingdom; [3]KING'S COLLEGE HOSPITAL, Endocrinology & Diabetes Dept, United Kingdom.

Context
Adrenocortical carcinoma is a rare cancer with an annual incidence of 0.7-2 cases per million population and 5-year survival of 31.2%. Adrenal insufficiency is a common and life shortening complication of ACC and little is understood about how it impacts on patients.
Objective
To understand patients' experience of the condition, its treatment, care process, impact of AI on ACC wellbeing, self-care needs and support.
Design
Systematic review of MEDLINE, EMBASES, CINAHL, PsycINFO and Open Grey for studies published until February 2021. All research designs were included. The findings underwent a thematic analysis and narrative synthesis. Studies quality was assessed using mixed method assessment tools.
Results
A total of 2837 citations were identified; 15 titles with cohort, cross sectional, case series and case report study designs met the inclusion criteria involving 479 participants with adrenal insufficiency secondary to adrenocortical carcinoma. Quantitative research identified impacts of disease and treatment on survivorship, the burden of living with AI/ACC, toxicity of therapies, supporting self-care and AI management. These impact factors included adjuvant therapies involved and their toxicities, caregivers/family supports, healthcare and structure support in place, specialist skill and knowledge provided by healthcare professional on ACC management. No qualitative patient experiences evidence was identified.
Conclusion
ACC appears to have high impact on patients' wellbeing including the challenges with self-care and managing AI. Evidence is needed to understand patient experience from a qualitative perspective.

DOI: 10.1530/endoabs.81.EP3

EP4

Clinical-laboratory and morphological predictors of pheochromocytoma progression

Anna Motrenko[1], Timur Britvin[2], Irena Ilovayskaya[1] & Larisa Gurevch[3]
[1]Moscow Regional Research and Clinical Institute (MONIKI), Neuroendocrine Unit, Department of Endocrinology, Moscow, Russian Federation; [2]Moscow Regional Research and Clinical Institute (MONIKI), Department of Endocrine Surgery; [3]Moscow Regional Research and Clinical Institute (MONIKI), Department of Pathology, Russian Federation.

According to the 4th edition of the WHO classification of endocrine organ tumors (2017), all pheochromocytomas are classified as malignant tumors (ICD-O code 8700/3). However, in the literature there are no unambiguous data on the significance of clinical and laboratory predictors of the aggressiveness of pheochromocytoma. The aim of the study was to verify possible predictors of pheo-progression using clinical data, the results of laboratory and instrumental

examination (including PASS and GAPP scales) of patients with a verified diagnosis of pheochromocytoma.
Material and methods
According to the data of this pilot retrospective study, data were analyzed from 27 patients with pheochromocytoma (16 women, 11 men) aged 22–73 years (median 51 years), who were operated on for the period from 2016 to 2021. 24-hour urine analysis for free metanephrines was determined by high performance liquid chromatography with tandem mass spectrometry with the addition of a preservative. The location and size of the pheochromocytoma was assessed by CT data with the determination of the native HU density. An immunohistochemical study was performed with antibodies to chromogranin A, synaptophysin, Ki-67, followed by an assessment of the potential for malignancy using the PASS and GAPP scales.
Results
There was a strong positive correlation between the PASS and GAPP scales ($r=0.720$), which is statistically significant ($P<0.01$). Both scales have a statistically significant positive correlation of mean strength with tumor size (PASS: $r=0.382$ / $P=0.049$; GAPP: $r=0.403$ / $P=0.037$). Correlation of these scales with the gender and age of patients, as well as the secretory activity of the tumor, was not revealed. A direct correlation was established between the PASS and GAPP scales and the size of the tumor.
Conclusion
According to our data, tumor size should be considered as a clinical predictor of metastatic potential of pheo, however gender, age, and functional activity of the tumor were not useful.
Keywords: pheochromocytoma; immunohistochemistry; PASS; GAPP.
DOI: 10.1530/endoabs.81.EP4

EP5

Adrenal incidentalomas in geriatric patients: Prevalence, radiological features, and hormonal profile

Faten Haj Kacem Akid[1], Abdelmouhaymen Missaoui[1], Mariem Belhoul[2], Wafa Belabed[1], Dhoha Ben Salah[1], Mnif Fatma[1], Nadia Charfi[1], Mouna Mnif[1], Nabila Rekik Majdoub[1,1], Mouna Elleuch[1] & Mohamed Abid[1]
[1]Hedi Chaker University Hospital, Endocrinology Departement, Sfax, Tunisia; [2]Faculty of Medicine of Sfax, Departement of Family Medicine, Sfax, Tunisia.

Background and Aims
The incidence of adrenal incidentaloma(AI) has been rising sharply due to the increased use of radiologic imaging. It shows evident variation with age, with the majority of the cases presenting in the 5th to 7th decade of life. This study aims to assess the prevalence of AI and its radiological features and hormonal profiles in the geriatric population.
Patients and Method
We conducted a retrospective descriptive study including 177 patients diagnosed with AI, referred to the Endocrinology Department of Hedi Chaker University Hospital, Sfax, Tunisia during 2011–2020. All patients have undergone clinical examination, adrenal CT, and biochemical workup for hormonal secretion.
Results
Among the 177 patients diagnosed with AI, 38.9% were 65 years and older. We focused our investigation on the geriatric population sample($n=69$). The mean age at diagnosis was 71.4 ± 4.2 years, with a female predominance(57.5%). At the time of diagnosis, older adults reported various unspecific "aging-related symptoms" such as asthenia(50%), weight loss(40%), and paresthesia(37.5%). Hypertension(67.5%), diabetes(42.5%), and dyslipidemia(30%) were the leading comorbidities in geriatric patients bearing AI. Ninety-five percent of AI were detected on CT scans performed mainly for nephritic colitis(42.5%) or abdominal pain(17.5%). Complementary centered adrenal CT featured adrenal adenomas in 90%, less frequently bilateral adrenal hyperplasia (7.5%), and macronodular adrenal hyperplasia(2.5%). AI was unilateral in 61%, mainly left-sided(54.5%), and bilateral in 39%. The mean size of AI was 24.1 ± 12.8 mm. 10% of aged patients were harboring AI larger than 40 mm. Non-contrast CT density was $<$ 10UH in 82.5%. As for the remaining patients(17.5%), enhanced CT showed an absolute washout $>$ 60% in 42.9% of cases. Based on the hormonal workup, 70% of elderly patients had non-secreting lesions. The functioning incidentalomas displayed autonomous cortisol secretion(32.5%), primary hyperaldosteronism(25%), or secondary hyperaldosteronism(21.8%). Only one senior had a secreting pheochromocytoma. AI with mixed hormonal secretion was recorded in 12.5%.
Conclusion
AI often affects the geriatric population, with an incidence reaching 10% after 70 years compared to 1–4% in younger adults. The vast majority of the AIs are non-functioning adenomas. Less common, some hormonal secretions, especially autonomous cortisol secretion and primary hyperaldosteronism, may be individualized in elderly patients bearing AI, although the hormonal excess often remains subclinical. Due to frailty and comorbidities frequently associated with advanced age, surgical management should be discussed on a case by case basis and proposed for seniors harboring lesions suspected of malignancy or overt hormonal secreting tumors: pheochromocytoma, cortisol secreting adenoma, etc
DOI: 10.1530/endoabs.81.EP5

EP6

Application of machine learning techniques in a qualification for a surgical treatment of adrenal tumors

Marta Wielogórska[1], Marcin Adamski[2], Vitalii Ulychnyi[1], Beata Podgórska[1], Katarzyna Siewko[1], Anna Popławska-Kita[1], Małgorzata Szelachowska[1], Adam Krętowski[1,3] & Agnieszka Adamska[1]
[1]Medical University of Białystok, Department of Endocrinology, Diabetology and Internal Medicine, Białystok, Poland; [2]Bialystok University of Technology, Faculty of Computer Science, Poland; [3]Medical University of Bialystok, Clinical Research Centre, Poland.

Background
The gradual increase in the detection rate of adrenal incidentalomas makes them a common clinical problem. The vast majority of them are benign adrenocortical adenomas. Nevertheless every patient with adrenal incidentaloma requires performing number of tests to exclude pheochromocytoma, autonomous cortisol secretion, adrenal carcinoma and primary hyperaldosteronism. Evaluation of whether adrenal incidentalomas are malignant or functional and continuing patient follow-up to assess the necessity for surgery assumed important place in endocrinology practice.
Objective
The aim of the study was to compare several machine learning techniques in a qualification for a surgical treatment of adrenal tumors and choose the most accurate algorithm as a valuable adjunct tool for decision-making.
Methods
A retrospective, single-center study was performed on hospitalized patients with adrenal incidentaloma between 2017 and 2019. From a database comprising 264 patients with adrenal incidentaloma, clinical data for 30 patients who underwent adrenalectomy due to suspicion of primary aldosteronism, pheochromocytoma, Cushing's syndrome, or adrenal cancer were extracted. All included patients underwent the endocrine work-up aimed to study the hormonal status of adrenal incidentalomas and every adrenal lesion was assessed with CT scan. On the basis of postoperative histopathological examinations, proper qualifications were confirmed in 20 out of 30 selected patients. Several machine learning algorithms, including Support Vector Machine, Multilayer Neural Network, C4.5 Decision Tree, Random Forest, k-Nearest Neighbours, Naïve Bayes, Zero R, One Rule, Logistic Regression, were trained to qualify the patients for an adrenalectomy. Finally, attribute selection technique was used to assess their usefulness in classification.
Results
The highest average accuracy was obtained for Support Vector Machine with linear kernel and soft margin – 90% of properly classified subjects. The Neural Network gave the second best result and was able to classify with an accuracy of 86%. Statistical evaluation using Pair-T Student modified for dependent samples was significantly better in comparison to baseline approach Zero-R ($P<0.05$). The most commonly selected by classifiers attributes were tumor homogeneity (100%), maximum diameter of the tumor (100%) and obesity (98%). Nevertheless prior attribute selection did not improve accuracy of trained algorithms.
Conclusions
Presented results show that application of machine learning methods in qualifying patients for an adrenalectomy may improve the decision process. The new training machine learning-based methods might be used to simplify making therapeutic decisions in adrenal incidentaloma patients and reduce the time from the initial identification of adrenal incidentaloma to the final decision about surgery.
DOI: 10.1530/endoabs.81.EP6

EP7

A phase III trial of recombinant human growth hormone in pediatric patients with growth failure caused by chronic kidney disease

Hong Xu[1], Xiaoshan Tang[1], Qian Shen[1], Jing Chen[1], Xiaoyan Fang[1], Aihua Zhang[2], Fei Zhao[2], Qiuxia Chen[2], Wenyan Huang[3], Ping Wang[3], Liwen Sun[3], Huijie Xiao[4], Ke Xu[4], Xiaorong Liu[5], Zhi Chen[5], Chaoying Chen[6], Juan Tu[6], Yubing Wu[7], Xiuli Wang[7], Jianhua Mao[8], Zhihong Lu[8], Jingjing Wang[8], Xiaojing Nie[9], Zihua Yu[10], Jun Huang[9], Cuihua Liu[11], Guanghai Cao[11], Yufeng Li[12], Yaju Zhu[12], Jianjiang Zhang[13], Miao Wang[13], Mo Wang[14] & Haiping Yang[14]
[1]Children's Hospital of Fudan University, Shanghai Kidney Development and Pediatric Kidney Disease Research Center, National Children's Medical Center, Department of Nephrology, Shanghai, China; [2]Nanjing Children's Hospital Affiliated to Nanjing Medical University, Department of Nephrology, Nanjing, China; [3]Shanghai Children's Hospital, Shanghai Jiao Tong University, Department of Nephrology and Rheumatology, Shanghai, China; [4]Peking University First Hospital, Department of Pediatrics, Beijing, China; [5]Beijing Children's Hospital affiliated with Capital Medical University, Department of Nephrology, Beijing, China; [6]Children's Hospital Affiliated to Capital Institute of Pediatrics, Department of Nephrology, Beijing, China; [7]Shengfing Hospital Affiliated to China Medical University, Department of Pediatric, Shenyang, China; [8]The Children's Hospital, Zhejiang University School of Medicine, Department of Nephrology, Hangzhou, China; [9]The 900th Hospital of Joint Logistic Support Force, Department of Pediatrics, Fuzhou, China; [10]Fujian Children's Hospital, Affiliated Hospital of Fujian Medical University, Department of Nephrology, Rheumatology and Immunology, Fuzhou, China; [11]Children's Hospital Affiliaten of Zhenzhou University, Department of Nephrology and Rheumatology, Zhenzhou, China; [12]Xinhua Hospital Affiliated to Shanghai Jiao Tong University School of Medicine, Department of Pediatric Nephrology, Shanghai, China; [13]The First Affiliated Hospital of Zhengzhou University, Department of Pediatric, Zhengzhou, China; [14]Children's Hospital of Chongqing Medical University, Department of Nephrology and Rheumatology, Chongqing, China.

Background and objective
Children with chronic kidney disease (CKD) have impaired growth that leads to short stature in adulthood and treatment with recombinant human growth hormone (rhGH) is associated with improved growth. This study aimed to evaluate the efficacy and safety of daily rhGH (Jintropin®) in children in China with growth failure caused by CKD prior to transplantation.
Methods
Prepubertal patients (2–13 years old) with CKD-related short stature were enrolled in this multicenter, randomized, open-label, negative-controlled study (NCT03535415). Eligible patients were randomized 1:1 to receive daily rhGH 0.05 mg/kg/day administered subcutaneously or control (no rhGH given, only relevant examinations were performed) for up to 52 weeks. The primary endpoint was improvement in (Δ) height standard deviation score (HT SDS). Secondary endpoints included improvements in height velocity (HV), bone maturation (bone age [BA]/chronological age [CA]), insulin-like growth factor 1 standard deviation score (IGF-1 SDS), IGF-1/IGF binding protein-3 (IGFBP-3) molar ratio, and safety.
Results
A total of 68 patients were randomized to either treatment or control; 11 patients (treatment: 7; control: 4) dropped out, 8 (treatment: 5; control: 3) of whom due to transplantation. At week 52, ΔHT SDS from baseline was 0.747 ± 0.579 ($P < 0.001$) and 0.173 ± 0.470 ($P = 0.039$) in the treatment and control groups, respectively (intergroup $P < 0.001$). Least-squares mean difference between both groups was 0.582 (95% confidence interval 0.323–0.842). Statistically significant improvements were also observed in those who received treatment compared with those in the control group for ΔHV (7.021 ± 3.795 cm/year vs 2.566 ± 3.577 cm/year; intergroup $P < 0.001$), ΔIGF-1 SDS (1.697 ± 2.098 vs -0.171 ± 1.506; intergroup $P < 0.001$), ΔIGF-1/IGFBP-3 molar ratio (0.046 ± 0.073 vs 0.001 ± 0.041; intergroup $P < 0.001$), and Δheight (9.87 ± 2.89 cm vs 6.43 ± 2.72 cm; intergroup $P < 0.001$). Δ(BA/CA) was 0.041 ± 0.074 and 0.008 ± 0.079 in the treatment and control groups, respectively (intergroup $P = 0.118$). Most treatment-emergent adverse events (TEAEs) were mild to moderate; 19 patients (treatment: 10; control: 9) experienced serious adverse events, and 5 in the treatment group temporarily discontinued rhGH due to TEAEs. 7 reported drug-related TEAEs, which included elevated blood insulin, scoliosis, glycosuria, musculoskeletal discomfort, hyperinsulinemia, and abnormal liver function.
Conclusion
Daily rhGH 0.05 mg/kg per day for 52 weeks was effective and well tolerated in children with short stature caused by CKD. At the end of the study, significant improvements in ΔHT SDS, ΔHV, ΔIGF-1 SDS, ΔIGF-1/IGFBP-3 molar ratio, and Δheight were observed with treatment.

DOI: 10.1530/endoabs.81.EP7

EP8

The spectrum of CYP21A2 copy number variations and gene mutations by MLPA in a pediatric Romanian population with 21-hydroxylase deficiency

Sorina Schipor[1], Ioana Nedelcu[1], Camelia Procopiuc[1], Elena Braha[1], Madalina Boboc[1], Andreea Brehar[1], Andrei Muresan[1], Alina Dumitrica[1], Oana-Monica Popa[1], Andra Caragheorgheopol[1], Dana Manda[1], Susana Vladoiu[1] & Iuliana Gherlan[1,2]
[1]C.I. Parhon National Institute of Endocrinology, Research Department, Bucureşti, Romania; [2]Carol Davila University of Medicine and Pharmacy, Bucharest, Romania.

Objective
The analysis of the copy number variation of *CYP21A2* gene in a cohort of 21-hydroxylase deficiency (21-OHD) pediatric patients in a tertiary referral center from Romania.
Methods
A total of 24 patients (21 female and 3 male, 7:1 female to male sex ratio) with previously biochemically and clinically diagnosed 21-OHD were enrolled in this study from October 2020 to October 2021. The age at the diagnosis was 4.6 ± 4.8 years (mean ± S.D.). All clinical and biochemical data were collected. Genomic DNA was extracted from peripheral blood leukocytes, and copy number variations along with several point mutations of *CYP21A2* gene were detected by multiple ligation-dependent probe amplification (MLPA) using MRC-Holland SALSA MLPA P050-C1 kit and Coffalyser.net software. The study has been approved by Ethical Committee of the Institute.
Results
Clinical and biochemical phenotype revealed 13 patients (54.17%) with classic and 11 patients (45.83%) with non-classic form of 21-OHD. Salt-wasting phenotype was diagnosed in 8 patients in whom MLPA analysis results were: large deletion/rearrangement in *CYP21A2* (2 patients with homozygous *CYP21A2* deletion and 2 patients with fused *CYP21A1P/CYP21A2* gene (chimeras)); 2 patients with heterozygous g.655A/C > G (I2G) mutation, 1 patient compound heterozygous for P31L/I172N and one patient heterozygous for I172N mutation. In 5 patients with classic simple virilizing 21-OHD MLPA analysis showed: *CYP21A1P* deletion (2 patients), *CYP21A1P* duplication (1 patient), I2G/I172N (2 patients). The MLPA analysis in the remaining 11 patients with non-classic form of 21-OHD indicated: heterozygous gene deletion and I172N mutation (2 patients), partial *CYP21A1P* deletion (1 patient), *CYP21A2* duplication (1 patient), *CYP21A1P* duplication (1 patient), homozygous mutation I172N and a heterozygous P31L mutation (1 patient), with a normal profile in 5 patients.
Conclusions
Copy number variation analysis is a very useful tool in 21-OHD molecular diagnosis, especially in classic salt-wasting patients but a complete precise diagnosis should be complemented by *CYP21A2* sequencing analysis.

DOI: 10.1530/endoabs.81.EP8

EP9

Pheochromocytoma during pregnancy: diagnosis and treatment challenges

Imen Halloul, Ach Taieb, Ben Abdelkerim Asma, Saad Ghada, El Fekih Hamza, Hasni Yosra, Maaroufi Amel, Kacem Maha, Chaieb Molka & Ach Koussay
Farhat Hached University Hospital, Department of Endocrinology and Diabetes, Sousse, Tunisia.

Introduction
Pheochromocytoma in pregnancy is rare with an incidence of 0.007%. A timely diagnosis is essential since fetal and maternal mortality depends on the early treatment. Our object is to report a pheochromocytoma diagnosed in a patient at the beginning of the pregnancy and to highlight the particularity in the therapeutic care.
Case presentation
A 32-year-old female patient was admitted to our endocrinology department for exploration of palpitation associated with headache and sweats. She had a family history of diabetes and hypertension and no history of pituitary adenoma or hyperparathyroidism. The symptoms were concomitant to food intake, and evolving for 02 years. The patient decreased her diet to avoid the symptoms, therefore, losing 09 kg. Clinically, her systolic blood pressure was ranging between 140 and 170, and diastolic between 80–90 mmHg. Pheochromocytoma was suspected and confirmed with increased plasma normetanephrine and metanephrine levels (10* the normal range). Abdominal CT scan showed a heterogenous mass of the left adrenal gland (5*4 cm) with spontaneous density of 40UH. Shortly after, the patient discovered she was 9 weeks pregnant. We started

treatment with doxazosin, and blood pressure values were normalized. At 18 weeks of menstrual age, laparoscopic adrenalectomy of the left adrenal gland was performed without any complications during or after surgery. The tumor was confirmed to be a 7-cm pheochromocytoma in histological exam. After surgery, blood pressure was normal without treatment and post-operative measurements of serum normetanephrines and metanephrines were normal. At 30 weeks of menstrual age, the fetus was healthy.

Conclusion

Maternal and fetal mortality du to pheochromocytoma decreases to less than 15% if the diagnosis was made antepartum. Symptoms in pregnant patients do not differ from symptoms in non-pregnant patients. However, they may worsen with advancing pregnancy due to an increased pressure on the tumor by the abdominal distension, fetal movements and uterine contractions. When the diagnosis is made within the first 24 weeks of pregnancy and adequate α-blockade can be established, tumor removal is recommended in the second trimester via laparoscopic surgery. Decisions for those patients should be made by an experienced multidisciplinary team.

DOI: 10.1530/endoabs.81.EP9

EP10

A case of ChAdOx1 vaccine-induced thrombocytopaenia and thrombosis syndrome leading to bilateral adrenal haemorrhage and adrenal insufficiency

Agathoklis Efthymiadis[1], Dalia Khan[2], Sue Pavord[2] & Aparna Pal[1]
[1]Oxford Centre for Diabetes, Endocrinology and Metabolism, Oxford University Hospitals NHS Foundation Trust, Oxford, United Kingdom; [2]Department of Haematology, Oxford University Hospitals NHS Foundation Trust, Oxford, United Kingdom.

Introduction

Vaccine-induced thrombosis and thrombocytopenia (VITT) after vaccination against SARS-CoV-2 with the adenoviral vector-based vaccines ChAdOx1 and Ad26.COV2.S has been associated with adrenal pathology, such as bilateral adrenal vein thrombosis, adrenal cortex haemorrhage and adrenal insufficiency in six percent of patients[1].

Case report

We report the case of a 23-year-old healthy woman who presented at eight days after ChAdOx1 vaccination with a low platelet count of 43×10^9/l, raised D Dimers $>100\,000$ ng/ml and multiple lobar and segmental pulmonary emboli. Anti-platelet factor 4 antibodies were detected confirming definite VITT in accordance with the UK diagnostic criteria. At sixteen days post-vaccine, further imaging showed bilateral adrenal haemorrhage, non-occlusive splenic vein thrombosis and right ventricular thrombosis. Her cortisol level was <25 nmol/l. She was treated with anticoagulation, plasmapheresis, immunosuppression and steroid replacement. She had high anti-spike titre and positive anti-nucleocapsid titres for SARS-CoV-2. She developed seizures secondary to posterior reversible encephalopathy, requiring intensive care. After 4 weeks in hospital, she was discharged on warfarin, hydrocortisone and fludrocortisone replacement. Short synacthen tests three and nine months later showed no recovery of adrenal function, although magnetic-resonance-imaging of the adrenal glands showed resolving adrenal haemorrhage.

Discussion and conclusions

Adrenal insufficiency secondary to bilateral adrenal vein thrombosis and adrenal cortex haemorrhage should be suspected in patients with vaccine-induced thrombosis and thrombocytopenia (VITT) and treated promptly. Adrenal haemorrhage can occur as the initial presentation of VITT or days to weeks after the development of thrombosis in other sites. Completion of vaccination schedule against SARS-CoV-2 post VITT using an mRNA-based vaccine should be recommended to patients post-VITT, as mRNA-based vaccines have not been associated with VITT. There is paucity of data regarding the potential for recovery of adrenal function after bilateral adrenal haemorrhage in the context of VITT and thus more studies are needed to inform clinical practice. The need for disease registries for rare conditions, such as VITT, is crucial as direct cooperation and sharing of information by clinicians might enable quicker identification of disease patterns than would have been possible via established reporting tools of adverse events.

Reference

1. Pavord S, Scully M, Hunt BJ, Lester W, Bagot C, Craven B, et al. Clinical Features of Vaccine-Induced Immune Thrombocytopenia and Thrombosis. N Engl J Med. 2021 Oct;385(18):1680–9.

DOI: 10.1530/endoabs.81.EP10

EP11

The concentration of metanephrine and normetanephrine in the most common indications for biochemical monitoring

Romana Marušić[1,2] & Tatjana Bačun[1,3]
[1]Faculty of Medicine Osijek, Josip Juraj Strossmayer University of Osijek, Osijek, Croatia, Osijek, Croatia; [2]National Memorial Hospital Vukovar, Department of Internal Medicine, Vukovar, Croatia; [3]Clinical Hospital Centre Osijek, Department of Internal Medicine, Osijek, Croatia.

Objectives

Pheochromocytomas are rare neuroendocrine tumors that originate in chromaffin cells of the adrenal medulla and excessively secrete catecholamines, which leads to a multitude of different symptoms. The most common symptoms include headaches, palpitations and sweating. Because of a diverse clinical picture, they pose a major challenge in diagnostics and often go unidentified. The diagnosis is confirmed by measuring plasma and 24-hour urinary metanephrine and normetanephrine. The aim is to determine the most common indications for biochemical testing by sex and age and the association between the concentrations of metanephrine and normetanephrine and indications, sex, and age.

Study design

Cross-sectional study with historical data.

Participans and methods

The study was conducted on subjects in whom the concentration of metanephrine and normetanephrine in plasma was determined in 2019. A list of patients was collected from the Clinical Institute for Laboratory Diagnostics at the Osijek Clinical Hospital by accessing the laboratory information system. Data (indication for biochemical testing, sex, age) was collected from the Department of Nephrology for each patient by accessing the hospital information system.

Results

The study was conducted on 224 respondents (42.9% men and 57.1% women). The most common indication for biochemical testing is adrenal incidentaloma (61.6%) and symptoms of pheochromocytoma (18.3%). There is no significant difference in the distribution of patients according to gender. The median age of participants with adrenal incidentaloma and participants with previously treated pheochromocytoma is higher compared to subjects with hereditary risk for pheochromocytoma and hypertension before they turned 20 years old. There is no significant association between the values of metanephrine and normetanephrine and the indication for biochemical testing. Metanephrine values are significantly lower in women. There is no significant association between age and metanephrine values, while the association between age and normetanephrine values is positive and significant, but very weak.

Conclusion

Higher values of metanephrine are associated with males and higher values of normetanephrine are associated with older age. Adrenal incidentalomas and pheochromocytoma-indicating symptoms are very common in the general population, while the incidence of pheochromocytoma is extremely rare. Given the risk of missing a diagnosis, it is important to know the indications for biochemical testing to make a timely diagnosis and prevent complications.

Keywords: adrenal gland; catecholamines; hypertension; paraganglioma; pheochromocytoma

DOI: 10.1530/endoabs.81.EP11

EP12

QTc interval in patients with pheochromocytoma and paraganglioma

Dina Rebrova[1], Elisey Fedorov[1], Igor Chinchuk[1], Vladimir Rusakov[1], Leonid Krasnov[1], Ilya Sleptsov[1], Roman Chernikov[1], Ilya Sablin[1], Natalya Vorokhobina[2], Sergei Fogt[2], Ilya Shcherbakov[1], Shamil Shihmagomedov[1], Ekaterina Zgoda[1] & Arseny Semenov[1,3]
[1]Saint Petersburg State University, Saint Petersburg State University Hospital, St. Petersburg, Russian Federation; [2]North-Western State Medical University n.a. I.I. Mechnikov, Department of Endocrinology, St. Petersburg, Russian Federation; [3]Saint Petersburg State University, Medical Faculty, Saint-Petersburg, Russian Federation.

Introduction

Prolonged QTc interval is a known risk factor for developing ventricular tachyarrhythmias. QTc prolongation is often reported in patients with pheochromocytoma, however the literature data on this issue are rather heterogeneous. Here we report the results of QTc measurement in patients with pheochromocytoma and paraganglioma (PPGL) in comparison to hormonally inactive benign adrenal tumors.

Methods
The test group included 204 patients with pheochromocytoma and 2 with paraganglioma. 27 people with hormonally inactive benign adrenal tumors (HIBAT) served as a control group. QT interval was measured during standard 12-lead ECG before surgical intervention for the disease, and then corrected with Bazett formula (QTcB). The interval was categorized into gender-specific categories. For women, the cutoff points were $\leq$450 ms (normal), 451 to 470 ms (borderline), and $>$470 ms (prolonged), and for men $\leq$430 ms (normal), 431 to 450 ms (borderline), $>$450 ms (prolonged). The pattern of arterial hypertension (i.e. paroxysmal, sustained or mixed type) was evaluated according to complaints, anamnesis and clinical examination results. Numerical data are presented
Results
Medians of QTcB were similar and reached 416 [392, 436] ms in patients with PPGLs and 413 [398, 435] ms in patients with HIBAT ($P=0.975$, Mann–Whitney U test). The intervals were categorized in test group and control group as normal in 169 (82.04%) and 21 (77.77%), borderline in 22 (10.68%) and 5 (18.52%), prolonged in 15 (7.28%), and 1 (3.70%) patient respectively. The hypothesis that the clinical course type of PPGL may influence QTcB was tested. Patients who had sustained or mixed type of tumor-induced arterial hypertension, which may indicate continuous catecholamine exposure, were compared to those with paroxysmal hypertension or asymptomatic disease. In the first subgroup QTcB counted 413 [389, 432] ms, in second it was 428 [400, 451] ms ($P=0.011$, Mann–Whitney U test). The number of patients with borderline or prolonged QTcB was 21 (13.55%) in first subgroup and 16 (31.37%) in second ($P=0.007$, Yates's chi-squared test, odds ratio 2.9 [95%CI: 1.4, 6.2]).
Conclusion
Our data suggest that pheochromocytoma and paraganglioma may be associated with increased QTc, however this effect is limited to certain risk groups. Patients with sustained tumor-induced hypertension, which probably means prolonged catecholamine exposure, are at risk of prolonged QTc.

DOI: 10.1530/endoabs.81.EP12

EP13

A challenging case of hypertension: an ACTH-secreting pheochromocytoma

Nicola Lanzo[1], Gaia Francesca Maria Fazzino[1], Francesca Manzella La Barbera[1], Bohdan Patera[1], Silvia Lepanto[1], Federica Martina Bianchi[1], Ilaria Clementi[1], Eliana Piantanida[1,2] & Maria Laura Tanda[1,2]
[1]Insubria University, Department of Medicine and Surgery, Varese, Italy; [2]Ospedale di Circolo e Fondazione Macchi - ASST Sette Laghi, Endocrine Unit, Varese, Italy.

Pheochromocytoma is a rare catecholamine-secreting tumour arising from chromaffin cells in the adrenal medulla and one of the main causes of endocrine hypertension. We here report the case of a 48-year old man admitted to the Internal Medicine Department for evaluation of resistant hypertension. The patient presented with headache, sweating, palpitations, pitting edema, hypertension and hypokalemia both resistant to conventional polytherapy. He was therefore investigated for endocrine causes of hypertension with evidence of urinary metanephrines above the upper reference limit. Besides, an abdominal CT scan showed a left adrenal mass highly suspicious for pheochromocytoma. Calcitonin and PTH levels were within the normal range. Further investigations showed high ACTH and blood cortisol levels. The latter remained unsuppressed after low-dose and high-dose dexamethasone suppression tests (1289 µg/l and 1302 µg/l, respectively). To rule out Cushing's disease, a pituitary MRI was performed, without evidence of sellar abnormalities. All other anterior pituitary hormone levels were within the normal range, except for biochemical central hypothyroidism. The severe Cushing syndrome associated with hypokalemia along with the very high ACTH level (319 ng/l, normal values 7–63 ng/l) supported an ectopic source of ACTH. A total body CT scan confirmed only the previously known left adrenal mass lesion. The right adrenal gland was of normal appearance. The mass showed only selective enhancement in its caudal portion with 123I-MIBG scintigraphy, so a somatostatin receptor scintigraphy was performed which resulted positive. Treatment with metyrapone 250 mg every six hours and thyroxine replacement were initiated to control hypercortisolism and restore euthyroidism before surgery. After proper alfa- and beta-adrenoreceptor blockade treatment, a left adrenalectomy was performed. Hydrocortisone was given before and immediately after the operation, while cortisone acetate was employed afterwards. At two months follow-up, normalization of ACTH levels (24 ng/l) and urinary metanephrines was observed. Histopathology confirmed an ACTH-secreting pheochromocytoma associated with adrenal hyperplasia, with prevalence of the *pars intermedia*, with no signs of angio- or neuroinvasion nor necrosis, low mitotic index, no expression of SDHB and immunostaining positive for ACTH, synaptophysin, chromogranin A, GATA 3. Ectopic ACTH-production is most often related to small cell lung carcinomas or, rarely, to neuroendocrine carcinoids. Few cases of sporadic ACTH-producing adrenal-medullary tumours have been described. Despite its rarity, in those cases where hypertension is burdened by severe hypokalemia and hyperglycemia, an ACTH-secreting pheochromocytoma may be suspected. This condition should be excluded for its high mortality rate and since proper pre-operative management is essential.

DOI: 10.1530/endoabs.81.EP13

EP14

Adrenal sarcomas – Exceptionally rare or more common than thought? Prevalence in adrenalectomy specimens over 12 months period and presenting features.

Nur Azman[1], James Lawrence[2], Matthew Hayes[3], James Douglas[3] & Jana Bujanova[11]
[1]University Hospital Southampton NHS Foundation Trust, Endocrinology Department, Southampton General Hospital, Southampton, United Kingdom; [2]Salisbury District Hospital, Endocrinology Department, Salisbury, United Kingdom; [3]University Hospital Southampton NHS Foundation Trust, Urology Department, Southampton General Hospital, Southampton, United Kingdom.

Adrenal/periadrenal sarcomas are very rare entity of adrenal tumours. An epidemiological analysis of primary adrenal cancers found prevalence of adrenal sarcoma of 1.3% compared to adrenocortical carcinoma (ACC) 43.8%, neuroblastoma 39.7%, pheochromocytoma 10.9% and non-Hodgkin's lymphoma 4.3% (1). In 2021, 26 adrenalectomies in adults were performed in our institution. 12/26 had malignant histology. 9/26 lesions were $>$ 6 cm. 7/9 lesions $>$ 6 cm were malignant (2 adrenal sarcomas, 2 ACC, 2 infiltrative renal cancer, 1 metastatic melanoma). Adrenal sarcoma was detected in 2/26 adrenalectomized specimens. We present two cases of adrenal sarcoma detected over 12-month period in University Hospital Southampton, United Kingdom. Case 1: 35-year-old woman presented with right abdominal pain for over one year. Ultrasound showed right suprarenal mass. CT CAP and adrenal MRI confirmed large tumour 4.9$\times$6.1$\times$5.7 cm adjacent to or arising from right adrenal gland and indents IVC. No metastases. Urine metanephrines, aldosterone, renin, 1 mg ODST were normal. Working diagnosis was non-functioning ACC. Patient underwent open adrenalectomy and post-operatively her pain resolved. Histology revealed high grade leiomyosarcoma (pT2 N0 G3) adjacent to adrenal with narrow excision margin. Patient opted against adjuvant chemotherapy and remains under surveillance. Imaging 8 months post-op showed no evidence of recurrence. Case 2: 70-year-old man presented with two months history of left flank and back pain, weight loss, and elevated CRP (159 mg/l). CT detected suspicious 7.8 cm heterogenous left adrenal mass extending to splenic hilum. Metanephrines, lymphoma screen- normal, 1 mg ODST-raised (72 nmol/l). Patient underwent open adrenalectomy, splenectomy and wedge excision of the liver due to intraoperative findings of liver metastases. Histology confirmed high grade epithelioid angiosarcoma. Restaging CT post-op showed lung, liver metastases and local recurrence in resection bed. He commenced palliative paclitaxel chemotherapy, with good radiological response. Adrenal sarcomas should be considered in any age in differential diagnosis of indeterminate adrenal masses especially when $>$ 6 cm, associated with ipsilateral pain and raised CRP. 1 mg ODST can be raised due to raised metabolic rate associated with high-grade malignancy. The duration of symptoms could range from few weeks to 12 months. In our second case with metastatic disease, surgical debulking of primary tumour provided significant pain relief and increased patient's quality of live and prognosis. Both patients are alive at the time of writing.
Reference
(1) Chandrasekar T *et al*. The who, when, and why of primary adrenal malignancies: Insights into the epidemiology of a rare clinical entity. Cancer. 2019 Apr 1;125(7):1050–1059

DOI: 10.1530/endoabs.81.EP14

EP15

Don't break my heart: sparing the knife in SDHB mutated cardiac paraganglioma treated with cabozantinib

Lindsay Carafone, William Archibald, Adrienne Victor & Inga Harbuz-Miller
University of Rochester, Rochester, United States.

Introduction
Cardiac paragangliomas are rare endocrine neoplasms. Surgical resection is first line treatment. Here, we describe a case of cardiac paraganglioma where surgical resection was aborted due to involvement of important cardiac structures. Systemic therapy was instead pursued with tyrosine kinase inhibitor cabozantinib.
Case
A 64-year-old man with a past medical history significant for tobacco use and poorly controlled type 2 diabetes mellitus presented with chest pain, several months of progressive fatigue and 15 pound unintentional weight loss. Echocardiogram revealed a 6.9×5.8×4.9 cm right-sided cardiac mass. Biopsy was performed demonstrating cytopathology consistent with paraganglioma. Laboratory studies revealed chromogranin A 1,038 ng/ml (normal <93 ng/ml), plasma normetanephrine 1.87 nmol/l (0–0.89 nmol/l) and plasma metanephrine 0.14 nmol/l (0–0.49 nmol/l). Ga-68 DOTATATE Positron Emission Tomography/Computed Tomography (PET/CT) scan revealed DOTATATE avidity within the region of the cardiac mass. No additional lesions or metastatic foci were identified. Next-generation sequencing performed on the tissue biopsy demonstrated an SDHB mutation (H244D) at a variant allele frequency of 62.2%. Surgical resection was attempted and aborted due to the paraganglioma encasing the right coronary artery and the tricuspid valve. Systemic therapy was initiated with tyrosine kinase inhibitor cabozantinib. Dose reduction was required due to development of palmar-plantar erythrodysesthesia. Subsequent surveillance Ga-68 DOTATATE PET/CT scan revealed partial response to treatment at two months with increasing central photopenia of the cardiac mass from 94 standardized uptake value (SUV) to 54 SUV. The patient had biochemical response with decreasing chromogranin A and norepinephrine levels.
Conclusion
Treatment of cardiac paraganglioma ideally consists of local resection, however this is not always possible due to involvement of critical structures of the heart. Systemic therapy for paragangliomas is largely based on small, retrospective studies. Our case illustrates an unresectable cardiac paraganglioma with response to cabozantinib as evidenced by radiologic and biochemical data. Radionucleotide therapy is a potential future treatment option for this patient.

DOI: 10.1530/endoabs.81.EP15

EP16

Optimization of familial hypercholesterolemia diagnosis through LDL cholesterol correction formula for lipoprotein(a) levels

Rosana Urdaniz Borque[1], Sergio Roman Gimeno[1], Elena Pérez Galende[11], Gema Gonzalez Fernandez[11], Borja Sanz Martín[2] & José Antonio Gimeno Orna[1]
[1]Lozano Blesa University Clinical Hospital, Endocrinology, Zaragoza, Spain; [2]Reina Sofía Hospital of Tudela, Tudela, Spain.

Introduction
For the clinical diagnosis of heterozygous familial hypercholesterolemia (HeFH) validated algorithms are used, with the Dutch Lipid Clinic Network (DLCN) Criteria being the most recommended in our environment. One of the items that scores for the system proposed by the DLCN is the value of LDL cholesterol. However, LDLc levels can be distorted by lipoprotein a (Lpa(a)) levels.
Objective
To analyze the change in the validity of the DLCN criteria for the diagnosis of HeFH with pathogenic mutation confirmed when using the LDLc.
Methods
Observational, retrospective, cross-sectional, and analytical study in a cohort of 91 patients with clinical diagnostic criteria for probable or defined familial hypercholesterolemia according to the DLCN criteria, followed in our Lipid Unit at Lozano Blesa University Clinical Hospital, from 1 May 2019 to 31 December 2020. The DLCN criteria have been calculated based on LDLc values, and LDLc corrected for Lp(a) [according to the corrected LDLc formula = LDLc – 0.30*Lp(a)]. In all the statistical test performed, significant values of $P<0.05$ were considered. Several ROC (Receiver Operating Characteristic) curves have been generated between the initial LDLc and that LDLc corrected by Lp(a) values to predict the presence of genetic mutation. Corresponding cross tables have been made between LDLc (initial and corrected) and genetic mutation; as well as between the DLCN score (obtained with uncorrected LDLc) and genetic mutation.
Results
We included 91 patients (51.65% women, mean age at diagnosis 48.80±12.96 years). 43.95% of them did not present mutation in the genetic study for HeFH. Lp(a) in subjects with no known mutation was 24.70 ± 86.10 mg/dl compared to 22.50 ± 60.3 mg/dl in patients with known mutation. The area under the ROC curve of the LDLc variable and the presence of mutation in the genetic test was higher in the case of LDLc corrected by Lp(a) (AUC=0.639,$P=0.038$) than in the uncorrected LDLc (AUC=0.623,$P=0.065$). This improves the specificity of the LDLc variable to predict genetic mutation if used corrected by Lp(a): 70% versus 62.74% if used uncorrected. When using the LDLc corrected by Lp(a) for the calculation of the DLCN score, 66.66% of the patients were reclassified from probable diagnostic group to a possible diagnosis, without presenting 56.26% of them a known genetic mutation.
Conclusions
The use of adjustment of LDL cholesterol levels according to Lp(a) levels in the diagnosis of HeFH facilitates a more specific diagnosis than with the use of unadjusted LDLc.

DOI: 10.1530/endoabs.81.EP16

EP17

Associated factors with metabolic syndrome in elderly patients harboring adrenal incidentaloma: A comparative study

Faten Haj Kacem Akid[1], Abdelmouhaymen Missaoui[1], Mariem Belhoul[2], Wafa Belabed[1], Dhoha Ben Salah[1], Mnif Fatma[1], Nadia Charfi[1], Nabila Rekik Majdoub[1], Mouna Elleuch[1] & Mohamed Abid[1]
[1]Hedi Chaker University Hospital, Endocrinology Department, Sfax, Tunisia; [2]Faculty of Medicine of Sfax, Department of Family Medicine, Sfax, Tunisia.

Background and Aims
Numerous studies have suggested that metabolic syndrome (MetS) is related to adrenal incidentaloma (AI) in young adults. Limited data about MetS in geriatric patients diagnosed with AI are available, despite the high incidence of this adrenal disease in the elderly. This study aims to assess the prevalence of MetS and its associated factors in aged patients harboring AI.
Patients and Method
We conducted a retrospective, comparative, and analytical study including 69 patients aged 65 years and above diagnosed with AI. All patients have undergone clinical examination, adrenal CT, and biochemical workup at the Endocrinology Department of Hedi Chaker University Hospital, Sfax, Tunisia, from 2011 to 2020. MetS was diagnosed based on the National Cholesterol Education Program's Adult Treatment Panel III (ATP III) criteria. We compared two groups:
[MetS+]: elderly subjects with MetS ($n=17$)
[MetS-]: elderly subjects without MetS ($n=52$)
Results
There was no significant age diffrence between both groups ([MetS+]:72.1 vs [MetS=] 71.0 years old; $P=0.82$). Female gender was significatly associated with MetS ([MetS+] 82.4% vs [MetS-] 39.1%; $P=0.006$). Patients bearing bilateral AI were significantly more affected by MetS ([MetS+] 58.8% vs [MetS-]: 4.3%; $P=0.000$) compared to those having unilateral AI. Smaller incidentaloma size seems to aggravate substabtially the risk of developping MetS in the elderly (incidentaloma size in [MetS+] 21.0 vs [MetS-]:26.7 mm; $P=0.009$). Both groups had similar electrolyte profile except higher phosphatemia which was statistically linked to the prescence of MetS ([MetS+] 1.30 vs [MetS-]: 0.96 mmol/l; $P=0.018$). We noted no significant correlation between hormonal hypersecretion and MetS in older adults, since there was a comparable distribution of functioning ([MetS+] 46.7% vs [MetS-] 40.0%) and nonfunctioning AI([MetS+] 53.3% vs [MetS-] 60%; $P=0.693$) in the two groups.
Conclusion
AI is associated with a higher cardiometabolic risk. This risk seems to increase in advanced age. Metabolic abnormalities are classically attributed to hormonal hypersecretion, especially in Cushing's syndrome. However, several studies have recently proven that insulin resistance and metabolic dysregulation also occur in nonfunctioning AI. Our results suggest that bilateral and smaller AI may worsen the risk of metabolic disturbances in geriatric patients, regardless of their secreting profile. Further research is needed to elucidate this hypothesis.

DOI: 10.1530/endoabs.81.EP17

EP18

Cardiovascular risk factors in mild adrenal autonomous cortisol secretion in a Caucasian population

Agnieszka Adamska[1], Vitalii Ulychnyi[1], Katarzyna Siewko[1], Anna Popławska-Kita[1], Małgorzata Szelachowska[1], Marcin Adamski[2], Angelika Buczyńska[3] & Adam Krętowski[1,3]
[1]Medical University of Białystok, Department of Endocrinology, Diabetology and Internal Medicine, Poland; [2]Bialystok University of Technology, Faculty of Computer Science, Poland; [3]Medical University of Białystok, Clinical Research Centre, Poland.

Background
Cardiovascular (CVS) risk factors could be present in patients with mild adrenal autonomous cortisol secretion (MACS), which could account for up to 50% of patients with adrenal adenomas. However, the most frequent CVS risk factors in MACS have not been established.
Objective
The aim of the present study was to analyse the difference in CVS risk factors in patients with MACS in comparison to those with non-functioning adrenal tumour (NFAT).
Materials and Methods
A total of 295 patients with adrenal incidentaloma who were hospitalised in the single-center between 2017 and 2019 were included in this retrospective study. All patients underwent a 1 mg overnight dexamethasone suppression test (DST). We divided our group into those who showed suppression in the DST (NFAT) and those who did not show suppression in the DST (MACS). In the studied groups, we analysed the presence of CVS risk factors, such as obesity, prediabetes (PD), type 2 diabetes mellitus (T2DM), hypertension, hyperlipidaemia, and chronic kidney disease.
Results
In our study, 18.9% of patients were defined as MACS, and the remaining 80.1% of patients were defined as NFAT. In the group with MACS, we observed obesity in 33.9%, whereas in NFAT, the prevalence of obesity was 34.7% ($P=0.9$). Hypertension was diagnosed in 78.5% of MACS vs. 69.5% of NFAT ($P=0.2$), whereas chronic kidney disease was observed in 32.1% of MACS vs. 28.5% of NFAT ($P=0.7$). Accordingly, we did not find differences in the diagnosis of prediabetes in MACS vs. NFAT (26.8% vs. 34.3% ($P=0.35$)). Importantly, T2DM was diagnosed in 41% of MACS vs. 23% of NFAT ($P<0.01$). Interestingly, we observed a higher frequency of occurrence of hyperlipidaemia in NFAT (72.4%) vs. MACS (53.6%) ($P=0.01$). Accordingly, in patients without T2DM, MACS was observed in 15.2%, in comparison to 29.5% in patients with T2DM ($P<0.01$).
Conclusions
In our retrospective analyses, we found that T2DM is more prevalent in MACS than in NFAT, whereas hyperlipidaemia is more prevalent in NFAT. Accordingly, no differences were observed in the incidence of obesity, hypertension, prediabetes, or kidney damage in NFAT and MACS patients. This could suggest that mild hypercortisolaemia is not associated with a higher CVS risk in comparison to NFAT.

DOI: 10.1530/endoabs.81.EP18

EP19

Niemann-Pick disease type B and bilateral adrenal incidentalomas

Hamza Elfekih[1,2], Sinda Allegue[1], Monia Zaier[2,3], Oumayma Zarrouk[11], Hayfa Farid[1], Amel Maaroufi[1,2], Maha Kacem[1,2], Molka Chadli Chaieb[1,2], Yosra Hasni[1,2] & Koussay Ach[1,2]
[1]Farhat-Hached University Hospital, Endocrinology-Diabetology Department, Sousse, Tunisia; [2]Faculty of Medicine Ibn El Jazzar, University of Sousse, Sousse, Tunisia; [3]Farhat-Hached University Hospital, Department of Clinical Hematology, Sousse, Tunisia.

Introduction
Niemann Pick disease is a rare autosomal recessive lysosomal storage disorder caused by a deficiency in acid sphingomyelinase. Usually discovered in childhood, it can affect liver, spleen and pulmonary function. Here, we report the case of a Niemann Pick type B disease in an adult associated with bilateral adrenal incidentalomas.
Observation
A 45-year-old male patient was found to have bilateral adrenal incidentalomas associated with hepatomegaly and multinodular splenomegaly, discovered by an abdominal CT scan that was requested during his follow-up for inguinal and umbilical hernia. MRI and CT scan with contrast showed bilateral adrenal hyperplasia and a 26 mm non-adenoma in the medial arm of the right adrenal gland. The patient's clinical examination and biological workup were normal. Short synacthen test ruled out adrenal insufficiency. Plasma metanephrines and low-dose dexamethasone suppression test excluded adrenal hypersecretion. During etiological workup of the splenomegaly, the patient underwent a bone marrow biopsy revealing sea-blue histiocytosis. In addition, a serum acid sphingomyelinase activity assay revealed a deficiency (<0.3 µmol/l per hour) confirming the Niemann-Pick disease type B.
Discussion
The prevalence of adrenal incidentalomas is approximately 5% in the general population and they are bilateral in 7.8 to 15% of cases. Systematic etiological investigation of bilateral adrenal lesions is necessary to exclude malignancies and hypersecretions. Niemann-Pick diseases are characterized notably by hepatosplenomegaly and gradual deterioration in pulmonary function. Its association with bilateral adrenal hyperplasia, adrenal masses and sea-blue histiocytosis has not been previously reported in the literature.

DOI: 10.1530/endoabs.81.EP19

EP20

Adrenal hemangioma with subclinical cushing's syndrome

Ould Kablia Samia[1], Mouna Benfiala[1], Benabdelatif Katia[1], Reda Kassa[2] & Amira Bouchenna[1]
[1]Central Hospital of the Army, Endocrinology, Algiers, Algeria; [2]Douira Hospital, Histopathology, Algiers, Algeria.

Introduction
Adrenal cavernous hemangioma is a rare tumor with few cases reported in the world. Usually this adrenal masses are incidentally discovered and non functional.
Case report
We describe the case of a 63 year old male patient with a history of hypertension and treated prostate. He was referred to our endocrinology department with complaints of his left lower back. At the admission the BMI was 21 kg/m^2, his blood pressure was 160/90 mmHg and the heart rate was 84 beats /mn. In the clinical examination there were no clinical signs of hypercortisolism or catecholamine or mineralocorticoid excess. The abdominal enhanced C T showed a left large heterogeneous adrenal tumor of 50 mm with hemorrhage, necrosis and calcification, the C T value of solid part was 30 UH. The laboratory evaluation revealed a morning cortisol level of 179 nmol/l after a 1 mg overnight dexamethasone suppression test and a low ACTH concentration. The plasma metanephrine, normetanephrine, aldosterone level and renine activity were normal. All these features make it difficult to distinguish from a primary adrenal cortical carcinoma and then required operative management. An adrenalectomy was performed and the tumor was safely completely resected with no evidence for local invasion. The results of pathological examinations were in favor of a cavernous hemangioma of the left adrenal gland.
Conclusion
Adrenal cavernous hemangioma is a rare tumor that can have a very large size, and it is difficult to differentiate from adrenal cortical carcinoma clinically or radiologically.

DOI: 10.1530/endoabs.81.EP20

EP21

Metabolic and cardiovascular consequences of hormone replacement by hydrocortisone in adrenal insufficiency

Ines Charrada, Alaya Wafa, Boubaker Fadia, Najoua Lassoued, Zantour Baha, Berrich Olfa & Sfar Mohamed Habib
Endocrinology-Diabetology and Internal Medicine Service CHU Tahar Sfar Mahdia Tunisia, Mahdia, Tunisia.

Introduction
During adrenal insufficiency (AI), glucocorticoid treatment is supposed to be neutral on the metabolic parameters of patients. However, recent data from the literature report that this corticosteroid replacement therapy increases the metabolic risk. The aim of our work was to determine the metabolic and cardiovascular impact of hydrocortisone (HC) replacement therapy during peripheral AI.
Patients and methods
This was a descriptive and analytical study involving 77 patients with peripheral AI (66 women and 11 men), all treated with HC. For each patient, we determined the length of the disease, the duration of the follow-up, the daily and cumulative dose of HC, the evolution of metabolic parameters (weight, blood pressure, glycemia, lipid parameters), and the Framingham score under HC.
Results
The mean age was 40.5 years (range: 22-63 years). The mean duration of evolution was 7.7 years. The study of metabolic and cardiovascular parameters after treatment with hydrocortisone showed weight gain in 96.1% of patients (overweight: 46.75% and obese: 40.25%). We noted that 41.5% of patients had developed hypertension, 54.54% had pre-diabetes, 37.66% had diabetes mellitus, 52% had dyslipidemia. We noted a significant positive relationship between daily HC dose and the development of obesity ($P<10^{-4}$), hypertension (P: 0.003), diabetes mellitus (PP: 0.025) and dyslipidemia (P: 0.004), respectively. We found a significantly positive relationship between, on the one hand, disease duration, cumulative HC dose and, on the other hand, obesity (P:0.05/P:0.029), hypertension ($P<10^{-4}$/$P<10^{-4}$), and glycemic homeostasis disorders

(*P*: 0.03/*P*: 0.02), respectively. For cardiovascular risk, we noted an elevation of the Framingham score after HC treatment (>20% in 6 patients), with a positive correlation between this score and, respectively, disease duration (*P*: 0.036), cumulative HC dose (*P*: 0.022), female sex (*P*: 0.001) and menopause (*P*: 0.044). In the same setting, four patients had experienced a cardiovascular event, and were all on a HC dose ≧30 mg/d.
Conclusion
The metabolic and cardiovascular risk of corticosteroid replacement therapy with HC during AI appears to be real. It increases with the duration of the disease and the cumulative dose of HC. Regular monitoring of metabolic and cardiovascular parameters is therefore essential with constant re-evaluation of the dose of this drug in these patients.

DOI: 10.1530/endoabs.81.EP21

EP22

Adrenal ganglioneuroma: presentation of two cases

Athanasia Michou, Zoi Efstathiadou, Paraskevi Komzia, Apostolos Gogakos, Efstathios Divaris, Georgia Kourkouta & Marina Kita "Hippokration" General Hospital of Thessaloniki, Endocrinology, Thessaloniki, Greece.

Introduction
Adrenal ganglioneuroma (AGN) is a rare (about 470 described cases), benign tumor arising from the neural crest tissue. These tumors are usually asymptomatic and incidentally detected. They have variable radiological features that often raise suspicion of malignancy. AGN are diagnosed at a mean age of 50 years, have no gender preference and are rarely associated with genetic syndromes.
Aim
The presentation of two male patients, 24 and 53 years old with adrenal incidentalomas and a final diagnosis of AGN.
Case 1
A 24-year-old male patient, with a history of asthma, was referred for evaluation of a left adrenal tumor incidentally discovered on a chest CT performed due to an exacerbation of his respiratory symptoms. The tumor, measuring 1.4 cm, had smooth borders but showed increased density (30 HU). On MRI, the tumor showed mild signal enhancement in T2 sequences and poor enhancement with delayed uptake of paramagnetic substance. Clinical and laboratory workup of the patient were normal. The patient was normotensive and testing for cortisol, metanephrines and adrenal androgens (DHEAS, 17OHPRG), no functionality was detected. The patient underwent a laparoscopic adrenalectomy, the histological examination of which showed morphological features of AGN.
Case 2
A 53-year-old male patient with no previous comorbidities was diagnosed with a large incidentaloma on the right adrenal gland, during a diagnostic work up for fever of unknown etiology. On CT, the incidentaloma had a size of 11×7.5×6.5 cm, high density (>30 HU) and very low absolute and relative contrast media washout. Clinical examination of the patient revealed no signs of hypercortisolism or other pathological findings. Haematological and biochemical tests were normal. Similarly, hormonal workup exclude hypersecretion (normal circadian cortisol rhythm (morning 9.8 μg/dl, evening 1.6 μg/dl), normal 24-hour metanephrines fractions [normetanephrine =261 μg/24 h (<780), metanephrines =41 μg/24 h (<375)] and normal adrenal androgens DHEAS and 17OHPRG. Due to the size of the tumor and the imaging characteristics, which were not compatible with an adrenal adenoma, a retroperitoneal endoscopic right adrenalectomy was performed. Histological examination revealed an AGN with scattered microcalcifications without evidence of necrosis and atypia. The patient, after 4 years of follow-up, remains disease free.
Conclusion
AGNs usually have a benign course. Nevertheless, their imaging features guide patients to their surgical removal to establish a definitive diagnosis and determine prognosis. Age of diagnosis ultimately may not play a decisive role in the differential diagnosis of AGN.

DOI: 10.1530/endoabs.81.EP22

EP23

Determination of 18-hydroxycortisol, 18-oxocortisol by HPLC–MS/MS in the differential diagnosis of various forms of primary aldosteronism

Natalia Romanova, Nadezhda Platonova & Ekaterina Troshina The National Medical Research Centre for Endocrinology, Therapeutic Endocrinology Department, Moscow, Russian Federation.

Introduction
Aldosterone synthase participates in the key reactions of aldosterone synthesis – 11-hydroxylation, 18-hydroxylation and, finally, 18-oxidation. In recent works devoted to evaluating the effectiveness of hybrid steroids in the differential diagnosis of subtypes of primary aldosteronism (PA), it is worth emphasizing the experience of using high-performance liquid chromatography – tandem mass spectrometry (HPLC-MS/MS), which allows detecting even very low concentrations in peripheral plasma (the lower limit for 18-oxocortisol is 0.25 ng/dl).
Objective
To evaluate differences in the synthesis of steroid end products by HPLC-MS/MS at PA.
Material and methods
Retrospective evaluation of blood serum samples from 136 patients with a verified diagnosis of primary aldosteronism. In accordance with standard protocols, the parameters of steroidogenesis were evaluated – aldosterone, 18-oxocortisol, 18-hydroxycortisol, 18-hydroxycorticosterone, 20b-dihydrocortisone, cortisone, cortisol, testosterone, 21-deoxycortisol, corticosterone, 11-deoxycortisol, androstenedione, 11-deoxycorticosterone, DHEA, 17-OH progesterone, 17-OH pregnenolone, progesterone, pregnenolone, androstenedione, adrenosterone, 11-hydroxyandrostendione by HPLC–MS/MS.
Results
As part of the study, in 136 patients with aldosterone-producing adenoma (APA) ($n=56$), idiopathic hyperaldosteronism (IHA) ($n=24$) and 56 with hormonally inactive tumors (HIT), a study of steroidogenesis was conducted, including the determination of the end products of steroid synthesis – 18-hydroxycortisol, 18-oxocortisol by HPLC–MS/MS. Thus in patients with APA, the levels of 18-oxocortisol, 18-hydroxycortisol, 18-hydroxycorticosterone, pregnenolone, determined by HPLC–MS/MS, were statistically significantly increased compared to the study of those in patients with hormonally inactive tumors (18-Oxocortisol Me(PA) 0.75 [0.13; 1.98] ng/dl, Me(HIT) 0.1 [0.06; 0.14] ng/dl, $P<0.05$; 18-Hydroxycortisol Me(PA) 5 [2.52; 10.95] ng/dl, Me(HIT) 2.4 [2; 3.44] ng/dl, $P<0.05$; 18-Hydroxycorticosterone Me(PA) 3.48 [1.97; 7.02] ng/dl, Me(HIT) 1.76 [1.25; 2.52] ng/dl, $P<0.05$; Pregnenolone Me(PA) 2.22 [1.4; 3.07] ng/dl, Me(HIT) 1.38 [0.98; 2.19] ng/dl, $P<0.05$).
Conclusions
Thus, the expediency of determining 18-oxocortisol and 18-hydroxycortisol by HPLC–MS/MS in the differential diagnosis of various forms of PA has been proved.

DOI: 10.1530/endoabs.81.EP23

EP24

Complex adjuvant treatment of patients with two-component adrenocortical cancer (clinical case)

Alexey Krivosheev[1], Timur Britvin[2], Anna Motrenko[3], Larisa Gurevch[4] & Irena Ilovayskaya[5]
[1]Moscow Regional Research and Clinical Institute (MONIKI), Department of Endocrine Surgery, Russian Federation; [1]Moscow Regional Research and Clinical Institute (MONIKI), Department of Endocrine Surgery; [3]Moscow Regional Research and Clinical Institute (MONIKI), Neuroendocrine Unit, Department of Endocrinology, Moscow, Russian Federation; [4]Moscow Regional Research and Clinical Institute (MONIKI), Department of Pathology, Russian Federation.

Adrenocortical cancer (ACC) is a tumor of the adrenal cortex, clinical manifestations, recurrence, and progression potential are determined by its biological characteristics. Morphological diagnosis of tumors of the adrenal glands in some cases presents significant difficulties. According to the WHO classification of tumors of the endocrine organs (4th revision, 2017), in addition to the classical one, myxoid, sarcomatoid and oncocytic histological variants of ACC are distinguished. According to a number of studies, the oncocytic variant is characterized by a less aggressive clinical course. In our work, we present a clinical case of combined treatment of two-component hormonally active (hypercorticism and virilization) adrenocortical carcinoma. After radical surgical treatment, histological examination was verified a polyclonal adrenocortical carcinoma, represented by two components different in cellular composition and architecture. Most of the tumor is of classical structure (Weiss score 4), the second component is an oncocytic variant of ACC (2 major and 2 minor Lin-Weiss-Bisciglia criteria). An immunohistochemical (IHC) study of the oncocytic component of tumor revealed expression of subtype somatostatin 2 receptors (SSTR2), KI67 index was 21%. There was no expression SSTR2 in classical component, the Ki67 proliferation index was 10%. Chromogranin A expression was absent in both tumor components. Invasion of periadrenal adipose tissue, Ki67 10% or more in both tumor components, positive expression of SSTR2 served as the basis for starting adjuvant drug treatment with mitotane in combination with long-acting somatostatin analogs. There was no progression of

the disease during 30 months of patient monitoring. To date, mitotane remains the only drug for the treatment of ACC with proven efficacy. A number of targeted drugs interacting with specific tumor receptors have been proposed, but their use is limited a low efficiency. Recently, reports have been published on the expression of SSTR in tumor tissue, as well as on the effect of synthetic somatostatin analogs on the growth of ACC cell lines. A feature of this clinical case is the development of polyclonal adrenocortical carcinoma, with different functional activity, histostructure, proliferation index and receptor status of its components, which suggests a different malignant potential of tumor components and emphasizes the need for accurate morphological verification of adrenocortical tumors for individualization of treatment. The progression-free period more than 30 months after radical surgical treatment gives grounds for the use of somatostatin analogs in the drug treatment of ACC, but its effectiveness requires further study and evaluation.

DOI: 10.1530/endoabs.81.EP24

EP25

Acute adrenal crisis following COVID-19 in a patient with 11β-hydroxylase deficiency

Hamza Elfekih[1,2], Manel Dridi[1], Asma Ben Abdelkarim[1,2], Siwar Kahloun[1], Yosra Hasni[1,2], Amel Maaroufi[1,2], Maha Kacem[1,2], Molka Chadli Chaieb[1,2] & Koussay Ach[1,2]
[1]Farhat-Hached University Hospital, Endocrinology-Diabetology Department, Sousse, Tunisia; [2]Faculty of Medicine Ibn El Jazzar, University of Sousse, Sousse, Tunisia.

Introduction
11-Beta-hydroxylase deficiency (11β-OHD) is the second most common cause of congenital adrenal hyperplasia. It leads to the accumulation of steroids precursors prior to the enzyme defect, notably 11-deoxycorticosterone (DOC), leading therefore to low renin hypertension and hypokalemia. Hence, patients with 11β-OHD are reportedly protected from adrenal crisis. Here, we report a case of a male with 11β-OHD presenting with acute adrenal insufficiency.
Observation
A 40-year-old male, following in our department for congenital adrenal hyperplasia due to 11β-OHD, was admitted for abdominal pain and vomiting. He had also headaches, chills without shortness of breath, that started one day before his admission leading to the diagnosis of Covid-19 infection. The patient was receiving glucocorticoid replacement therapy (hydrocortisone 30 mg b.i.d.) with good compliance. On examination, he had a blood pressure of 120/70 mmHg despite discontinuation of antihypertensive treatments (Calcium channel blocker, Beta-blocker and spironolactone). His heart rate was 114 bpm and his blood oxygen saturation rate was 95%. Laboratory analysis showed normal serum potassium level of 4.2 mmol/l, functional acute kidney failure and elevated C-reactive protein of 49 mg/l. The patient received hydrocortisone hemisuccinate 200 mg the first day with an improvement of his symptoms.
Discussion
Acute adrenal crisis is exceptional in patients with 11β-OHD. The diagnosis in our case was based on abdominal pain, vomiting, the abnormally normal blood pressure and serum potassium level, and the favorable progression after hydrocortisone hemisuccinate. It was hypothesized that regular treatment with hydrocortisone in these patients will suppress ACTH secretion and leads to a reduced accumulation of steroids precursors that may expose them to the risk of developing acute adrenal crisis in case of hydrocortisone therapy interruption or in the absence of doses adjustment in stressful conditions.

DOI: 10.1530/endoabs.81.EP25

EP26

A rare cause of a surrenal mass

Coskun Ates, Erhan Hocaoglu, Ensar Aydemir, Filiz Mercan Saridas, Özen Öz Gül, Soner Cander, Canan Ersoy & Erdinc Erturk
Uludag University Faculty of Medicine, Endocrinology and Metabolic Diseases, Bursa, Turkey.

Introduction
Myxoid adrenocortical adenoma was described by Brown et al. in 2000 (1). Myxoid adrenal cortical adenoma with pseudo glandular structure is a particular histological variant and is extremely rare. Accurate diagnosis is based on the combined evaluation of clinical features, adrenal imaging, and pathological features. Immunohistochemical studies (cytokeratin, melan-A, USP10, chromogranin, vimentin) can distinguish adrenocortical adenoma from other retroperitoneal myxoid tumors (2).
Case
A 43-year-old male patient uses a bi-level positive airway pressure device for known obstructive sleep apnea syndrome. The patient described occasional high blood pressure had left flank pain in the last 15 days. No pathology was detected in the urinalysis performed by the urology and in the abdominal X-ray. Contrast-enhanced upper abdomen computed tomography was then performed on the patient. In his report, it was seen that there was a 29×27 mm mass lesion in the left adrenal gland with intense contrast enhancement in the arterial and venous phases. In the 1 mg dexamethasone suppression test performed by us, aldosterone, renin, adrenaline, noradrenaline, dopamine, metanephrine and normetanephrine levels were within the normal range. Doxazosin treatment was given to the patient who described occasional blood pressure attacks. The patient underwent laparoscopic left adrenalectomy two weeks later. No complications developed. Histopathological study showed that the mass was a myxoid adrenocortical adenoma with a pseudo glandular pattern. Immunohistochemically, vimentin, CD56, melan-A, CK8 were diffusely positive, while inhibin was focally positive. No immunoreactivity was found in cytokeratin 7, S-100, calretinin, synaptophysin, chromogranin A, TTF1, CK7, napsin, mesolthelin, WT-1, PanCK, CD99. The patient has been followed for 15 months after laparoscopic adrenalectomy. No pathology was detected in the control adrenal hormone profile and control computed tomography. Blood pressure is regulated.
Conclusion
Myxoid adrenocortical adenoma with pseudo glandular pattern may suggest adrenocortical metastasis or pheochromistoma by adrenal imaging method. Immunohistochemical markers are very useful in differential diagnosis.
References
1-Brown FM, Gaffey TA, Wold LE, Lloyd RV. Myxoid neoplasms of the adrenal cortex: a rare histologic variant. Am J Surg Pathol. 2000;24:396–401.
2-Zeng Z, Gu LJ, Zhou ZY, Liu L,Yan HL, Huang YB, Wang ZS, Chen J, Yuan JP. Myxoid adrenocortical adenoma with a pseudo glandular pattern: a case report and literature review Int J Clin Exp Pathol 2017;10(8):8908–8915.

DOI: 10.1530/endoabs.81.EP26

EP27

Impact on quality of life and sleep of hydrocortisone hormone replacement in adrenal insufficiency.

Ines Charrada, Alaya Wafa, Boubaker Fadia, Houcem Mrabet, Zantour Baha, Berrich Olfa & Sfar Mohamed Habib
Endocrinology-Diabetology and Internal Medicine Service CHU Tahar Sfar Mahdia Tunisia, Mahdia, Tunisia.

Introduction
Hydrocortisone (HC) is the most widely used replacement molecule in the treatment of adrenal insufficiency (AI). This substitution treatment is far from ideal especially as it is impossible to reproduce the nycthemeral cycle of cortisol with its current galenic form which has a short half-life. The aim of our work was to determine the impact of HC treatment of peripheral AI on the long-term quality of life and sleep.
Patients and methods
This is a descriptive and analytical study involving 77 patients with peripheral AI (66 women and 11 men), all treated with HC. For each patient, we determined the duration of the disease, the daily and cumulative dose of HC, the number of times HC was taken, the SF-36 quality of life score and the Pittsburgh sleep quality score in 58 patients.
Results
The mean age was 40.5 years (range: 22–63 years). The mean duration of progression was 7.7 years. We found that the percentage of patients with impaired quality of life was higher than in the healthy Tunisian adult population (79.31% vs. 51%), with a lower mean SF-36 global score (54.9 vs. 69.4). We noted a better quality of life in case of three HC intakes compared to two (*P*: 0.006). Regarding sleep quality, we found that 24% of patients had a sleep disorder of the type insomnia of the second part of the night with early awakening, without any correlation with the HC dose. This prevalence was higher than in the general adult population (24% vs. 9.7%). This quality of sleep seems to be better in case of three intakes of HC (morning, noon and afternoon).
Conclusion
Our results agree with those of the literature, since it appears that a 3-dose schedule was more beneficial for quality of life and long-term sleep. However, even with these HC dosing regimens, we remain far from the physiological rhythm of cortisol, and new modified-release HC preparations (DuoCort/Chronocort) could allow to better mimic the nycthemeral cycle of cortisol in patients suffering from AI.

DOI: 10.1530/endoabs.81.EP27

EP28

Addison disease masquerading as hyperemesis gravidarum and good fetal outcome.

Stela Vudu[1], Ina Dusa[1], Veronica Gonta[2], Neonila Tofan[2], Aristia Seremet[1] & Lorina Vudu[1]
[1]State University of Medicine and Pharmacy "Nicolae Testemitanu", Endocrinology, Chisinau, Moldova; [2]Republican Clinical Hospital, Endocrinology, Chisinau, Moldova.

Here we report the case of a woman with first presentation of Addison disease in pregnancy that went undiagnosed until postpartum period. She gave birth to a healthy child by vaginal delivery at 40 weeks of pregnancy. Our patient is a 31 years pregnant woman with unremarkable medical or familial history. At 8 weeks of pregnancy she was complaining of nausea, vomiting, loss of appetite and fatigue, leading to hospitalization. The physical examination revealed a blood pressure of 80/50 mmHg, a check-up that included blood and urine analyses did not reveal any abnormalities. She received treatment with saline and glucose perfusion, vitamin B and was discharged after one week, with persistent symptoms attributed to hyperemesis gravidarum. At 16 weeks of gestation the patient noticed a bronze appearance of the skin. Her condition was deteriorating, with accentuation of fatigue and 9 kg weight loss, leading to another 2 hospitalizations due to presumed hyperemesis gravidarum. Neverthless at 40 weeks of gestation she gave birth to a healthy child by vaginal delivery. 2 months later she was hospitalized in the endocrinology department due to extreme fatigue and persistent gastrointestinal symptoms. At admission the patient's blood pressure was 85/55 mmHg, pulse – 88 beats/minute and respiratory rate – 20 breaths/minute. She had tanned skin and hyperpigmented spots on gums, tongue and mucosa of cheeks. Laboratory data showed: ACTH 1006 (0–46 pmol/l), cortisol 2.41 (69–690 nmol/l). A diagnosis of primary adrenal insufficiency was established and intravenous hydrocortisone hemisuccinate was initiated. Thereafter, the patient was transferred to oral cortisone, and discharged on the 5th day. Currently the patient is in good condition, taking tablets of Cortisone 25 mg at 0800 h and 12.5 mg at 1200 h, and is breastfeeding.

Discussion

Addison disease (AD) is a rare condition, usually due to autoimmune destruction of the adrenal cortex. Addison disease complicating pregnancy is even rarer, about 100 pregnancies being reported worldwide. Untreated Addison disease during pregnancy leads to increased maternal mortality and fetal growth retardation. Nausea and vomiting due to adrenal insufficiency may be confused with typical symptoms of pregnancy. Generalized hyperpigmentation – a hallmark of Addison disease may be seen in normal pregnancy, but dark spots on lips and mouth mucosa should prompt adrenal insufficiency evaluation.

Conclusion

First diagnosis of Addison disease during pregnancy may be challenging due to misleading symptoms attributed to normal pregnancy. Differential diagnosis of severe and prolonged hyperemesis gravidarum should include adrenal insufficiency.

DOI: 10.1530/endoabs.81.EP28

EP29

Pheochromocytoma in the elderly: treatment challenges

Imen Halloul, Ach Taieb, Saad Ghada, Ben Abdelkerim Asma, El Fekih Hamza, Hasni Yosra, Maaroufi Amel, Kacem Maha, Chaieb Molka & Ach Koussay
Farhat Hached University Hospital, Department of Endocrinology and Diabetes, Sousse, Tunisia.

Introduction

Pheochromocytoma is a rare neuroendocrine tumor with a prevalence ranging from 0.05% to 0.1%. Those tumors are usually diagnosed in young adults. However, they can also affect children and the elderly, with sporadic cases being more common in older patients. Giving the recent increases in life expectancy and improvements in imaging techniques, there has been an increase in the number of pheochromocytoma in the elderly.

Case presentation

An 85-year-old female patient was admitted to our endocrinology department for exploration of adrenal incidentaloma. She was followed for hypothyroidism and hypertension for 10 years now. The mass was discovered at an abdominal CT scan when the patient developed vomiting and abdominal pain. The mass was a heterogeneous 65 mm tumor of the left adrenal gland, with a spontaneous density of 55 UH and was in contact to the left renal vein. Biological explorations confirmed the presence of a pheochromocytoma with an elevated level of metanephrines and normetanephrines (5* the normal range). Treatment with doxazosin was administered for 2 weeks in preparation for surgery. A left adrenalectomy was performed without incidents. Histologically, the tumor was confirmed to be a benign pheochromocytoma. The follow-up showed a complete remission with a normal blood pressure and a normal level of plasmatic metanephrine.

Conclusion

Management of pheochromocytoma is delicate in the elderly population, giving the comorbidities associated. Thus, surgical removal should be made by an experienced multidisciplinary team to avoid post-operative complications. Meticulous preparation for surgery is crucial with a particular attention on maintaining balance between the adrenal disease and comorbidities.

DOI: 10.1530/endoabs.81.EP29

EP30

Rare case of SIADH related hyponatremia in sarcoidosis

Bhavna Sharma & Mushtaqur Rahman
Northwick Park Hospital, United Kingdom.

Disorders of sodium metabolism in sarcoidosis are predominated by diabetes insipidus; SIADH is extremely rare, restricted to sporadic case reports. We present the case of a 68 year old South Asian female presenting with a 3 year history of chronic, mild hyponatraemia, which was asymptomatic apart from mild lightheadedness. She had a history of stable sarcoidosis that was not requiring treatment, based on lung pathology. Despite fluid restriction, serum sodium remained around 128 mmol/l; serum osmolality was 263 mOsm/kg, urine osmolality 296 mOsm/kg, and urine sodium 76 mmol/l. TSH was normal, 3.52 mIU/l. A Short synacthen test was normal: baseline serum cortisol of 497 nmol/l, rising at 30 mins to 809 and at 60 mins to 1002. IGF-1 and HbA1c were normal. Serum ACE was raised, 82U/L.A CT Chest/Abdomen/Pelvis revealed two calcified paratracheal lymph nodes and stable apical thickening in both lungs, with slightly more marked subpleural reticulation in right upper lobe of lung. An MRI scan of the brain showed no gross pituitary pathology. The patient was managed with oral slow-sodium 2 tabs bd and furosemide 20 mg od. In light of the hyponatremia, active management of the sarcoidosis was reconsidered in case of neurosarcoidosis and for this, an MRI scan of the brain with the use of gadolinium needs to be undertaken first

DOI: 10.1530/endoabs.81.EP30

EP31

Spontaneous haemorrhage of an adrenal angiomyolipoma: case report

Paloma González Lázaro, Maria Zhao Montero Benitez, Cristina Montalban Méndez, Pedro Jimenez Torrecilla, Amparo Lomas Meneses & Ines Gomez García
La Mancha Centro Hospital Center, Endocrinology, Alcázar de San Juan, Spain.

Introduction

Angiomyolipomas are rare mesenchymal tumours arising from the perivascular epithelioid cells. They are benign endocrinologically inactive tumours with a histological structure consisting of variable amounts of adipose, thick-walled blood vessels and smooth muscle cells. Commonly, angiomyolipomas occur in the kidney with few extra renal case reports in adrenals.

Case Report

We report the case of a 76-year-old-man with personal history of hypertension and hypercholesterolemia, who presents as an incidental finding on ultrasound performed by urology due to an episode of acute urine retention, a 91 mm right adrenal mass, which on scan is suggestive of adenoma. The hormonal study (cortisoluria, metanephrines and aldosterone) was negative for functionality and, DHEA sulfate revealed normal results. Due to the large size, the patient underwent an open right adrenalectomy and was discharged home just over 1 week post-operatively without incidences. Histology showed a soft tissue tumour composed of mature adipose tissue, proliferating thick-walled vessels and in a smaller quantity proliferation of smooth muscle, with focal spindle and epithelioid cells Immunostains for Melan-A (Fig. 4) and HMB-45 were focally positive. Desmin and smooth muscle actin were also focally positive, confirming the presence of smooth muscle in the tumour, also there were present cystic areas occupied by devitalized tissue and fibrino-hematic material. These histological features are consistent with an spontaneous adrenal hematoma of an angiomyolipoma.

Discussion

This case report describes spontaneous haemorrhage of an adrenal angiomyolipoma picked up incidentally on imaging. A review of the literature revealed 18

previously reported cases of adrenal angiomyolipoma. Of these, 15 were sporadic and 3 were reported in patients with tuberous sclerosis or lymphangioleiomyomatosis]. There were 2 reported cases of spontaneous haemorrhage. Management of these lesions has been guided by the limited number of case reports in the literature. It is general consensus that smaller lesions detected incidentally should be managed non-surgically and their size should be kept under surveillance. Surgical management has been proposed for lesions which are either symptomatic and/or greater than 5 cm. Laparoscopic adrenalectomy has successfully been used, but larger lesions are best removed using open adrenalectomy

Conclusion

Adrenal angiomyolipomas are rare benign tumours that have the ability to reach a large size and potential to bleed. Here we report the 3er case reported on literature of spontaneous haemorrhage in an adrenal angiomyolipoma, which was successfully treated with open adrenalectomy.

DOI: 10.1530/endoabs.81.EP31

EP32

Interference in aldosterone assay revealed by hemolysis.

Martine Deckers[1], Tamira Klooker[2], Jacquelien Hillebrand[3], Sjoerd van den Berg[4] & Prim de Bie[1]
[1]OLVG lab BV, Clinical Chemistry, Amsterdam, Netherlands; [2]Flevoziekenhuis, Internal Medicine, Almere, Netherlands; [3]Amsterdam UMC, Clinical Chemistry, Laboratory of Endocrinology, Amsterdam, Netherlands; [4]Erasmus MC, Internal Medicine, Rotterdam, Netherlands.

We report an interference in an immunoassay for aldosterone, which potentially could have led to a wrongful diagnosis and unnecessary surgery. The interference was serendipitously recognized due to a preanalytical error. A 59-year-old female patient with hypertension was referred to the department of endocrinology after an adrenal incidentaloma was detected. Because of her hypertensive history, screening for primary hyperaldosteronism was performed. An elevated aldosterone and a raised aldosterone/renin ratio was measured. To confirm the diagnosis of primary hyperaldosteronism a saline infusion test was performed. However, Aldosterone could not be reliably measured by our own immunoassay (Liaison XL) due to hemolysis in the sample taken after 2L saline infusion. This sample, together with the sample before infusion, was sent to our referral laboratory, where aldosterone was measured by LC–MS/MS. Low concentrations of aldosterone were measured by LC–MS/MS in both samples, rejecting the diagnosis hyperaldosteronism. Strikingly, the basal aldosterone concentration as measured by LC–MS/MS was much lower comparted to the concentration as measured by the Liaison XL immunoassay, raising suspicion of an assay interference. Confirmative testing with a repeat sample, using an additional immunoassay (Lumipulse 2100) and a dilution experiment all pointed towards a method specific interference in our own immunoassay. These results showed that the patient did not have primary hyperaldosteronism and that her incidentaloma was hormonally inactive. In retrospect, based on these results dynamic testing would not have been necessary. Surgical intervention was not performed and the patient was treated with antihypertensive drugs. Since in most laboratories aldosteron results from both screening and confirmative tests are derived from the same method, analytical interference in an immunoassay is difficult to detect. This especially holds true if there is a high clinical probability for primary hyperaldosteronism as in this case due to presence of hypertension and the finding of an adrenal incidentaloma. This may also explain the low number of publications on this type of interference in the literature.

DOI: 10.1530/endoabs.81.EP32

EP33

Large adrenal tumor in paucisymptomatic ACTH – independent Cushing syndrome's patient – a clinical case

Maria-Alexandra Mohora[1], Raluca Trifanescu[1,2], Caragheorgheopol Andra[3], Iordachescu Carmen[3], Hortopan Dan[3] & Catalina Poiana[1,2]
[1]C.I. Parhon National Institute of Endocrinology, Pituitary and Neuroendocrine Disorders, Bucureşti, Romania; [2]Carol Davila University of Medicine and Pharmacy, Endocrinology, Bucureşti, Romania; [3]C.I. Parhon National Institute of Endocrinology, Bucureşti, Romania.

Background

Cushing's syndrome is represented by the cummulation of signs and symptoms of excess glucocorticoids and has many potential causes. Approximately 20 percent of all cases are represented by ACTH-independent adrenal tumors – with a majority of these being represented by cortisol secreting adrenal adenomas. Generally, a large adrenal tumor has over 5 cm in diameter and the risk of it being malignant raises proportionately with the dimensions. Large adrenal tumors are rare and the management and surgical indication is patient-specific.

Case report

A 20 years old female presented for weight gain (30 kg in the last 3 years), bradimenorrhea, hirsutism and treatment-resistant acne, referred by a dermatologist. Clinical exam revealed general obesity with little central redistribution, facial and shoulders pustular acne, vessel fragility (bruises and hematomas), purple axillary striae and hirsutism (Ferriman score = 29). Blood pressure was normal upon multiple examinations. The patient had upper-normal 0800 h cortisol values (19.19 μg/dl) with suppressed 0800 h plasma ACTH (1.05 pg/ml), with loss of circadian secretion rhythm (late-night serum cortisol – 15.8 μg/dl) and lack of cortisol suppression both after 1 mg overnight dexamethasone (17.8 μg/dl) and after 2 mg × 2 days dexamethasone suppression test (19.7 μg/dl). She also had increased free urinary cortisol levels (324 μg/24 h) and late-night salivary cortisol (19.1 nmol/l). She also had increased androgens (testosterone and androstenedione), with a FAI of 14, with upper-normal values of DHEA-S, without suppression after the dexamethasone dynamic tests. Glucose metabolism was normal, with normal HOMA-IR score. Abdominal MRI was performed, revealing a large left adrenal tumor 6.7/5.6/6.3 cm and a hypo-plastic right adrenal gland. **The diagnosis was** ACTH-independent Cushing syndrome due to adrenal tumor secreting cortisol and androgens, with radical-surgery indication.

Treatment

Taking into account the potential malignancy, the patient underwent open surgery. The histopathological examination revealed an 8/7/7 cm cortical adrenal adenoma, without any malignancy characteristics. The immunohistochemistry analysis is pending.

Follow-up

Postoperatively, the patient showed adrenal insufficiency. Five months later, the basal cortisol value was low (0.97 μg/dl) with a slighly raised value of ACTH (56.64 pg/ml). The MRI confirmed total removal of the left adrenal tumor and a slightly smaller right adrenal gland.

Conclusion

Despite having a large adrenal tumor, our young patient had a paucisymptomtic ACTH – independent Cushing syndrome. Morning cortisol values aren't enough to exclude hypercortisolism especially in young patients.

DOI: 10.1530/endoabs.81.EP33

EP34

Single centre experience of assessment of adrenal incidentalomas – it's time for a change

Thin Kyi Phyu Naing, Husay Janebdar, Neetha Jose, Janak Saada, Mark Rochester, Khin Swe Myint & Rupa Ahluwalia
Norfolk & Norwich University Hospital, United Kingdom.

Background

Adrenal incidentalomas (AIs) refer to adrenal masses discovered on imaging performed for conditions unrelated to suspected adrenal diseases. In an ageing population with improving radiological modalities, the detection of AIs has increased. While most are benign, non-functioning adenomas, some may represent functioning and/or malignant disease including adrenal carcinoma. Investigating AIs can be time-consuming and anxiety-inducing for patients, while under-investigation can result in missing life-threatening diagnoses. Thus, AI investigation pathways should be streamlined to achieve both efficiency and cost-effectiveness.

Method

A review of management of AIs was conducted in a large, tertiary centre within the United Kingdom. The size and laterality of lesions including attenuation, functional status and multidisciplinary team (MDT) meeting outcomes were assessed. This is an ongoing audit and the full data analysis will be available at the time of presentation.

Results

A total of 182 patients with AIs were referred between 2019 and 2022. 91 patients were seen in 2021, the data for which is presented below.

Discussion

Under current hospital guidelines, (based on the European Society of Endocrinology's 2016 recommendations), all patients with AIs undergo biochemical testing and clinical assessment followed by discussion at the adrenal MDT meeting. Similar to published evidence, our data demonstrates that the majority of AIs are benign and non-functioning (84%). Thus, the investigation pathway should be remodelled to avoid unnecessary clinic appointments. For those with benign, non-functional adenomas, a nurse-led or virtual consultation could be offered. Face-to-face appointments for further examination and treatment should be reserved for those with functioning and/or malignant lesions.

Given the low risk of malignancy or functional lesions amongst AIs and the expected rise in incidence of reported AIs, it's imperative to optimise current practice and avoid further strain on clinical services.

Total patients (2021)	91
Biochemistry completed and discussed in MDT	53
Awaiting results and/or MDT outome	38

Laterality of lesions	Number of patients	%
Unilateral	48	91
Bilateral	5	9

Diagnosis	Number of patients	Average size of adenoma (mm)	%
Non-functioning adenoma	45	30	84
Autonomous adenoma	8	26	16
Phaeochromocytoma	0	–	0
Primary adrenocortical malignancy	0	–	0
Metastases	0	–	0

Initial imaging modality	Number of patients	%
CT with contrast	43	82
CT without contrast	5	9
MRI	5	9

Radiology MDT outcome	Number of patients	%
Benign	47	89
Indeterminate	6	11
Malignancy	0	0

Clinic outcome	Number of patients	%
Discharge	45	84
Monitor	8	16
Treat	0	0

DOI: 10.1530/endoabs.81.EP34

EP35

Carbohydrate metabolism disorders in patients with Addison's disease

Dhoha Ben Salah, Khouloud Boujelben, Asma Zargni, Mouna Elleuch, Maalej Souhir, Mouna Mnif, Mnif Fatma, Nadia Charfi, Nabila Rekik Majdoub, Faten Haj Kacem Akid & Mohamed Abid
Hedi Chaker Hospital, Diabetology and Endocrinology Department, Sfax, Tunisia.

Introduction
In adults with Addison disease, over glucocorticoid replacement therapy is associated with an increased morbidity and decreased life expectancy, related to low bone mineral density and cardiometabolic outcomes. The aim of our study was to assess the prevalence of carbohydrate metabolism disorders in patients with Addison disease and identify its predictive factors.
Patients and methods
A cross sectional study including 50 patients diagnosed with Addison disease with a mean duration of glucocorticoid replacement of 13.9 years. Biochemical markers of glucose metabolism were evaluated.The prevalence of type 2 diabetes and its complications were analyzed. Patients presenting type 1 diabetes were excluded from our study.
Results
The mean age of patients was 49.5 ± 13.9 years (18–78 years) with significant female predominance and a sex ratio of 0.25.High blood pressure (52%) and diabetes mellitus (52%) were the most common family histories. Mean fasting blood glucose at the diagnosis of Addison disease was 4.6 ± 0.6 mmol/l (3.6–5.4 mmol/l). Mean glycated hemoglobin (HbA1c) was 4.6 ± 0.7%(3.8–5.5%).No patient had prediabetes nor diabetes at the diagnosis. At the time of our study, disorder of carbohydrate metabolism was found in over a third of patients (38%) after a mean duration of Addison disease of 17.5 ± 5.4 years (4–35 years).Among those patients, 31.6% had type 2 diabetes. Diabetic retinopathy occurred in 2 patients and one patient complained of diabetic neuropathy. Daily and cumulative dose were higher in patients with diabetes compared to those with normal blood sugar level (27,5 ± 5 mg/day versus 25.6 ± 6.9 mg/day; 506.2 ± 277.2 mg versus 355.4 ± 282.9 mg) without significant difference. As well, longer Addison disease duration was found in patients presenting diabetes compared to those with a normoglycemia (19.8 ± 9.9 versus 13.2 ± 8.4 years; $P = 0.1$).
Conclusion
At the present time, despite of the worldwide availability of replacement therapy in Addison disease, exposure to supraphysiological dose of corticosteroids leads to altered insulin secretion and decreased hepatic and muscular insulin sensitivity, that result in risk exacerbation of carbohydrate metabolism disorders.

DOI: 10.1530/endoabs.81.EP35

EP36

Evaluation of the efficacy of osilodrostat in five patients with Cushing's syndrome: A single-center study

Naoko Hashimoto[1], Satomi Kono[2], Takashi Kono[1], Shimatsu Akira[3], Alberto Pedroncelli[4] & Tomoaki Tanaka[2]
[1]Chiba University, Department of Molecular Diagnosis, Graduate School of Medicine, Chiba, Japan; [1]Chiba University, Department of Molecular Diagnosis, Graduate School of Medicine, Chiba, Japan; [3]Omi Medical Center, Kusatsu, Japan; [4]Recordati AG, Basel, Switzerland.

Context
Osilodrostat (Osi), a potent inhibitor of 11β-hydroxylase, blocks the conversion of 11-deoxycortisol to cortisol and improves hypercortisolism in patients with Cushing's syndrome (CS). Here, we report a study evaluating the efficacy of Osi in five non-Cushing's disease (CD) CS patients treated with Osi in Japan.
Subjects and Results
Five patients with non-CD CS were treated with Osi at Chiba University [primary disease breakdown: 4/5 patients with adrenal Cushing's syndrome (cortisol-producing adenoma (CPA): 3, primary macronodular adrenal hyperplasia (PMAH): 1) and 1 with an adrenocorticotropic hormone (ACTH)-producing tumor originating from the thymus]. The mean age was 38.4 years, the male to female ratio was 1:4, and the mean duration of treatment was 3.4 months for the 3 patients who underwent CPA surgery after receiving Osi, 15 months for the patient with an ACTH-producing tumor and 18 months for the patient with PMAH. The maximum dose of Osi ranged from 4 mg/day to 10 mg/day. Three patients had been treated with metyrapone before Osi was administered. The maximum dose of metyrapone ranged from 1000 mg/day to 5000 mg/day. Osi was administered after approximately one-month wash-out period. The mean urinary free cortisol level before administration was 2162 μg/day (251-5420), which decreased markedly to a mean of 13 μg/day (8.3-20.6) after treatment, all of which were normalized. Laparoscopic surgeries were performed safely. The major adverse events were related to the Osi mechanism of action, such as adrenal insufficiency/hypofunction and fatigue, and no grade 4 adverse events were observed. The three patients with CPA were cured by surgery after preoperative Osi administration. None of the patients discontinued Osi because of safety.
Conclusion
Osi efficiently normalized symptoms and rapidly and persistently lowered urinary cortisol levels in patients with CS due to adrenal or ectopic ACTH. Our findings show that Osi is an effective treatment option and contributes to safely undergoing surgery for CPA patients.

DOI: 10.1530/endoabs.81.EP36

EP37

Clinical sexual dimorphism in patients with nonfunctioning adrenal incidentaloma

Antoan Stefan Sojat[1], Miomira Ivovic[2], Ljiljana Marina[2], Bogdan Dugic[3], Milina Tancic-Gajic[2], Zorana Arizanovic[1], Dunja-Simona Petkovic[4], Kristina Saravinovska[4], Tijana Petkovic[1], Natalija Antic[1], Aleksandra Kendereski[2] & Svetlana Vujovic[2]
[1]Clinic for Endocrinology, Diabetes and Metabolic Diseases, University Clinical Centre of Serbia, Department for Obesity, Metabolic and Reproductive Disorders, Belgrade, Serbia; [2]Clinic for Endocrinology, Diabetes and Metabolic Diseases, University Clinical Centre of Serbia, Faculty of Medicine, University of Belgrade, Department for Obesity, Metabolic and Reproductive Disorders, Belgrade, Serbia; [3]School of Electrical Engineering, University of Belgrade; [4]Faculty of Medicine, University of Belgrade, Belgrade, Serbia.

Introduction
The incidence of adrenal incidentaloma (AI) increases with age. According to epidemiological studies they are more frequent in women than in men.
Aim
The aim was to determine the possible clinical sexual dimorphism in patients with nonfunctional adrenal incidentaloma (NAI).
Patients and methods
This was an observational, cross-sectional study of 381 patients with AI that were functionally assessed in our Clinic. After exclusion of patients with overt adrenal hyperfunction, malignancy, cysts and patients with (possible) autonomous cortisol secretion the studied group consisted of 195 patients with NAI: 129 female and 66 males. Based on average menopause age of 51, we stratified women in two groups: < 51 and $\geqq 51$. For the sake of comparison, we age-matched the male group, and evaluated differences in body mass index (BMI), adrenal tumor size (ATS), localization, ACTH, 24 h cortisol, 1 mg dexamethasone suppression cortisol (1 mg DST), and prevalence of hypertension (HTA) and type 2 diabetes mellitus (T2DM).
Results
Female sex was predominant in the whole NAI cohort (F/M %: 66.1/33.8) as well as in both age groups (< 51, 44 patients – F/M %: 61.3/38.6 and $\geqq 51$, 151 patients – F/M %: 67.5/32.4) with no difference in gender frequency between younger and older patients. There was no difference in age, BMI, ATS, localization, ACTH, 24 h cortisol, 1 mg DST cortisol, HTA and T2DM prevalence between female and male patients. Upon stratification by age, older female patients had significantly higher BMI ($P=0.002$), higher 24 h cortisol ($P=0.017$) and more prevalent T2DM ($P=0.003$) than younger female patients, while HTA was equally prevalent in both female groups. In a linear regression, BMI was the most significant predictor of HTA in premenopausal female patients ($B=0.552$, 95%CI $B=0.006$–0.102, $P=0.028$).
Conclusion
Despite younger age and significantly lower BMI in premenopausal women with NAI, the frequency of HTA was the same as in the menopausal group with BMI being the most significant predictor. Our results add to the body of evidence that female gender plays a role as a cardiometabolic risk factor in NAI patients indicating the existence of clinical sexual dimorphism in patients with NAI.

DOI: 10.1530/endoabs.81.EP37

EP38

Endocrine emergencies during Ramadan

Yousra Settai, Nassim Essabah Haraj, Siham El Aziz & Asma Chadli
UHC IBN ROCHD, Endocrinology and Metabolic Disorders, Casablanca, Morocco.

Introduction
Ramadan, the holy month of fasting, is a stressful period that exposes to endocrine disturbances, which may decompensate some endocrinopathies or precipitate their revelation.
Objectives
To evaluate the incidence of endocrine emergencies during the month of Ramadan, and thus the risk of endocrine decompensation related to fasting.
Materials and methods
This is a prospective study conducted in the department of endocrinology and diabetology, including 47 patients who consulted for endocrine emergencies during Ramadan, in the period from April 13 to May 12, 2021. Data analysis was performed using SPSS version 25 software.
Results
The average age of our patients was 39 years (18–70 years), with a sex ratio of 3:1. Young people represented 78.7%. Before the month of fasting, 68% of the patients were known to have endocrinopathy (hyperthyroidism, hyperparathyroidism, adrenal insufficiency), 43% of whom admitted poor compliance with their treatment during Ramadan. Hyperthyroidism predominated in 48.9%, with 25.5% of acute adrenal insufficiency, 21.2% of acute hypocalcemia, and 4.2% of acute hypercalcemia. In 63.9% of the patients, no decompensation factor other than fasting was identified. Other causes were mainly pancreatitis (34%), underlying heart disease (16%), urinary tract infections (11%), and other causes (cholecystitis, tuboovarian abscess, pneumocystis, Guillain-Barré syndrome).
Conclusion
Ramadan fasting is a sacred ritual for Muslims, but it is not without risks since it exposes to hormonal disturbances that can reveal or decompensate certain endocrinopathies. Hence the need for a pre-Ramadan consultation to adapt the treatment and to discuss the possibility of fasting, with close follow-up during the holy month, to avoid the risk of complications.

DOI: 10.1530/endoabs.81.EP38

EP39

Hypertension during pregnancy: A diagnosis that should not be overlooked.

Wiem Saafi, Taieb Ach, Asma Ben Abdelkarim, Ghada Saad, Hamza Elfekih, Yosra Hasni, Maha Kacem, Molka Chaieb, Amel Maaroufi & Koussay Ach
Farhat Hached University Hospital, Endocrinolgy, Sousse, Tunisia.

Introduction
Hypertension disorders during pregnancy constitute a significant cause of maternal and perinatal mortality worldwide. Paragangliomas represent a rare cause of hypertension in gestation. The management of these endocrine tumors can be challenging, especially when diagnosed during pregnancy. We describe a case of a paraganglioma discovered in a pregnant woman.
Case report
We report the case of a twenty-seven-year-old female patient who presented to our endocrinology department with gestational diabetes when she was 27 weeks pregnant. At 20 weeks of gestation, she was explored for high blood pressure, and the diagnosis of gestational hypertension was retained and treated with calcium inhibitors. The patient continued to have elevated blood pressure with typical signs of the Menard triad. A pheochromocytoma was then suspected. Plasma metanephrine levels were twelve times above the normal range. Since the patient was pregnant, MIBG scintigraphy could not be practiced. Thoracic and abdominal MRI showed a retroperitoneal and right latero-aortic mass of 3.5 cm. The diagnosis of paraganglioma was established, we treated the patient with alpha-blockers. As for her diabetes, she required insulin therapy. Surgical treatment was postponed. She had regular control of her hypertension and diabetes. The obstetrical ultrasound did not show any abnormalities during control. The patient had cesarean delivery at 38 weeks of gestation with a positive outcome.
Conclusion
Paraganglioma represents a rare cause of hypertension during pregnancy. The association between hypertension and diabetes should be alarming, especially during the first weeks of gestation. The early diagnosis of this situation can make its management less complicated.

DOI: 10.1530/endoabs.81.EP39

EP40

Pheochromocytoma with subclinical and adrenocorticotropic hormone-independent Cushing Syndrome

Elyes Kamoun[1,2], Ibtissem Ben Nacef[1,2], Sabrine Mekni[1,2], Youssef Lakhoua[1], Nadia Mchirgui[1,2], Imen Rojbi[1,2] & Karima Khiari[1,2]
[1]Hospital Charles Nicolle, Endocrinology Department, Tunis, Tunisia; [2]Faculté de Médecine de Tunis, Tunis, Tunisia.

Introduction
Adrenal incidentaloma prevalence is rising with the advancement of imaging techniques. The hormonal work-up should always include free metanephrines for the diagnosis of a pheochromocytoma and 1 mg overnight dexamethasone suppression test for the diagnosis of autonomous cortisol secretion. These tumors have two distinct embryologic origin and don't usually coexist, and when they do, it occurs in case of an ectopic adrenocorticotropic hormone (ACTH) production by the pheochromocytoma. We herein describe a pheochromocytoma with an ACTH-independent possible autonomous secretion of cortisol.

Observation
We report the case of a 57 years old woman, with a history of an insulin-treated type 2 diabetes mellitus, high blood pressure treated with captopril and amlodipine, atrial fibrillation treated with beta-blockers and vitamin K antagonists, referred to our department for an adrenal incidentaloma. It was a left adrenal mass measuring 28*23*32 mm with a spontaneous density of 28HU, an absolute washout of 71% and relative washout of 40%. She didn't have any clinical sign of pheochromocytoma or Cushing syndrome. On laboratory investigation, she had a glycated hemoglobin of 8,7%, a low potassium level at 3.4 mmol/l and TSH levels at 1.38 µUI/ml. Adrenal hormonal work-up found urinary fractionated metanephrines levels at 364 nmol/creatinine (3*normal) and urinary fractionated normetanephrines levels at 463 nmol/creatinine (1.65*normal) confirming the diagnosis of pheochromocytoma. Cortisol levels after 1 mg overnight dexamethasone suppression test were at 87 nmol/l, confirming a possible autonomous secretion of cortisol with ACTH levels inferior to 5 pg/ml excluding an ectopic secretion of ACTH. Aldosterone and renin levels were assessed and a secondary hyperaldosteronism was discovered with aldosterone levels at 740 pmol/l, renin levels at 53 pg/ml and aldosterone/renin ratio at eight. Sex hormones and steroid precursors were normal. The diagnosis of a corticomedullary mixed tumor of the adrenal gland is suspected in our patient. Complementary work up didn't find osteoporosis, calcitonin and calcium levels were normal, transthoracic echocardiography concluded to a concentric hypertrophy of the left ventricule. The patient was put under alpha blockers and was referred to surgery.
Conclusion
This case illustrates the presentation of a corticomedullary mixed tumor, which is a rare adrenal tumor presenting as a pheochromocytoma with an ACTH-independent cortisol production. The pre and peri operative management includes the management of a pheochromocytoma and an autonomous cortisol secretion. Confirmation of this diagnosis relies on histology and immunohistochemistry.

DOI: 10.1530/endoabs.81.EP40

EP41

Papillary stasis edema revealing arterial hypertension in the context of an 11beta-hydroxylase deficiency

Rekik Mona[1], Kammoun Sonda[1], Ayedi Omar[1], Faten Haj Kacem Akid[2], Ben Amor Saloua[1] & Trigui Amira[1]
[1]Habib Bourguiba Hospital, Department of Ophthalmology, Sfax, Tunisia; [2]Hedi Chaker Hospital, Department of Endocrinology, Sfax, Tunisia.

Introduction
11-Hydroxylase deficiency is a rare form of congenital adrenal hyperplasia characterized by glucocorticoid deficiency, hypertension, hypokalemia and virilization in females. We report a case of congenital adrenal hyperplasia due to 11beta-hydroxylase deficiency revealed by bilateral papilledema in the context of arterial hypertension.
Case report
A 13-year-old patient, with no medical history, presented with complains of headache, vomiting and bilateral visual blurring. Visual acuity was 10/10 in both eyes. The fundus examination showed bilateral papilledema. Brain magnetic resonance imaging was normal. The blood pressure was at 17/10. Holter monitoring of blood pressure revealed high blood pressure levels. The patient also presented with hirsutism. The etiological assessments concluded with an adrenal enzymatic block caused by 11-hydroxylase deficiency. The patient was successfully treated with glucocorticoids.
Discussion
11beta-hydroxylase deficiency is the second cause after 21-hydroxylase deficiency of congenital adrenal hyperplasia, and accounts for about 5 to 8% of cases. 11beta-hydroxylase deficiency is clinically manifested by a syndrome of hyperandrogenism associated with arterial hypertension found in two out of three patients with this anomaly. In this case, the condition was revealed by bilateral stasis papilledema associated with arterial hypertension. Indeed, papilledema is the clinical expression of various conditions in children. Its management is urgent because vital and visual prognoses can be engaged. Stasis edemas are caused by general conditions, the leader of which is intracranial hypertension, whatever its etiology. A second cause that should not be overlooked is represented by malignant hypertension.
Conclusion
Papilledema in children poses many problems, including diagnostic ones. Its management is urgent because vital and visual prognoses can be engaged. The diagnosis and the treatment can be multidisciplinary involving ophthalmologist, radiologist and neuropediatrician and endocrinologist.

DOI: 10.1530/endoabs.81.EP41

EP42

Giant non-functioning adrenocortical carcinoma – the elephant in the room

Sing Yang Sim[1], Jana Bujanova[2], Matthew Hayes[2], Charles Tilley[2], Simon Crabb[2] & Lorena Arnez[1]
[1]St Mary Hospital, Diabetes and Endocrinology, Isle of Wight, United Kingdom; [2]University Hospital Southampton, Southampton, United Kingdom.

Adrenocortical carcinoma (ACC) is a rare malignancy with an incidence of 0.7–2.0 cases/million habitants/year, often with a dismal prognosis. Patients present with abdominal symptoms or symptoms of hormone excess. However, 15% are diagnosed incidentally. (1) A 59y male was referred with progressive lethargy, weight loss, dyspepsia and abdominal distension over the past 2 years. He was dismissive of 'the elephant in the room' and in denial. He was pushed to seek medical attention by his family when abdominal mass and cachexia could no longer be ignored. His weight was 63 kg, BMI 20.2 kg/m^2. He looked emaciated with no Cushing's stigmata.There was a large firm mass on the entire left half of his abdomen extending midline. CT chest/abdomen/pelvis showed 23 cm mass arising from the left adrenal gland, heterogenous with punctate calcification and central necrosis. Mass was hormonally non-functional apart from incomplete cortisol suppression on 1 mg overnight dexamethasone suppression test – 86 nmol/l ($<$50).
Results
Normetanephrine 1.67 µmol/24 h (0–3), Urine metanephrine 0.49 µmol/24 h (0–1.40), Urine 3-methoxytyramine 0.75 µmol/24 h (0.57–2.39), DHEA 12.9 µmol/l (1.3–9.8), testosterone 4.8 nmol/l, androstenedione 12.2 nmol/l (2.8–10.5), SHBG 30.9 nmol/l (15–48), FAI 13.9 (34–106), 17OHP 2.2 nmol/l, aldosterone renin ratio 30 pmol/mIU.
FDG PET CT showed a large avid necrotic left upper abdominal mass with SUV max 7 inseparable from the left adrenal gland. He underwent an open adrenalectomy. 6 kg organised mass with central necrosis was fully excised measuring 37$\times$21$\times$21 cm. Post-operative period was complicated by hyponatraemia despite Hydrocortisone cover. Histology showed positive staining for calretinin, inhibin and melan-A. Staining for PAX8, S100, chromogranin was negative. The appearances were consistent with ACC, Weiss Score 5 and ki-67-5.9%, T1, N0, M0, R0. Post-operatively he was very well, off steroids and back at work part-time. He was offered adjuvant mitotane but decided not to receive it. His circumstances were borderline-he did not meet ESMO guidelines for mitotane, although the ESE guidelines would suggest, that it could be considered 'on a case-by-case basis'.
Conclusion
To our knowledge, this is the largest and the second heaviest ACC ever reported. This case highlights a very wide heterogenicity in ACC behaviour from a very aggressive to indolent disease. A combination of patient psychological factors leading to delayed presentation and indolent behaviour of this ACC allowed it to reach colossal proportions, something we are unlikely to see again.
References
1 Rossella Libé Adrenocortical carcinoma (ACC): diagnosis, prognosis, and treatment Front Cell Dev Biol. 2015; 3: 45.

DOI: 10.1530/endoabs.81.EP42

EP43

Clinical case: adrenal cortical carcinoma

Vita Lizdeniene[1], Saule Cyrolyte[2], Ieva Meskinyte[2], Darius Pranys[3] & Raimonda Klimaitę[4]
[1]Hospital of Lithuanian University of Health Sciences, Kauno Klinikos, Department of Endocrinology, Kaunas, Lithuania; [2]Lithuanian University of Health Sciences, Kaunas, Lithuania; [3]Hospital of Lithuanian University of Health Sciences, Kauno klinikos, Department of Pathology, Kaunas, Lithuania; [4]Institute of Endocrinology, Medical Academy, Lithuanian University of Health Sciences, Kaunas, Lithuania.

Introduction
Adrenal cortical carcinoma (ACC) is a rare and aggressive malignancy. Most patients (80%) are asymptomatic at the time of diagnosis. ACC generally has a poor prognosis with a 5-year survival rate of 20–25%.
Case
A 37-year-old man came to the Hospital of Lithuanian University of Health Sciences Kaunas Clinics for general weakness, fatigue, intermittent abdominal pain, and weight loss ($\sim$ 10 kg in 9 months). During the abdominal US, the mass in the right adrenal gland was found. Physical examination: no clinical signs of hypercortisolemia and no changes in other endocrine systems were observed.

Laboratory tests
Diagnosis of pheochromocytoma and primary hyperaldosteronism excluded. 26.10.20 – 1 mg of Dexamethasone test – no suppression of cortisol was detected, low-dose and high dose Dexamethasone suppression tests – pathologic (Table 1).
Abdominal CT
In the right adrenal gland – ∼ 4.6×4.1 cm mass, non-homogeneous with microcalcifications, unevenly accumulates contrast. Laparoscopic right adrenalectomy was performed.
Macroscopic examination
Right adrenal gland 7.5×5×4 cm, in incisions yellowish 5×4.5×3.1 cm mass.
Microscopic examination
About 50% of the tumor consists of cells, which layout in lobular and alveolar structures. Cells are medium-sized with round, chromatic nuclei and a moderately abundant, mildly eosinophilic cytoplasm. Another component of the tumor takes up to 3.0 cm of the tumor itself and is formed by polymorphic medium-sized and large atypical cells with highly accentuated, polymorphic, and chromatic nuclei. The cells have mildly eosinophilic cytoplasm of varying abundance. Part of the tumor cells is monstrous. Narrow areas of tumor necrosis and wide inclusions of fibrous tissue were found. No overgrowth of the fibrous adrenal capsule was found.
Conclusion:
adrenal cortical carcinoma against the background of cortical adenoma pT1 Nx Mx LVI R0.
Chest and abdominal CT
Right adrenal gland is removed, no signs of metastases were observed, left-without changes.
DXA
Osteopenia. MEN1, Beckwith-Wiedemann, and Lynch syndromes were ruled out by genetic tests. Post-operative treatment included Hydrocortisone 20–30 mg/d replacement therapy. Renin, aldosterone, cortisol (in the background of Hydrocortisone use), ACTH, electrolytes – all in the normal range (Table 1).
Conclusion
Non-functioning adrenal carcinoma and its nonspecific clinic may be a challenge in the diagnosis of the disease and require careful clinical examination. Nonspecific clinics of adrenal cortical carcinoma can often lead to a late diagnosis, leading to local and systemic progression of the disease.

DOI: 10.1530/endoabs.81.EP43

EP44

Lipid profile in patients with Addison disease

Dhoha Ben Salah, Khouloud Boujelben, Abdelmouhaymen Missaoui, Faten Haj Kacem Akid, Mouna Mnif, Mnif Fatma, Nadia Charfi, Nabila Rekik Majdoub, Mouna Elleuch & Mohamed Abid
Hedi Chaker Hospital, Sfax-Tunisia, Department of Endocrinology, Diabetology.

Introduction
Long-term glucocorticoid replacement therapy in patients with Addison disease has been linked to an increased cardiovascular risk and consequent mortality. Our objective was to determine the frequency of dyslipidemia in patients with Addison disease and its potential predictive factors.
Patients and methods
This was a cross-sectional study, performed in the department of endocrinology in Hedi Chaker hospital –Sfax –Tunisia. Fifty patients with Addison disease were recruited between March 2020 and July 2021.Lipid profile at time of disease diagnosis and after glucocorticoid replacement was analyzed.
Results
The mean age of our patients was 49.5 ± 13.9 years (18–78 years).The female sex was the most affected with a sex ratio of 4. The disease duration was 13.9 ± 8.7 years on average with extremes between 5 and 35 years. Lipid profile at time of Addison disease diagnosis was normal in 81.5% of patients. For those presenting disturbed lipid balance, there were isolated hypercholesterolemia in two patients, hypertriglyceridemia in one patient and mixed dyslipidemia in 2 patients. At the time of our study, the prevalence of hyperlipidemia was 16% (8 patients), occurring after a mean duration of glucocorticoid replacement therapy of 13.6 years. The alterations in the lipid balance observed were mixed dyslipidemia in 5 patients, isolated hypercholesterolemia in one patient, hypertriglyceridemia in 2 patients and low HDL-cholesterol level in 5 patients. Among those patients, five patients were treated with statins and 2 patients with fibrates. One patient was on healthy diet. All lipid parameters increased at the time of the study compared to lipid profile at time of disease diagnosis: Total cholesterol level:4.3 ± 0.9 mmol/l vs 3.7 ± 1 mmol/l;Triglyceride level: 1.6 ± 1 mmol/l vs 1.2 ± 0.7 mmol/l;HDL-cholesterol level:1.4 ± 0.3 mmol/l vs 1.1 ± 0.5 mmol/l;LDL-cholesterol level:2.4 ± 0.6 vs 2 ± 0.6 mmol/l. There were no significant correlation between hyperlipidemia and cumulative hydrocortisone dose nor duration of glucocorticoid replacement therapy.
Conclusion
Our findings highlight the importance of controlling lipid status in patients with Addison disease. Identifing patients at risk of lipid metabolism disorders at the preclinical phase seems imperative to reduce cardiovascular complications of long-term glucocorticoid replacement therapy.

DOI: 10.1530/endoabs.81.EP44

EP45

Metabolic syndrome in patients with Addison disease

Dhoha Ben Salah, Khouloud Boujelben, Abdelmouhaymen Missaoui, Mouna Elleuch, Mnif Fatma, Mouna Mnif, Nadia Charfi, Nabila Rekik Majdoub, Faten Haj Kacem Akid & Mohamed Abid
Hedi Chaker Hospital, Department of Endocrinology, Diabetology, Sfax, Tunisia.

Introduction
Inadequate glucocorticoid replacement therapy in Addison disease leads to an increased risk of both cardiovascular disease and metabolic syndrome. The metabolic effects of long-life corticosteroid exposure are due to physiological mechanisms that are associated with carbohydrate metabolism disorder, dyslipidemia and insulin resistance. In this study, we aimed to determine the prevalence and predictive factors of metabolic syndrome in patients with Addison disease.
Patients and methods
A cross sectional study performed between March 2020 and July 2021, including 50 patients with Addison disease. Metabolic syndrome was assessed by referring to the National Cholesterol Education Program-Adult Treatment Panel III.
Results
Mean age was 49.5 ± 13.9 years (40 females versus 10 males). Average duration of the disease was 13.9 ± 8.7 years (5–35 years). All patients were on hydrocortisone replacement, taking daily 27.4 ± 6.7 mg (15–42.1 mg). The average weight was 72.5 kg (62–107 kg).Progressive weight gain was observed in 70% of patients. This gain was more pronounced during the first year of follow-up and estimated at 7.4 kg on average. Mean Body Mass Index (BMI) was 28.1 kg/m^2 (21,2–45,8 kg/m^2).Twenty four (48%) patients were obese. Mean waist circumference was 107 ± 11.8 cm (65–121 cm) for woman and 105.1 ± 9.6 cm (64–119 cm) for men. Android fat distribution was found in 60% of patients versus 12% at time of diagnosis. Glucose intolerance was found in over a third of patients (38%).Among those patients, 31,6% had type 2 diabetes. Hypertriglyceridemia was found in 2 patients. Five patients had low HDL-cholesterol level. Metabolic syndrome was found in 24% of patients versus only one patient at time of diagnosis. No significant correlation was identified between Addison disease duration and the occurrence of metabolic syndrome. Daily hydrocortisone dose was significantly higher among patients having metabolic syndrome ($P = 0.04$).As well, cumulative hydrocortisone dose was higher among those patients but without significant difference ($P = 0.5$).
Conclusion
Similarly, to anti-inflammatory corticotherapy, a broad range of metabolic effects including insulin resistance and profound alterations in carbohydrate and lipid metabolism impedes glucocorticoid replacement therapy.

DOI: 10.1530/endoabs.81.EP45

EP46

Ovarian cyst in woman treated with mitotane, side effects not to be ignored

Mouna Mezoued, Bessaid Khadidja & Malha Azzouz
Bologhine Hospital, Endocrinology, Alger, Algeria.

Introduction
Mitotane is an adrenolytic drug that is used as an adjuvant to treat adrenocortical carcinoma, The side effects of lysodren are numerous, but some of them are less known. We report a case of ovarian cyst in a woman of childbearing age. It is a 26 years old patient treated with Lysodren® for a locoregional recurrence of an adrenal cacinoma stage II of the ENSAT. After 9 months of treatment, the patient presented an amenorrhea, with the appearance of a large ovarian cyst of 50 mm, detected on the follow-up CT scan, which initially led to the suggestion of a recurrence. At presentation, FSH, luteinizing hormone (LH), were within the normal range, The levels of marker CA-125, occasionally controlled, remained normal. The cyst spontaneously disappeared 6 months after having stopped the treatment, and the patient became spontaneously pregnant having an uncomplicated delivery 2 years later.

Conclusion
Therapeutic concentrations of mitotane could be associated with the presence of benign ovarian cysts and amenorrhea, up to 50% of women. It is of clinical importance to be aware of this unwanted effect of mitotane, because finding a growing ovarian mass induces anxiety and may conduce to a misdiagnosis of ACC progression.

DOI: 10.1530/endoabs.81.EP46

EP47

Morning cortisol and circulating inflammatory cytokine levels: a mendelian randomisation study

Skanda Rajasundaram[1,2], Rezbieara Rahman[3], Benjamin Woolf[4], Steven Zhao[5] & Dipender Gill[3,6,7]
[1]Kellogg College, University of Oxford, Oxford, United Kingdom; [2]Imperial College London, Faculty of Medicine, London, United Kingdom; [3]St George's, University of London,, Clinical Pharmacology and Therapeutics Section, Institute for Infection and Immunity, London, United Kingdom; [4]University of Bristol, Medical Research Council (MRC) Integrative Epidemiology Unit, Bristol, United Kingdom; [5]The University of Manchester, Manchester Academic Health Science Centre, Centre for Epidemiology Versus Arthritis, Division of Musculoskeletal and Dermatological Science, Manchester, United Kingdom; [6]Imperial College London, Department of Epidemiology and Biostatistics, London, United Kingdom; [7]Novo Nordisk Research Centre Oxford, Old Road Campus, Oxford, United Kingdom.

Background
Cortisol is an essential steroid hormone released from the adrenal gland. Plasma cortisol levels follow a circadian rhythm under the control of the Hypothalamic–Pituitary–Adrenal axis, reaching peak levels in the morning. Cortisol has long been known to exert immunosuppressive effects and accordingly, glucocorticoids are central in treating inflammatory disease. Cortisol's propensity to downregulate certain pro-inflammatory cytokines and upregulate other anti-inflammatory cytokines is well-established. However, there remain gaps in our mechanistic understanding of how cortisol modulates various cytokines. Historically, studies have focussed on a small number of relatively well-established cytokines yet the effect of cortisol on many other cytokines remains uncertain.
Methods
Leveraging data from the CORtisol NETwork ($N=25\,314$) and FINRISK ($N=8293$) genome-wide association studies, we used two-sample Mendelian Randomisation (MR) to investigate the causal effect of genetically proxied increased morning cortisol levels on 42 circulating cytokines. MR utilises genetic variants in an instrumental variable framework to make causal inferences. By virtue of Mendel's Law of Segregation and Law of Independent Assortment, the inheritance of genetic variants is random. Furthermore, germline genetic variation corresponding to levels of morning cortisol and circulating cytokines is non-modifiable by the environment and temporally precedes the onset of clinically detectable changes in circulating cytokine levels. Thus, under specific assumptions, MR offers a method of investigating the causal effect of a morning cortisol on a comprehensive range of cytokines that is less vulnerable to confounding and reverse causation biases in comparison to traditional observational studies.
Results
Increased genetically proxied morning cortisol levels were associated with reduced levels of Interleukin 8 (IL-8) and increased levels of Macrophage Migratory Inhibitory Factor (MIF). A 1 s.d. increase in genetically proxied morning cortisol levels corresponded to a 0.767 normalised SD-unit decrease in IL-8 ($P=1.14\times10^{-4}$, 95% CI $=-1.157$ to -0.378) and a 0.806 normalised SD-unit decrease in MIF ($P=3.68\times10^{-5}$, 95% CI $=-1.189$ to -0.423). These findings remained statistically significant after applying the Bonferroni correction for multiplicity.
Conclusions
These results provide mechanistic insight into the immunomodulatory effects of cortisol. Clinically, our findings underline the therapeutic importance of steroids in inflammatory conditions where IL-8 and MIF play central roles in the pathophysiology of disease, e.g. Inflammatory Bowel Disease, Rheumatoid Arthritis and Systemic Lupus Erythematosus. Moreover, IL-8 and MIF may represent alternative therapeutic targets in these conditions, which could avoid some of the adverse effects of long-term glucocorticoid therapy.

DOI: 10.1530/endoabs.81.EP47

EP48

Fibrin clot properties and fibrinolysis in Cushing's syndrome

Christina Berr[1], Ewa Warchoł-Celińska[2], Julia Fazel[3], Anetta Undas[4,5,6] & Aleksander Prejbisz[2]
[1]Department of Endocrinology, I. Medical Clinic, University Hospital, University of Augsburg, Augsburg, Germany; [2]Department of Hypertension, National Institute of Cardiology, Warsaw, Poland; [3]Medizinische Klinik und Poliklinik IV, Klinikum der Ludwig-Maximilians-Universität München, München, Germany; [4]Innovative Laboratory Diagnostic Centre, John Paul II Hospital, Cracow, Poland; [5]Cracow Centre for Medical Research and Technologies, John Paul II Hospital, Cracow, Poland; [6]Department of Invasive Cardiology and Angiology, National Institute of Cardiology, Warsaw, Poland.

Background
Cushing's syndrome (CS) and hypertension (HT) are associated with alterations of coagulation. This is the first study that compares parameters of fibrin clot and fibrinolysis in CS with patients with essential hypertension (EHT) and healthy normotensive controls (HC).
Methods
The patients were recruited at the university hospital of Ludwig-Maximilians-Universität München (Germany) and the Department of Hypertension, Institute of Cardiology, Warsaw (Poland). We analyzed 31 patients (mean age: 42.9 ± 13.2 years, 25 females, 86% HT) with active CS (n = 25) and subclinical CS ($n=6$). They were compared with 31 age, sex and BMI matched patients with EHT (mean age: 44.3 ± 12.7 years, 25 females) and 31 age and sex matched HC (mean age: 43.8 ± 12.8 years, 25 females). The following variables were assessed: plasma fibrin clot permeability (Darcy's constant, Ks), clot lysis time (CLT) and a kinetics profile of thrombin generation i.a. the endogenous thrombin potential (ETP) with the use of a calibrated automated thrombogram. Immunoenzymatic and chromogenic assays were used to determine plasminogen activator inhibitor-1 (PAI-1) and plasma-activated thrombin-activatable fibrinolysis inhibitor antigen (TAFI).
Results
Fibrin clot structure in patients with CS is less dense in comparison to EHT, but comparable to HC (median Ks in CS 6.98 [5.53–8.91] vs. EHT 4.68 [3.96–6.11] 10^{-9} cm^2, $P<0.001$; CS 6.98 [5.53–8.91] vs. HC 7.89 [7.19–8.36] 10^{-9} cm^2, $P=0.09$). Higher density is generally found in patients with higher cardiovascular risk. Fibrin clot structure was most resistant to lysis in EHT (median CLT CS 97.10 [90.0–113.6] vs. EHT 110.5 [95.8–126.3] vs. HC 93.8 [79.2–104.0] min, CS vs. EHT $P<0.039$). Furthermore, CS patients present with a higher ETP as compared to healthy controls, but in EHT this is even more pronounced (median ETP in CS 1753.3 [1370.2–1881.4] vs. EHT 2087.6 [1946.0–2394.4], nM*min, $P<0.001$; CS 1753.3 [1370.2–1881.4] vs. HC 1132.6 [1048.1–1256.6] nM*min, $P<0.001$). Proteins inhibiting fibrinolysis such as PAI-1 and TAFI are significantly higher in CS than in EHT (mean PAI-1: CS 49.22 ± 26.43 vs. EHT 24.44 ± 23.79 ng/ml, $P<0.001$; mean TAFI: CS 131.25 ± 13.86 vs. EHT 95.03 ± 26.59 AG %, $P<0.001$).
Conclusion
Despite an overlap of hypertension in CS and EHT, we observe significant differences in fibrin clot structure and fibrinolysis in both entities. Fibrin clot density, CLT and ETP are more altered in EHT than in CS, whereas proteins inhibiting fibrinolysis are higher in CS.

DOI: 10.1530/endoabs.81.EP48

EP49

The different contribution of IGF1R and IR in mediating insulin-like growth factor 2 (IGF2) effects in adrenocortical carcinomas

Rosa Catalano[1], Emma Nozza[1], Emanuela Esposito[1], Anna Maria Barbieri[1], Giusy Marra[1], Donatella Treppiedi[1], Federica Mangili[1], Genesio Di Muro[1], Federico Arlati[1], Valentina Morelli[2], Maura Arosio[1,3], Giovanna Mantovani[1,3] & Erika Peverelli[1]
[1]University of Milan, Department of Clinical Sciences and Community Health, Milan, Italy; [2]Istituto Auxologico Italiano, IRCCS, Unit for Bone Metabolism Diseases and Diabetes, Milan, Italy; [3]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Endocrinology Unit, Milan, Italy.

Adrenocortical carcinomas (ACCs) are rare endocrine tumors with poor prognosis. They overexpress the insulin-like growth factor 2 (IGF2), that drives a proliferative autocrine loop by binding to IGF1R and IR. The majority of studies focused on IGF1R as mediator of IGF2 biological effects, but recently a high expression of IR, in particular of the isoform A, was observed in most ACCs, suggesting a potential role of this receptor in modulating IGF2 effects in adrenocortical tumorigenesis. However, the relative contribution of IGF1R and

IR to the biological effects of IGF2 in ACC is still unknown. Aim of this study was to investigate the specific roles of IGF1R and IR in mediating IGF2 tumorigenic effects in ACC. To this purpose we performed genetic silencing of both IGF1R and IR by transfecting H295R, MUC1 and primary ACC cells with specific siRNAs directed against IGF1R and IR. We found that the IGF2 anti-apoptotic effects were enhanced in H295R and ACC primary cultured cells silenced for both IGF1R ($-15.16\pm3.27\%$, $P<0.01$ and -45%, $P<0.05$, of caspase 3/7 activity, respectively) and IR ($-23.62\pm16.03\%$, $P<0.05$ and -32.4%, $P<0.001$, respectively). In addition, we demonstrated that IGF2 was still able to promote ERK and AKT phosphorylation after IGF1R and IR silencing in H295R and ACC primary cultured cells. Moreover, both IGF1R and IR silencing did not affect the IGF2-mediated proliferation in H295R. In MUC1 cells, IGF1R silencing did not alter IGF2-induced cell apoptosis and proliferation. Heterogeneous results were obtained in primary cultured cells obtained from 2 different ACC. In one of them IGF1R silencing decreased IGF2-induced cell proliferation, underlining the importance of this receptor in mediating IGF2-mitogenic effects. In the other one IGF2-mediated cell proliferation was reduced after IR, but not IGF1R, silencing. IGF1R, but not IR, knockdown reduced the antiproliferative effects of IGF1R/IR inhibitor Linsitinib in H295R and ACC primary cultured cells ($-32.76\pm20.81\%$ in control cells, $P<0.05$ and $-18.36\pm11\%$ in IGF1R silenced H295R cells, $P<0.05$), suggesting a main role of IGF1R in the response to Linsitinib. In conclusion, our data demonstrated a differential involvement of IGF1R and IR in mediating IGF2 tumorigenic effects in adrenocortical cancer cells.

DOI: 10.1530/endoabs.81.EP49

EP50

Urine steroid profiling as a tool for the treatment evaluation assessment in patients with adrenocortical carcinoma

Ludmila Iosifovna Velikanova[1], Natalia Vladimirovna Vorokhobina[2], Zulfia Rifgatovna Shafigullina[2], Valentina Victorovna Kalugina[2], Ekaterina Valerievna Malevanaya[1], Vagan Yurikovich Bohyan[3], Ivan Socratovich Stilidi[3] & Nikolai Evgenievich Kushlinskii[3]
[1]North-Western State Medical University named after I.I. Mechnikov, Chromatography Laboratory, Saint Petersburg, Russian Federation; [2]North-Western State Medical University named after I.I. Mechnikov, Endocrinology department, Saint Petersburg, Russian Federation; [3]Federal State Budgetary Institution "N.N. Blokhin National Medical Research Center of Oncology" of the Ministry of Health of the Russian Federation, Moscow, Russian Federation.

Background
The aim of the study was to evaluate urine steroid profiles by gas chromatography–mass spectrometry (GC–MS) in patients with adrenocortical carcinoma (ACC) to assess therapy efficacy.
Patients and Methods
39 ACC patients were examined before and after treatment. The median age was 47 years (41–60). The Weiss score was no less than 4 points. 10 patients were disease-free in the early postoperative period (up to 12 months after surgery). Metastases were detected 1–5 years after the surgery in 29 patients. The control group consisted of 25 patients with adrenocortical adenoma (ACA) without malignant features defined by the histologic analysis. The median age was 52 (47–61) years. We studied urine steroid profile using gas chromatograph–mass spectrometer SHIMADZU GCMS – TQ 8050. Statistical data was processed with software STATISTICA for WINDOWS (Version 10). Results comparison was made using Mann–Whitney test.
Results
ACC's main biomarkers urinary excretion rates [dehydroepiandrosterone (DHEA), etiocholanolone (Et), pregnanediol (P2), pregnanetriol (P3), pregnenediol (dP2), pregnenetriol (dP3)] did not differ between the disease-free postoperative ACC patients and the control group ($P>0.05$). The 3β,16,20-dP3 urinary excretion rate and the 3α16,20-dP3/3β,16,20-dP3 ratio were identified as the most discriminating markers in differentiating disease-free postoperative patients from preoperative ACC patients (receiver-operating characteristics (ROC) analysis revealed sensitivity = 100%, specificity = 96%, AUC = 0.99, cut-off < 194 μg/24 h and sensitivity = 85.7%, specificity = 92%, AUC = 0.87, cut-off > 3.4, respectively). Patients after surgery and chemotherapy had decreased urinary excretion rates of 3β,16,20-dP3 (cut-off < 100 μg/24 h sensitivity = specificity = 100%, AUC = 1,0) and the increase of 3α16,20-dP3/3β,16,20-dP3 ratio (cut-off > 2.7 sensitivity = 75%, specificity = 88%, AUC = 0.81) in comparison with the same patients' preoperative steroid profiles. Patients with recurrent ACC (in the postoperative period before the chemotherapy initiation or with the relapse occurrence after the completion of chemotherapy) had the similar excretion rates of ACC biomarkers as in the preoperative period.
Conclusion
Urine steroid profiling is a promising tool for the evaluation of treatment efficacy in ACC patients.

DOI: 10.1530/endoabs.81.EP50

EP51

Is there a difference in symptoms, catecholamine release and tumor size in pheochromocytomas diagnosed due to initially symptoms or incidenthalomas

Ingrid Nermoen[1,2,3] & Marte Henriksen Korneliussen[1]
[1]University of Oslo, Institute of Clinical Medicine, Oslo, Norway; [2]; [3]Akershus University Hospital, Norway.

Background
Pheochromocytoma is a rare adrenal tumor that can present with a variety of different symptoms. The cardinal symptoms are paroxysmal palpitations, headaches and sweating together with paroxysmal or persistent hypertension. Increasing use of CT scan contribute to the discovery of more adrenal incidentalomas and therefore more pheochromocytomas due to the workup of the incidentalomas. We intended to investigate if the presentation of the pheochromocytoma was different in the incidentaloma group, if so, what symptoms the tumor presented with, and if the tumors was different in size and metanephrine release.
Methods
Twenty-nine cases with pheochromocytomas examined and treated at Akershus University Hospital, Norway, during the last 20 years were reviewed. Age, year diagnosed, tumor characteristics, biochemistry, radiology, medical treatment before surgery, complications during surgery, and blood pressure measurement before, during and after the operation were registered.
Results
Of the 29 cases included, 70.4% presented as incidentalomas and 26.6% was discovered based on clinical symptoms and none due to genetic screening. The mean ($\pm$S.D.) age of the incidentalomas (58.0 ± 12.3) years was significantly higher than the patients diagnosed because of clinical suspicion (42.0 ± 9.9) years. Females were overrepresented in both groups and was in total 65.6%. There was no significant difference in blood pressure between the two groups (incidenthaloma vs clinical group), systolic 142.0 ($\pm$21.9) vs 154.2 ($\pm$18.8) mmHg, tumor size 4.9 ($\pm$3.0) vs 4.2 ($\pm$1.0) cm or normetanephrine median (range) 2.7 (0.7–26.2) vs 5.7 (3.1–44.0) nmol/l nor the excretion of metanephrine 1.5 (0.3–12.6) vs 1.4 (0.3–6.1) nmol/l. Out of the 19 incidentalomas 72.2% were retrospectively symptomatic and the most common symptoms were sweating, palpitations and headaches, followed by palpitations and tremor but these symptoms were rarely present at the same time. The last 10 years from 2010 to 2020, 15 incidenthalomas made up the 20 pheochromocytomas vs 4 of 7 from 2000 to 2010.
Conclusion
Our hospital diagnosed more pheochromocytomas the last years due to increasing discovery of incidentalomas on CT imaging and 72.2% of these incidenthalomas were retrospectively symptomatic. This points out the importance of investigating all incidentalomas biochemically and making a good medical history for symptoms as undiagnosed pheochromocytomas can be life-threatening.
Reference
H Falhammar *et al*. Initial clinical presentation and spectrum of pheochormocytoma: a study of 94 cases from a single center; Endocrine Connections (2018)7, 186–192

DOI: 10.1530/endoabs.81.EP51

EP52

Prevalence and clinical manifestations of neurogenic bladder dysfunction in type 2 diabetes: a population-based survey

Faten Haj Kacem Akid[1], Abdel Mouhaymen Missaoui[1], Mariem Belhoul[2], Wafa Belabed[1], Cyrine Chahaider[1], Dhoha Ben Salah[1], Mnif Fatma[1], Nadia Charfi[1], Mouna Mnif[1], Nabila Rekik Majdoub[1], Mouna Elleuch[1] & Mohamed Abid[1]
[1]Hedi Chaker University Hospital, Endocrinology Departement, Sfax, Tunisia; [2]Faculty of Medicine of Sfax, Departement of Family Medicine, Sfax, Tunisia.

Background and aims
Lower urinary tract (LUT) symptoms are one of the most common complications related to autonomous diabetic neuropathy. It is responsible for several dysfunctions due to distended bladder with a high risk of contracting retention.

The current survey aims to assess the clinical manifestations of neurogenic bladder dysfunction (NBD) and determine its prevalence in patients with type 2 diabetes (T2DM).
Patients and method
We conducted a cross-sectional descriptive study that included 200 patients with T2DM consulting at the Endocrinology Department of Hedi Chaker University Hospital, Sfax, Tunisia, from April 2019 to December 2019. We administrated the Urinary Symptom Profile (USP) questionnaire to all patients to assess clinical manifestations of NBD.
Results
The mean age was 59.3±10.6 years, with a female predominance (55.5%). Dyslipidemia (57%) and hypertension (49.7%) were the most common comorbidities. The duration of the evolution of diabetes was 11.0±7.9 years. Oral antidiabetic agents (OAD) and insulin therapy were prescribed in 40% and 13.6%, respectively. Most of the patients were receiving a mixed insulin-OAD treatment (44.2%). A glycemic imbalance was noted in 79.7%. Stress urinary incontinence prevailed in 22.5%. the discomfort linked to this dysfunction was mild or moderate in 53.3% and 42.2%, respectively. An overactive bladder was recorded in 70.5% and caused severe or extreme discomfort for 24.1% and 16.3% of patients, respectively. Near one-half of investigated patients (51.5%) reported dysuria. The latter disorder was responsible for serious distress for 26.2% of patients. In total, the prevalence of LUT dysfunction was as high as 79.5% of patients with T2DM.
Conclusion
NBD is a cluster of lower urinary tract disorders such as stress urinary incontinence, dysuria, and overactive bladder. NBD is considered a chronic diabetic complication [1]. The prevalence of NBD varies from 25% to 87% in different studies. Urodynamic studies remain the gold standard diagnostic tool. However, the USP questionnaire represents a simple and very sensitive questionnaire for screening of NBD in patients with diabetes in clinical practice [2]. Due to its frequency, NBD should be screened for in patients with diabetes suffering from LUT dysfunctions.
References
1. Golbidi, Saeid, and Ismail Laher. “Bladder dysfunction in diabetes mellitus.” Frontiers in pharmacology 1 (2010): 136.
2. Bansal, Rahul, et al. “Urodynamic profile of diabetic patients with lower urinary tract symptoms: association of diabetic cystopathy with autonomic and peripheral neuropathy.” Urology 77.3 (2011): 699–705.
DOI: 10.1530/endoabs.81.EP52

EP53

Syncope: an unusual presentation of a rare disease
Uzair Akbar Ali[1], Muhammad Sajjad Sadiq[2] & Elizabeth Ann Brosnan[2]
[1]St. Luke’s General Hospital, Kilkenny, Ireland; [2]Mayo University Hospital, Castlebar, Ireland.

Background
Syncope is common in healthy adolescents and young adults. It can happen due to hypotension secondary to orthostasis. Primary adrenal insufficiency is infrequently reported in patients presenting with syncope and dizziness caused by loss of vasopressor effect of catecholamines and volume depletion.
Clinical Case
A 17-year-old boy with a past medical history of learning disability and asthma presented to our health facility with an episode of syncope. He felt dizzy on standing and had transient loss of consciousness at the General Practitioner (GP) Surgery. He was feeling unwell and nauseous for past several days. His physical examination revealed darkening of skin (pigmentation) but rest of the examination was unremarkable. Initial baseline investigations including blood glucose were normal except mild hyponatremia with sodium levels of 134 mmol/l (135–145). CT scan of thorax, abdomen and pelvis was unremarkable. He was referred to the endocrinologist with a clinical impression of primary adrenal insufficiency. Further investigations including serum ceruloplasmin and iron studies were normal. Short synacthen test revealed cortisol levels of 46 nmol/l and 40 nmol/l at 30 and 60 minutes respectively. Adrenal antibodies were weak positive. He was treated as auto-immune adrenal insufficiency or Addison’s disease and given mineralocorticoid (fludrocortisone) and corticosteroids (hydrocortisone) regimen. Careful history taken with his mother revealed that he had vitiligo in the past but denied any significant family or drug history. His previous investigations showed high levels of TSH at different times ranging from 2.69 to 45.18 mIU/l (0.51–4.30). Anti TPO antibodies were tested and found significantly raised with a value of 220 IU/ml (0–40). The patient was given the diagnosis of autoimmune polyendocrine syndrome type 2 (APS-2). He was advised screening for antibodies against IA-2, insulin, GAD65 to test for type 1 diabetes predisposition and tissue transglutaminase autoantibodies to screen for coeliac disease. His family was finding it difficult to absorb all these information and asked for some time before proceeding to further tests. He was advised endocrine clinic follow ups.
Conclusion
This case report highlights the importance of arriving at the right diagnosis as signs and symptoms can be vague and mimic other conditions. Appropriate investigations, treatment and follow up can improve quality of life.
Key words: syncope, adrenal insufficiency, auto-immune.
DOI: 10.1530/endoabs.81.EP53

EP54

False positive metanephrines secondary to sinemet-diagnostic dilemmas in interpretation
Bhavna Sharma[1], Asjid Qureshi[1], Florian Wernig[2] & Shivashankar Seechurn[1]
[1]Northwick Park Hospital, United Kingdom; [2]Imperial College London, United Kingdom.

A 50 year-old lady was referred to the endocrine service for evaluation of significantly elevated 3-methoxytyramine (3-MT) levels. Past medical history included well controlled HIV and hypertension controlled by a single agent only (amlodipine). On one occasion, she was noted to have an elevated systolic blood pressure of 189 mmHg in clinic and therefore 24 h urinary metanephrines were requested. She did not have any other symptoms to suggest excess catecholamines. Systems review was unremarkable. There was no family history of endocrinopathies. She had recently been diagnosed with multiple system atrophy. A Dopamine Active Transporter scan revealed reduced uptake at the basal ganglia. She had been started on Sinemet 125 mg TDS by the neurologist and her symptoms, which include postural hypotension, greatly improved. In the endocrine clinic, her systolic blood pressure was 128 mmHg. The history was revisited and it transpired that on the day her blood pressure had been elevated, she had omitted her amlodipine. Physical examination did not reveal any obvious stigmata of an endocrinopathy. Blood tests showed normal electrolyte, renal function, bone profile and thyroid function. However, repeat 24 h urinary metanephrines were a follows: Metanephrine 488 nmol/ 24 h (NR 0-2000), normetanephrines 1139 nmol/24 h (NR 0-4400) and 3-MT 20 424 nmol/24 h (NR 0-2500). This confirmed a previous 24 urine collection result. It was thought that the isolated markedly raised 3-MT, a dopamine metabolite, was secondary to Sinemet which is a combination of carbidopa and levodopa. Sinemet could not be discontinued as it significantly improved her symptoms. A differential diagnosis of a dopamine secreting neuroendocrine tumour was a considered. Chromogranin A & B were evaluated and were normal. Her case was discussed at the regional adrenal MDT meeting. The MDT concluded that the markedly raised 3-MT were secondary to Sinemet and no further investigations such as functional imaging would be required. Interpreting biochemical markers in the presence of influencing factors and drugs can often be challenging. Abnormal results can trigger unnecessary investigations which can be distressing to the patient. This case highlights the importance of MDT discussions in such scenarios.
DOI: 10.1530/endoabs.81.EP54

EP55

The asymmetric adrenal in mice and men: Sexual dimorphism and potential hormonal consequences
Nicole Bechmann[1,2], Mats Leif Moskopp[3], Deepika Watts[4], Charlotte Steenblock[2], Waldemar Kanczkowski[2], Ben Wielockx[4], Stefan R Bornstein[2], Mirko Peitzsch[4] & Graeme Eisenhofer[2,4]
[1]Institute of Clinical Chemistry and Laboratory Medicine, University Hospital Carl Gustav Carus, Medical Faculty Carl Gustav Carus, Technische Universität Dresden, Germany; [2]Department of Internal Medicine III, University Hospital Carl Gustav Carus, Technische Universität Dresden, Germany; [3]Department of Neurosurgery, Vivantes Friedrichshain Hospital, Charité Academic Teaching Hospital, Germany; [4]Institute of Clinical Chemistry and Laboratory Medicine, University Hospital Carl Gustav Carus, Medical Faculty Carl Gustav Carus, Technische Universität Dresden, Germany.

Evidence indicates that the adrenals are sexually dimorphic and asymmetric. These differences may have implications for the prevalence and progression of adrenal diseases, which also show asymmetry and sexual dimorphism. The present study aims to characterize the morphological and metabolic differences associated with adrenal sex and asymmetry in mice and humans. Adrenals were compared bilaterally in male and female C57B/6NRj mice with regard to

morphological and hormonal characteristics. Female adrenals were consistently larger than male adrenals (330.2 ± 14.7 vs. 215.4 ± 15.8 µg protein/adrenal, $P < 0.001$). Although males had smaller adrenals, total contents of catecholamines were higher in males than in females (mean both adrenals: 3.8 ± 0.3 vs. 3.5 ± 0.2 µg catecholamines/adrenal). In contrast, adrenal contents of the two main adrenal steroids, corticosterone and aldosterone, were significantly higher in females than males. In females, the right adrenal was significantly smaller than the left adrenal (295.3 ± 19.0 vs. 365.2 ± 12.9 µg protein/adrenal, $P = 0.03$), whereas no clear differences were observed in males. In both sexes, total tissue catecholamines as well as corticosterone and aldosterone were higher in the left than the right adrenal. We confirmed these findings in three additional mouse strains (C57BL/6J, CD6 and Tie2 GFP/FVB). Furthermore, we performed a systematic review of adrenal imaging data in humans. Unlike in mice, women have smaller adrenals than men, but also in humans the left adrenal gland is larger than the right adrenal. Using adrenal vein samples and human adrenal tissue data, we will further characterize hormonal differences in patients. Characterization of differences between sexes and of adrenal asymmetry in mice and humans may have implications for prediction and diagnosis of adrenal disease, and it may also allow improved translation of results from experimental murine models to the clinic.

DOI: 10.1530/endoabs.81.EP55

EP56

Cushing disease in patient with chronic renal failure treated by hemodialysis: a case report

Ameni Terzi, Nadia Khessairi, Yasmine Mouelhi, Meriem Yazidi & Melika Chihaoui
Rabta hospital, Endocrinology, Tunis, Tunisia.

Introduction
The occurrence of Cushing's syndrome in individuals with chronic renal failure is notably rare. It represents a challenging diagnosis in the context of pre-existing chronic kidney disease due to commonly associated alterations in the hypothalamic–pituitary–adrenal axis function. Consequently, the interpretation of standard tests used to detect hypercortisolism can be peculiarly difficult and reveal concrete particularities in comparison to patients with normal renal function. We here present the case of a chronic hemodialysis patient who was diagnosed with Cushing syndrome disclosed by an adrenal incidentaloma.
Case presentation
In December 2021, a 67-year-old female was admitted to our department for exploration of a 23 mm left-sided adrenal nodule incidentally detected on a computed tomography (CT) performed about 6 months ago for suspicion of an arteriovenous fistula stenosis. Indeed, the patient started hemodialysis 3 times a week since 2014 for end-stage renal disease caused by tubulointerstitial nephritis. In addition, she underwent subtotal parathyroidectomy associated to right loboisthmectomy for tertiary hyperparathyroidism and multinodular goiter in 2015. Clinically, she didn't have hypercortisolism features except slender lower limbs and a recently diagnosed hypertension. Her body mass index was 28.75 kg/m^2. Biologically, she had hypertriglyceridemia and glucose intolerance. Subsequent endocrinological testing revealed negative plasma fractionated metanephrines and resistance to suppression of low dose (1 mg), 4 mg and high dose (8 mg) of dexamethasone: the early morning cortisol level was respectively 7.1 µg/dl, 2.6 µg/dl and 2.3 µg/dl. The plasma ACTH level performed twicely was 55 pg/ml and 31 pg/ml. It led to the practice of a brain MRI that was normal. A latterly conducted CT scan detected a left adrenal adenoma with a diameter of 31 mm, spontaneous density of 20 UH, relative washout of 49% and absolute wash out of 64%. The patient didn't have obstructive sleep apnea. Based on these findings, Cushing's syndrome secondary to a left adrenal tumor was diagnosed and the patient was presented for left adrenalectomy.
Conclusion
This is the first documented report outlining the coexistence of Cushing syndrome and tertiary hyperparathyroidism in an individual with end stage renal disease and the fourth known case of Cushing disease occurring in a long-term hemodialysis patient. This observation emphasizes the cortisol dynamics alterations broadly associated with renal failure. These pituitary adrenocortical function disturbances are mainly characterized by increased cortisol levels, heightened plasma ACTH levels and resistance to low dose dexamethasone suppression testing highlighting thereby the delicate diagnosis of Cushing disease in this context.

DOI: 10.1530/endoabs.81.EP56

EP57

Monitoring for the long-term metabolic complications in patients with subclinical cushing's syndrome: service evaluation

Jessica Yau[1] & Justyna Witczak[2]
[1]Cardiff University, School of Medicine, Cardiff, United Kingdom; [2]University Hospital of Wales, Centre for Endocrine and Diabetes Sciences, Cardiff, United Kingdom.

Introduction
Patients with subclinical Cushing's syndrome (SCS) are thought to have excess cortisol from an adrenal adenoma, secreting ACTH-independent cortisol that is not fully suppressed by the pituitary feedback system. High cortisol levels may be linked to metabolic complications. There are no specific guidelines on the surgical management of SCS.
Objective
To evaluate if patients with SCS are monitored and managed for metabolic complications due to cortisol excess.
Method
A retrospective service evaluation study on patients diagnosed with SCS from 2016 to 2019 at the University Hospital of Wales, United Kingdom. We identified 114 patients with a non-suppressed response to the overnight dexamethasone test (ODST), qualified as a 0900 h cortisol > 50 nmol/l. 48/114 were excluded either due to a further negative dexamethasone suppression test or no adrenal adenoma present on imaging. Data of 66 patients were collected on the monitoring and management for metabolic complications in July 2021.
Results
66 patients showed a mean age of 66 ± 12.74 s.d., a male to female ratio of 2:1. 89% (59) had a single adenoma, 11% (7) had bilateral adenomas, and the mean lesion size was 2.82 cm ± 1.34 s.d.. 70% (46) of patients had at least one known metabolic complication present. The four metabolic complications present were hypertension (65%), diabetes mellitus (21%), dyslipidaemia (15%), and osteoporosis/osteopenia (27%). 21% (14) of patients had a history of cardiovascular disease (CVD). The majority had one to three metabolic risk factors (RF) screened; four patients had all four RF tests done; positive results for HbA1c (7/22), lipid profile (11/33), blood pressure (24/43), and DEXA scan (18/21). 28 (42%) patients had been discharged, 12 (18%) were deceased. Surgery was discussed in 26 patients (39%); 10/26 were offered and ultimately 8 underwent the surgery. The criteria to be offered surgery were only clear in 4/8 (50.0%) patients, as they had a lesion > 4 cm. 6/8 surgical patients had at least one metabolic complication, and 5/8 had a minimum of one positive RF result. All the adrenal adenomas removed were shown to be benign in the histopathology studies.
Conclusion
SCS is linked with other metabolic complications; improvement in monitoring of these complications will help the patient receive the required treatment earlier to reduce their CVD risk. More defined surgical criteria could aid clinicians in decision-making. Non-surgical patients may benefit from continued monitoring of metabolic risk factors/complications even after discharge.

DOI: 10.1530/endoabs.81.EP57

EP58

Inadequate peroxisomes activity – a rare cause of Adrenal Insufficiency

Nicoleta Chelaru[1], Laura-Mihaela Trandafir[2,3], Christina-Maria Ungureanu[1,3], Otilia-Elena Frasinariu[2,3] & Ioana Vasiliu[2,3]
[1]Saint Spiridon County Hospital, Iaşi, Romania; [2]Saint Mary Emergency Children Hospital, Iasi, Romania; [3]"Grigore T. Popa" University of Medicine and Pharmacy of Iaşi, Iasi, Romania.

Introduction
Zellweger Spectrum Disorders, one of the two groups of Peroxisome Biogenesis Disorders (PBD-ZSD) are rare, complex autosomal recessive genetic anomalies characterised by mutations in any of the PEX genes which are responsible for defective peroxisomes activity. The peroxisomes are organelles that play a primary role mainly in the lipid metabolism of almost all the cells of the body, hence their defective biosynthesis, assembly or biochemical functions turn PBD-ZSD into a multi-organ disease. The disease progression is variable, with a wide spectrum of clinical phenotypes and may include the onset of adrenal insufficiency.
Case report
We report the case of a 2 year-old girl who was previously diagnosed with a malfunctioning PEX6 protein as a result of biallelic pathogenic variants in PEX6 gene. The medical history work-up draws attention to the overall developmental delay, psychomotor retardation, partial vision and hearing loss and seizures under treatment with antiepileptic drugs. Among the clinical features we emphasize the

small size, craniofacial dysmorphism, dysphagia, poor feeding and hepatomegaly. Laboratory data revealed elevated liver functions, abnormal coagulation profile and modified adrenal tests: elevated adrenocorticotropic hormone (ACTH) with normal morning cortisol level. The diagnosis of subclinical adrenal insufficiency was confirmed by the impaired plasma cortisol response following the Synacthen test. Hydrocortisone supplementation was recommended during stressful situations and intercurrent illness.
Discussion
Our patient's clinical picture fits with an intermediate PBD-ZSD. Given the complexity of the disease, the management of PBD-ZSD is multidisciplinary and it focuses mostly on symptomatic or supportive treatment. These patients need close monitoring for adrenal insufficiency onset, which may by life-threatening if the diagnosis is delayed. Experts recommend yearly endocrinological check-ups by measuring serum morning cortisol and ACTH. Also, the endocrinological management may include vitamin D supplementation and bisphoshonates treatment, as patients with PBD-ZSD are at risk for osteopenia over time.

DOI: 10.1530/endoabs.81.EP58

EP59

Screening of primary aldosteronism among egyptian hypertensive population

Marwa Fathy[1], Mona Mansour[2], Ahmed Rabie[2], Fatma Abd Elhafiz[3], Randa Salam[1] & Abeer Awad[2]
[1]Faculty of Medicine-Cairo University, Internal Medicine-Endocrinology Unit, Cairo, Egypt; [2]Faculty of Medicine-Cairo University, Cairo, Egypt; [3]Faculty of Medicine-Cairo University, Clinical Pathology, Cairo, Egypt.

Background
Hypertension is a common condition that affects many people all over the world. It could be associated with several complications especially in cases of resistant hypertension. Many clinical practice guidelines recommend screening for primary aldosteronism especially in persons with resistant hypertension owing to the worse prognosis when compared with blood pressure-matched essential hypertension.
Objective
The study aimed to screen for primary aldosteronism in high-risk hypertensive Egyptian patients, and to determine the challenges faced in the diagnosis.
Material and Methods
50 high-risk hypertensive patients were recruited from the Outpatient Endocrinology Clinic out of 200 hypertensive patients in the period from February 2019 and April 2021. Creatinine, Glycosylated hemoglobin (HBA1c), lipid profile, potassium level, sodium level, plasma aldosterone concentration (PAC), active renin concentration (ARC), and aldosterone/ renin ratio (ARR) were assessed in all patients.
Results
A series of 50 hypertensive patients screened for PA (26 females and 24 males) with a mean age of 41.88 ± 11.91 s.d.. We found that 41 (82%) patients were receiving antihypertensive medications and 9 (18%) patients didn't receive treatment for hypertension previously. 9 (18%) patients kept on no treatment, 6 (12%) patients were kept on the same anti-hypertensive medications, and 35 (70%) of them were shifted to other anti-hypertensive drugs. 4 patients out of total 50 patients had a positive ARR (>46), while 13 (26%) patients out of total 50 hypertensive patients had low renin levels. There was a statistically significant relation between serum aldosterone/ renin ratio (ARR) and serum potassium (K) with P-value $=0.001$ (Figure 4), also a statistically significant relation between serum aldosterone/ renin ratio (ARR) and (systolic blood pressure, diastolic blood pressure) with P-value $=0.001$ was found.
Conclusion
we recommend routine screening for PA in high-risk hypertensive patients that could offer targeted treatment before adverse cardiovascular consequences develop.

Keywords: High-risk hypertensive patients; Primary aldosteronism; Plasma aldosterone concentration; Active renin concentration; Aldosterone/ renin ratio.
DOI: 10.1530/endoabs.81.EP59

EP60

Adrenal incidentaloma: clinical and metabolic characteristics and follow-up results, a 10-year experience

Yasin Araç[1], Guzin Yaylali[2] & Senay Topsakal[2]
[1]Meric Town Public Hospital, Edirne, Turkey; [2]Pamukkale University, Department of Endocrinology and Metabolic Diseases, Denizli, Turkey.

Objective
In this retrospective study we investigated the clinical and radiological characteristics, hormonal status and metabolic components of the patients with adrenal incidentaloma(AI). Additionally, we investigated whether tumor size or hormonal status changes during long-term follow-up and the effect of these on metabolic parameters.
Methods
The data of 384 patients who were followed up with the diagnosis of AI between 2010 and 2020 were retrospectively analyzed. All patients underwent radiological, hormonal and metabolic evaluation and prospective follow-up.
Results
374 patients (248 female (%64)) enrolled to this study. 348(%90.6) of them were reported as adenomas and 31(%8.07) of them as non-adenomas and 4(%1.04) of them were indeterminate. The mean adenoma diameter was approximately 2 centimeters and was mostly detected on the left (%48.9). %13,81 of the subjects(n = 53) were functioning and among functional adenomas 9 subjects(%2.34) have autonomous cortisol secretion(ACS), 7 subjects(%1.82) have primary hyperaldosteronism, 4 subjects(%1.04) have pheochromocytomas, and 39 subjects(%10.1) have possible autonomous cortisol secretion. In patients with bilateral incidentalomas, the mean diameter of adenomas was higher than unilateral incidentalomas with a diameter of 24.22 mm in comparison to 20.36 mm. Similarly, in patients with bilateral incidentalomas, systolic and diastolic blood pressure was higher than unilateral incidentalomas (135.83 ± 20.27,130.02 ± 18.84% and 79.25 ± 11.56, 78.52 ± 10.11, respectively). Moreover, our study revealed that the frequency of diabetes, hypertension and hyperlipidemia in patients with possible autonomous cortisol secretion was %37, %63, %22.2, respectively. Of 384 patients, 9.11% ($n = 35$) underwent surgery. The most common pathological finding was adrenocortical adenoma ($n = 19$, %54). The median follow-up duration of patients was 48.91 months. Of 384 patients, %44.7 ($n = 172$) were followed up regularly with CT/MRI. During the follow-ups, the diameter of adenomas (%11.6) has increased by more than 10 mm. Of 384 subjects, %56.7 ($n = 218$) were followed with hormonal evaluation and 6 patients have developed possible autonomous cortisol secretion and 3 patients have developed autonomous cortisol secretion. Moreover, 1 subject has been developed primary hyperaldosteronism.
Conclusions
The main findings of the present study are that there was no relevant tumor growth after 5 years of follow-up and that the conversion rate to subclinical or clinical hypercortisolism was low and there were no new cases of pheochromocytoma. Only one subject has shown the development of primary hyperaldosteronism. Our study revealed a significantly increased risk of developing DM, HT and HL in patients with possible autonomous cortisol secretion.

DOI: 10.1530/endoabs.81.EP60

EP61

Prevalence, clinical and biochemical peculiarities of metabolic syndrome in aged patients bearing adrenal incidentaloma

Faten Haj Kacem Akid[1], Abdelmouhaymen Missaoui[1], Mariem Belhoul[2], Wafa Belabed[1], Dhoha Ben Salah[1], Mnif Fatma[1], Nadia Charfi[1], Mouna Mnif[1], Nabila Rekik Majdoub[1], Mouna Elleuch[1] & Mohamed Abid[1]
[1]Hedi Chaker University Hospital, Endocrinology Department, Sfax, Tunisia; [2]Faculty of Medicine of Sfax, Department of Family Medicine, Tunisia.

Background and Aims
Growing scientific evidence supports the hypothesis of an increased cardiometabolic risk in patients harboring adrenal incidentalomas (AI). This risk would be higher in aging populations and patients with functioning adenomas. The current study aims to determine the clinical and biochemical characteristics of metabloic syndrome(MetS) and assess its prevalence in older patients with AI.
Patients and Method
We conducted a retrospective descriptive study including 69 patients aged 65 years and above diagnosed with AI. All patients have undergone clinical examination, adrenal CT, and biochemical workup at the Endocrinology Department of Hedi Chaker University Hospital, Sfax, Tunisia, from 2011 to 2020. MetS was diagnosed based on the National Cholesterol Education Program's Adult Treatment Panel III (ATP III) criteria.
Results
The mean age at diagnosis was 71.4 ± 4.2 years, with a female predominance (57.5%). Seventy percent of elderly patients had non-secreting AI. The functioning incidentalomas displayed autonomous cortisol secretion (32.5%), primary hyperaldosteronism (25%), or secondary hyperaldosteronism (21.8%). One senior had a secreting pheochromocytoma. Hypertension was the most

common metabolic disorder encountered in 77.5% of aged patients. The mean Body mass index was 28.5 ± 5.4 kg/m^2. Our elderly population was frequently overweight (32.5%) or obese (40%). Abdominal obesity affected remarkably the female gender (87% in females versus 35.3% in males) with a mean waist circumference of 106 cm in females and 99 cm in males. We noticed a glucose metabolism disorder in 70%: mainly diabetes mellitus in 60%, impaired fasting glucose in 7.5%, and impaired glucose tolerance in 2.5%. Most senior patients had disturbed lipid profiles. HypoHDLemia prevailed in 45.7%, while hypertriglyceridemia and hypercholesterolemia were found in 17.5% and 28.2%, respectively. The prevalence of MetS in our sample of geriatric patients carrying AI was 24.6%.

Conclusion

Recent scientific data has concluded that AI defines a novel risk factor of MetS [1]. We could hypothesize that AI (despite its hormonal profile) may be associated with a subtle excessive cortisol secretion, hardly labeled clinically and biochemically, which could cause an acquired condition of insulin resistance [2]. Along with multiple age-related mechanisms, this condition would be clinically manifest and result in overt MetS in the geriatric population.

References

1. Ribeiro Cavalari, al. "Nonfunctioning adrenal incidentaloma: a novel predictive factor for metabolic syndrome." Clinical endocrinology 89.5 (2018): 586–595.
2. Peppa, Melpomeni, et al. "Insulin resistance and metabolic syndrome in patients with nonfunctioning adrenal incidentalomas: a cause-effect relationship?." Metabolism 59.10 (2010): 1435–1441.

DOI: 10.1530/endoabs.81.EP61

EP62

Synchronous adrenal gland masses in a patient: clinical case

Mafalda Martins Ferreira, Mariana Lavrador, Cátia Araújo, Joana Reis Guiomar, Carolina Moreno, Patrícia Oliveira & Isabel Paiva
Centro Hospitalar e Universitário de Coimbra, Endocrinologia, Diabetes e Metabolismo, Coimbra, Portugal.

We describe the case of a 69-year-old woman with bilateral adrenal incidentalomas identified in CT-scan: on the right, a 57 mm heterogeneous mass with < 10 Hounsfield units(HU) with absolute washout of 16%; on the left a 13 mm mass with 35UH, intense contrast enhancement but washout of 66%. She had a recent onset of diabetes, hypertension, androgenic alopecia and facial hair. The systolic blood pressure remained persistently > 160 mmHg despite receiving four antihypertensive drugs. She referred multiple episodes of syncope in the orthostatic position without palpitations, facial flushing or diaphoresis. She had no malignancy history nor had any apparent syndromic physical features. Her BMI was 32.3 kg/m^2, waist circunference of 110 cm with thin members and she presented with androgenic alopecia, submental hair lacking other Cushing features. Hormonal tests showed elevation of plasmatic metanephrines: metanephine 79.9 pg/ml (< 60), normetanephrine 214.6 pg/ml (< 120); 3-metoxityramin of 12.7 pg/ml (< 14); 1 mg dexamethasone suppression test of 4.7 µg/dl with supressed ACTH < 5 pg/ml; and elevation of total-testosterone 1.2 ng/ml (< 0.90), DHEA-SO4 1.54 µg/ml (0.15–0.8) and androstenedione 6.7 ng/ml (0.5–3.4). 17-hydroxyprogesterone: 0.67 ng/ml (0.1–2.3). 18 F-FDOPA PET confirmed a pheochromocytoma on the left adrenal gland without metastatic lesions. She began treatment with phenoxybenzamine. Gadolinium MRI suggested a adrenocortical carcinoma on the right. Urology proposed right adenomectomy and total adrenalectomy of the left adrenal gland, then converted to total adrenalectomy of the right gland and parcial adrenalectomy of the left because the pheochromocytoma was macroscopically hard to find even with patient mobilization. Histopathology was consistent with a pheochromocytoma on the left adrenal gland (PASS-score 4/20) and adenoma on the right. After surgery there was normalization of the levels of metanephrines and androgens. Synacthen showed a 60 minute cortisol of 10 µg/dl. She was discharged with 10 mg hydrocortisone once a day. The genetic study is in process.

Discussion

There are few reports on bilateral adrenal masses since they are uncommon, especially if from different etiologies. This patient had simultaneously a pheochromocytoma and a cortisol plus androgen-producing adenoma confirmed by normalization of hormones after its resection – androgen-hypersecretion by benign tumors is also unusual since is more typical of carcinomas. The surgeon was faced with the need to decide the type of surgical approach at the last minute: there are few recommendations on adrenal surgery but there is general consensus to perform total adrenelectomy on pheochromocytoma-affected glands. However, complete normalization of metanephrines and eventual future adrenocortical-hormone sufficiency are good outcome predictors.

DOI: 10.1530/endoabs.81.EP62

EP63

Malignant pheochromocytoma with bone, pulmonary and brain metastases

Cátia Araújo, Mafalda Martins Ferreira, Mariana Lavrador, Carolina Moreno, Patrícia Oliveira, Carla Baptista & Isabel Paiva
Centro Hospitalar Universitário de Coimbra, Serviço de Endocrinologia, Diabetes e Metabolismo, Coimbra, Portugal.

Introduction

Pheochromocytomas are rare neuroendocrine tumors whose malignancy is defined by the presence of metastases that may appear several years later. The appropriate follow-up time remains uncertain.

Clinical Case

We present the case of a woman with a history of pheochromocytoma who underwent complete resection at 48 years old. The genetic evaluation was negative for mutations on RET, VHL, SDHB or SDHD genes. At 66 years old, a thoracic vertebral metastasis appeared on MIBG-I123 scintigraphy. The biopsy of the lesion was consistent with neuroendocrine tumor metastasis. The patient was submitted to radiotherapy, radioisotope therapy and kyphoplasty. The radioisotope therapy with MIBG-I123 proved to be ineffective. Therapy with an antagonist of the alpha-adrenergic receptors (phenoxybenzamine) was initiated. In the next eleven years, the MIBG-I123 scans and lombar CT showed progression of bone metastases and doubt about the possibility of liver lesions. Over these years, plasma metanephrine and 3-methoxytyramine remained normal but normetanephrine showed marginal and progressive elevations. At 77 years, the patient underwent a second radioisotope treatment with MIBG-I123, once again ineffective. 3 months later, the patient was admitted with fatigue, respiratory failure and gait imbalance. Chest CT showed miliary pulmonary spread. Bronchoalveolar lavage immunocytochemistry was compatible with NET metastases. 18F-DOPA PET/CT confirmed pulmonary and massive liver metastases and new bone lesions. Cranial CT scan showed cerebellar, lenticular, frontal and hypothalamic–pituitary involvement suggestive of secondary lesions. Despite the pituitary involvement, there was no hormonal deficiency. Plasma normetanephrine increased. The clinical condition worsened and the patient ended up dying 2 months later.

Conclusions

Metastases typically involve bone, liver and lung – cerebral metastases are rare. MIBG-I123 scintigraphy can detect metastases susceptible to radioisotope therapy, but about a third of patients do not respond. Even in the absence of obvious high-risk characteristics, malignancy can occur and it is not easy to predict. This case illustrates the importance of life-long follow-up in these tumors and the unpredictability of occurrence of metastatic lesions.

DOI: 10.1530/endoabs.81.EP63

EP64

Pheochromocytoma experience

Zafer Pekkolay
Dicle University Faculty of Medicine, Endocrinology, Diyarbakır, Turkey.

Aim

This study aims to evaluate patients with a diagnosis of pheochromocytoma.

Method

This retrospective case–control study includes data from a tertiary endocrine center from January 1, 2010, to December 31, 2020. Demographic, laboratory, operation/pathology data of patients with pheochromocytoma were recorded.

Results

A total of 38 patients (20 patients (52.6%) were male) were included in the study. Median age 48 years (17–81) IQR:18. Tumor localization (right/left/bilateral: 23/9/6) was most common on the right at a rate of 60.5%. Six patients had bilateral tumors. Five patients (three from the same family) had MEN 2A syndrome, and one patient had MEN 2B syndrome. All MEN syndromes had medullary thyroid cancer. One patient had pheochromocytoma, medullary thyroid cancer, and parathyroid adenoma. Neurofibromatosis was detected in one patient. Median tumor size was 6,5 cm (1.6-24) IQR: 3.3 Metanephrine level median: 666(18-23115) IQR:2793(52–341 µg/day) Normetanephrine level median: 3342(187-18900) IQR: 3378(88–444 µg/day) All patients had a normal aldosterone/renin ratio. There was no response to dexamethasone suppression in 10.5 percent of the patients. Mean calcitonin level in patients with medullary thyroid cancer: 2306.5. Normetanephrine was elevated in 92% of patients. Metanephrine elevated in 65% of patients. Normetanephrine and metanephrine were found to be elevated at the same time in 80% of those with bilateral masses.

Conclusion

Pheochromocytoma is seen equally in both gender. It is mainly localized in the right adrenal. It often secretes norepinephrine. Epinephrine/norepinephrine is

often increased in bilateral disease. MEN syndrome is common in bilateral disease.

Keywords: Pheochromocytoma, adrenal mass, endocrine hypertension

DOI: 10.1530/endoabs.81.EP64

EP65

False positive metanephrines in high risk patient for pheochromocytoma

Ricardo Fonseca, Catarina Roque & Ana Sofia Osório
Hospital Fernando Fonseca, Amadora, Portugal.

Background
False positive results are common in the screening of pheochromocytoma. Even in high risk patients with disorders related to multiple endocrine neoplasia it's crucial to exclude possible interferences with analytical methods.
Clinical case
A 69 year-old man was submitted to total thyroidectomy, due to a 11 mm hypoechogenic nodule suspicious of papillary carcinoma (FNA). Histology confirmed medullary carcinoma pT1b. The surgery department ordered the screening for primary hyperparathyroidism and pheochromocytoma and sent the case to Endocrinology. Initial 24 h urinary metanephrines (HPLC) were increased [861 µg/24 h (<302)], but urine was collected shortly after surgery. The patient didn't have paroxistic symptoms and the abdominal CT showed normal adrenal glands. The tests were repeated one month later without known interferences (taking tamsulosin, atorvastatin, omeprazole and levothyroxine): metanephrines were normal in plasma and urine [plasmatic 38 pg/ml (<65), urinary 132 µg/24 h (<302)], but the urinary normetanephrines were elevated 4 fold [2005 µg/24 h (<527) while plasmatic remained normal [110 pg/ml (<196)]. RET gene study didn't show mutations. Given the discrepancy of the results, the metanephrines and normetanephrines were repeated after tamsulosin withdrawal for 15 days, which resulted in normal plasmatic and urinary levels [24 h urinary metanephrines 158 µg/24 h (<302), normetanephrines 213 µg/24 h (<527); plasmatic metanephrines 45 pg/ml (<65), normetanephrines 35 pg/ml (<196)].
Discussion
There are many interferences with nor/metanephrine tests. Anesthetics and some analgesics are known interferences, but there is a comprehensive list of possible medications associated with false positive results. In this case, the first metanephrines were interpreted as interference caused by surgery and anesthetics given that metanephrine levels normalized later. After hospital discharge normetanephrines increased in spite of low risk of disease (RET gene negative for mutations, normal adrenal glands in abdominal CT). Tamsulosin is an alpha-adrenergic blocker with local prostatic action, unexpected to have significant changes in normetanephrines, but only after 15 days of drug discontinuation the results were normal.

DOI: 10.1530/endoabs.81.EP65

EP66

Effects of cumulative doses of corticosteroids on the recovery of patients with COVID-19

Mitra Kazemijahromi[1], HamidReza Samimagham[2], Reza Reza Farrokh Seresht[2] & Soroosh Soroosh Jaber Ansari[2]
[1]Endocrinology and Metabolism Research Center, Hormozgan University of Medical Sciences, Bandar Abbas, Iran; [2]Clinical Research Development Center,Shahid Mohammadi Hospital, Hormozgan University of Medical Sciences, Bandar Abbas, Iran.

Background
Corticosteroids suppress the immune system and have been proposed as a treatment for the severe form of (COVID-19) due to their potential ability to inhibit the COVID-19-induced cytokine storm. We aimed to evaluate the effects of cumulative doses of corticosteroids on the recovery of COVID-19 patients.
Methods
In this descriptive cross-sectional study, we retrospectively evaluated patients with COVID-19 (confirmed by [PCR]) receiving corticosteroids at Shahid Mohammadi Hospital, Bandar Abbas, Iran during June-October 2020. All patients had been admitted to the general wards and not the intensive care unit. COVID-19 was not severe in any of the patients. Beside corticosteroids, all patients had received similar standard COVID-19 treatment according to the National COVID-19 Committee protocols. In addition to the demographic features of the patients including age and gender, COVID-19 symptoms, respiratory rate (RR), lactate dehydrogenase (LDH) level, C-reactive protein (CRP) level, oxygen saturation (SpO2), lymphocyte percentage and count on admission and at the last evaluation before discharge were extracted from the patients' medical files.
Results
A total of 200 patients with confirmed COVID-19 were included in this study. The mean age of the patients was 51.65 ± 9.35 years and 117 (58.5%) were male. The administered corticosteroid was dexamethasone in 55%, methylprednisolone in 32.5%, and prednisolone in 12.5%. The mean administered cumulative corticosteroid dose was equal to 82.69 ± 59.40 mg prednisolone. All COVID-19 symptoms, including fever, cough, dyspnea, headache, body ache, and anosmia decreased in the patients. However, there was no significant difference between patients using < 65 mg of corticosteroids and those using ≧ 65 mg of the medicine regarding the final status of symptoms. The increase in SpO2 was significantly higher in patients using < 65 mg of corticosteroids ($P = 0.008$). Moreover, the proportion of patients with negative final CRP was significantly higher in this group ($P < 0.001$). On the contrary, hospital length of stay was significantly shorter in patients using ≧ 65 mg of corticosteroids ($P = 0.034$). The two groups had no significant differences in terms of LDH levels, lymphocyte percentage and count, RR, and the final status of lung infiltration ($P > 0.05$).
Conclusions
While the cumulative dose of corticosteroids equal to < 65 mg of prednisolone is associated with increased SpO2 and decreased CRP in COVID-19 patients, it leads to prolonged hospital stay compared to the ≧ 65 mg dose of corticosteroids.

DOI: 10.1530/endoabs.81.EP66

EP67

Arterial hypertension in elderly patients carrying adrenal incidentaloma: epidemiological,clinical and therapeutic features

Faten Haj Kacem Akid[1], Abdelmouhaymen Missaoui[1], Mariem Belhoul[2], Wafa Belabed[1], Dhoha Ben Salah[1], Mnif Fatma[1], Nadia Charfi[1], Mouna Mnif[1], Nabila Rekik Majdoub[1], Mouna Elleuch[1] & Mohamed Abid[1]
[1]Hedi Chaker University Hospital, Endocrinology Department, Sfax, Tunisia; [2]Faculty of Medicine of Sfax, Depatment of Family Medicine, Tunisia.

Background and Aims
Arterial hypertension (AH) is one of the most common comorbidities in the elderly. The association of adrenal incidentaloma (AI) with AH in older patients may influence the clinical and therapeutic outcomes of the latter condition. In the current study, we aimed to assess the prevalence of AH and its clinical and therapeutic features in geriatric patients bearing AI.
Patients and Method
We conducted a retrospective descriptive study including 69 patients aged 65 years and above diagnosed with AI. All patients have undergone clinical examination, adrenal CT, and biochemical workup at the Endocrinology Department of Hedi Chaker University Hospital, Sfax, Tunisia, from 2011 to 2020.
Results
The mean age at diagnosis was 71.4 ± 4.2 years, with a female predominance (57.5%). Hypertension was the most common metabolic disorder encountered in 77.5% of aged patients carrying AI. The mean systolic blood pressure was 132 mmHg (extremes = 100–180). The mean diastolic blood pressure was 75 mmHg (extremes = 50–120). AH was newly diagnosed in 10% of cases thanks to a 24-hour ambulatory blood pressure monitoring during the AI clinical assessment. For the patients already diagnosed with AH, the average duration of hypertension was 8.9 ± 7.2 years. Most elderly patients with AI had stage I high blood pressure (87.1%) at diagnosis. Stage II (9.7%) and stage III (3.2%) AH were less frequently encountered. Antihypertensive monotherapy was proposed for 51.9% of patients. Antihypertensive bitherapy (29.6%) or tritherapy (11.1%), quadritherapy (3.7%) were less prescribed. Target organ damage related to AH was observed in 37%, mainly renal (29.4%) and neurological (22.2%) complications. Primary hypertension was the most common form in 70% of cases. Secondary AH was diagnosed in 30% of aged patients having AI due to autonomous cortisol secretion (32.5%), primary hyperaldosteronism (25%), or secondary hyperaldosteronism (21.8%). One senior had a secreting pheochromocytoma. Bilateral AI (92.3%) is subsequently more associated with AH in aged patients than unilateral AI (57.7%) ($P = 0.027$). We did not establish any significant correlation between the AI size and the severity of AH.
Conclusion
Although the prevalence of AH increases with aging, secondary hypertension must be excluded in hypertensive aged patients with AI, mainly autonomous cortisol hypersecretion and pheochromocytoma. The studied population shared the same clinical and therapeutic features as the general hypertensive population. Despite its hormonal profile, bilateral AI is a significant predictive factor of the onset of AH in the elderly.

DOI: 10.1530/endoabs.81.EP67

EP68

Clinical sexual dimorphism in patients with adrenal incidentaloma and (possible) autonomous cortisol secretion

Ljiljana Marina[1], Miomira Ivovic[2], Antoan Stefan Sojat[1], Bogdan Dugic[3], Milina Tancic-Gajic[2], Zorana Arizanovic[1], Kristina Saravinovska[4], Dunja-Simona Petkovic[4], Tijana Petkovic[1], Natalija Antic[1], Aleksandra Kendereski[2] & Svetlana Vujovic[2]
[1]Clinic for Endocrinology, Diabetes and Metabolic Diseases, University Clinical Centre of Serbia, Department for Obesity, Metabolic and Reproductive Disorders, Belgrade, Serbia; [2]Clinic for Endocrinology, Diabetes and Metabolic Diseases, University Clinical Centre of Serbia, Faculty of Medicine, University of Belgrade, Department for Obesity, Metabolic and Reproductive Disorders, Belgrade, Serbia; [3]School of Electrical Engineering, University of Belgrade, Belgrade, Serbia; [4]Faculty of Medicine, University of Belgrade, Belgrade, Serbia.

Introduction
Many diseases of the adrenal cortex show a higher prevalence in women than men with incidence increasing with age in both genders.
Aim
The aim was to determine the possible sexual dimorphism in patients with adrenal incidentaloma (AI) and (possible) autonomous cortisol secretion ((P)ACS).
Methods
This was an observational, cross-sectional study of 381 patients with AI that were functionally assessed in our Clinic. After exclusion of patients with overt adrenal hyperfunction, malignancy, cysts and nonfunctional AI, the studied group consisted of 186 patients with (P)ACS: 138 female and 48 males. Based on average menopause age of 51, we stratified women in two groups: < 51 and $\geqq 51$. For the sake of comparison, we age-matched the male group, and evaluated differences in body mass index (BMI), adrenal tumor size (ATS), localization, ACTH, 24 h cortisol, 1 mg dexamethasone suppression cortisol (1 mg DST), and prevalence of hypertension (HTA) and type 2 diabetes mellitus (T2DM).
Results
Female sex was predominant in the whole cohort (F/M % 74.2/25.8) and in both age groups (< 51 years, 33 patients – F/M % 87.8/12.2 and $\geqq 51$ years, 153 patients – F/M % 71.2/28.8), with a higher frequency in younger group when compared to males ($P=0.048$). There was no difference in age, BMI, ATS, localization, ACTH, 24 h cortisol, 1 mg DST cortisol, HTA and T2DM prevalence between female and male patients. Older male patients had a higher prevalence of T2DM ($P=0.035$) than younger males with 24 h cortisol level being the most significant predictor of T2DM ($P=0.047$). There was no difference in prevalence of HTA, nor other significant differences between younger and older male patients. In the female group, there was no difference in HTA and T2DM prevalence between younger and older patients. In older female patients ATS was the most significant predictor of T2DM ($B=0.247$, 95% CI $B=0.002$–0.018, $P=0.011$) while BMI was the most significant predictor of HTA ($B=0.301$, 95% CI $B=0.009$–0.031, $P=0.002$), whereas there were no detectable significant predictors in younger females for both T2DM and HTA.
Conclusion
Female gender is a predisposing factor for subtle cortisol hypersecretion in patients with AI, while also being a predisposing factor for cardiometabolic comorbidities in women younger than 51 years of age, thus pointing to a relevant clinical sexual dimorphism that could aid in providing a decision-making process and tailored treatment.

DOI: 10.1530/endoabs.81.EP68

EP69

Epidemiological and clinical data and factors of poor blood pressure control in known hypertensive patients in the Sfax region

Fatma Mkaouar[1], Fatma Mnif[2], Khouloud Boujelben[2], Jihen Jdidi[3] & Mohamed Abid[2]
[1]Hedi Chaker, Medecine Interne, Sfax, Tunisia; [2]Hedi Chaker, Endocrinologie, Sfax, Tunisia; [3]Hedi Chaker, Medecine Communautaire et Preventive, Sfax, Tunisia.

Introduction
Hypertension is a very common chronic disease worldwide. Its imbalance is one of the main causes of cardiovascular and neurodegenerative complications.
Patients and Methods
We collected data from hypertensive patients who voluntarily presented for screening on both diabetes and hypertension screening days.Poor blood pressure control was defined as systolic blood pressure (SBP) greater than or equal to 140 mmHg and/or diastolic blood pressure (DBP) greater than or equal to 90 mmHg. The Student t test and the Chi-squared test were used.A threshold of statistical significance was set at 5% for the different tests used.
Results
These were 389 patients who were known to be hypertensive among 2012 patients who were collected at the diabetes and hypertension screening days (19.3%). The median age of the known hypertensives was higher than that of the nonknown (60 years versus 50 years). Men were significantly more affected by hypertension than women (60.7% versus 39.3%) ($P<0.001$).Most of the known hypertensives had a family history of hypertension with a frequency of 64.5% ($P<0.001$). One hundred and fifty known hypertensive patients were diabetic (38.6%) versus 238 who were diabetic without associated hypertension (15.2%) with a $P<0.001$. Smoking was found in 23.1% of known hypertensive patients versus 28.7% of those without hypertension ($P=0.02$). Alcohol consumption was found in 8.2% of the known hypertensive subjects versus 11.7% of the non-known hypertensive subjects ($P=0.05$). A minority was on diet (11.2%). The majority were on monotherapy (58.4%). The use of two hypotensive drugs was for 58 subjects (17.6%). The remaining 42 subjects were on triple therapy (12.8%).The mean SBP was 138.2 mmHg with extremes ranging from 98 mmHg to 215 mmHg and the mean DBP was 82.5 mmHg with extremes ranging from 50 mmHg to 120 mmHg. It was noted that 58.6% of hypertensive patients were poorly balanced.Almost half of the women were well balanced (50.3%) whereas only 35.6% of the men had a good balance of their BP ($P=0.004$). For both subjects with a family history of hypertension and those without, the frequency of well-controlled BP was almost the same (41%). Known diabetics had a balanced BP in 44.3% of cases, whereas this balance was achieved in only 39.6% of the non-diabetics ($P=0.35$).
Conclusion
The management of hypertension is part of the management of all cardiovascular risk factors, which also indicate the therapeutic attitude and target blood pressure values.

DOI: 10.1530/endoabs.81.EP69

EP70

Adverse events associated with supraphysiological glucocorticoid dosing in congenital adrenal hyperplasia (CAH): results of a structured literature review

Vijay Sharma[1], Helen Coope[2], Kamran Maskin[2], Lotta Parviainen[2], John Porter[2], Michael Withe[2] & Anne-Marie Barnes[1]
[1]BresMed Health Solutions Ltd, United Kingdom; [2]Diurnal, United Kingdom.

Objectives
Congenital adrenal hyperplasia (CAH) is a rare condition caused by enzyme deficiency in cortisol biosynthesis. Patients with CAH require lifelong therapy, with the aim of replacing deficient hormones (cortisol +/− aldosterone) and reducing excess androgen production. Guidelines state that the lowest effective glucocorticoid (GC dose) should be used; however, current GC therapy is suboptimal, and supraphysiological GC doses are used to reduce excess androgens. This study aimed to evaluate the published evidence on long-term adverse events (AEs) associated with GC dosing in CAH.
Methods
A structured, comprehensive literature review was conducted to identify evidence for the link between supraphysiological GCs dosing and long-term AEs of interest to the CAH population: such as cardiovascular disease (CVD), osteoporosis/bone health, obesity, diabetes, reduced growth, and poor fertility.
Results
In total, 4,874 records were identified, and 53 studies were included. There is a lack of prospective randomised controlled trials comparing standard GC regimens. Available literature report heterogeneity of patient populations, treatment regimens and study duration. Studies show that complex and multiple dose GC regimens are used in CAH, and both over- and underdosing are associated with AEs. The relationship between GC dosing and bone health was most widely reported with 17 papers reporting a link between excess GC dosing and poor bone health. Fracture risk was shown to increase in older patients. Sixteen articles reported a link between GC dosing and obesity and associated metabolic syndrome including fat mass and lean body weight. These studies reported that higher GC dosing was associated with higher BMI. Thirteen articles reported a link between GC dosing and height / growth in CAH patients providing evidence for an important link between GC dosing and growth period, with high doses of GC during adolescence being associated with lower final height. Four articles linked diabetes markers, such as HbA1c levels, glucose metabolism, and insulin resistance, with GC dosing. Other relationships supported by the literature were the links between GC dosing and patients' health related quality of life, and CVD/associated risk factors.

Conclusion
This literature review identified a wealth of evidence to support relationships between supraphysiological GCs dosing and long-term AEs in CAH. There is an unmet need for a treatment for CAH that provides optimal cortisol replacement at a physiological dose, thereby reducing AEs associated with excess GC dosing.

DOI: 10.1530/endoabs.81.EP70

EP71

Adrenal incidentaloma rate during coronavirus disease 2019 (COVID-19) pandemic

Ozge Telci Caklili[1], Arzu Poyanli[2], Esin Duvek[2], Eda Canipek[2], Alpay Medetalibeyoglu[3], Hulya Hacisahinogullari[1], Ozlem Soyluk Selcukbiricik[1], Nurdan Gul[1] & Ayse Kubat Uzum[1]
[1]Istanbul University, Faculty of Medicine, Endocrinology and Metabolism, Istanbul, Turkey; [2]Istanbul University, Faculty of Medicine, Radiology, Istanbul, Turkey; [3]Istanbul University, Faculty of Medicine, Internal Medicine, istanbul, Turkey.

Background
Adrenal incidentaloma (AI) is described as an adrenal mass detected on imaging not performed for adrenal disease. In coronavirus disease 2019 (COVID-19) pandemic, chest CT evaluation was performed for all ages in adults. In this study, we aimed to detect adrenal adenoma(s) which were identified with chest CT, during COVID-19 diagnostic work-up to find AI prevalence in our population.
Methods
All patients who underwent chest CT examination for COVID-19 at Istanbul University Faculty of Medicine between March 15, 2020 and June 15, 2020, were screened. Patients' demographic characteristics were recorded from their medical records. Patients with a history of malignancy were excluded. Images were assessed by two radiologists and consulted with an experienced senior radiologist.
Results
A total of 4449 patients' CT images were screened. There were 4108 patients with no lesion (control group) and 248 (5%) patients with at least one lesion (adrenal group). The mean age of the control group was 46.67 ± 17.07 and the adrenal group was 60.65 ± 16.83 years ($P < 0.001$). In 248 patients, there were 134 patients with at least one adrenal nodule (3% among all screened CT images). The mean age of the patients was 58.70 ± 15.09 years. Thirty-four patients had a right nodule, 78 patients had a left nodule and 22 had bilateral nodules. When nodule size and Hounsfield unit (HU) were compared there was no statistically significant difference between the left adrenal gland and right adrenal gland ($P = 0.57$ and $P = 0.97$, respectively).
Conclusion
Our data showed an AI rate of 3% and the majority of nodules were in the left adrenal gland.

DOI: 10.1530/endoabs.81.EP71

EP72

Bone impact of hydrocortisone hormone replacement in adrenal insufficiency.

Ines Charrada, Alaya Wafa, Najoua Lassoued, Boubaker Fadia, Zantour Baha, Berrich Olfa & Sfar Mohamed Habib
Endocrinology-Diabetology and Internal Medicine Service CHU Tahar Sfar Mahdia Tunisia, Mahdia, Tunisia.

Introduction
The treatment of adrenal insufficiency (AI) is based on long-term glucocorticoid substitution. Hydrocortisone (HC) is the most commonly used substitution molecule. The aim of our work was to determine the long-term bone impact of patients with peripheral AI.
Patients and methods
This is a descriptive and analytical study involving 77 patients with peripheral IS (66 women and 11 men), all treated with HC. For each patient, we determined the duration of the disease and the daily and cumulative dose of HC, and performed a phosphocalcic assessment, an alkaline phosphatase (ALP) determination, and a bone densitometry (BMD) performed in 30 patients.
Results
The mean age was 40.5 years (range: 22–63 years). The mean duration of evolution was 7.7 years. We found that among the patients who had a BMD, 75% had bone demineralization at the time of the study, which was more marked in the cancellous bone (spinous site). This prevalence was high compared to the Tunisian adult population (75% vs 45.7%). This demineralization was positively correlated with the cumulative dose of HC (mean cumulative dose (g) $= 60 \pm 80.4$ in patients with normal BMD vs 132 ± 86.4 in patients with bone demineralization; $P = 0.042$), and was more frequent but not significantly so in postmenopausal women. However, we did not find any correlation between bone demineralization and daily HC dose and disease duration, respectively. Biologically, at the time of the study, ALP was elevated and hypocalcemia was present in 15% and 26.7% of patients, respectively. However, we did not find any correlation between these two biological abnormalities and the daily dose of HC, the cumulative dose and the duration of the disease respectively.
Conclusion
Hormone replacement therapy of peripheral AI with HC seems to be a risk factor for bone demineralization, especially with the higher cumulative dose of this corticoid. Further studies are needed to better define the cumulative dose threshold at which bone densitometry monitoring is indicated.

DOI: 10.1530/endoabs.81.EP72

EP73

A rare cause of Cushing's syndrome

Vittoria Favero[1], Carmen Aresta[2], Chiara Parazzoli[1], Valentina Morelli[2] & Iacopo Chiodini[1,2]
[1]University of Milan, Department of Medical Biotechnology and Translational Medicine, Milan, Italy; [2]IRCCS Istituto Auxologico Italiano, Department of Endocrine and Metabolic Diseases, Milan, Italy.

Introduction
Aggressive ACTH-independent Cushing's syndrome is rare and frequently related to malignant adrenocortical tumor. However, in exceptional situations, ectopic steroids secretion has been described.
Case report
We report the case of an 87 years-old woman referred to our clinic in September 2020 after a low trauma sacral fracture. Her recent medical history revealed the onset, in the previous months, of severe hypokalemia, uncontrolled type 2 diabetes (glycated hemoglobin 9.2%), worsening of arterial hypertension and spontaneous bruising. Because of the medical history, a Cushing's syndrome (CS) was suspected and after exclusion of exogenous glucocorticoid use, specific tests were carried out. Laboratory findings confirmed the diagnosis of CS: 24-hour urine free cortisol $> 4 \times$ ULN, cortisol after 1-mg overnight dexamethasone suppression test of 58.8 µg/dl, undetectable adrenocorticotropic hormone (ACTH) levels, and hypokalemia. The subsequent abdominal CT scan revealed normal adrenal glands, but showed a suspicious 8-cm pelvic mass, which was suggestive of malignancy. Unfortunately, given the old age and the severe clinical picture, no further investigations were feasible and a medical therapy with metyrapone was initiated. After few weeks of therapy, we observed an improvement of glucose and pressure control and the restoration of normal potassium levels, even though the clinical picture remained severe. After six months a clinical improvement was observed, and the patient could undergo an abdomen MRI for better characterizing the pelvic mass. This second radiologic evaluation showed a significant increase of the pelvic mass diameter, which had doubled, reaching the diameter of 17 centimeters. Because of the rapid tumor growth and the presence of ACTH independent hypercortisolism, the patients could be suspected to be affected by an ectopic cortisol secreting adrenocortical carcinoma. Histological confirmation would be necessary, but surgical options or other invasive procedures are not feasible.
Discussion
Ectopic adrenal carcinomas may result from adrenal embryonic remnants. Adrenocortical neoplasms arising in ectopic locations are extremely rare, and cortisol-secreting ones are even rarer, with only a few cases reported in the literature. The treatment of ectopic adrenocortical carcinoma does not differ from that of eutopic tumors. However, ectopic adrenocortical carcinomas are, in general, aggressive and poorly differentiated and they are, therefore, associated with a high mortality rate.

DOI: 10.1530/endoabs.81.EP73

EP74

Magnetic iron oxide nanoparticles for the delivery of thermal therapy for the treatment of primary aldosteronism

Anna Sorushanova[1], Padraig Donlon[1], Obdulia Covarrubias-Zambrano[2], Jose Covarrubias[2], Sunitha Varghese[2], Peter Owens[3], Martin O'Halloran[44], Punit Prakash[5], Stefan Bossmann[2] & Michael Conall Dennedy[1]
[1]National University of Ireland Galway, Clinical Pharmacology, Ireland; [2]The University of Kansas Medical Center, Department of Cancer Biology,

United States; [3]National University of Ireland Galway, Centre for Microscopy & Imaging, Ireland; [4]National University of Ireland Galway, Translational Medical Device Lab, Ireland; [5]Kansas State University, Department of Electrical and Computer Engineering, United States.

To minimise damage to surrounding tissues, targeted delivery of therapeutics to the tumour is highly desirable, and the development of nanotechnology has shown promising results. Magnetic iron oxide nanoparticles (MIONPs) have been gaining traction over the years for applications such as drug delivery, molecular imaging and delivering hyperthermia for treatment of various cancers (1). MIONPs have great therapeutic potential as they can be produced in various sizes and shapes, with the ability to modify the surface by coating the nanoparticles. MIONPs have the ability to be activated by external magnetic field to generate heat and to cause hyperthermia (2). Translationally, the delivery of thermal therapy offers an option for minimally invasive definitive treatment of primary aldosteronism, an endocrinopathy of aldosterone excess/dysregulation which represents the commonest secondary form of hypertension. In this study, MIONPs have been used at different concentrations to evaluate nanoparticle uptake and rate of uptake by adrenal cortical and endothelial cells, as well as gain understanding of the location of nanoparticles within the cell. Magnetic iron oxide nanoparticles (MIONPs) were provided by The University of Kansas. Adrenal Cortical cell-lines (MUC1, H295R and HAC15) and Endothelial cell-line (HUVEC) were used in this study. MIONPs were added at concentrations of 0.5, 5, 10, 20 and 50 μg/ml to the cells and incubated overnight. MIONP up-take efficiency, rate of uptake and cytotoxicity was assessed by Flow Cytometry. Confocal Microscopy was used to image the cells following MIONP incubation. Cellular proliferation was assessed by Xcelligence system and ala-marBlue. Cellular respiration was assessed by "Seahorse" technology. MIONP location within the cells was assessed by transmission electron microscopy (TEM). Following overnight incubation with MIONPs, Flow Cytometry showed significant uptake by MUC1, HAC15 and HUVEC cells at 10 μg/ml MIONP concentration. Confocal and TEM images revealed MIONPs in the cytoplasm and in the vesicles for all cell types (Fig. 1 and 2). Live Confocal imaging showed MIONP phagocytosis specific uptake by the HAC15 cells.

References

1. Chaves (*et al.*), International Journal of Nanomedicine: 5511–5521, 2017.
2. Wang (*et al.*), Beilstein Journal of Nano-technology: 444–455, 2012.

DOI: 10.1530/endoabs.81.EP74

EP75

Adrenal incidentaloma: metabolic profile of non-secretory adrenal adenomas

Soumiya Berrabeh[1], Fatimzahra Bentebbaa[1], Ouafae Elmehraoui[1], Imane Assarrar[2], Dounia Zerrouki[1], Siham Rouf[3] & Hanane Latrech[3]
[1]Mohammed VI University Hospital Center Oujda, Faculty of Medicine and Pharmacy Oujda, University Mohammed First Oujda, Endocrinology-Diabetology and Nutrition Department., OUJDA, Morocco; [2]Mohammed VI University Hospital center Oujda, Faculty of Medicine and Pharmacy Oujda, Université Mohammed Premier Oujda, Endocrinology-Diabetology and Nutrition Department, OUJDA, Morocco; [3]Mohammed VI University Hospital center Oujda, Faculty of Medicine and Pharmacy Oujda, University Mohammed First Oujda, Endocrinology-Diabetology and Nutrition Department, Laboratories of Epidemiology, Clinical Research and Public Health, OUJDA, Morocco.

Introduction

The performance of medical imaging leads to the incidental discovery of many silent and ignored tumor lesions. The term "adrenal incidentaloma" (AI) is a neologism for an adrenal mass discovered incidentally during an abdominal imaging examination, not motivated by the exploration of adrenal pathology, most of the time asymptomatic. Several authors hypothesize that adrenal adenomas could be a manifestation of the metabolic syndrome and that the prevalence of insulin resistance indicators (diabetes, hypertension, obesity) is high in patients with an adrenal incidentaloma. The aim of this work is to research among our patients with non-secreting adrenal adenoma, abnormalities of markers of metabolic syndrome in order to identify patients at high metabolic and vascular risk, which may prompt us to reconsider the management of these non-functioning tumors.

Material and methods

A prospective and descriptive study of 50 cases of adrenal incidentalomas, including 24 cases of non-secreting adenomas, collected in the endocrinology, Diabetology and Nutrition department of the CHU Mohamed VI of Oujda. The data were collected from the medical records and processed by SPSS V21 software

Results

Non-secreting adenoma represents 48% of AI. The mean age of our patients with non-functional adenoma was 62.4 ± 10.5 years with female predominance (70.8%). Among 24 patients, eight had a BMI >30 kg/m2, a mean waist circumference of 103.8 mm in women and 108.5 mm in men, 11 patients were hypertensive and 6 were diabetic (25%). Fourteen patients had low HDL cholesterol including 5 male and 9 female patients. Moreover, nine patients had elevated triglycerides. Sixty-six percent of patients satisfied the definition of metabolic syndrome according to the IDF 2005 criteria (International Diabetes Federation), including 10 women and 6 men. Regarding cardiovascular risk, according to the recommendations of the European Society of Cardiology, 70.8% of patients were classified at very high risk and 29.2% at high cardiovascular risk.

Discussion/Conclusion

Non-functional adrenal adenomas are often associated with metabolic syndrome which is a major risk factor for cardiovascular or thromboembolic events, hence the need to consider cardiovascular risk in patients with non-secretory adrenal adenoma for optimal management.

Keywords: adrenal incidentaloma, *metabolic profile,* cardiovascular risk

DOI: 10.1530/endoabs.81.EP75

EP76

Pulmonary thromboembolism as the initial presentation of ACTH-independent Cushing's Syndrome

Daniela Dias[1], Ines Damasio[2], Helder Simões[1], Filipa Serra[1], Luisa Fontes[3], Carlos Leichsenring[4], Nuno Pinheiro[4] & Inês Sapinho[1]
[1]Hospital CUF Descobertas, Endocrinology, Lisbon, Portugal; [2]Oncology Institute Francisco Gentil, Endocrinology, Lisboa, Portugal; [3]Hospital CUF Descobertas, Internal Medicine, Lisbon, Portugal; [4]Hospital CUF Descobertas, Surgery, Lisboa, Portugal.

Cushing's syndrome (CS) is associated with a considerable risk of complications including thromboembolic events (TE). They occur mostly within the first 2–3 months postoperatively. When present before surgery, CS has high rates of perioperative mortality and morbidity. The benefit of steroidogenesis inhibitors after TE is not fully known. Furthermore, little guidance is available regarding TE assessment/management in CS. We report a case of a 34-year-old male admitted in our emergency department for a presyncope episode during minimum physical activity. He described severe fatigue that had progressively worsened over 3 months. He experienced progressive weight gain of 10 kg and the appearance of extensive purple trunk striae in the last year. His past medical history included hypertension, obesity and obstructive sleep apnea. His blood pressure was 100/78 mmHg, his heart rate 150 bpm and oxygen saturation was 99%. Laboratory tests revealed: hemoglobin 15 g/dl, leukocytosis 13,200/mm3, AST 259 U/L (15–37), ALT 653 U/L (16–63), indirect hyperbilirubinemia 1.20 mg/dl, D-dimer 70.370 ng/ml (<500), NT-proBNP 125 pg/ml, troponin T 663 ng/l. CT scan pulmonary angiography found extensive pulmonary embolism involving the right and left pulmonary arteries with extension to lobar arteries, also revealed a 35 mm solid tumor on his left adrenal gland. Lower limb color doppler ultrasound demonstrated deep venous thrombosis in the right popliteal vein. Anticoagulant therapy was initiated. The patient was hospitalized for treatment and further investigation. Elevated urinary free-cortisol(UFC) levels were noted (936 μg/24 h;1389 μg/24 h;28–213), ACTH level was undetectable (<5 pg/ml), salivary cortisol showed loss of circadian rhythm (32.8 nmol/l- 0800 h; 32.5 nmol/l-0011 h), and low dose dexa 1 mg plasma cortisol result was 26.4 μg/dl and low DHEA-S of 76 μg/dl (80–560). These results were compatible with ACTH-independent CS. He started on metyrapone to control the hypercortisolaemia (maximum 1500 mg 8–8 h). Ketoconazol was not an option given the elevated liver enzymes. There was an initial reduction in 24 hours UFC within a few weeks of initiation of metyrapone. However, the UFC level failed to normalize, after 7 months of medical therapy alone(UFC 706 μg/24 h).An uneventful laparoscopic left adrenalectomy was subsequently performed, with hydrocortisone started for empiric treatment of secondary adrenal insufficiency. Postoperative histopathology confirmed an adrenal adenoma. He completed 3 months of rivaroxabane. Presently, 5 months after surgery, he remains on hydrocortisone. Studies on medical therapy directed to lower cortisol values and their effects in TE risk are sparse. Additional studies are needed to reinforce well defined guidelines regarding CS and its thrombotic complications.

DOI: 10.1530/endoabs.81.EP76

EP77

Adrenocortical carcinoma: experience of a tertiary center

Ana Rita Elvas, Joana Couto, Raquel G Martins, Jacinta Santos, Teresa Martins & Fernando Rodrigues
Portuguese Oncology Institute of Coimbra, Department of Endocrinology, Coimbra, Portugal.

Introduction
Adrenocortical carcinoma (ACC) is a rare endocrine malignancy with poor prognosis. Objective: The aim of this study is to characterize patients with ACC followed at a tertiary center. Material and Methods: Retrospective analysis of clinical records of patients with histopathological diagnosis of ACC followed in our clinic. Results and conclusions: We reviewed 11 patients. The average age at diagnosis was 57.3 ± 15.2 years and 63.6% were females. Seven patients had a functioning adrenal carcinoma. At diagnosis, 72.7% of the patients presented weight loss, 36.4% back pain and 27.3% referred asthenia. Two patients presented Cushing's syndrome, one hirsutism and three arterial hypertension and hypokalaemia. Regarding imaging data, the tumour was detected almost exclusively through abdominal computed tomography (CT); dimensions ranged from 3.8 to 20 cm with a median size of 10 cm; 54.5% were located on the left adrenal gland; 28.6% had signs of necrosis; 27.3% presented local invasion and 36.4% distant metastasis. Prognostic stratification based on ENSAT tumour stage was used; two (18.2%) patients were in stage I, four (36.4%) in stage II, one (9.1%) in stage III and four (36.4%) in stage IV. Ten patients (90.9%) underwent adrenalectomy, 70% through laparotomy. Presence of residual tumour could not be assessed(Rx) in 50% of the patients; total resection was reported in 10%; microscopic (R1) or macroscopic (R2) res ection margins were observed in 30% and 10%, respectively. The Weiss Score ranged from 3 to 6 (median of 3) and the Ki67 proliferative index ranged from 2 to 20 (median of 7). Postoperatively, 4 (36.3%) patients received only mitotane treatment and 3 (27.3%) patients were given systemic chemotherapy combined treatment with mitotane. Adjuvant radiotherapy was applied in two patients; and other two required palliative radiotherapy. One patient who received mitotane did not report any drug side effects. The symptoms reported were mostly gastrointestinal disturbances (81.4%, $n=5$); one patient presented neurotoxicity and other reported skin lesions and mucositis. Two patients even had to discontinue treatment du e to intolerance. Disease specific mortality was 85.7%. The mean overall survival was 62.1 ± 14.7 months for stages I + II (ranging from 33.3 to 90.9 months) and 8.8 ± 2.9 months for stages III + IV (ranging from 3.1 to 14.5 months), $P=0.005$. ENSAT staging at diagnosis was the major prognostic factor in our series.

DOI: 10.1530/endoabs.81.EP77

EP78

Subthreshold cortisol deficiency-another ray in the spectrum?

Foteini Adamidou, Paraskevi Komzia & Marina Kita
Ippokration General Hospital, Department of Endocrinology, Thessaloniki, Greece.

Introduction
In Endocrinology, subclinical disorders meet certain diagnostic laboratory thresholds, but are by definition asymptomatic. Subthreshold disorders in Endocrinology have not been defined. We describe two cases of cortisol deficiency, primary and secondary, with normal baseline cortisol, which were by presentation clinical, but could be characterized as subthreshold by biochemical cut-off criteria.
Case 1
A 47-year-old woman was referred for assessment of adrenal reserve, one year after a complicated admission following a road accident. Her past medical history was remarkable for Hashimoto's thyroiditis on thyroxine. During her hospitalization with multiple injuries and subdural hematoma, she developed multiple complications, including bilateral adrenal hemorrhage. On examination the patient complained of fatigue; she was hemodynamically stable, but skin and mucosal hyperpigmentation was noted. Multiple measurements of am serum ACTH revealed values between 428–800 pg/ml (10–60) with preservation of circadian rhythm and of cortisol between 10 and 20 ng/ml (6–22). Other relevant labs were: TSH 3.67 mIU/ml, DHEAS 75 μg/dl (150–475), plasma renin activity 13.88 ng/ml/h (0.48–4.88), aldosterone 13.7 ng/dl (4–30). Response to 250 μg tetracosactrin stimulation was borderline at 60' (17.8 μg/dl). Pituitary MRI was normal. Adrenal CT showed normal/small adrenal glands, with complete resolution of hemorrhage. Antibodies to 21-hydroxylase were negative. Serum cortisol-binding protein was 3.8 mg/dl (1.7–3.1) while on oral contraceptives. She was started on hydrocortisone 10–0–5 mg with resolution of symptoms. Four years following the initial presentation, the patient had an am cortisol of 11.89 ng/ml, ACTH 24.5 pg/ml, DHEAS 21 μg/dl and normal response to tetracosactrin stimulation (0' 16.2 μg/dl, 30' 20.16 μg/dl, 60' 21.77 μg/dl), indicating full delayed recovery of the axis.
Case 2
A 87-year-old woman was hospitalized because of severe fatigue, nausea and associated hyponatremia at 125 mmol/l. Her past medical history was significant for hypertension treated with carvedilol 6.25 bid. Her am serum ACTH and cortisol on repeated measurements were 13.6 pg/ml (10–60) and 11.8 μg/dl respectively. Response to 250 μg tetracosactrin stimulation was borderline at 60' (17.9 μg/dl). Prolactin was 1.89 ng/ml, TSH 0.255 mIU/l, FT4 0.61 ng/dl (0.6–1.49) and FSH 1.79 mIU/ml. Pituitary MRI was normal. The cause of hypopituitarism remained unknown. She was started on hydrocortisone 10-0-5 mg and thyroxine 25 μg/d, with resolution of symptoms and electrolyte normalization. A challenge trial of cortisol discontinuation led to symptomatic relapse.
Conclusions
Clinical cortisol deficiency with normal baseline serum cortisol can be defined as subthreshold condition. Concurrent ACTH measurements and stimulation tests are necessary to unmask the problem. The definition should not contest current diagnostic cut-offs or the principle of quaternary prevention.

DOI: 10.1530/endoabs.81.EP78

EP79

A multidisciplinary team for diagnosis and management of primary hyperaldosteronism

Meir Frankel[1], Gabriel Munter[1], Sophia Magen[2] & Anthony Verstandig[1]
[1]Shaare Zedek Medical Center, Jerusalem, Israel; [2]Laboratory Division, Shaare Zedek Medical Center, affiliated to Faculty of Medicine, Hebrew University, Jerusalem, Israel.

Background
Primary hyperaldosteronism (PH) is a syndrome caused by excess aldosterone secretion, which leads to hypertension and hypokalemia and increased risk for target organ damage. The overproduction of aldosterone at the adrenal gland can be unilateral or bilateral. For unilateral disease the best treatment is unilateral adrenalectomy. According to international guidelines, most of the patients should have adrenal venous sampling (AVS) to distinguish between bilateral and unilateral disease. At 2018 we established a multidisciplinary team for diagnosis and management of primary hyperaldosteronism. The aim of this study was to investigate all cases of PH treated in our institute since establishment, including advantages and pitfalls of AVS procedure.
Methods
A retrospective study was performed on a cohort including all patients that were diagnosed and treated at Shaare Zedek Medical Center during 2018–2021. All patients had adrenal imaging (CT or MRI) followed by AVS as needed. Data collection included demographic, clinical and biochemical information, detailed results of AVS procedures and follow up after. AVS protocol and interpretation of the results were done according to International clinical practice guidelines.
Results
During the described period, 22 patients were diagnosed with PH. Mean age 51.6 ± 10, 19/22 (86%) males. All patients had hypertension and 18/22 (82%) had hypokalemia. 21 of them had an AVS. All AVS procedures were done by one invasive radiology specialist. In 17/21 (81%) the AVS results were fully successful, with improvement during time, from 70% at the first ten patients to 90% at the last ten patients. In 4/21 (19%) there was difficulty to locate the right adrenal vein; even though, in 3/4 patients there was evidence for lateralization according to indirect interpretation of the results, overall 20/21 (95%) had a conclusive lateralization result. In 8/21 (38%) adrenal imaging wasn't accurate in confirming lateralization side. No significant complications of the AVS were observed. 11/16 patients with unilateral disease had unilateral adrenalectomy, all of them became normotensive with less medications or no medical treatment for hypertension.
Conclusion
Establishment of a multidisciplinary team can improve management and treatment for patients with primary hyperaldosteronism. Learning curve for AVS can be achieved after 10 cases. With the limitation of adrenal imaging to locate the hyperaldosteronism source, AVS is a critical step in the diagnosis of primary hyperaldosteronism, and with a good implementation process it is a safe and efficient procedure.

DOI: 10.1530/endoabs.81.EP79

EP80

Adrenal insufficiency presenting as hypercalcemia and acute kidney injury

Nauman Jadoon
Queen Elizabeth University Hospital, United Kingdom.

Introduction
Hypercalcemia is uncommon in patients with adrenal insufficiency. It is common in patients with primary hyperparathyroidism and malignancy.
Case
This is a case of primary adrenal insufficiency presenting as acute kidney injury and hypercalcemia. The patient was referred with 10 days history of vomiting, decreased appetite, lethargy and abdominal pain. A week before admission, she developed pleuritic chest pain worsening with inspiration. Her admission bloods showed acute kidney injury (eGFR 38 ml/min), hyponatremia (121 mmol/l), hyperkalaemia (5.7 mmol/l), and hypercalcemia (3.11 mmol/l). Workup for primary hyperparathyroidism and screening for malignancy were negative. Basal cortisol was undetectable (<30 nmol/l) and adrenocorticotrophic hormone level was raised (1030 ng/l). Administration of hydrocortisone and intravenous fluids resulted in dramatic resolution of hypercalcemia and electrolyte abnormalities within 48 h.
Conclusion
This case shows that adrenal insufficiency can may present with hypercalcemia and acute kidney injury and should be considered while evaluating cause of hypercalcemia in patient especially if investigations for common causes are negative.

DOI: 10.1530/endoabs.81.EP80

EP81

Percutaneous ethanol ablation of large adrenal tumor

Inmaculada Venegas Nebreda, Nerea Egaña Zunzunegui, Cristina Elías Ortega, Ane Amilibia Achucarro & Alfredo Yoldi Arrieta
Hospital Universitario de Donostia, San Sebastian, Spain.

Introduction
Percutaneous ablation has been used over the years for the minimally invasive treatment of liver, kidney, thyroid and, although less frequent, adrenal cysts. We describe the case of a young patient with a large adrenal cyst treated with ethanol ablation, avoiding adrenalectomy.
Clinical case
We present a 32-year-old woman who is referred to Endocrinology due to a 10 cm adrenal incidental finding in an MRI performed due to disc herniation. As her personal history, she presented gestational Diabetes (DM) in both her pregnancies with subsequent type 2 DM and hypertension. Her treatment includes Metformin and Enalapril. She does not have a Cushingoid phenotype. She reports mild abdominal discomfort, occasional headaches and palpitations. Her blood analysis show HbA1c 6.1% with fasting glucose of 153 mg/dl, with metanephrines, Nugent test and urinary free cortisol in the normal range. The CT scan reveals a thin-walled cystic image of 10 cm in diameter, with no apparent interior content and with a probable diagnosis of a right adrenal cyst. After discussing the case in the endocrine tumor committee, we present the patient with the two available alternatives: adrenalectomy or percutaneous ablation with ethanol. After explaining both options to the patient, she chooses sclerosis because it is less aggressive. Under local anaesthesia, 500 ml of yellow liquid are evacuated with the subsequent introduction of 100 ml of ethanol. After 1 hour, another 100 ml of fluid are evacuated to sclerosize the lesion. Upon examination, no adrenal cells are identified in the sample. The patient is discharged the same day. One month after the ablation, the patient undergoes a control ultrasound where a 90% reduction in cyst volume is observed. In another control at 4 months the cyst remains stable in size.
Discussion
Adrenal cysts are rare lesions which may sometimes reach a considerable size. They may result in complications such as infection, haemorrhage, rupture or compression of adjacent structures. Percutaneous ethanol ablation may be a valid alternative to adrenalectomy in patients with large or recurrent cysts.

DOI: 10.1530/endoabs.81.EP81

EP82

Glucocorticoids and androgen secreting adrenocortical adenoma: A case report and literature review

Ali Alqahtani, Mohammed Almehthel & Mohammed Almohaya
King Fahad Medical City, Obesity, Endocrinology and Metabolism Center, Riyadh, Saudi Arabia.

Background
The presence of Adrenocorticotropic hormone (ACTH)-independent Cushing syndrome that is associated with androgen hypersecretion is extremely rare in benign adrenal tumors. Precise recognition and management of this association will have a great impact on the management of such patient.
Clinical case
We describe a case of a 35-year-old lady who presented with 2 years history of difficult-to-control hypertension, symptoms of androgen excess along with Cushing features. Further workup revealed lack of serum cortisol suppression after overnight 1-mg dexamethasone suppression test [493 nmol/l (17.8 μg/dl)] along with 24-h urine free cortisol of 1020 μg/24 h (reference range: 21–292 μg/24 h) and Adrenocorticotropic hormone (ACTH) level of 1.18 pmol/l (reference range: 1.03–10.70 pmol/l). Androgens profile was consistent with high Dehydroepiandrosterone (DHEA) level [22 umol/l (reference range: 2–11.1 umol/l)] and serum testosterone level was 2.18 nmol/l (reference range: 0.38–1.97 nmol/l). There was no biochemical evidence of hyperaldosteronism or pheochromocytoma. Subsequent imaging confirmed the presence of large heterogeneous left adrenal mass ($4.4\times7\times4.6$ cm) with enhancing solid and cystic/necrotic components and small round calcifications. A left robotic adrenalectomy was performed uneventfully. The histopathologic findings were consistent with the diagnosis of an adrenocortical adenoma as there were no features of malignancy seen as per modified Weis criteria. Postoperatively, the patient had undetectable cortisol level with marked improvement in her blood pressure.
Conclusion
An unusual case of adrenocortical adenoma that is associated with plurihormonal hypersecretion is described. Clinicians should be aware of such rare association when evaluating a patient with a similar context.

DOI: 10.1530/endoabs.81.EP82

EP83

Giant pheochromocytoma: wich management?

Sara Ijdda, Rafi Sana, Ghizlane El Mghari & El Ansari Nawal
University Hospital Center Mohamed VI, Departement of Endocrinology, Diabetes, Metabolic Disease and Nutrition, MARRAKECH, Morocco.

Introduction
Malignant pheochromocytomas present a real challenge for practitioners. This entity of tumors is rare, with complex characterization, and heterogenocity in their evolution and prognosis. Given the rarity of this tumor group, there is no consensus on the therapeutic management. The management must be in a multidisciplinary framework. Through this illustrative case, we propose a literature review of this rare entity with discussion of the different therapeutic options in a metastatic situation.
Observation
A 23-year-old patient, with no pathological history, admitted for etiological assessment of a right adrenal mass revealed by isolated right low back pain evolving 5 years previously. An ultrasound was carried out having objectified two tissue masses of the liver of secondary appearance, then a complement by an adrenal scan objectified a voluminous tumoral process at the right adrenal, very vascularized seat of a zone of necrosis with liver metastases. Methoxylates were negative, urinary free cortisol was normal, and dexamethasone suppression test was positive. The patient underwent a right adrenal-nephrectomy complicated by renal failure due to tubular necrosis. The anatomopathological study was in favor of a pheochromocytoma. Bone scintigraphy revealed humeral metastases. As part of a multidisciplinary decision, chemotherapy (CVD), metabolic radiotherapy and treatment with iodine 131 MIBG were proposed. The patient is currently being monitored in France, since she was admitted there for doctoral studies. The 1-year follow-up after surgery showed a reduction in the volume of hepatic metastases, as well as an improvement in renal function with clinical and radiological monitoring as a therapeutic option.
Discussion/Conclusion
Malignant pheochroocytomas represent 10 to 15%. They are defined by the presence of metastases at sites devoid of chromaffin. In the absence of curative treatment and the presence of long survivors, monitoring may be a therapeutic option. The treatment is justified by the presence of a large tumor volume, the presence of an uncontrollable hormonal syndrome and radiological progression.

Cytoreductive surgery should reduce symptoms and improve response to other treatments.For slowly progressive metastatic pheochromocytomas, treatment with 131I-MIBG has been recommended as first-line treatment, with 177Lu-DOTATOC being a potential alternative for those with positive somatostatin receptor metastases; chemotherapy combining Dacarbazine, Vincristine and Cyclophosphamide, may be considered for progressive disease. Prospective trials, in terms of targeted therapies, are necessary for a better characterization of these tumors in order to identify the appropriate treatment. The prognosis of theses tumors remains unfortunate.

DOI: 10.1530/endoabs.81.EP83

EP84

The primary aldosteronism rollercoaster: hypoaldosteronism as a potential postoperative complication

August Palma[1], Lihua Hu[1], Heok Cheow[1], Iosif Mendichovszky[1], Vasilis Kosmoliaptsis[1], Alison Marker[1], Waiel Bashari[1,2], Russell Senanayake[1,2] & Mark Gurnell[1,2]
[1]Wellcome Trust-MRC Institute of Metabolic Science, Addenbrooke's Hospital, Cambridge Biomedical Campus, Cambridge, United Kingdom; [2]University of Cambridge, School of Clinical Medicine, Cambridge, United Kingdom.

Introduction
Primary aldosteronism (PA) is a common and potentially reversible cause of secondary hypertension, characterised by resistance to standard antihypertensive therapy and possible hypokalaemia. Lateralisation investigations, including adrenal vein sampling (AVS), are required to distinguish between unilateral or bilateral disease, with unilateral disease representing a potentially surgically curable form of PA. The majority of patients proceeding to adrenalectomy remain well postoperatively, with complete resolution of hypokalaemia. Rarely, patients can develop hypoaldosteronism postoperatively, due to prolonged suppression of the contralateral zona glomerulosa. There remains a lack of guidance on how to predict and monitor hypoaldosteronism in PA patients undergoing adrenalectomy. We will illustrate these challenges within two cases.
Cases
Case 1: A 58-year-old fit and otherwise healthy female was referred with a 20-year history of hypertension (on three antihypertensive agents) and unprovoked hypokalaemia (K = 2.9 mmol/l). Following diagnosis of PA, lateralisation studies confirmed unilateral left adrenal disease. She underwent an uncomplicated left adrenalectomy. At her 1-month postoperative review, she reported symptoms of postural hypotension with fatigue. A short synacthen test (SST) was normal. However, serum electrolytes revealed hyperkalaemia (K = 6.1 mmol/l), hyponatraemia (Na = 129 mmol/l) and renal impairment (creatinine = 129 μmol/l). Additional biochemical testing revealed plasma renin concentration (PRC) 62 mU/L and plasma aldosterone concentration (PAC) 104 pmol/l. Following commencement of fludrocortisone, there was significant clinical and biochemical improvement (serum K = 4.9 mmol/l, Na = 135 mmol/l, creatinine = 84 μmol/l). A subsequent attempt to withdraw fludrocortisone therapy was associated with recurrence of hypoaldosteronism. *Case 2*: A 55-year-old male was referred with a 10-year history of hypokalaemia and resistant hypertension (average BP 170/11 mmHg on four antihypertensive agents). He had a history of mild renal impairment (baseline creatinine 107 μmol/l). Following diagnosis of PA, he was commenced on Eplerenone which successfully achieved a normotensive state. Lateralisation studies confirmed unilateral left adrenal disease, and the patient proceeded to left adrenalectomy without complication. At his 1-month post-operative review, he was found to be hyperkalaemic with renal impairment (creatinine 176 μmol/l). His PAC was undetectable (< 70 pmol/l); SST was normal. Following commencement of fludrocortisone, there was a rapid improvement in his biochemistry (K = 5.1 mmol/l, Na = 141 mmol/, creatinine 113 μmol/l).
Conclusion
Although considered to be a relatively rare (~5%) complication in patients with PA undergoing unilateral adrenalectomy, hypoaldosteronism is a potentially serious manifestation. Factors that may predict its development include severity of PA (e.g. presence of hypokalaemia). Our cases highlight the importance of attempting to identify those patients who are at higher risk of postoperative hypoaldosteronism, ensuring that there is a strategy for close biochemical surveillance postoperatively in these patients.

DOI: 10.1530/endoabs.81.EP84

EP85

Assessment of glucolipid metabolism in patients with Cushing's syndrome caused by adrenal adenoma

Jie Li[1], Jiaxin Zhang[1], Guimei Yang[1], Xintong Hou[1], Dan Yang[1], Jing Yang[1], Yi Zhang[2] & Yunfeng Liu[1]
[1]First Hospital of Shanxi Medical University, Department of Endocrinology, Taiyuan, China; [2]Shanxi Medical University, Department of Pharmacology, Taiyuan, China.

Backgrounds
Based on anthropometry and blood biochemical tests, this study aims to analyze the variation of glucose and lipid metabolism in Cushing's syndrome (CS) patients caused by adrenal adenoma combining with flash glucose monitoring system (FGMS) and dual-energy X-ray absorptiometry (DEXA).
Methods
According to the strict diagnostic and exclusion criteria, seven healthy controls (HCs) and seven CS patients were collected in this study. First, the anthropometric parameters and blood biochemical indexes of all subjects were collected. Subsequently, their body composition of the whole body were measured by DEXA. Finally, all were equipped with a sensor of FGMS, and the blood glucose levels were recorded. According to the data of FGMS, the related indexes of blood glucose variation were calculated. The data between HCs and the CS group were analyzed by T-test or Mann–Whitney test.
Results
(1) Anthropometric parameters: compared with HCs, the CS group showed the higher waist circumference and waist-to-hip ratio (all $P < 0.005$); (2) Blood biochemical indexes: the levels of HbA1c%, TG, TC and LDL-C in the CS group were higher than those in HCs (all $P < 0.005$), while FBG and FINS were generally unaffected in the CS group than in HCs; (3) Data related FGMS: compared with HCs, the changes of general blood glucose alterations, within-day and day-to-day glucose variability, and the percentage of blood glucose above the standard range (PT3) were significantly higher, and the percentage of blood glucose within the standard range (PT2) was significantly lower (all $P < 0.005$); (4) Data related DEXA: a significantly increased fat ratio in Android area (represent for midsection fat) was found in the CS group (all $P < 0.005$), but no increase or decrease in fat or lean tissue of other areas were observed; (5) Fast insulin, HOMA-β index and HOMA-IR index of CS group tend to be higher than HCs, but there are no significant difference.
Conclusion
The homeostasis of glucolipid metabolism in the CS group was significantly destroyed, but impaired islet β-cell function and IR were not observed. A limitation of our study is its relatively small sample size due to the rare occurrence of CS.

DOI: 10.1530/endoabs.81.EP85

EP86

Head and neck paraganglioma: exploring the metastasizing potential. Case report

Laura Teodoriu[1,2], Andreea Boboc[3], Ana-Maria Patrascu[44], Stefana Bilha[1], Letitia Leustean[1], Maria-Christina Ungureanu[1], Cipriana Stefanescu[5] & Cristina Preda[1]
[1]University of Medicine and Pharmacy Gr. T Popa, Endocrinology, Iasi, Romania; [2]Regional Institute of Oncology, Endocrinology, Iasi, Romania; [3]Regional Institute of Oncology, Surgery, Iasi, Romania; [4]Regional Institute of Oncology, Pathology, Iasi, Romania; [5]University of Medicine and Pharmacy Gr. T Popa, Nuclear Medicine, Iasi, Romania.

Introduction
Paragangliomas (PGLs) are tumors originating from neural crest-derived cells situated in the region of the autonomic nervous system ganglia. Head-and-neck PGLs (HNPGLs) originate from the sympathetic and parasympathetic paraganglia, most frequently from the carotid bodies and jugular, tympanic and vagal paraganglia, and are usually non-catecholamine secreting.
Case report
We present the case of a 60 years old male patient, which was admitted at Endocrinology Department for differential diagnosis of bilateral cervical lymph nodes, which occurred over past 10 years, with a clinical exacerbation in the last year. His thyroid ultrasound results were suggestive only for a Hashimoto's thyroiditis, with hormonal tests implying hypothyroid status. In the context of bilateral lymph nodes, with MRI that indicated a potential haemalogical malignancy, the left lateral cervical formation has been biopsied and the histopathological result concluded: head and neck paraganglioma. Immunohistochemical result indicates that our HNPGL might have malignancy potential: increased tumor dimensions (over 10 cm identified on MRI exam), Ki 67 positive

in 3% of the tumor cells, sustentacular cells and low expression of S100 in those cells. Other immunohistochemical staining highlighted positive synaptophysin, chromogranin and GATA3. Our patient was not expressing catecholamine secretion clinical features but we recommend complete hormonal exploration: normetanephrine, 3-methoxytyramine and neuron-specific enolase (NSE), tests in working progress. We will recommend full exploration of adrenal glands also, to exclude synchronous affection.
Conclusion
His case will be reviewed by multidisciplinary committee to conclude proper therapeutic management: surgery, radiotherapy or somatostatin analogs and potential PRRT after specific functional imaging. With integral neuroendocrine tumor markers and functional imaging results we'll be able to determine if this paraganglioma is malignant or not.

DOI: 10.1530/endoabs.81.EP86

EP87

Managing Immune checkpoint inhibitors and adrenal insufficiency in acute setting

Mahamud Bashir, Kirtanya Ramachandran, Rebecca Volmy, Alexanderia Williams, Akunna Elonu, Gloria Elekwa, Lamis Fahal, Hassan Rehmani, Homagni Roy & Gideon Mlawa
Queens Hospital, London, United Kingdom.

The introduction of immune checkpoint inhibitors (ICIs) in clinical management of cancer has had an undeniable impact in management of cancer patients. Currently there are several ICIs are used across Europe including but not limited to, pembrolizumab, atezolizumab, and ipilimumab. Even though their clinical efficacy is reputable, they have the potential of causing serious immunotherapy-related adverse events' (irADRs) in several organ systems including endocrine organs. With the ever-growing use of ICIs, case reports are emerging with increasing frequency of rare yet life-threatening endocrine dysfunctions, particularly involving the pituitary, thyroid and less frequently adrenals.
Case presentations
Case 1)A 64 y/o patient was admitted under medical team with features of adrenal insufficiency. He had background of metastatic poorly differentiated adenocarcinoma of lung(T4N3M1c), for which he was treated with pembrolizumab (from October 2019 – May 2020), cisplatin, premetrexed, simvastatin 20 mg OD, ezetimibe 10 mg OD and analgesia. She presented with general fatigue, loss of appetite and mouth ulcers since ICI therapy. He was given iv hydrocortisone and the patient improved clinically. On physical examination, the patient's looked tired and his HR was 116 bpm. Blood test showed his cortisol to be 8 nmol/l, TSH: 4.39 mU/L. He was discharged on prednisolone 10 mg OD which was reduced to 7.5 mg. 2)A 59 years with a background of right eye choroidal melanoma for which she underwent primary enucleation in January 2019 and was subsequently started on Pembrolozumab. She also has other comorbidities like T2DM, HTN, IHD for which she is being medically managed. She was admitted with general fatigue, vomiting and she was hypotensive and her lab findings showed her cortisol to be very low at 28 nmol/l. She was also in in fast AF and AKI. The oncology team reviewed her, and she was started on IV methyl prednisolone and IV fluids following which her AKI resolved. She was discharged on hydrocortisone 10 mg BD.
Discussion/ conclusion
Adrenal insufficiency (AI) is a rare irADRs of ICI therapy. If left untreated AI is life-threatening and unlike other autoimmune complication of ICI use AI is irreversible with patients often require long term steroid therapy. Baseline endocrinology tests like TFT, glucose(HbA1C), cortisol need to be done at initiation of treatment and monitored regularly. Based on our findings from this case we believe that it is important that the patients are educated regarding risk of AI and follow up monitoring for signs of AI be put in place post therapy with ICI.

DOI: 10.1530/endoabs.81.EP87

EP88

Management of primary hyperaldosteronism and the role of adrenal venous sampling; a single-center experience

Carlien De Herdt[1], Philipse Eva[2], D'Archambeau Olivier[3], Ysebaert Dirk[4], Snoeckx Annemiek[3], Peeters Bart[5] & Christophe De Block[2]
[1]Antwerp University Hospital, Endocrinology-Diabetology-Metabolism, Edegem, Belgium; [2]Antwerp University Hospital, Endocrinology-Diabetology-Metabolism, Edegem, Belgium; [3]Antwerp University Hospital, Radiology, Edegem, Belgium; [4]Antwerp University Hospital, Endocrine and Transplantation Surgery, Edegem, Belgium; [5]Antwerp University Hospital, Clinical Biology, Edegem, Belgium.

Background
Primary hyperaldosteronism (PA) is a prevalent, but underdiagnosed syndrome. Diagnosis and treatment have been relatively constant since the development of the latest Endocrine Society guidelines in 2016.
Study objective
Baseline characteristics, treatment and follow-up of subjects with PA referred for adrenal venous sampling (AVS) in a tertiary hospital since 2009 are presented.
Results
Thirty five subjects (M/F: 17/18, mean age 49 ± 10 years) underwent AVS. Reasons for screening were; therapy-resistant hypertension (46%), sustained blood pressure > 150/100 mmHg (20%), hypertension and an incidental mass (3%), hypertension with hypokalaemia (28%). One subject without hypertension had a positive screening for PA in the work-up of an adrenal incidentaloma. Echocardiogram showed left ventricular hypertrophy in 19 subjects (54%). Plasma aldosterone/ renin ratio (ARR) was above the threshold of 24 (pg/ml) /(μu/ml) in most (94%) subjects. With a mean plasma aldosterone (PAC) of 306 pg/ml, 88% had a PAC > 150 pg/ml. A combination of an elevated PAC and ARR was seen in 81%. Saline infusion test was still performed in 60% of subjects of which 81% had a PAC above 100 μg/ml and 19% between 50 and 100 μg/ml. AVS showed unilateral aldosterone hypersecretion in 12 and bilateral hypersecretion in 11 subjects. In 9 subjects the right adrenal vein was not reachable and in 3 subjects there were analytical problems. Discrepancy in lateralization between CT adrenals and AVS was seen in 57%; normal CT vs AVS with lateralization (2 subjects), normal CT vs AVS with bilateral hypersecretion (4 subjects), adrenal adenoma on CT with lateralization on the contrary adrenal (2 subjects), adrenal adenoma on CT without lateralization on AVS (5 subjects). Of the 12 subjects with lateralization, 9 underwent unilateral adrenalectomy of which 3 could stop all antihypertensive drugs, but all could reduce medication from 5 to 2, average. Of the 12 subjects with a non-diagnostic AVS, 6 underwent unilateral adrenalectomy with the histological confirmation of an aldosterone producing adenoma and antihypertensive drugs could be stopped postoperatively in 3 subjects.
Conclusion
Since 2009 only 35 subjects were referred to undergo AVS which suggests the underdiagnosis of PA. Hypertension and hypokaliëmie are not mandatory characteristics of PA but were present in 97% and 57%, respectively. The number of patients with unilateral vs bilateral aldosterone hypersecretion was similar. 57% had a discrepancy in lateralization between AVS and CT adrenals. Antihypertensive drugs could be stopped in 40% of subjects who underwent unilateral adrenalectomy.

DOI: 10.1530/endoabs.81.EP88

EP89

Alternative treatment in Bilateral Macronodular Adrenal Hyperplasia with possible adrenal hypersensitivity to Angiotensin II

Aurora Calisi, Enrichetta Gigante, Raffaele Pepe, Valeria Creato & Francesco Cipollone
SS Annunziata, UOC Clinica Medica, Chieti, Italy.

Bilateral Macronodular Adrenal Hyperplasia (BMAH) is an uncommon cause (< 2%) of endogenous Cushing's syndrome, characterized by enlarged adrenal glands Althought the exact pathogenetic mechanism remains unclear, recently, it has been reported that aberrant expression of ectopic receptors, such as AVP, GIP, angiotensin II (AT1 receptor) catecholamine, LH, 5HT4 agonists, and leptin, evoked cortisol secretion, which escapes from cortisol-mediated feedback in BMAH. Here we report a case of BMAH that suggested an aberrant response to angiotensin II via AT1 receptor in cortisol hypersecretion. A 66-yr-old man was admitted to a hospital for stroke,medically treated since beyond the established thrombolytic window. On admission he presented severe hypertension (BP 230/140 mmHg). On the hypothesis of secondary hypertension we performed in−depth analysis. Laboratory test documented undetectable plasma ACTH level (1,6 pg/ml) and high level of 24−h urinary free cortisol (983 mg/die). Plasma cortisol was not suppressed (12,8 μg/dl) after the administration of 1 mg dexamethasone overnight. Abdominal Magnetic Resonance Imaging demostrated nodular enlargement of bilateral adrenal glands. Moreover, renine and aldosterone levels were high (respectively 83 mU/ml and 74 ng/dl) and Angio-CT revealed right renal artery stenosis. These results indicated a diagnosis of Cushing's syndrome due to BMAH with suspected adrenal hypersensitivity to angiotensin II. Therefore, Renal Artery Stenosis Angioplasty (PTA) was performed and the patient underwent a revised assessment which revelead

normal level of plasma ACTH, urinary free cortisol and renine and aldosterone. Although it is well known that angiotensin II stimulates aldosterone secretion mainly through angiotensin II receptor (AT1), there has been no evidence, to our knowledge, that angiotensin II affects cortisol secretion in vivo. In our case, PTA blocked the aberrantly increase of plasma cortisol level. Therefore, it is possible that the adrenal hypersensitivity to angiotensin II is involved in the pathogenesis of BMAH and that angiotensin II aberrantly stimulated cortisol secretion via AT1 receptor. A similar case report described a case of BMAH with adrenal hypersensitivity to angiotensin II, treated with bilateral adrenalectomy [1]. In summary, we have reported a case of BMAH with possible hypersensitivity to angiotensin II. Further investigations are required to clarify the significance of abnormal adrenal response to angiotensin II.

1. ACTH-Independent Macronodular Adrenal Hyperplasia. Nakamura *et al.* Endocrine, vol. 15, 2001

DOI: 10.1530/endoabs.81.EP89

EP90

Tumor enlargement in adrenal incidentaloma is related to glaucoma and statin treatment: are there two new prognostic features?

Alice Ferrero[1], Tommaso Daffara[2], Chiara Mele[2], Marco Zavattaro[3], Martina Romanisio[2], Beatrice Cavigiolo[3], Samuele Costelli[2], Marina Caputo[3,4], Paolo Marzullo[3], Flavia Prodam[3,4] & Gianluca Aimaretti[3]
[1]Endocrinology, Università del Piemonte Orientale, Department of Translational Medicine, Novara, Italy; [2]Endocrinology, Università del Piemonte Orientale, Department of Translational Medicine, Novara, Italy; [3]Endocrinology, Università del Piemonte Orientale, Novara, Italy., Department of Translational Medicine, Novara, Italy; [4]Department of Health Sciences, Università del Piemonte Orientale, Novara, Italy.

Aim
The uncertainty on the management of small adrenal incidentalomas (AIs) in guidelines still represents a challenge in real clinical practice. The aim of the study was to identify risk factors for morphological or functional changes during follow-up by using clinical, radiological, and pathological features.
Methods
We retrospectively evaluated demographic (gender and age at diagnosis), clinical (weight, height, body mass index, smoking habit, comorbidities), radiological characteristics (localization, diameter, HU for CT scan; T1 and T2, and the loss of intensity at chemical shift for MRI) and biochemical parameters of adrenal hypersecretion of 177 AIs (2007-2021). To detected risk factors for tumor enlargement or hypersecretion, diseases associated with AIs were included if the prevalence was higher than 2%. Patients were divided into two groups according to dimension during follow-up (group A: radiological stability; group B: tumor enlargement at radiological scans).
Results
90.4% of patients belongs to group A, while 9.6% to group B. Chronic obstructive pulmonary disease (COPD), neoplasms, and glaucoma were the most frequent associated diseases. Group B showed larger diameter at diagnosis ($P=0.09$), higher aldosterone ($P<0.001$), DHEAS ($P=0.007$), ARR ($P=0.01$), lower DRC ($P<0.04$) levels and higher weight than group A. Open laparotomy was chosen most frequently in group B ($P<0.004$). AI diameter was negatively correlated with age ($r -0.159$, $P<0.04$), 17-OHP levels ($r -0.461$, $P=0.05$), statin treatment inversely to the drug potency ($r -0.193$, $P<0.02$), and positively with ACTH ($r 0.198$, $P=0.06$) and urinary normetanephrine levels ($r 0.248$, $P<0.01$). Analyzing AIs changing over time, an enlargement occurred within 36 months of follow-up and only glaucoma was an independent predictor of it ($B=3.370$, exβ $=29.077$; $P<0.005$). Considering concomitant treatments, at 36 months of follow-up, 100% of subjects showing an enlargement were not taking statins, compared to 45.2% of subjects with stable disease ($P=0.06$). Subjects suffering from glaucoma, atrial fibrillation, impaired glucose metabolism (T2DM or IGT), COPD (in males only) had a lower dimensional change-free survival than non-affected.
Conclusions
The presence of glaucoma and treatment with statins seems to be a risk and a protective factor, respectively, for an AI enlargement. Further prospective studies of validation are needed. If subtle undetectable cortisol hypersecretion and proliferation cellular mechanisms have a role are two topics for further research.

DOI: 10.1530/endoabs.81.EP90

EP91

Silent clinical presentation of a rare genetic disorder

Diandra Carmen Giuca[1], Dan Hortopan[2], Suzana Vladoiu[1], Adriana Padure[1], Andra Caragheorgheopol[1], Andreea Kremer[1] & Iuliana Gherlan[1,3]
[1]"C.I.Parhon" National Institute of Endocrinology, Bucharest, Romania; [2]Gral Medical Center, Bucharest, Romania; [3]"Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania.

Introduction
Carney complex is a rare autosomal dominant genetic disorder which develops secondary to mutation in the PRKAR1A gene located in the 17q22-24 region. It is commonly characterised by the association between spotty skin pigmentation, cardiac myxoma and secretory endocrine tumors.
Case presentation
A 15.8-year-old boy known with PRKAR1A mutation diagnosed based on his personal history – cutaneous papiloma of the neck resected at the age of 6 years, bilateral testicular microlitiasis, right testicular teratoma resected at the age of 9 years, embolic stroke secondary to left atrial myxoma resected at the age of 10 years was adressed for tall stature. His family history is negative. Clinical examination reveals a height of +2.03 S.D. (+1.54 DS compared to his familial target height), a height growth velocity of 6 cm per year (+3.86 S.D.), BMI 19 kg/sm; no other specific findings are met. Thyroid function and neck ultrasound are normal. Prolactin, hypophiseal-gonadal axis and androgens are within the normal range. Testicular ultrasound reveals the presence of persistent bilateral microlitiasis, but tumor markers (BhCG and alfa-fetoprotein) are negative. IGF1 (468.5 ng/ml, +1.65 SDS), IGFBP3 (5401 ng/ml) have normal values, with a supressed growth hormone of 1.28 ng/ml after oral glucose dynamic testing. Bone age is comparable to the chronological age (16.5 years old). Serum ACTH (1 pg/ml) and 0800 h cortisol (10.78 μg/dl) levels and free urinary cortisol (240.87 μg/24 h) raise the susspicion of ACTH-independent hypercorticism. Liddle test shows paradoxal stimulation of both serum and free urinary cortisol after dexamethasone intake (baseline, day 2 and 6 serum cortisol of 4.46, 9 and 18.43 μg/dl, respectively; baseline, day 3 and 6 free urinary cortisol of 39.26, 81.85 and 903.15 μg/dl, respectively), thus confirming the diagnosis of adrenal hypercorticism. Abdominal MRI shows no pathological changes of the adrenal glands. The most probable diagnosis in this case is primary pigmented adrenal hyperplasia which often accompanies PRKAR1A mutation.
Discussion
The therapeutic approach is bilateral adrenalectomy, but given the absence of clinical glucocorticoid changes, patient's family decision is to follow-up. He remains in observation for his height, but for the moment growth hormone excess can be excluded. This case particularities consists in the large range of clinical features of the Carney complex at an early age; still, one of the important feature of the syndrome –hypercorticism– was present in a subtle, subclinical manner and it was identified in a proactive evaluation.

DOI: 10.1530/endoabs.81.EP91

EP92

Very high urinary free cortisol levels in patients treated with tuberculostatics

Catarina Roque, Ana Sofia Osório & Ricardo Fonseca
Hospital Professor Doutor Fernando Fonseca, Endocrinology, Lisbon, Portugal.

Introduction
Pharmacologically induced false positive results in urinary free cortisol levels (UFCL) have been ascribed to 11βHSD-2 inhibition or direct interference on HPLC. Few drugs have been implicated by mechanisms not yet confirmed.
Case Reports
We report 3 patients with active pulmonary tuberculosis (TB) and very high UFCL, 2-6× above the upper limit of reference [mean levels 3411 μg/24 h (RR 167-827)]. The 2 males and the woman aged 31 to 60 y.o. had hypertension, one had diabetes mellitus and the other HIV. None had stigmata of Cushing syndrome. Known causes of falsely elevated UFCL were not found (eg. polyuria, synthetic steroid use). Acute disease could justify hypercortisolism but we kept the patients under observation to confirm UFCL normalization. On the first out-patient appointment the UFCL remained very high (mean 2431 μg/24 h) 1, 5 and 6 months after hospital discharge. On the second out-patient appointment, after completion of the anti-TB (HRZE) treatment, all patients had normal UFCL (mean 477 μg/24 h). We reviewed the files for active diseases, comorbidities and treatments: the one common situation was active TB and though acute disease could justify hypercortisolism initially, we considered it less likely to justify the more than 2 fold UFCL elevation in the clinically stable patient after hospital

discharge. The drugs used by the 3 patients during hospitalization, continued after the first and discontinued before the second out-patient appointments were Isoniazid and Rifampicin, which we suspect to cause this previously undescribed pharmacological interference. Rifampicin has been implicated in false positive dexamethasone suppression tests.

Conclusions

We report the association of very high UFCL in patients without stigmata of Cushing syndrome treated with anti-TB regimens containing Isoniazid and Rifampicin. Hopefully in the future we will confirm the underlying mechanism and appraise the impact of this finding on the exclusion criteria for adrenal insufficiency in these specific group of patients.

DOI: 10.1530/endoabs.81.EP92

EP93

Detection of late-onset adrenal hyperplasia in girls with peripubertal virilisation, a case stady

Bessaid Khadidja[1] & Mouna Mezoued[1,2]
[1]Public Hospital Establishment of Bologhine, Algiers, Algeria; [2]Bologhine Hospital, Endocrinology, Algiers, Algeria.

Introduction

Non-classical congenital adrenal hyperplasia (NCCAH) is considered to be a common monogenic inherited disease, with an incidence range from 1:500 to 1:100 births worldwide. NCCAH is often peri or post pubertal pauci or even asymptomatic. We report the case of a young girl with severe hirsutism and sexual ambiguity, despite late disclosure.

Observation

This is the case of a 16-year-old girl, with a history of menarche at the age of 14, presenting since puberty a spaniomenorrhea with rapidly worsening hirsutism. The clinical examination finds a normal height at 160 cm, a BMI at 21 kg/m^2, severe hirsutism scored at 33 according to Ferriman and Galway with signs of virilization and defeminization associating alopecia of the frontal gulfs, muscle hypertrophy, hoarseness tract, significant clitoral hypertrophy and breast atrophy. The biological assessment found elevated testosterone at 2.83 ng/ml, baseline 17OHP at 5.98 ng/ml, and 47.6 ng/ml after synacthen, normal plasma cortisol at 543 nmol/l, ACTH at 162 pg/ml. The abdominopelvic ultrasound objectified an aspect of micro polycystic ovaries. CT of the adrenal glands and pelvic MRI are without abnormalities. The diagnosis of NCCAH was retained. The patient was treated with cyproterone acetate and valerate of estradiol.

Discussion

Despite the high incidence, there is a low genotype-phenotype correlation, which explains why NCCAH diagnosis is usually delayed or even never carried out, since many patients remain asymptomatic or are misdiagnosed as suffering from other hyperandrogenic disorders.

DOI: 10.1530/endoabs.81.EP93

EP94

The burden of illness associated with adolescent and adult congenital adrenal hyperplasia: results of a structured literature review

Uzmah Sabar[1], Helen Coope[2], Kamran Maskin[2], Lotta Parviainen[2], John Porter[2], Mike Withe[2] & Matthew Woods[1]
[1]BresMed Health Solutions Ltd, Sheffield, United Kingdom; [2]Diurnal Limited, Cardiff, United Kingdom.

Objectives

Congenital adrenal hyperplasia (CAH) is a rare condition caused by enzyme deficiency in cortisol biosynthesis. The aim of this study was to evaluate the burden of illness associated with child/adolescent and adult CAH.

Methods

A structured, comprehensive literature review was conducted to identify articles describing the burden and treatment landscape of CAH. Literature databases (MEDLINE, Embase, the Cochrane Library and EconLit), websites and conference proceedings were searched. Searches were performed in 2016 and updated in June 2020; eligible articles presented evidence for child/adolescent (aged $\leq$18 years where reported) or adult CAH, for $\geqq$1 topic of interest (natural history; risk factors; epidemiology; clinical characteristics; humanistic, caregiver and economic burden; treatment options; or clinical guidelines). The evidence presented here focusses on the humanistic, caregiver and economic burden of child/adolescent and adult CAH.

Results

A total of 3,711 citations were identified and 338 were included. A total of 89 (adults) and 86 (adolescents) references were identified that reported humanistic, caregiver or economic burden data respectively. Compared to the general population, patients with CAH (irrespective of age) were found to be significantly shorter and experienced poor bone health, increased occurrences of cardiometabolic events (including obesity, hypertension and insulin resistance), were at risk of developing adrenal crises (which contributed to excess mortality), and in adolescent/adult CAH, had impaired male and female fertility (with adolescents commonly experiencing precocious puberty). Both adolescent and adult patients with CAH were also at risk of developing psychosocial health issues compared to the general population, with adult patients experiencing emotional trauma related to their condition and subsequently finding it difficult to speak about their illness. The reported generic HRQL (no CAH specific instruments were identified) in CAH was varied, with increased impairment observed in more severe forms of CAH and in general, HRQL frequently more impaired in women compared with men. Although the literature was sparse, it did indicate that CAH is associated with a substantial caregiver burden; parents of children/adolescents with CAH reported high levels of anxiety, depression and worry for their loved one. Furthermore, CAH was also associated with a notable economic burden, with significantly higher annual healthcare costs compared to matched controls ($P=0.007$ for patients aged 18–40 years; $P<0.001$ for patients aged $\geqq$40 years).

Conclusions

Our review highlights that CAH is a complex and debilitating disease which is associated with significant humanistic, caregiver and economic burden in both child/adolescent and adult CAH patients.

DOI: 10.1530/endoabs.81.EP94

EP95

Congenital adrenal hyperplasia due to 21-hydroxylase deficiency and hypertension: a case report

Chayma Besrour, Rojbi Imen, Mekni Sabrine, Majdoub Marwa, Lakhoua Youssef, Ben Nacef Ibtissem & Khiari Karima
Hospital Charles Nicolle, Endocrinology, Tunis, Tunisia.

Introduction

Congenital adrenal hyperplasia (CAH) due to 21-hydroxylase deficiency is the most common of the CAH, it is also the most common of the autosomal recessive diseases. Hypertension is generally absent, and its presence should lead to an investigation of another cause.

Observation

We report the case of a 26-year-old young man, descendant from a second-degree consanguineous marriage with a family history of the death of a brother at the age of 25 days of severe dehydration, who is followed in our department for HCS with HTA. The diagnosis of CAH was suspected at the age of 9 days due to dehydration with electrolyte disorders. Hormonal assays confirmed the diagnosis in front of a high level of 17-OH progesterone. At the age of 3 years old, he was operated for right testicular ectopia and at the age of 8 years old, we discovered a hypertension. The etiological assessment concluded to a secondary hyperaldosteronism.

Discussion

The 21-hydroxylase deficiency is generally not associated with hypertension, taking into consideration the hypocortisolism and the aldosterone deficiency depending on the level of the block. Hyperaldosteronism associated with 21hydroxylase deficiency constitutes a new entity recently reported by a few studies, but its pathophysiological mechanism remains unclear.

DOI: 10.1530/endoabs.81.EP95

EP96

Ectopic Cushing's syndrome

Guranda Maisuradze & Salome Kalandadze
New Hospitals, Tbilisi, Georgia.

Introduction

Ectopic Cushing's syndrome (ECS) is a condition caused by an ACTH-secreting tumor outside the pituitary or adrenal glands. Most cases are caused by neuroendocrine tumors of the lung, pancreas, thymus or medullary carcinoma of the thyroid. Small-cell carcinomas of the lung are probably the most common cause of biochemical hypercortisolism. About 15% of Cushing's syndrome cases are due to ECS.

Case description
A 27-year-old male patient presented to the clinic with a 4-months history of weakness, swelling, moon face, purple striae on the skin of the abdomen and thighs, hypertension, and hyperglycemia. On examination: BMI – 30.8 kg/m^2, T/A – 160/100 mmHg. Investigations: 0800 h Cortisol-474.0 ng/ml (64.1–209.4), ACTH-201 ng/l (12–62), FPG-168 mg/dl, HbA1c-4.6%, ALT-79($<$ 41), electrolytes-N; 1600 h Cortisol-383.93 (30–160); urinary free Cortisol-153 µg/24 hours (3.5–45). After hypercortisolism was confirmed, further tests were done to determine the cause. MRI scans of the brain, abdomen and pelvic with no pathology. Next we performed MRI scan chest – 11 $\times$ 14 mm solid pulmonary nodule appeared in the left lower lobe. ECS was diagnosed. Diet, regimen and Metformin were recommended. Patient was referred to the thoracic surgeon.
Conclusion
The best treatment for ECS is surgical removal of the tumor. This is usually possible when the tumor is benign. However, many tumors are malignant, and have metastasized before cortisol excess has been diagnosed. Surgical removal is not possible in these situations, and drugs to suppress cortisol secretion may be given. Surgical removal of the tumor may lead to full recovery, but there is a chance of the tumor coming back. Survival for people with ectopic tumors depends upon the outcome associated with the particular tumor type.
References
1. Ilias I, Torpy DJ, Pacak K, *et al*. Cushing's syndrome due to ectopic corticotropin secretion: twenty years' experience at the National Institutes of Health. J Clin Endocrinol Metab 2005; 90:4955. 2.Neary NM, Lopez-Chavez A, Abel BS, *et al*. Neuroendocrine ACTH-producing tumor of the thymus-experience with 12 patients over 25 years. J Clin Endocrinol Metab 2012; 97:2223. 3.Orth DN. Ectopic hormone production. In: Endocrinology and metabolism, 2nd, Felig P, Baxter JD, Broadus AE, Frohman LA (Eds), McGraw-Hill, New York 1987. p.1692.
DOI: 10.1530/endoabs.81.EP96

EP97

Adrenal insufficiency revealed during a septic shock
Rym Belaid, Anissa Ben Bouzid, Nada Ban Abdelaziz, Naourez Abid & Raja Amri
Mohamed Tahar's Maamouri Hospital, Internal Medecine Department, Nabeul, Tunisia.

Introduction
Acute adrenal insufficiency (AAI) is a rare but life-threatening condition. It may occur in 50 to 60% of septic shocks (SS). Its diagnosis can be difficult as symptoms are sometimes nonspecific. Herein, we report the case of a female patient with an AAI revealed during SS.
Abstract
A 30-year-old woman with a history of celiac disease since the age of 25 on a gluten-free diet, presented to the emergency department with abdominal pain, vomiting, fever and profound asthenia evolving for five days. Physical examination revealed an increased pulse rate of 120 beats per minute, a rapid respiratory frequency of 40 cycles per minute, fever (38.8) and low arterial hypotension of 60/40 mmHg. The abdomen was diffusely painful. Blood investigations showed leukocytosis (14000), mildly increased C-reactive protein (CRP) (84 mg/l), hypoglycemia (0.5 g/l), severe hyperkalemia (7.22 mmol/l) and hyponatremia (122 mmol/l). Arterial blood gas test noted a metabolic acidosis. A Computed Tomography (CT) scan of the lungs, abdomen and pelvis was normal. The urine culture was positive. The diagnosis of septic shock due to urinary tract infection was then initially retained. The patient was treated with vasoactive drugs and appropriate antibiotic therapy. The evolution was marked by the persistence of abdominal pain, arterial hypotension, hypoglycemia and hydro electrolytic disorders. The diagnosis of acute adrenal insufficiency was therefore suspected and then confirmed by a low serum cortisol level of 1.6 µg/dl (6.–18). The patient received intravenous hydrocortisone hemisuccinate and parenteral rehydration.- Clinical and biological improvement was noticed in few days.
Conclusion
Our case illustrates the difficulty of the diagnosis of an AAI during SS. Thus, acute adrenal insufficiency must be suspected in the context of SS especially in patients with hyperpigmentation; hyponatremia and/or hyperkalemia, a medical history of autoimmune disease or an increased vasopressor dependency. Parenteral rehydration and intravenous hydrocortisone hemisuccinate should be initiated immediately, even before laboratory confirmation of the diagnosis.
DOI: 10.1530/endoabs.81.EP97

EP98

Adrenal crisis revealing factitious hypoglycaemia in a pregnant woman
Anis Grassa, Nadia Khessairi, Yezza Hajer, Fatma Chaker, Meriem Yazidi & Melika Chihaoui
Rabta Hospital, Endocrinology, Tunis, Tunisia.

Introduction
Factitious hypoglycaemia in adults is usually due to exogenous intake of insulin or hypoglycaemia sulfonamides. This occult intake is most often voluntary and the diagnosis is not always obvious.
Observation
We report the case of a 37-year-old pregnant woman at 15 weeks of amenorrhoea, followed for addisson's disease since 3 years and not diabetic, was referred to our department for acute adrenal insufficiency following the discontinuation of her replacement therapy for more than 3 months. The main symptoms were asthenia, vomiting, abdominal pain and recurrent hypoglycaemia. She was treated with intravenous high-dose hydrocortisone, with improvement of the symptoms except for randomly scheduled hypoglycaemia resistant to correction.She denied taking any medication other than those given by the nurses and the hypoglycemia continued. Investigations such as plasma measurements of insulinemia, C-peptide, hypoglycaemia sulfonamides were done concomitantly as a venous glycemia at 0.4 g/l and were respectively 87.81 µIU/ml (normal: 2.6–24.9), 8.59 ng/ml (normal: 1.1–4.4) and 135 µg/ml. The diagnosis of factitious hypoglycemia by taking sulfonamides was confirmed. The day before and during hospitalization, the patient had admitted to sneaking glibenclamide tablets and the drug was seized.
Conclusion
Factitious hypoglycaemia represents a challenge for the clinician, on the one hand the patient tries to hide certain proofs on the other hand it remains an elimination diagnosis, especially if an organic cause is preexisting as it is in our observation.
DOI: 10.1530/endoabs.81.EP98

EP99

Geant myolipoma adrenal: report of two cases and literature review
Benabdelatif Katia, Mouna Benfiala, Bensalah Meriem, Lachkhem Aicha & Ould Kablia Samia
Central Military Hospital, Algiers, Algeria.

Introduction
Adrenal myelolipoma is a rare, benign and nonfunctional tumor composed of mature adipose and hematopoietic cells. It is often of incidental finding (8%) and the diagnosis is based on radiological imaging. We report two cases of giant adrenal myelolipoma and discuss the diagnostic and therapeutic aspects of this pathology.
Observation
Patient D.K 40 years old, hospitalized for adrenal mass revealed by right back pain radiating to the right hypochondrium, without signs of endocrine hypersecretion. Clinical examination showed sensitivity of the right lumbar fossa. 24-hours urinary methoxyl derivatives and dexamethasone suppression test were correct. The patient underwent the removal of the abdominal masse and anatomo-pathological examination showed adrenal myelolipoma. Patient A.M, 51 years old, with a personal history of simple mammary and renal cysts, consulted for an adrenal incidentaloma of 65 cm discovered on pelvic MRI during exploration of myxomatous uterus. Clinically, the patient did not present signs of endocrine hypersecretion or abdominal pain. Hormone levels returned normal. Abdominal scan revealed a large left adrenal mass with spontaneous density of – 45 HU, heterogeneous, 60*18*78 mm, without any sign of vascular invasion or neighbouring organs. The patient underwent a left adrenalectomy. Anatomo-pathological study showed adrenal myolipoma.
Conclusion
Unlike other adrenal incidentalomas, adrenal myelolipoma is a rare, benign tumor that is often asymptomatic with special radiological features. Management is based on clinical and radiological follow up of asymptomatic forms. Surgical treatment is reserved for large, symptomatic or complicated adrenal myelolipomas.
DOI: 10.1530/endoabs.81.EP99

EP100

Management of pituitary apoplexy

Ajay Sinha
NMCH, Medicine, Patna, India.

Introduction
Pituitary apoplexy is a rare clinical emergency with an incidence of 2–7% in pituitary adenomas. There does not exist any evidence-based standards of optimum care for the patients. A key controversy in management is related to the functioning of acute neurosurgical intervention. The nature of clinical presentation precludes robust randomised controlled trials. Practical guidelines are derived from high-quality observational studies. On this background, we report the management of pituitary apoplexy in a large cohort of patients treated at a single tertiary referral centre.
Methods
This retrospective study evaluates the clinical presentation, management and clinical outcomes presenting with pituitary apoplexy during 2020–2021.
Results
80 patients with 34 females were included. Among these patients, 10 patients had been previously diagnosed with a pituitary tumour. The common symptoms were visual disturbance, headache, diplopia and cranial nerve involvement. 32 patients had undergone surgery, while 48 patients were conservatively managed. All 32 patients had visual disturbances, while 59% of them had recovered fully. Among these patients, 76% made full recovery while 33 had visual disturbances. In the surgical group, 84% required hydrocortisone, 15% withdrew treatment, 69% required thyroxine, 34% required sex steroids, 9% started growth hormone. In the conservatively managed patients, 79% started hydrocortisone, 13% stopped doing so, 60% required thyroxine, 46% started sex steroids, 19% started growth hormones.
Conclusion
This data represents the largest case series from a single centre. We propose that patients with acute apoplexy who have mild or stable symptoms/signs can be managed conservatively with careful monitoring; only rarely is there a need to change from conservative to surgical management in these patients.

DOI: 10.1530/endoabs.81.EP100

EP101

Visfatin as a potential serum marker of adrenal gland cancers

Nadia Sawicka-Gutaj, Hanna Komarowska, Aleksandra Derwich, Elżbieta Wrotkowska & Marek Ruchala
Poznan University of Medical Sciences, Department of Endocrinology, Metabolism and Internal Medicine, Poznań, Poland.

Introduction
There are not many studies specifying the role and contribution of adipocytokines in biology of adrenal gland cancer. Many research show correlation between increased level of serum visfatin and malignant potential, stage progression and prognosis. *Visfatin/ NAMPT* overexpression has been found in a various type of malignances. So far, to the best of knowledge, this is the first research studying the role of visfatin in diagnosis of adrenal cortical carcinoma.
Patients and methods
This was a prospective observational study with a consecutive enrollment. Twenty two patients with adrenal gland cancers and 34 patients with benign adrenal tumors were recruited.
Results
Patients with adrenal gland cancers have higher serum visfatin concentrations as compared to controls (Me 7.7 ng/ml vs 5.9 ng/ml, $P=0.0017$). Also, ROC curve analysis detected visfatin concentrations higher than 7.1 ng/ml as a biomarker of adrenal cancers ($P=0.0007$; sensitivity 59.1%, specificity 85.3%). Visfatin serum concentrations in patients with adrenal cancers did not differ between men and women. In the whole group, visfatin positively correlated with the tumor size ($P=0.0193$, $r=0.318$).
Conclusion
Visfatin is a potential serum marker of adrenal gland cancers.

DOI: 10.1530/endoabs.81.EP101

EP102

Factors associated with metabolic syndrome in tunisian psychiatric patients

Abdel Mouhaymen Missaoui[1], Salem Jdira[2], Oumeyma Trimeche[1], Houda Hsine[2], Wafa Abbes[2] & Ines Khochtali[1]
[1]Fattouma Bourguiba University Hospital, Endocrinology Departement, Monastir, Tunisia; [2]Gabes Regional Hospital, Departement of psychiatry, Gabes, Tunisia.

Introduction
Metabolic Syndrome (MetS) is a bunch of metabolic disturbances related to insulin resistance and is considered a global public health problem. The screening and management of MetS is particularly challenging in psychiatric practice.
Objectives
We aim to identify clinical and therapeutic factors associated with MetS in a Tunisian psychiatric population.
Methods
We conducted a descriptive and analytical cross-sectional study involving 126 patients who attended the psychiatry department at Gabes regional hospital, Tunisia, from 2019 to 2020. MetS was diagnosed based on the 2005-IDF criteria. We compared two subgroups:
* [MetS+]: Patients with MetS ($n=32$)
* [MetS−]: Patients without MetS ($n=94$)
Results
[MetS+] patients were significantly older ([MetS+]:52.1 ± 10.5 versus [MetS−]:43.3 ± 12.7 years; $P=0.001$). The onset of psychiatric symptoms was significantly earlier in [MetS−] ([MetS+]:36.0 ± 14.1 versus [MetS−]:26.8 ± 11.0 years; $P=0.004$). No significant gender nor addictive behaviours diffrences were reported in both subgroups. The two shared an unprivileged educational and socioeconomic backgrounds. Married patients were more affected by MetS ([MetS+]: 65.6% versus [MetS−]:43.6%; $P=0.006$). Schizophernia and psychotic disorders(50%), and mood disorders(18.8%) were more recorded in [MetS+] unlike anxiety disorder (18.1%) which was more prevalent in [MetS−], without any statistic significance. Mental patients are more likely to develop MetS when prescribed anxiolytics (OR = 3.4; $P=0.034$; 95% CI[1.7–10.8]) or atypical antipsychotics (OR = 9.3; $P=0.001$; 95% CI[2.4–36.2]).
Conclusions
Screening psychiatric patients for comorbid MetS is recommended both before and during treatment. The initial drug selection should take into consideration specific metabolic profiles. The opportune identification of MetS can facilitate early lifestyle interventions and treatment to reduce the cardiometabolic risk in this vulnerable population.

DOI: 10.1530/endoabs.81.EP102

EP103

Metastatic adrenal carcinoma? When not everything is what it seems...

Daniel Medina Rivero[1], Isabel Mateo Gavira[2] & Francisco Javier Vílchez López[2]
[1]San Fernando, San Fernando, Spain; [2]Hospital Universitario Puerta del Mar, Cádiz, Spain.

69-year-old male, with a history of bipolar disorder under treatment, smoker and high blood pressure. He is referred for left adrenal injury detected incidentally by secondary hypertension study. Abdominal CT shows a mass of 67.7 × 51.8 × 52.3 mm in the left adrenal area, with radiological characteristics of malignancy and aggressive behavior, contacting the left renal pole and upper splenic pole, compatible with adrenal carcinoma vs. metastasis. The functional study is negative. In the extension study, a 10.2-mm right apical pulmonary nodule with nonspecific characteristics and a high-density lesion in the spinal canal at the level of the 9th costal arch compatible with a tumor lesion were detected. The PET-CT does not rule out the malignancy of both lesions. To differentiate whether the adrenal lesion is a primary or metastatic lesion, it was decided to perform FNA, which was inconclusive on 2 occasions. Finally, surgical intervention of the mass was chosen, with an initial approach of en bloc removal of the left adrenal gland, spleen and left kidney, although it was finally possible to perform an isolated left adrenalectomy as no invasion of neighboring organs was observed during the surgical act. The definitive pathological anatomy is compatible with anastomosing hemangioma, an exceptional variant of adrenal tumor, difficult to differentiate radiologically from adrenal carcinoma but that presents benign behavior, which completely changes management and prognosis.

DOI: 10.1530/endoabs.81.EP103

EP104

Establishment of humanized mouse humoral immunity evaluation system using the pregnancy immune system

Atsushi Yasuda[1], Toshiro Seki[1], Natsumi Kitajima[1], Masami Seki[2] & Yoshie Kametani[1]
[1]Tokai University School of Medicine, Japan; [2]Seirei Numazu Hospital, Japan.

(Aims) Regulation of humoral immunity is important to develop vaccines for infectious disease and cancer. However, human and mouse humoral immune systems contain different molecular mechanisms, and the evaluation of efficacy is difficult in the pre-clinical investigation. Humanized mice with reconstructed human immune system are useful for drug discovery of molecular-targeted drugs related to the immune system, and evaluation of antibody production by vaccines. The development of a good model for evaluating the antibody-producing ability has been awaited. However, it was difficult to develop antigen-specific IgGs in the mice, because the maintenance of fully developed T cells and B cells was not successful. We focused on the fact that the mother during pregnancy accepts the other, the foetation, while maintaining the production of specific antibodies, and attempted to produce humanized mice based on the expression of pregnancy-related protein interleukin-4 (IL-4). As we found that the mice can secrete antigen-specific antibodies, futher experiments were performed. (Materials and Methods) We immunized the 20mer HER2 peptide CH401MAP, which we developed as a breast cancer vaccine model, into NOG-hIL-4-Tg mice transplanted with healthy donor's peripheral blood mononuclear cells (PBMCs). Then, the subsets and activation level of T cells was confirmed by flow cytometry. Glucocorticoid receptor (GR) was quantified by realtime-RT-PCR. Moreover, the antibody production performance was confirmed by ELISA/LC-MS. (Results and Discussion) As a result, in the presence of high concentration of IL-4, antigen-specific IgG antibody production was detected in the plasma of PBMC-transplanted NOG-hIL-4 mice. Because glucocorticoid suppresses not only humoral immunity but also innate and cellular immunity, we analyzed the relationship among GR expression levels, the profile of human lymphocyte subsets and the humoral immunity status of PBMC-transplanted NOG-hIL-4 mice. The results showed that NOG-hIL-4-Tg splenocytes had significantly lower human GR mRNA levels than conventional NOG splenocytes after immunization. Moreover, B-cell proportion and antigen-specific IgG concentration in plasma showed strong negative correlations with the GR mRNA level. It was considered that IL-4 decreased GR expression to increase the viability of B cells and to induce the proliferation and class switching of clones producing specific antibodies. This system may help mother's immunity to protect their body from the infectious diseases and cancer. Moreover, it may help producing and sending pathogen-specific IgGs to their fetus.

DOI: 10.1530/endoabs.81.EP104

EP105

Serum cortisol immunoassay performance in the overnight dexamethasone suppression test.

Jonathan Atkins[1], Laura Owen[2,3], Jonathan Clayton[4], James M Hawley[1], Jonathan Scargill[4] & Brian Keevil[1]
[1]Wythenshawe Hospital, Manchester University NHS Foundation Trust, Manchester, UK; [2]Salford Royal Hospital, Northern Care Alliance NHS Foundation Trust, Manchester, UK; [3]The University of Manchester, Manchester, UK; [4]Royal Oldham Hospital, Northern Care Alliance NHS Foundation Trust, Greater Manchester, UK.

Background
The 1 mg overnight dexamethasone suppression test (ONDST) is recommended for the differential diagnosis of Cushing's syndrome and the investigation of adrenal incidentalomas. However, diagnostic performance of the test relies on accurate methods to quantitate cortisol in serum. Although the variable performance of serum cortisol immunoassays has been well-documented, little has been published on their performance following the ONDST.
Aims
Assess the performance of three common immunoassay platforms (Roche Elecsys II, Abbott Alinity & Siemens Centaur) when compared to a liquid chromatography tandem mass spectrometry (LC–MS/MS) method.
Methods
Samples ($n=77$) sent to the laboratory as part of an ONDST were retrieved prior to disposal and stored at −80°C until commencement of the study. Samples were pseudononymised, aliquoted and frozen prior to distribution to participating laboratories for immunoassay analysis. Samples with cortisol >250 nmol/l and samples with cortisol lower than the limit of quantitation for each assay were excluded. Immunoassay results were compared to a routine LC–MS/MS serum cortisol method that is metrologically traceable to a candidate reference measurement procedure. Statistical analysis was done, for total results and split into male and female cohorts, through Passing-Bablok regression and Bland-Altman plots.
Results
The Roche gen II compared well, with a mean bias of −2.4 nmol/l and a Passing-Bablok regression fit of $y=-1.332+0.9857x$. This bias was not affected by sex. The worst comparison was observed with the Abbott immunoassay. The mean bias here was −17.7 nmol/l, with a Passing-Bablok regression fit of $y=-5.565+0.8362x$. This negative bias was exacerbated in the samples taken from female patients (−20.9 nmol/l) vs male patients (−15.0 nmol/l). The Siemens assay had a mean bias of 3.2 nmol/l and a Passing-Bablok regression fit of $y=0.9035+1.044x$. This positive bias was worse in male patients (6.7 nmol/l) vs female patients (0.01 nmol/l).
Conclusions
Method-dependent variation exists in the analysis of serum cortisol as a part of ONDSTs. Of the immunoassays, Roche gen II and Siemens more closely aligned with LC–MS/MS. Use of the Abbott immunoassays may result in the underestimation of cortisol and a reduction in ONDST diagnostic sensitivity, particularly in female patients. Clinicians should be aware of the performance of their local assay and on the basis of this data there is evidence to support assay-specific cut-offs for the ONDST.

DOI: 10.1530/endoabs.81.EP105

EP106

11-deoxycorticosterone producing adrenal hyperplasia as a very unusual cause of endocrine hypertension: case report and systematic review of the literature

Queralt Asla Roca[1,2,3], Helena Sardà Simó[1,2,4], Enrique Lerma Puertas[2,4,5], FELICIA ALEXANDRA HANZU[6,7,8], Eulàlia Urgell Rull[2,9], José Ignacio Pérez García[2,10], Susan Webb Youdale[1,2,4,11] & ANA AULINAS MASO[1,2,3,11]
[1]Hospital de la Santa Creu i Sant Pau, Endocrinology and Nutrition, Barcelona, Spain; [2]Institut de Recerca – Hospital de la Santa Creu i Sant Pau, Barcelona, Spain; [3]University of Vic, Medicine, Vic, Spain; [4]Universitat Autònoma de Barcelona, Medicine, Bellaterra, Spain; [5]Hospital de la Santa Creu i Sant Pau, Pathological Anatomy, Barcelona, Spain; [6]Hospital Clínic, Endocrinology and Nutrition, Barcelona, Spain; [7]Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Barcelona, Spain; [8]Universitat de Barcelona, Medicine and Health Sciences, Barcelona, Spain; [9]Hospital de la Santa Creu i Sant Pau, Biochemistry, Barcelona, Spain; [10]Hospital de la Santa Creu i Sant Pau, General and Digestive Surgery, Barcelona, Spain; [11]Carlos III Health Institute, Centro de Investigación Biomédica en Red de Enfermedades Raras (CIBER-ER, Unit 747), Madrid, Spain.

11-deoxycorticosterone (DOC) is an aldosterone precursor synthesized from progesterone and converted to corticosterone in the adrenal cortex. DOC overproduction due to an adrenal lesion is a very rare cause of mineralocorticoid-induced hypertension. The objective of this study is to provide the most relevant clinical features that clinicians dealing with patients presenting with the hallmarks of hypertension due to DOC-producing adrenal lesions should be aware of. We report a case of a patient with a DOC producing adrenal hyperplasia and provide a systematic review of all published cases (PubMed, Web of Science) until 2021. A 53-year-old woman without any previous history of hypertension consulted to the Emergency Department for high blood pressure (BP), muscle aches and stiffness. Blood test showed serum potassium of 1.73 mmol/l. After being admitted to the Intensive Care Unit and the hospitalization ward, she was diagnosed of a left functional adrenal mass due to non-aldosterone dependent mineralocorticoid secretion (aldosterone: 81.94 pmol/l; reference range 187–930 and plasma renin activity: undetectable), namely excessive DOC production (35.8 ng/dl; reference range 2–15). A left adrenalectomy was performed. Macroscopy revealed a cortical adenomatous hyperplasia and microscopy excluded atypia, mitosis or necrosis, with a Ki67 index positive in <1% of cells. After surgery, her potassium levels normalized and BP and DOC levels significantly improved. The systematic review of the literature identified 44 cases (including ours). Most cases (30, 68%) affected women with a mean age of 42.8±15.6 years and presented with high BP and hypokalaemia (average: 2.65±0.61 mmol/l). Median (interquartile range) time from onset of first suggestive symptoms to diagnosis was 24 (56) months. DOC levels were a median of 15.8 (18.9) times above the upper limit of the normal reference range reported in each article and overproduction of more than one hormone was seen in 29 (66%) cases. Carcinoma was the most common histological type (48.8%). Median tumour size was 64 (67.5) mm. Reduced 11β-hydroxylase and 17α-hydroxylase enzyme activities were the most frequent immunohistochemical findings. Malignant compared to benign lesions were

larger (97 vs 40 mm, $P=0.0001$), had higher DOC levels (20.3 vs 6.2 times above the upper limit of normal, $P=0.041$) and shorter time of evolution (11 vs 42 months, $P=0.029$). In conclusion, DOC-producing adrenal lesions are very rare, affecting mostly middle-aged women with a primary aldosteronism-like clinical presentation and carcinoma is the most frequent diagnosis. Measuring DOC levels when low aldosterone levels are present in hypertensive patients is advisable.

DOI: 10.1530/endoabs.81.EP106

EP107

Cushing's syndrome due to primary bilateral macronodular adrenal hyperplasia in medical treatment. A case report

Susana Bacete Cebrián[1], Vanessa Triviño[1], Beatriz Ugalde Abiega[2], Javier Modamio[1], Mikaela Zubillaga[1], Olalla Meizoso-Pita[1], Isabel Huguet[1], Inmaculada Moreno-Ruiz[1], Iciar Martin Timon[1] & Cristina Sevillano-Collantes[1]
[1]Hospital Universitario Infanta Leonor, Endocrinología y Nutrición, Madrid, Spain; [2]Hospital Ramón y Cajal, Madrid, Spain.

Background
Primary bilateral bilateral macronodular adrenal hyperplasia is a cause of Cushing's syndrome. It is characterised by a large enlargement of the adrenal glands at the expense of multiple non-pigmented nodules. There is inefficient steroidogenesis.
Summary of the case
A 58-year-old woman with a history of extreme obesity, type 2 diabetes mellitus, hypertension and dyslipidaemia was admitted to our hospital for cellulitis and anaemia secondary to a post-traumatic haematoma. The endocrinology department was consulted for hyperglycaemia. Clinical examinations revealed a Cushing's phenotype. Blood hormone analysis revealed hypercortisolism, confirmed by elevated urinary cortisol. The primary origin was confirmed by the absence of basal cortisol suppression after dexamethasone 1 mg. An abdominal CT scan revealed enlargement of both adrenal glands consisting of multiple nodular hypodense lesions with low attenuation values. Associated hyperproduction of catecholamines, aldosterone and androgens, and 21-hydroxylase deficiency were ruled out. A 131-iodine-cholesterol scan was requested, which showed intense early bilateral uptake of both adrenals with a final diagnosis of bilateral adrenal hyperplasia scan. Genetic study detected the probably pathogenic variant c.394dup p.(Ala132Glyfs*55) in heterozygosis in the ARMC5 gene.Our patient was diagnosed with long-standing primary Cushing's syndrome due to bilateral macronodular adrenal hyperplasia caused by a heterozygous mutation in the ARMC5 gene; associated with secondary complications: extreme obesity with severe functional limitation, arterial hypertension, type 2 diabetes mellitus, dyslipidaemia, chronic hypokalaemia and metabolic alkalosis, recurrent spontaneous haematomas and depressive syndrome. Surgical treatment was proposed, but was ruled out due to the maximum surgical risk due to her comorbidities. We therefore started medical treatment with ketoconazole, titrating the dose up to 800 mg per day, achieving disease control, after normalisation of hypercortisolism. During admission, functional limitation of the lower limbs was added, and an X-ray of the lumbar spine was performed, awaiting bone densitometry, which revealed vertebral crushing, and zolendronic acid was started. At present, our patient has been hospitalised for a year as a social problem. She remains functionally and cognitively limited due to persistent depression.
Conclusion
Primary bilateral macronodular adrenal hyperplasia as a cause of Cushing's syndrome is rare. The initial management of this pathology is surgical, but there are patients with extensive comorbidity in whom this is not possible, and we have to opt for medical treatment. It is important to address all associated comorbidity as it is a pathology with a slow clinical course, but which greatly impairs the quality of life of patients.

DOI: 10.1530/endoabs.81.EP107

EP108

Assessing health-related quality of life in patients with Addison disease

Dhoha Ben Salah, Khouloud Boujelben, Abdelmouhaymen MISSAOUI, Faten Haj Kacem Akid, Mnif Fatma, Mouna Mnif, Nadia Charfi, NABILA REKIK MAJDOUB, Mouna Elleuch & Mohamed Abid
Hedi Chaker Hospital, Department of Endocrinology, Diabetology, Sfa, Tunisia.

Introduction
Conventional glucocorticoid replacement therapy has been suggested to increase morbidity in patients with Addison disease and fail to restore their quality of life (QOL). The aim of our study was to assess QOL in patients with Addison disease and to identify factors that determine their QOL.
Patients and methods
This cross-sectional study was carried out at the department of Endocrinology in HediChaker hospital-Sfax –Tunisia, from March 2020 to July 2021.Fifty patients with Addison disease were recruited both outpatient and hospitalization departments. Healthrelated quality of life was measured using the 36-item Short-Form Health Survey (SF-36).The questionnaire contained eight domains:physical functioning (PF), role physical (RP), bodily pain (BP) general health (GH), vitality (VT), social functioning (SF), role emotional (RE) and mental health (MH). An overall mean score of less than 66.7 means impaired quality of life.
Results
Mean age of patients and duration of Addison disease was $49,5 \pm 13,9$ years and $13,9 \pm 8,7$ years.The female sex was the most affected with a sex ratio of 4. The majority of patients (72%) were unemployed.Approximately half of patients were overweight (BMI $\geq$ 25) (48%) and had a sedentary lifestyle (66%). All patients were on hydrocortisone replacement, taking daily $27,4 \pm 6,7$ mg (15–42,1 mg). Mean cumulative hydrocortisone dose was $374,636 \pm 283,821$ mg (60–1184, 94 mg). Overall SF-36 scores were on average $65,7 \pm 4,1$.QOL was impaired in 65% of patients. Both daily and cumulative hydrocortisone doses were higher in patients having an impaired QOL but without significant difference. No correlation was identified between QOL and duration of glucocorticoid replacement therapy.
Conclusion
Patients with Addison disease experience significant impairment in their health QOL, which is linked particularly to metabolic and bone consequences of long-term glucocorticoid replacement therapy. The assessment of QOL in patients with Addison disease may help to ameliorate patient's wellbeing.

DOI: 10.1530/endoabs.81.EP108

EP109

Primary adrenal insufficiency due to bilateral adrenal hemorrhage-adrenal infarction in a patient with systemic lupus erythematosus and antiphospholipid syndrome

Katerina Bouki[1], Vasiliki Venetsanaki[1], Maria Chrysoulaki[1], Aikaterini Pateromichelaki[2], George Bertsias[2], VASILIKI DARAKI[1], Konstantinos Spanakis[3], Grigoria Betsi[1], Nikolaos Sbyrakis[4], Maria Sfakiotaki[1], Kalliopi Kontolaimaki[1], Eleni-Konstantina Syntzanaki[1], Rodanthi Vamvoukaki[1], Panagiotis-Nikolaos Tsakalomatis[1], Prodromos Sidiropoulos[2] & PARASKEVI XEKOUKI[4]
[1]University General Hospital of Heraklion, Endocrinology and Diabetes Clinic, HERAKLION, CRETE, Greece; [2]University General Hospital of Heraklion, Rheumatology and Clinical Immunology Clinic, HERAKLION, CRETE, Greece; [3]University General Hospital of Heraklion, Radiology Department, Department of Medical Imaging, HERAKLION, CRETE, Greece; [4]University General Hospital of Heraklion, Emergency Department, HERAKLION, CRETE, Greece.

Background
Systemic lupus erythematosus (SLE) is an autoimmune disease with multisystem involvement and varied presentation but its association with adrenal insufficiency is rarely reported.
Case presentation
A 30-year-old female presented to the emergency department with fever, lethargy and syncopal episodes during the last 48 h. She complained of general weakness, abdominal pain, nausea, vomiting, weight loss and anorexia for five months. Symptoms deteriorated progressively but were attributed to cholelithiasis for which she underwent a cholecystectomy one month prior, without symptom resolution. She had been hospitalized two years ago due to acute myocarditis and pulmonary embolism and was diagnosed with systematic lupus erythematosus (SLE) and secondary antiphospholipid syndrome (APS). Treatment included hydroxychloroquine, mycophenolic acid (MMF), tinzaparin and periodical corticosteroid treatment. At presentation, physical examination revealed severe hypovolemia, anuria, abdominal tenderness and skin and mucosal hyperpigmentation. Laboratory evaluation revealed anemia, hyperkalemia, hyponatremia, hypercalcemia, troponinemia, prolonged clotting time tests, acute renal insufficiency (serum creatinine:6,5 mg/dl) and pyuria. Primary adrenal insufficiency was suspected and was later confirmed by a low plasma cortisol level (1 μg/dl). She was initially admitted to the Intensive Care Unit (ICU) and treated with fluid resuscitation, continuous hydrocortisone infusion, inotropic agents, antiarrhythmics, anticoagulants, antibiotics and blood transfusions with a good

clinical response. Low levels of C3, C4 combined with high titres of SLE-related autoantibodies, lupus anticoagulant and a positive direct Coombs test were suggestive of clinically active SLE. Anti-adrenal antibodies were negative. Adrenal computed tomography performed on the seventh day revealed high density bilateral adrenal enlargement with fluid stranding of the adjacent fat probably due to recent bilateral adrenal haemorrhage. The patient remained in the ICU for three days and was then transferred to the Endocrine and subsequently to Rheumatology Clinic for further treatment. She was discharged 18 days later, on corticosteroids, hydroxychloroquine, MMF, bisoprolol, acenocoumarol and instructions about stress steroid dosing.
Discussion
Bilateral adrenal involvement in our patient was probably a manifestation of a hypercoagulable state due to APS, which can cause adrenal vein thrombosis, followed by adrenal haemorrhagic infarction, although haemorrhage due to tinzaparin therapy cannot be excluded. Addison disease is rare in patients with SLE however, adrenal failure in the presence of elevated antiphospholipid antibodies has been reported. High index of clinical suspicion is required in patients with lupus or APS presenting with unexplained symptoms and adrenal insufficiency should be included in the differential diagnosis.

DOI: 10.1530/endoabs.81.EP109

EP110

Tertiary adrenal insufficiency revealing Gayet-Wernicke encephalopathy

Kaoutar Rifai, Loubna Guissi, Farah Kamel, Hind Iraqi & Mohamed Elhassan Gharbi
Ibn Sina University Hospital, Endocrinology, Rabat, Morocco.

Introduction
Gayet-Wernicke encephalopathy (WE) is a rare neurological disorder, caused by thiamine (vitamin B1) deficiency. We report a case of tertiary adrenal insufficiency revealing Gayet-Wernicke encephalopathy.
Case presentation
A 45-year-old women was admitted with abdominal pain, vomiting and weakness. Her medical history was significant for a long-term self-medication with corticosteroids and chronic vomiting. Clinical examination revealed a cushingoid appearance (discrete facial erythrosis, protuberant abdomen, skin fragility). The Laboratory results revealed a natraemia of 136 mmol/l, a kalaemia of 4 mmol/l, and an 0800 h serum cortisol level of 50 ng/ml. The diagnosis of tertiary adrenal insufficiency was made and treatment with parenteral hydrocortisone hemisuccinate was started. The evolution was characterized by the development of nystagmus, confusional state and flaccid tetraparesis. Brain MRI was consistent with Gayet-Wernicke encephalopathy. Parenteral vitamin B1 was initiated. As a result the symptoms of nystagmus and confusion subsided, but the patient retained motor sequelae.
Discussion
Wernicke encephalopathy (WE) is an acute neurological condition resulting from thiamine deficiency, most often secondary to chronic alcoholism, but can also occur in the context of chronic vomiting. WE is characterized by a clinical triad of ophthalmoparesis with nystagmus, ataxia and confusion. Brain MRI may reveal hyperintense signaling in the periventricular thalamus, mammillary bodies and periaqueductal gray matter. Early and adequate treatment with thiamine is necessary to avoid death or progression to permanent brain damage.
Conclusion
Our case illustrates the seriousness of self-medication with corticosteroids ranging from a simple tertiary adrenal insufficiency to a serious pathology such as Gayet-Wernicke encephalopathy.
References
Wernicke Encephalopathy.Vasan S, Kumar A.2021 Aug 11. In: StatPearls.
Thiamine in the treatment of Wernicke encephalopathy in patients with alcohol use disorders.Latt N, et al. Intern Med J. 2014.

DOI: 10.1530/endoabs.81.EP110

EP111

The "RESCUE" Trial: 11β-Hydroxysteroid Dehydrogenase Type 1 (HSD-1) Inhibition for ACTH-Dependent Cushing's Syndrome

Frank Czerwiec[1], Jeffrey Drajesk[2], Sarah Hooper[1], Kimberly Hunsicker[3], Robert Jacks[5], Jamie MacPherson[4], Tonya Marmon[5] & David Katz[3]
[1]Sparrow Pharmaceuticals, Inc., Clinical Development, Portland, OR, United States; [2]Sparrow Pharmaceuticals, Inc., Program Management, Portland, OR, United States; [3]Sparrow Pharmaceuticals, Inc., Executive Management, Portland, OR, United States; [4]Sparrow Pharmaceuticals, Inc., Regulatory Affairs, Portland, OR, United States; [5]Sparrow Pharmaceuticals, Inc., Consultant Statistician, Portland, OR, United States.

Background
HSD-1, an intracellular enzyme, converts cortisone to cortisol in tissues where cortisol excess is associated with morbidity including liver, adipose, bone, brain, muscle, skin, and eye. SPI-62 is a potent and specific HSD-1 inhibitor in development for treatment of Cushing's syndrome and autonomous cortisol secretion, and as adjunctive therapy to prednisolone in polymyalgia rheumatica. In Phase 1 clinical trials SPI-62 was generally well tolerated and associated with maximal liver and brain HSD-1 inhibition. SPI-62 decreased urinary cortisol metabolites indicating a similar decrease of hepatocellular cortisol in this important target tissue. After a corresponding transient decrease, circulating cortisol homeostasis was restored by ACTH increase which also resulted in a moderate adrenal androgen increase. SPI-62's effects on androgens did not result in adverse effects. Urinary free cortisol was unaffected. The RESCUE trial will assess SPI-62 safety and efficacy in patients with a dysregulated HPA axis, ie., ACTH-dependent Cushing's syndrome.
Methods
In this randomized, placebo-controlled, crossover, multinational, Phase 2 clinical trial, adult patients ($n=26$) with ACTH-dependent Cushing's syndrome with active and consistently elevated urinary free cortisol (UFC) will be randomized to receive SPI-62 and placebo for 12 weeks each. A diagnosis of an inadequately treated pituitary adenoma (Cushing's disease) or ectopic ACTH or CRH producing tumor based on established criteria is required. Evidence of Cushing's associated morbidities including at least 2 of A) insulin-resistance/type-2 diabetes mellitus, B) dyslipidemia, C) hypertension, or D) osteopenia is required. Subjects must not have had recent Cushing's surgical, radiation other approved or experimental medical therapies for cortisol excess. Medical conditions or treatments likely to interfere with study assessments or subject safety are also excluded. The primary outcome is pharmacological suppression of the urinary ratio of hepatic 5- and 3-steroid reductase metabolites of cortisol and cortisone (tetrahydrocortisol + allotetrahydrocortisol)/tetrahydrocortisone). Safety is assessed by adverse events, vital signs, ECG, and clinical laboratory analyses including effects on HPA/HPG axis biomarkers. Efficacy is assessed by reduction of Cushing's features and morbidities of hyperglycemia, dyslipidemia, adiposity, hepatic steatosis, hypertension, glaucoma, osteopenia, muscle strength, cognition, sleep, and mood. Assessments include tumor-imaging by MRI, ocular tonometry, timed up-and-go and hand-grip strength tests, dual-energy x-ray absorptiometry, oral glucose tolerance, continuous glucose monitoring, and ambulatory blood pressure monitoring.
Results
This trial is ongoing; results are pending.
Discussion
This Phase 2 explores SPI-62 safety, HSD-1 inhibition, effects on HPA/HPG axes, and clinical effects in patients with ACTH-dependent Cushing's syndrome.

DOI: 10.1530/endoabs.81.EP111

EP112

The ACSPIRE trial: 11β-hydroxysteroid dehydrogenase type 1 (HSD-1) inhibition for autonomous cortisol secretion and adrenal cushing's syndrome

Frank Czerwiec[1], Jeffrey Drajesk[2], Sarah Hooper[1], Kimberly Hunsicker[1], Robert Jacks[5], Jamie MacPherson[4], Tonya Marmon[5] & David Katz[3]
[1]Sparrow Pharmaceuticals, Inc., Clinical Development, Portland, OR, United States; [2]Sparrow Pharmaceuticals, Inc., Program Management, Portland, OR, United States; [3]Sparrow Pharmaceuticals, Inc., Executive Management, Portland, OR, United States; [4]Sparrow Pharmaceuticals, Inc., Regulatory Affairs, Portland, OR, United States; [5]Sparrow Pharmaceuticals, Inc., Consultant Statistician, Portland, OR, United States.

Background
HSD-1, an intracellular enzyme, converts cortisone to cortisol in tissues where cortisol excess is associated with morbidity including liver, adipose, bone, brain, muscle, skin, and eye. SPI-62 is a potent and specific HSD-1 inhibitor in development for treatment of autonomous cortisol secretion (ACS) and Cushing's syndrome, and as adjunctive therapy to prednisolone in polymyalgia rheumatica. In Phase 1 clinical trials SPI-62 was generally well tolerated and associated with maximal liver and brain HSD-1 inhibition. Single and multiple SPI-62 doses decreased urinary cortisol metabolites indicating a similar decrease of hepatocellular cortisol in this important target tissue. After a corresponding

transient decrease, circulating cortisol homeostasis was restored rapidly by ACTH increase which also resulted in a moderate adrenal androgen increase. SPI-62's effects on ACTH and androgens did not result in adverse effects. Urinary free cortisol was not affected. The ACSPIRE trial will assess SPI-62 safety and efficacy in patients with dysregulated cortisol production due to ACS or adrenal Cushing's syndrome (aCs) for the first time.
Methods
In this randomized, placebo-controlled, multinational, Phase 2 clinical trial, adult patients with ACS or aCs with otherwise benign adrenal adenomas, persistently elevated morning cortisol after verifiably adequate dexamethasone suppression, and at least two morbidities associated with hypercortisolism [A) insulin-resistance/type-2 diabetes mellitus, B) dyslipidemia, C) hypertension, or D) osteopenia] will be randomized to receive SPI-62 or placebo for 12 weeks. Subjects must have declined, delayed, or been deemed ineligible for adrenalectomy and not recently taken approved or experimental medical therapies for cortisol excess. Medical conditions or treatments likely to interfere with study assessments or subject safety are also excluded. Efficacy at 12-weeks is assessed by reduction of cortisol-associated morbidities of hyperglycemia and dyslipidemia while also examining, adiposity, hepatic steatosis, hypertension, inflammatory cytokines, osteopenia, muscle strength, cognition, sleep, and mood. Safety is assessed by adverse events, vital signs, ECGs, clinical laboratory analyses. Pharmacology is assessed by effects on HPA/HPG axis biomarkers and suppression of the urinary ratio of hepatic 5- and 3-steroid reductase metabolites of cortisol and cortisone (tetrahydrocortisol + allotetrahydrocortisol)/tetrahydrocortisone). Assessments include timed up-and-go and hand-grip strength tests, dual-energy x-ray absorptiometry, oral glucose tolerance test, continuous glucose monitoring, and 24-hour ambulatory blood pressure monitoring.
Results
This trial is ongoing; results are pending.
Discussion
This Phase 2 explores SPI-62 safety, HSD-1 inhibition, effects on HPA/HPG axes, and clinical effects in patients with ACS and aCs.

DOI: 10.1530/endoabs.81.EP112

EP113

Adrenal venous sampling in patients with hyperaldosteronism

Ángel Rebollo-Román[1], M[a] del Carmen Serrano Laguna[1], María-Eugenia Pérez-Montilla[2], Paloma Moreno-Moreno[1] & MARIA ANGELES GALVEZ MORENO[2]
[1]Hospital Universitario Reina Sofía, UGC Endocrinología y Nutrición, Córdoba, Spain; [2]Hospital Universitario Reina Sofía, UGC Radiodiagnóstico y Cáncer de Mama, Córdoba, Spain.

Objective
Adrenal venous sampling (AVP) is a reliable procedure to differentiate if in patients with primary aldosteronism (PA) aldosterone production is unilateral or bilateral and guide the treatment of these patients. Our objective was to describe their characteristics and the outcomes of the AVPs.
Methods and patients
Observational longitudinal clinical study between July 2020 and September 2021 in patients who underwent AVP in our Hospital.
Results
10 patients included. Mean age: 50.9 ± 14.67 years. 60% women. IMC: 26.64 ± 4.05 kg/m^2. 80% patients with an adenoma in the CT: 20% in the right gland, 50% in the left and 10% in both. 20% of patients without adenoma in CT. Reason of PA screening: 40% resistant high blood pressure (HBP), 20% HBP and adrenal adenoma and 40% HPA and hypokalemia. All patients received HBP treatment. 70% of patients took potassium supplementation. In 90% of patients catheterization of both adrenal glands was successful. 66.7% of them showed a left lateralization. 33.3% with no lateralization. Among the 5 patients with successful AVS and adenoma in CT, in 4 of them AVS lateralization matched the image. In 1 patient AVS lateralized to the opposite side. In 1 patient AVS showed left lateralization although no adenoma was seen in CT.All patients with successful catheterization underwent surgery according to the AVS result. 71.4% of them could stop HBP medication.
Conclusion
– In spite of the limited number of AVS performed in our center, AVS is successful in most of the patients (90%) in our series.
– In most patients (80%) AVS lateralization results matched the side of the adenoma in the CT image if it was present. In one patient there was lateralization although no image was seen in CT.
– After surgery most patients in our series can stop their HBP medication.

DOI: 10.1530/endoabs.81.EP113

EP114

Late diagnosis of adrenoleukodystrophy in an adult patient with tetraparesis and addisonian crisis.

Apostolos Gogakos[1], Aliki Aggelaki[2], Apostolos Dougalis[2], Georgia Kourkouta[1], Marina Kita[1] & Zoi Efstathiadou[1]
[1]"Hippokration" General Hospital of Thessaloniki, Greece; [2]Fourth Department of Internal Medicine, "Hippokration" General Hospital of Thessaloniki, Greece.

Introduction
Adrenoleukodystrophy (ALD) is a rare, X-linked inherited, genetic disease, characterized by a disorder of peroxisome metabolism, leading to the accumulation of very long-chain fatty acids (VLCFAs) mainly at the central nervous system and the adrenal glands. It usually occurs in childhood, but there are types of the disease that manifest later in life.
Case
A 57-year-old man with a history of progressive spastic paresis, starting at the age of 25, was admitted due to weakness and hypotension, nausea, abdominal pain, and blurred vision. Fever and severe hyponatremia (Na 108 mmol/lt) were present. Due to the clinical-laboratory picture and reported episodes of hypoglycemia, basal cortisol and ACTH levels were determined, which were indicative of primary adrenal insufficiency [cortisol 2.5 μg/dl, ACTH 360 pg/ml (7–64)]. The diagnosis was confirmed by a short synacthen test (250 μg tetracosactide) with a maximum cortisol response of 1.43 μg/dl. The patient was discharged fever-free and electrolytically stable on hydrocortisone and fluorohydrocortisone replacement therapy. Considering the neurological history and the newly diagnosed Addison's disease, the possible diagnosis of adrenoleukodystrophy was suspected. The new MRI imaging of the brain showed no typical focal lesions while cervical spinal cord atrophy was reported, a typical finding of adrenomyeloneuropathy, one of the most common forms of the disease in adult patients. He underwent a long-chain fatty acid test that confirmed the diagnosis.
Conclusion
The patient suffered spastic tetraparesis without an identified neurological diagnosis for many years. The diagnosis of coexisting primary adrenal insufficiency led to the diagnosis of adrenoleukodystrophy. Adrenomyeloneuropathy is a less severe form of adrenoleukodystrophy, with the onset of symptoms in adolescence or adulthood. This form of the disease does not involve brain damage and should be included in the differential diagnosis of men with adrenal insufficiency or neurological motility disorders of unknown causes.

DOI: 10.1530/endoabs.81.EP114

EP115

Paraneoplastic Cushing's syndrome in metastatic poorly differentiated carcinoma of the kidney

Sandra Ghenoiu[1], Teodor Constantin[2], Costel Daniel Serban[3], Cristina Capatina[1,4] & Catalina Poiana[1,4]
[1,]"C.I.Parhon" National Institute of Endocrinology, VI, Bucharest, Romania; [2,]"C.I.Parhon" National Institute of Endocrinology, Bucharest, Romania; [3]Emergency Clinical Hospital "Dr. Bagdasar-Arseni", II, Bucharest, Romania; [4,]"Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania.

Introduction
Paraneoplastic Cushing's syndrome is attributed to ectopic ACTH release from a non-pituitary tumor. The lung is frequently the primary site of the underlying neoplasm but sometimes, in cases of advanced metastatic disease, determining the origin may be challenging.
Case presentation
A70-year-old man was reffered to our centre for generalised bone pain, lethargy, and important weight loss in the last six months. Before admission, a contrast-enhanced CT scan of thorax and abdomen revealed multiple lung nodules, mediastinal lymphadenopathy, spinal bone lesions suggestive of metastases (with considerable size and extension in the spinal canal), bilateral adrenal masses (with washout percentage >55%) and a large heterogeneous renal mass. The patient presented poor general condition, immobilisation (mainly due to intense bone pain), pale skin and maleolar petechiae; classical clinical features of hypercortisolism were not present. Moderate hypercalcemia, high inflammatory markers, severe ACTH dependent Cushing's syndrome and low PTH level were noticed. Spine MRI confirmed the osteolytic lesions and also the spinal cord

compression due to important tumoral processes affecting thoracic vertebrae. A percutaneous biopsy of a vertebral metastasis revealed a highly anaplastic tumoral process with renal orgin. Mifepristone and analgesic treatment were initiated with biochemical control of Cushing's syndrome, but the patient died within 6 weeks from diagnosis.
Conclusions
ACTH-dependent hypercortisolism source is difficult to identify in a patient presenting with multi-organ masses. Although rare, the renal origin of ectopic Cushing's syndrome should not be disregarded.

DOI: 10.1530/endoabs.81.EP115

EP116

Metyrapone treatment in bilateral macronodular adrenal hyperplasia: a report of two cases

Vittoria Favero[1], Carmen Aresta[2], Chiara Parazzoli[1], Iacopo Chiodini[1,2] & Valentina Morelli[2]
[1]University of Milan, Department of Medical Biotechnology and Translational Medicine, Milan, Italy; [2]IRCCS Istituto Auxologico Italiano, Department of Endocrine and Metabolic Diseases, Milan, Italy.

Introduction
Primary bilateral macronodular adrenal hyperplasia (PBMAH) is potentially responsible for variable degree of cortisol excess. In patients with PBMAH the complete remission of cortisol hypersecretion can be achieved only by performing bilateral adrenalectomy, leading to a persistent hypocortisolism and to a consequent need of a lifelong glucocorticoid replacement therapy. Therefore, bilateral adrenalectomy is worth doing only in patients with severe hypercortisolism, while a medical treatment could be a valid alternative for patients with mild Cushing's syndrome (mCS), particularly in the presence of possibly related clinical conditions (i.e. diabetes, hypertension and bone fragility). In this scenario, steroid synthesis inhibitors, such as metyrapone, have been proposed as possible therapeutic options. We report two cases of PBMAH with mCS treated with low doses of metyrapone (mean dose of 500 mg). Before and after 6 months of therapy, an assessment of clinical consequences of mCS was performed with a 24-hour ambulatory blood pressure monitoring (ABPM) and an oral glucose tolerance test (OGTT).
Case reports
Case 1. A 68 years old male with history of scarcely controlled arterial hypertension. The basal OGTT was consistent with a diabetes diagnosis (fasting glucose levels 128 mg/dl, 2-hour OGTT glucose levels 202 mg/dl). After 6 months of treatment, he achieved: i) the remission of diabetes (fasting glucose levels 97 mg/dl. 2-hour OGTT glucose levels 122 mg/dl) with no changes in anti-diabetic therapies; ii) the ABPM documented improvement in mean blood pressure values (147/80 mmHg and 121/63 mmHg, respectively before and 6 months after treatment). Case 2. A 79 years old female with a history of osteoporosis with 4 clinical vertebral fractures, arterial hypertension and depressive disorder. Before starting the therapy, she had an impaired fasting glucose (104 mg/dl) with a normal response to the glucose load (post-OGTT glucose levels 96 mg/dl). After six months of therapy, we observed: i) the normalization of basal glucose levels (90 mg/dl) and the persistence of a normal OGTT response (132 mg/dl); ii) the important reduction of anti-hypertensive medications with ABPM documented stable mean blood pressure values (119/68 mmHg); iii) the striking amelioration of the depressive disorder and cognitive function. In both patients metyrapone was well tolerated without signs or symptoms of hypocortisolism. In the first patient, potassium levels decreased during the treatment period but remaining within the normal range.
Discussion
Our observations suggest that low doses of metyrapone are well-tolerated and can improve blood pressure and glycemic control in PBMAH and mCS

DOI: 10.1530/endoabs.81.EP116

EP117

Unusual case of adrenal insufficiency

Ana Matijaca
Clinical Hospital Dubrava, Department of Endocrinology, Diabetes and Metabolic Diseases, Zagreb, Croatia.

33-year old obese but otherwise considered 'healthy' patient was admitted to department of surgery due to wet gangrene of left foot. Lower leg amputation was done. As patient was obese with ITM 44 kg/m^2 endocrinologist was consulted. In overnight 1 mg dexamethason supression test cortisol was 72 nmol/l, HbA1c was 5.7%, TSH was 8 mIU/l, level of 25-OH D vitamin below lower range and arterial blod pressure was normal (130/80 mmHg). Patient had central obesity with muscle wasting and gynecomastia, but did not have any purple stirae, bruises, fat pads or hypertension. During stay worsening of clinical condition with respiratory insufficiency due to sepsis occured and patient was transfered to Critical care unit. Debridemenet and re-amputation were needed so few surgical procedures were done and dexmedetomidine for sedation was repeatedly given during few days. After stabilisation of clinical state polyuria was noticed and although patient was normotensive and sodium and potassium level as plasma osmolality were normal, level of cortisol was checked and found to be below level of detection ($<$ 11 nmol/l). Level of pituitary hormones was normal: TSH 2,7 mIU/l, FSH 18,54 IU/l and slightly elevated LH 15,19 and prolactin 646 mIU/l together with ACTH 10,7 pmol/l. Level of peripheral thyroid hormons and testosteron was normal (FT4 12,44 pmol/l, testosterone 9,39 nmol/l) as were SHBG 57,1 nmol/l. CT radiography of adrenal glands showed no signs of necrosis or haemorrhage of the adrenals which morphology was normal. Short test with 250 ug Synacthen iv. was done and showed no adequate adrenal response, cortisol was 100 nmol/l after 30' and 107 nmol/l 60' after stimulation. After one week of supstitution with hydrocortison (20 + 10 mg per os daily) as surgical treatment was over and discharge was planned, afternoon dose of hydrocortisone was omitted and level of cortisol on 0800 h was 83 nmol/l. We concluded that partial recovery of adrenal gland happened but patient was recommended to continue with low dose hydrocortison supplementation (10 + 5 mg tbl). Control work –up in Outpatient clinic was scheduled. Aim of this case presentation is to remind of possible causes of adrenal failure, not only due to sepsis but also malnutrition, drugs – in this particular case dexmedetomidine and to recall other possible mechanisms of adrenal failure in severe or critically ill patients, even in those who might first seem to have Cushing syndrome as was the case with this patient.

DOI: 10.1530/endoabs.81.EP117

EP118

Virilizing adrenal oncocytoma: about 2 cases report

Mouna Mezoued, Bessaid Khadidja & Malha Azzouz
Bologhine Hospital, Endocrinology, Alger, Algeria.

Introduction
Oncocytomas of adrenal glands are extremely rare and usually present as incidentally detected masses. The aim of this presentation is to report tow cases of a virilizing androgen-secreting adrenal oncocytoma.
Case description
Case 1: A 27-year-old female was admitted to our clinic with a 116 mm left adrenal incidentaloma. The patient's main symptom was hirsutism. Upon investigation, elevated values of testosterone, and DHEA-S were found. Contrast-enhanced abdominal CT and MRI scans revealed a heterogenous large left mass (diameter 116 $\times$ 95 mm) with necrotic areas, and a clear distinction from the adjacent structures. The patient underwent a surgical adrenalectomy. The histological examination of the tumor revealed a borderline adrenocortical oncocytoma. Case 2: A 25 years-old woman, presenting a recent and progressive virilization syndrome. Hormonal evaluation showed elevated serum testosterone and delta-4-androstenedione levels, normal urinary free cortisol level and incomplete suppression of cortisol at the 1 mg dexamethasone suppression test. CT scan of the abdomen revealed a 60$\times$50 mm right adrenal mass. The patient benefited from an adrenelectomy. The histological examination of the tumor revealed a benign adrenocortical oncocytoma

DOI: 10.1530/endoabs.81.EP118

EP119

A case of autoimmune polyglandular syndrome type 2

Nino Zavrashvili, Ketevan Chanturishvili, Natia Margvelashvili, Ketevan Gvazava & Natia Shonia
Tbilisi Institute of Medicine, Endocrinology Department, Tbilisi, Georgia.

Autoimmune polyglandular syndromes (APS) are a group of immune-endocrine syndromes that cause autoimmune destruction of multiple endocrine organs. The most common in this group is APS type 2, which frequently presents with primary

adrenal insufficiency with autoimmune thyroid disease and/ or type 1 diabetes mellitus. We present a case of 46 year old male, with no significant medical history who presented in our clinic with: weakness, fatigue and weight loss for the preceding last 3 months. On the examination he was found to have hypotension, tachycardia, hyper pigmentation of the skin and vitiligo. Based on the lab reports and physical exam findings diagnosis primary adrenal insufficiency, Graves Hyperthyroidism and vitiligo was made corresponding with the Autoimmune Polyglandular Syndrome type 2. Treatment with Hydrcortisone, Fludrocortisone and Thionamides was started in our patient resulting in significant improvement in patient's symptoms. After achieving euthyroidism, the thionamide dose was gradually decreased and later discontinued after a year of treatment. Patient remains euthyroid to present day and continues only adrenal hormone replacement therapy with both glucocorticoid and mineralocorticoid. Patient is on regular follow up and is clinically well. He is given the instructions of "sick day rules" to change the hydrocortisone dose appropriately. Patient consent for publication is obtained. The Case report will be accompanied with the corresponding pictures depicting pre and post treatment appearance of the patient.

DOI: 10.1530/endoabs.81.EP119

EP120

COVID-19 pandemic and alternative options to classical pathways: real life experience

Benedetta Zampetti, Iuliana Pauna[2], Sara Andreani[2], Emanuela Isabella Carioni[1], Daniela Dallabonzana[1], Roberto Attanasio[3], Marco Boniardi[2] & Renato Cozzi[3]
ASST Grande Ospedale Metropolitano Niguarda, Endocrinology Department, Milano, Italy; [2]ASST Grande Ospedale Metropolitano Niguarda, General Oncologic and Mini-invasive Surgery Department, Milano, Italy; [3]Scientific Committee Associazione Medici Endocrinologi, International Chapter of Clinical Endocrinology, Italy.

COVID-19 pandemic obliged physicians to find out alternative options to classical pathways, to lower viral spread and related dangers as well as to cope with redeployment of personnel and resources. We describe here two cases in whom surgery for adrenal Cushing's syndrome (CS) and pheochromocytoma (PHEO) was deferred due to the unavailability of surgical facilities.
Case no 1: A 69-yo woman was evaluated for CS. Type 2 diabetes mellitus was diagnosed some years before and a 35-mm right adrenal mass incidentally found at US; no endocrine work-up was performed. Progressively clinical picture worsened and physical examination suggested ACTH-independent hypercortisolism, confirmed by endocrine work-up performed in January 2020. The whole picture was so severe that she was not considered suitable for surgery that became anyway inaccessible due to pandemic. Ketoconazole was given up to 400 mg/day with a progressive reduction in CLU values. Due to the occurrence of symptomatic hypoadrenalism, a block-and-replace therapy with cortisone acetate was started, obtaining a progressive and persistent improvement in clinical/biochemical picture. Due to the persistence of pandemic and the unavailability of surgical facilities for not urgent surgeries, patient is still waiting surgery. Case no 2: In an 83-yo woman, abdominal plastic surgery was complicated by hypertensive crisis, acute pulmonary edema, cardiogenic shock, acute renal failure; multiple stenoses were disclosed at coronary-angiography, reverse Takotsubo at ventriculography. Abdominal CT disclosed a 45×31 mm left-adrenal lesion consistent with PHEO, confirmed by Endocrine-workup. Recovery of systolic function and pressure control were obtained with doxazosin (in addition to ongoing lowering blood pressure treatment. The planning of adrenal resection was postponed due to an adrenal hematoma developed while on LMWE treatment; the subsequent CT showed hematoma reabsorption but in the meanwhile there was the outbreak of the pandemic. The patient was monitored throughout subsequent months with telemedicine controls, confirming optimal pressure control; she underwent laparoscopic-adrenalectomy without any perioperative complications. A post-op CT and hormonal evaluation did not disclose any tumor remnant/relapse and the patient has an optimal pressure without any anti-hypertensive treatment.
Conclusion
This change of the mainstay of treatment for adrenal hypersecreting lesions due to pandemic could offer a new therapeutic paradigm of these diseases in cases when surgery is contraindicated for severe comorbidities.

DOI: 10.1530/endoabs.81.EP120

EP121

Primary hyperaldosteronism and graves 'disease, a rare combination

Randa Salam
Cairo University, Internal Medicine, Endocrinology, Cairo, Egypt.

Introduction
Primary hyperaldosteronism is a known cause for secondary hypertension. In addition to its effect on blood pressure, aldosterone exhibits proinflammatory actions and plays a role in immunomodulation of autoimmunity. Autoimmune hyperthyroidism (Graves' disease) and primary hyperaldosteronism rarely coexist but underlying mechanisms associating the two are still unclear.
Case report
A 32-year-old female referred to endocrine unit for further evaluation and management of hypertension and hypokalemia. She was on three antihypertensive medications at the time of presentation but had poor blood pressure control. She also had nonspecific body aches and intermittent muscle cramps palpitation and sweating with associated heat intolerance, recent weight loss, for the past 2 months. She did not have any virilizing features. She was not on diuretics or any long-term medications except three antihypertensive medications. None of her family had hypertension, strokes, or sudden deaths at younger age. Examination, pulse: 110 /minute, blood pressure: 140/100 mmHg while on antihypertensive therapy BMI: 23 kg/m2. There was a small diffusely enlarged goiter without any tenderness. Bilateral mild exophthalmos normal eye movements and vision. Investigations:potassium, 2.1 mmol/l (3.5–5) Patient with hypertension, hypokalemia, possibility of primary hyperaldosteronism was considered. Aldosterone: renin ratio (ARR) was measured after correcting the potassium value and adjusting the interfering medications ARR was 198 [ng/dl]/[ng/ml/hr] ($n: < 20$) A contrast enhanced computed tomography (CT) of abdomen showed a right-sided homogenously dense (density of 9.5 Hounsfield Units {HU}) adrenal lesion measuring $2.0 \times 1.5 \times 0.8$ cm Evaluation of the thyroid status revealed evidence of hyperthyroidism: TSH $<$ 0.08 μIU/ml (0.27–4.0), free T4—4.60 ng/dl (0.7–1.9), and free T3—7.36 pg/ml (2–4.4). Ultrasound scan of the thyroid showed diffusely enlarged gland with increased echo pattern and vascularity on Doppler studies, compatible with Graves' disease Thyrotoxicosis was managed with antithyroid drugs (Carbimazole)30 mg/day titration till she was on 10 mg/day and once patient rendered euthyroid, laparoscopic right adrenalectomy was performed. Antithyroid medications were discontinued after 12 months after which patient achieved remission of Graves' disease.
Conclusion
Primary hyperaldosteronism (PA) is a leading endocrine cause for secondary hypertension, particularly in resistant hypertension Recent studies have demonstrated role of aldosterone on immunomodulation together with its effects on adaptive immune system, suggesting the possible rare link with development of autoimmune disorders

DOI: 10.1530/endoabs.81.EP121

EP122

Malignant pheochromocytoma: a case report

Ghita Khamel, Kamel Farah, Kaoutar Rifai, Hind Iraqi & Mohamed Hassan Gharbi
Ibn Sina University Hospital, Endocrinology, Rabat, Morocco.

Introduction
Pheochromocytoma (PHEO) is an adrenal medulla tumor secreting catecholamines. Malignancy is defined by the presence of metastases in non-chromaffin tissue. Its optimal management requires experienced multidisciplinary teams.We report the case of a patient followed for malignant pheochromocytoma
Comment
58-year-old patient operated for a pheochromocytoma in 2016, then lost sight of. The evolution was marked 6 years later by the installation of right lumbar pain associated with a Menard triad evolving in a context of weight loss not figure. Clinical examination found right lumbar contact with tenderness on palpation, associated with swelling next to the left scapula. The dosage of urinary methoxylated derivatives shows a normetanephrine level twice the normal. The adrenal CT shows a right interhepato-renal lesional process invading the hepatic parenchyma measuring: 8.4×10.5 cm. As part of the extension assessment, a CTAP CT scan was performed showing an inter hepatorenal tissue mass invading the liver and the thoracic wall in favor of tumor recurrence with secondary pancreatic and bone localizations at the level of the femoral head, and lysis scapular bone. MIBG scintigraphy and PET FDG are not available The file was

staffed in mulidisciplinary meeting, the therapeutic decision was to complete with palliative chemotherapy with VP 16 cisplatine A genetic study is requested in search of a mutation of the SDHB gene
Discussion
The prevalence of metastatic pheochromocytomas varies between 5 and 26%. Only the presence of lymph node or distant metastases affirms malignancy; histological examination does not provide certain information Secondary localizations are most often pulmonary, hepatic and bone.The diagnosis of recurrence can be made through MIBG scintigraphy despite a normal hormonal balance. Surgery is rarely curative, but tumor reduction or resection of metastases particularly reduces cardiovascular risk. Treatment with 131I-MIBG is an interesting alternative in the management of malignant pheochromocytomas when chemotherapy is indicated as first-line treatment in the event of an inoperable tumor or failure of metabolic radiotherapy.
Conclusion
Our case illustrates the importance of clinical, biological and even morphological monitoring of all patients operated for pheochromocytoma, which must be continued for a long time (15 years) given the possibility of late revelation of metastases. In spontaneous evolution, the 5-year survival is generally less than 50%. Due to the current absence of an effective treatment for malignant tumors, several palliative therapies allow tumor reduction and improved survival.

DOI: 10.1530/endoabs.81.EP122

EP123

The Adrenal that inCYSTS on causing pain

Christopher Horne[1], Charles Tilley[2], Martin Smith[3] & C Richard W Lockyer[4]
[1]University Hospital Southampton, Endocrinology, Southampton, UK; [2]University Hospital Southampton, Pathology, Southampton, UK; [3]Salisbury District Hospital, Endocrinology, Salisbury, UK; [4]University Hospital Southampton, Urology, Southampton, UK.

Adrenal lymphangiomatous cysts are rare, often found incidentally, but can also present in association with abdominal/loin pain or hypertension.[1] They have occasionally been reported in association with hormone over secretion of either aldosterone, cortisol or catecholamines. We present a case of a 40-year-old serving soldier who was suddenly awoken with severe left sided abdominal and flank pain. Over the course of several months, he was forced to take time off work, required opiate analgesia and experienced significant psychological burden because of the severity of symptoms. His initial work up involved a cystoscopy (due to dipstick haematuria) which was normal and a CT of the abdomen which showed a left sided 3.5 cm cystic, partially calcified adrenal lesion. Full endocrinological workup revealed the lesion to be non-functioning. He was normotensive. The size of the adrenal cyst was not thought to correlate with the severity of his pain (and a follow up CT showed no growth or intracyst haemorrhage), but in the absence of an alternative explanation, the patient chose to proceed to a laparoscopic left adrenalectomy. His pain immediately resolved postoperatively, he discontinued all analgesia and returned to work. Histology showed multiloculated cyst lined by flattened endothelial-like cells. Immunohistochemistry confirmed expression of D2-40, CD31 and CD34 consistent with cystic adrenal lymphangioma. Whilst most small adrenal cysts are asymptomatic, adrenal cystic lymphangiomas have been associated with back/abdominal/loin pain in 48% and hypertension in 14% cases.[1,2] This suggests that these endothelial cysts are more likely to cause symptoms regardless of their size. The possible mechanisms of pain in relatively small cysts with no evidence of prior bleed could include retroperitoneal irritation, local cytokine release, abnormal lymphatic drainage, but what exactly causes this phenomenon, especially if pain is severe, remains a mystery. Management of the adrenal cyst and decision on whether to proceed to surgery remains dependent on the size and clinical imperative. However, this case provides an example of small adrenal cyst having life changing implications, had it not been removed. Recognition that small adrenal cystic lymphangiomas can cause such symptoms may help inform future clinical decision making.
References
1. Adrenal Gland Lymphangiomas. Indian J Surg. 2015 Dec;77(3):1334–1342
2. Cystic lymphangiomatous lesions of the adrenal gland: A clinicopathological study of 37 cases including previously unreported cysts with papillary endothelial proliferation. Pathol Res Pract. 2019 Jun;215(6):152385

DOI: 10.1530/endoabs.81.EP123

EP124

A case report of 24 years old female with stage IV adrenocortical carcinoma in vilnius university santaros clinics.

Modesta Alekniene[1,2], Greta Kazakeviciute[1,2], Karolina Charciunaite[1], Gintare Naskauskiene[1,2] & Zydrune Visockiene[1,2]
[1]Vilnius University Hospital Santaros Klinikos, Center of Endocrinology, Vilnius, Lithuania; [2]Vilnius University Faculty of Medicine, Clinic of Internal Diseases, Family Medicine and Oncology, Vilnius, Lithuania.

Introduction
Adrenocortical carcinomas (ACC) are rare and frequently aggressive tumors that may be functional (hormone-secreting) – causing Cushing's syndrome and/or virilization, or nonfunctional – presenting as an abdominal mass or as an incidental finding. We describe a rare case of stage IV adrenocortical carcinoma which first manifested as treatment resistant Cushing's syndrome**.**
Case report
In september of 2021**,** a 24-year-old female came with a complaint of acne and weight gain. During the process of anamnesis collection other symptoms characteristic to hypercortisolism were identified – rounding and flushing of the face, widening of the neck, abdominal weight gain, limb weakening and thinning, increase in blood pressure and thirst. In initial blood test results biochemical parameters testosterone and plasma metanephrines were within normal limits. Serum cortisol was elevated (1049,9 nmol/l), also secondary hypothyroidism was found. Low-dose dexamethasone test was performed and no suppression was observed, cortisol after suppression test remained high – 797 nmol/l. We confirmed autonomous cortisol secretion after disturbed circadian cortisol rhythm, high levels of the 24-hour urinary free cortisol, suppressed adrenocorticotropic hormone were found. Following that, chest, abdominal, pelvis computed tomography (CT) scan was performed and right adrenal mass was identified (90 × 62 × 127 mm), with metastases in the liver and in nearby lymph nodes. Interdisciplinary team decided on a treatment plan consisting of radical surgery followed by a postoperative chemotherapy treatment with mitotane. 2021-10-15 radical surgery was performed and she started the rehabilitation process. After surgery she felt better, she lost weight, her blood pressure became normal. 2021-10-28 histological test results came and adrenocortical carcinoma with metastases in liver was confirmed. 2021-11-29 treatment with doxorubicin, cisplatin and etoposide has begun, but after the first 3 days of treatment – chemotherapy induced cardiotoxicity appeared. She was hospitalized 2021-12-02. 2021-12-06 Abdominal CT scan showed tumor recurrence and progression. Due to hypokalemia, hypercortisolism – etomidate therapy was given, starting from 40 mg a day, through 8 h intravenously. 2021-12-22 mitotane was given, starting from 2000 mg per day. One more cycle of chemotherapy was tried, but her condition rapidly deteriorated and on 2022-01-05 she died.
Conclusion
Our case showed that despite the rarity of the tumor and young patient's age it is important to perform further clinical evaluation in any patient with unexplained symptoms characteristic to hypercortisolism.

DOI: 10.1530/endoabs.81.EP124

EP125

A case of Cushing's disease caused by pituitary macroadenoma

Guranda Maisuradze[1] & Salome Kalandadze[2]
[1]New Hospitals, Endocrinology, Diabetes and Metabolism, Tbilisi, Georgia; [2]New Hospitals, Tbilisi, Georgia.

Introduction: Cushing's disease (CD) accounts for approximately 80% of cases of Cushing's syndrome. Almost all patients with CD have a pituitary adenoma. The tumors are usually microadenomas, only approximately 5 to 10 percent are macroadenomas. Pituitary adenomas arise from epithelial pituitary cells and account for 10–15% of all intracranial tumors. Pituitary imaging is important in confirming the diagnosis of pituitary macroadenoma and also for determining the differential diagnoses of other sellar lesions. Case report: A 27-year-old woman was referred with a 2-week history of headache, blurred vision, edema, amenorrhoea, acne and 14 kg weight gain. Three months previously, her gynecologist had diagnosed hyperprolactinemia (PRL-1053 U/ml) and had started treatment with Cabergoline ¼ tab. 2 times per week. She stopped the treatment without doctor's permission. On examination, there was no galactorrhoea and no purple stretch marks, BMI-19 kg/m^2, BP-110/70 mmHg, P-76', regular. Investigations: MR scan of brain – *chiasm-compressing* adenoma with suprasellar extension 1.2x2.0x1.5 cm, CT scan – *without adrenal hyperplasia,* PRL-1053 U/ml (102-496), TSH-0.696 mIU/ml (0.27-4.2), FT4-10.76 pmol/l (12-22), FT3-3.09 pmol/l (3.1-6.8), LH < 0.100 mIU/ml (2.4-12.6),

FSH-0.954 mIU/ml (3.5-12.5). Serum ACTH and Cortisol were not performed properly, the patient couldn't menaged collecting 24 h urine as well. All other investigations were in normal range. She was diagnosed with macroadenoma pituitary, hyperprolactinemia, central hypothyroidism, secondary hypogonadism. We prescribed Dopamine agonist and Levothyroxine. 2 weeks later she presented new Lab results: 08:00 ACTH-25.03 pg/ml (7.2-63.3), Cortisol-1271 nmol/l (172-497). The high-dose dexamethasone test was performed; proper fall of cortisol was not achieved. CD was diagnosed and she was referred for adenomectomy to neurosurgeon. Buffalo Hump and purple stretch marks first appeared some days before surgery. Transsphenoidal adenomectomy was performed. After surgery replacement therapy has begun.

Conclusion

Patients with macroadenomas are more likely to have supranormal plasma ACTH concentrations than are those with microadenomas (83 versus 45 percent), and the concentrations are less likely to fall with high doses of dexamethasone, as it was described in our case. The treatment of choice for patients with CD is transsphenoidal surgery and resection of the pituitary tumor.

Reference

1. Katznelson L, Bogan JS, Trob JR, et al. Biochemical assessment of Cushing's disease in patients with corticotroph macroadenomas. J Clin Endocrinol Metab 1998; 83:1619. 2. Woo YS, Isidori AM, Wat WZ, et al. Clinical and biochemical characteristics of adrenocorticotropin-secreting macroadenomas. J Clin Endocrinol Metab 2005; 90:4963.

DOI: 10.1530/endoabs.81.EP125

EP126

Disorders of sexual development due to congenital adrenal hyperplasia

Fatima Zahra Outtaleb[1], Amal Tazzite[2] & Hind Dehbi[1,2]
[1]Ibn Rochd University Hospital, Laboratory of Medical Genetics, Casablanca, Morocco; [2]Faculty of Medicine and Pharmacy, Hassan II University, Cellular and Molecular Pathology Laboratory, Casablanca, Morocco.

Disorders of sexual development are defined as any congenital condition, in which the development of the chromosomal, gonadal, or anatomical sex is atypical. Congenital adrenal hyperplasia is one of the most common etiology of those disorders, whiwh may be responsible for acute adrenal insufficiency in the neonatal period. The objectives of this case report are to underline the interest of the diagnosis and the genetic counseling for this pathology characterized by an autosomal recessive transmission. It is a child aged of 3 months at the time of diagnosis, the last of a sibling of nine children, with a history of four deaths in the siblings, and who presented at the age of 2 months with an acute adrenal insufficiency syndrome, revealing congenital adrenal hyperplasia due to 21-hydroxylase deficiency. Clinical examination revealed a sexual ambiguity (hypospadias and cryptorchidism). The rest of the clinical examination did not find any dysmorphism or other associated abnormalities. The inguino-scrotal ultrasound revealed a pelvic structure in the shape of a uterus and the absence of testicles. The karyotype on two different samples confirmed the female chromosomal sex of the child, with a normal formula of 46.XX. Genetic counseling with molecular study are planned. Disorders of sexual development are the result of anomalies that have arisen during the sex differentiation of the individual. The diagnosis of these abnormalities requires in particular cytogenetic and molecular analyses. Prenatal diagnosis is performed in high-risk pregnancies and prenatal treatment with dexamethasone seems effective in preventing genital anomalies in affected female fetus.

DOI: 10.1530/endoabs.81.EP126

EP127

A newly diagnosed Cushing's syndrome after a visit at the Emergency Department

Marina Iliescu[1], Mihaela Tarna[1], Marian Andrei[1], Luminita Nicoleta Cima[1,2], Carmen Sorina Martin[1,2] & Fica Simona[1,2]
[1]Spitalul Universitar de Urgenţă Elias, Bucureşti, Romania; [2]Carol Davila University of Medicine and Pharmacy, Bucureşti, Romania.

Cushing's syndrome results from an excess exposure to glucocorticoids which can result from various causes, divided into ACTH-dependent and ACTH-independent etiologies. An example of ACTH-independent causes are adrenal masses which are either benign adenomas, representing the majority of adrenal mass cases, or by malignant neoplasms. We present the case of a 52 yo woman who presented at the Emergency Department (ER) with thoracic pain and palpitations, for which several cardiac investigations where performed including a thoracic CT scan in order to exclude a pulmonary embolism (PE). The CT scan infirmed the PE, but revealed masses on both adrenal glands. The left adrenal gland showed a heterogeneous, hypodense aspect with a nodule of 1,7 cm and 106 HU. The right adrenal gland showed an homogeneous, hypodense aspect of -13 HU. Therefore the patient was transfered to the Endocrinology Department. Physical examination revealed an obese patient with central fat distribuition, lean proximal parts of the limbs, buffalo hump, hirsutism and kyphotic attitude of the spine. The patient was known with a history of arterial hypertension grade 3, uncontrolled despite treatment with 4 antihypertensive drugs and she complained of mechanical back pain. The routine blood tests were normal, except a mixted dyslipidemia. We excluded pheochromocytoma and primary hyperaldosteronism. Cortisol circadian rhythm was abnormal and basal plasma ACTH low. The cortisol secretion did not suppress after administration of 1 mg overnight of dexamethasone. Severe osteoporosis was diagnosed after DXA evaluation with a vertebral fracture at T4 level. After diagnosing Cushing's syndrome due to primary bilateral macronodular adrenal hyperplasia we decided to perform unilateral adrenalectomy because our patient had moderately increased cortisol production, but with clinical evidence of cortisol excess and the left adrenal was larger on CT scan. Unfortunately, we were not able to screen for aberrant receptors or perform adrenal venous sampling. The particularity of this case is the fact that the patient presented at the ER complaining of nonspecific thoracic pain and the diagnosis of Cushing's syndrome was suspected via an imaging which was not perfomed for evaluation of an adrenal disease.

DOI: 10.1530/endoabs.81.EP127

EP128

Case report of rare adrenocortical oncocytoma with cushing's syndrome and liver hemangiomas

Khatuna Chakvetadze[1], Tamar Shervashidze[2] & Armaz Mariamidze[3]
[1]JSC EVEX – Kutaisi Referral Hospital, Outpatient Diagnostic Department, Kutaisi, Georgia; [2]David Abuladze Georgian-Italian Clinic, Outpatient, Georgia; [3]Pathology Research Center, Georgia.

Introduction

Hormonally active adrenocortical oncocytoma is a very rare neoplasm. Adrenal oncocytomas are mostly considered as non-functioning, benign tumors, with the size of generally >6 cm and lack of pathognomonic features on radiological examinations.

Case Report

A 41-year-old woman was referred to the endocrinologist in April 2021 due to weight gain, resistant arterial hypertension and menstrual irregularities for the last several years. She has been infertile for 10 years, though 5 years ago she delivered a preterm baby girl by the 35th week of pregnancy. Physical examination revealed cushingoid characteristic features: dorsal cervical fat pad, moon facies, fragile skin and thin extremities. Cushing syndrome was confirmed by an overnight 1 mg dexamethasone suppression test, an elevated free cortisol on a 24-hour urine collection, suppressed ACTH level and low DHEA-S level. Primary hyperaldosteronism was excluded by an oral salt loading test. Urinary metanephrines were normal. HBA1C-6.0%. Abdominal CT and MRI revealed left sided adrenal heterogeneous lesion (adenoma) measuring 2.3X2.8X2.2 cm with a calcification focus in the periphery. She was also revealed small liver hemangiomas and NAFL disease. In July 2021 the patient underwent laparoscopic left adrenalectomy. To prevent postoperative adrenal insufficiency, the patient was medicated with hydrocortisone. The operative adrenal gland measured 6x2.5x2.5 cm, with a nodule of 2.5x2.2x2.0 cm of well-defined limits, yellowish. The histological and immunohistochemical analysis revealed the diagnosis of adrenocortical neoplasm with predominance of oncocytic cells in solid-trabecular structures (adrenocortical oncocytoma), having uncertain malignant potential. The doses of hydrocortisone were tapered slowly and stopped 3 months later. 6 months after surgery her cortisol, DHEA-S and electrolyte levels were normal, without any radiologic evidence of recurrence. She is currently in follow up.

Discussion

Adrenocortical oncocytomas are extremely rare tumors with almost 200 published cases, first reported in 1986 by Kakimoto. Although it is by definition, non-functioning, recent data indicate that 17.0-31.5% of adrenal oncocytomas have hormonal activity. By origin oncocytomas are epithelial tumours composed of large eosinophilic cells, due to mitochondria-rich cytoplasm. The frequency of non-functioning oncocytomas is higher in female. The diagnosis of these neoplasms is mostly based on histological and immunohistochemical analysis. The Lin-Weiss-Bisceglia risk system is used to distinguish malignant oncocytic tumors, with major and minor criteria for differentiation. Small oncocytomas are commonly benign tumors, but in our clinical case the hormonally active oncocytoma, with two minor criteria (necrosis and capsular invasion), was classified as having uncertain malignant potential, thus suggesting important prognosis and need for close follow-up.

DOI: 10.1530/endoabs.81.EP128

EP129

Altered steroid metabolism in patients following severe trauma: the golden hour study

Conor Bentley[1,2,3], Jon Hazeldine[1,2], Laura Bravo[4], Angela Taylor[5], Lorna Gilligan[5], Fozia Shaheen[5], Animesh Acharjee[2,4,6], Georgios V Gkoutos[2,4,6,7], Mark Foster[1,2,7], Wiebke Arlt[5] & Janet Lord[1,2]
[1]Institute of Inflammation and Ageing, University of Birmingham, Birmingham, UK; [2]National Institute for Health Research Surgical Reconstruction and Microbiology Research Centre, Queen Elizabeth Hospital Birmingham, Birmingham, UK; [3]School of Sport, Exercise and Rehabilitation Sciences, University of Birmingham, Birmingham, UK; [4]Institute of Cancer and Genomic Sciences, Centre for Computational Biology, University of Birmingham, Birmingham, UK; [5]Institute of Metabolism and Systems Research, University of Birmingham, Birmingham, UK; [6]Institute of Translational Medicine, University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK; [7]Royal Centre for Defense Medicine, Birmingham, UK.

Background
Advancements in medical care have significantly improved survival after major traumatic injury and the main risks are now sepsis and multi-organ failure. An understanding of the hormonal, inflammatory and metabolic changes that occur following trauma is still evolving but it is clear that they impact significantly upon patient prognosis. To date, studies that have examined trauma-induced changes in steroid metabolism have analysed samples taken from patients post-hospital admission, culminating in marked variability in the time of first blood sample. Here we investigated the major changes in steroidogenesis following trauma, focusing on the immediate time after injury.
Methods and Results
We recruited 31 male trauma patients (mean age 28.1 years range 19–59) who had an initial blood sample taken within 1-hour of injury, with subsequent samples taken 4–12 and 48–72 h post-injury. Our control cohort was 35 healthy male volunteers (mean 30 years; range 18–50). Sixteen serum steroids were quantified by liquid chromatography tandem mass spectrometry using a Waters Acquity UPLC and a Xevo-XS mass spectrometer;

- precursors; progesterone, 17hydroxyprogesterone,
- glucocorticoids; 11-deoxycortisol, cortisol, cortisone,
- mineralocorticoids; 11-deoxycortocosterone, corticosterone,
- androgen precursors; DHEAS, DHEA, androstenedione,
- androgens; testosterone, DHT,
- 11-oxygenated androgens; 11-hydroxy-androstenedione, 11hydroxy-testosterone, 11keto-androstenedione and 11keto-testosterone.

Eleven of the sixteen steroids were significantly increased 1 h after injury in comparison to healthy controls. Maximum concentrations of these steroids were observed one hour post injury, concentrations then decreased at 4–12 h and reached levels similar (or lower than) healthy controls 48–72 h after injury. The exceptions were cortisone, 11Keto-androstenedione, 11Keto-testosterone, testosterone and DHT. The concentrations of testosterone and DHT decreased one hour post injury when compared to healthy controls, then decreased further at 4–12 and again at 48–72 h post injury. To estimate when trauma-induced steroid metabolism changes occurred we employed generalised additive models (GAMs) to the samples collected within the first hour of injury. GAMs allowed us to estimate the time excretion of each steroid was altered compared to the healthy controls. The modelling estimated injury-induced changes in steroid precursors 9 min post trauma then in a sequential manner reflecting steroidogenesis to active androgens at 35 min, demonstrating rapid disruption of both adrenal and gonadal steroid biosynthesis.
Conclusions
These data show major changes in steroidogenesis following trauma, for the first time focusing on the immediate time after injury. Whether those patients that have ultra-early changes in steroid metabolism are associated with poor patient outcome warrants further investigation.

DOI: 10.1530/endoabs.81.EP129

EP130

More than a coincidence? a true risk factor in spontaneous coronary dissection: hypothyroidism

Aymen Noamen, Khalil Bahri, Houssem Ben Ayed, Sarra Chenik, Nadhem Hajlaoui & Wafa Fehri
Military Hospital of Tunis, Cardiology, Tunis, Tunisia.

Introduction
Spontaneous coronary artery dissection (SCAD) is an uncommon cause for acute coronary syndrome (ACS). It has been linked to many conditions such as physical exertion, emotional stress, fibromuscular dysplasia, autoimmune diseases. Recent studies suggest high prevalence of hypothyroidism in unselected consecutive patients with SCAD compared with a control group of ACS patients without SCAD with more distal dissections on curly vessels.
Case report
A 51 years old woman with no particular medical history except for hyperthyroidism diagnosed 5 months prior and treated with anti-thyroid drugs, presented to the emergency department for sudden constrictive chest pain following an unusual physical exertion. The EKG showed a regular sinus rhythm of 75 bpm and ST segment depression in the apico-lateral and inferior leads. Troponin levels were high (>40.000 ng/l) and the rest of the lab tests were unparticular. The patient received anti-ischemic treatment and was transferred to our department. At the admission to the intensive care unit, the patient was pain-free, and the EKG showed a sinus regular rhythm with complete regression of the previous patterns, she was then promptly transferred to the cath lab where coronary angiography was performed and showed a tubular dissection of a tortuous mid left anterior descending artery without flow limitation, concordant with type 2 SCAD. The decision then was to perform angioplasty with a DES covering the length of the diseased segment. The transthoracic echocardiography showed an akinetic apex, a left ventricle ejection fraction of 40% and an apical thrombus. The thyroid hormones dosage revealed a hypothyroidism, which was most likely iatrogenic due to the anti-thyroid drugs; subsequent dose lowering was put into effect for an eventual interruption. The patient was discharged with uneventful clinical course.
Conclusion
SCAD is still a topic of interest with unresolved pathophysiology and multiple factors that have been linked to it like thyroid disorder. More studies are needed in this context, which could potentially help elucidate the mechanisms involved in this phenomenon.

DOI: 10.1530/endoabs.81.EP130

EP131

Adrenal insufficiency revealed during a diabetic pregnancy: a case report

Oussama Jaddi, Zineb Ait Si Ali, Sana Rafi, Ghizlane EL Mghari & Nawal EL Ansari
Mohammed VI University Hospital, Department of Endocrinology, Diabetology, Metabolic Diseases and Nutrition, Marrakech, Morocco.

Introduction
Adrenal insufficiency is rarely diagnosed during pregnancy. In the absence of treatment it is associated with high maternal-foetal morbidity and mortality. We report the case of a twenty-one years old female patient, diagnosed with adrenal insufficiency during a diabetic pregnancy of 12 weeks of gestation.
Observation
Twenty-one years old female patient, diagnosed with type 1 diabetes since the age of 15, Referred to our department for the follow-up of her diabetes with an unplanned, evolving pregnancy estimated at 12 weeks of gestation. The patient reported multiples episodes of hypoglycemia reaching 0.42 g/l and persistent asthenia. The clinical examination showed a blood pressure of 100/68 mmHg, heart rate of 71 bpm, and BMI of 22.86 kg/m^2. Suspicion of adrenal insufficiency is confirmed by a low baseline cortisol of 13 µg/dl for an average of 25.1 µg/dl according to the term (12 weeks of gestation). The patient initially received hydrocortisone 30 mg/d reduced after to 20 mg/d with a favorable evolution after the replacement therapy. Adrenal insufficiency of autoimmune cause in the context of autoimmune polyendorcrinopathy, is the most likely etiological diagnosis. The results of the etiological investigation are in progress.
Conclusion
Adrenal insufficiency can occur during pregnancy and be life-threatening if not treated appropriately. However with a correctly adapted hormonal substitution during pregnancy the evolution is favorable in most cases. During delivery, the treatment must be increased and administered by injection as during surgery. The diagnosis can sometimes be difficult due to confusion with the signs of pregnancy or in case of association with diabetes which could be responsible for a delayed management.

DOI: 10.1530/endoabs.81.EP131

Calcium and Bone

EP132

Association of preoperative therapy by native form vitamin D and hypocalcemia after parathyroidectomy in primary hyperparathyroidism patients

Alina Elfimova[1], Anna Eremkina[1], Olga Rebrova[2,3], Elena Kovaleva[1] & Natalia Mokrysheva[4]
[1]Endocrinology Research Center, Department of Parathyroid Disease, Moscow, Russian Federation; [2]Endocrinology Research Center, Moscow,; [3]Pirogov Russian National Research Medical University, Department of Medical Cybernetics and Informatics, Moscow, Russian Federation; [4]Endocrinology Research Center, Director, Moscow, Russian Federation.

Background
Primary hyperparathyroidism (PHPT) is a common endocrine disorder resulting from oversecretion of parathyroid hormone (PTH) in parathyroid glands. Hypocalcemia can occur in the postoperative period after parathyroidectomy (PTE) and can be challenging to control and requires varying doses of supplementation. Vitamin D deficiency can worsen the severity of PHPT and promote the development of "hungry bone syndrome" due to increased influx of calcium into bone after PTE.
Aim
To estimate the association of preoperative cholecalciferol therapy and development of hypocalcemia in 1–3 days after PTE in patients with PHPT.
Methods
Patients with PHPT, serum 25-hydroxyvitamin D (25(OH)D) <20 ng/ml (vitamin D deficiency), and serum total calcium <3 mmol/l were included. Exclusion criterion was the therapy with drugs affecting calcium-phosphorus metabolism – cinacalcet, denosumab or bisphosphonates (either as monotherapy or as a part of combination therapy). All patients underwent selective PTE at the Endocrinology Research Center in 1993–2010 or 2017–2020. PTH, total calcium, phosphorus were measured on 5 days – 4 years before surgery and before therapy by cholecalciferol (if any). 25(OH)D, alkaline phosphatase (AP), osteocalcin, c-terminal telopeptide of type 1 collagen (CTX-1) and dual-energy X-ray absorptiometry were measured on 4-365 days before surgery.
Results
Among 117 included patients, 110 (94%) were female and 7 (6%) male with median age 58 [49; 65] years. 21 patients took cholecalciferol for 2 weeks–2 months at a dose according to the replenishment of vitamin D deficiency and 96 did not. No significant difference was found in demographical (sex, age at surgery), clinical (severity of bone mass density loss) and laboratory parameters (PTH, total calcium, phosphorus, AP, osteocalcin, CTX-1, 25(OH)D) between these groups of patients. Patients with cholecalciferol therapy had significantly less frequent postoperative hypocalcemia (10% vs 63%, $P<0.001$, χ^2). Cholecalciferol intake is negatively associated with hypocalcemia, RR $=0.15$, 95% CI: 0.03–0.51.
Conclusions
Taking cholecalciferol before PTE for 2 weeks–2 months reduces the risk of postoperative hypocalcemia by 2–33 times in patients with PHPT.

DOI: 10.1530/endoabs.81.EP132

EP133

Metabolic parameters in patients with primary hyperparathyroidism before and after parathyroidectomy

Ekaterina Bibik[1], Ekaterina Dobreva[1], Anastasia Miliutina[2], Alina Elfimova[1], Anna Eremkina[1] & Natalia Mokrysheva[3]
[1]Endocrinology Research Centre, Department of Parathyroid Pathology and Mineral disorders, Moscow, Russian Federation; [2]Endocrinology Research Centre, Department of Registries of Endocrinopathies, Moscow, Russian Federation; [3]Endocrinology Research Centre, Moscow, Russian Federation.

Background
Metabolic syndrome may be the nonclassical feature of primary hyperparathyroidism (PHPT) because an increased incidence of various glucose and lipid disorders is often observed in patients with this disease. Earlier we showed PHPT patients had higher serum triglycerides and higher rate of insulin resistance compared to the control group. Dynamics of metabolic parameters after surgery is ambiguous.
The aim
of this study was to compare metabolic parameters in patients with PHPT before and after parathyroidectomy.
Material and Methods
24 patients with PHPT (median age 37 years [33; 41]) underwent biochemical and hormone evaluation, standard oral glucose tolerance test, euglycemic hyperinsulinemic and hyperglycemic clamps, bioelectrical impedance analysis of the body composition before and 1 year after surgery. The exclusion criteria were the GFR $<$ 60 ml/min/1.73 m^2, severe comorbid illness, body mass index (BMI) ≥ 32 kg/m^2, diabetes mellitus, using drugs affecting glucose, lipid and calcium balance. Control group ($n=20$) was sex-, age- and BMI-matched without any endocrine pathology (median serum albumin-adjusted calcium (Ca_{adj}) 2.24 [2.15; 2.28]mmol/l, parathyroid hormone 40.19 [31.10; 51.04]pg/ml).
Results
Except one patient who had glucose intolerance others had normal glucose metabolism according to standard lab tests. 54.2% had normal weight, 41.7% was overweight and just 1 person had obesity I, herewith 45.8% of all had over visceral fat. Insulin resistance (by M-index) was detected in 54.2% cases. PHPT patients had higher serum triglycerides (1.13 [0.94; 1.39] vs 0.79 [0.63; 1.01]mmol/l), lower M-index (5.60 [4.25; 7.45] vs 7.9 [7.0; 10.6]mg/kg*min) and higher C-peptide and insulin levels in both phases of pancreas secretion compared to the control group ($P<0.05$ for all). After radical parathyroidectomy we detected decreased fasting glucose (5.04 [4.63; 5.23] vs 4.69 [4.48; 5.00]mmol/l, p $=0.031$), uric acid (297.7 [246.4; 365.6] vs 261.58 [238.52; 350.37]μmol/l, p $=0.044$) levels and insulin level of second secretion phase (AUC 1150.2 [960.8; 1447.9] vs 982.0 [805.8; 1375.7], p $=0.039$) but any significant changes of lipid profile and M-index as well as body composition weren't revealed. We found negative correlation between Caadj and total cholesterol levels ($r=-0.50$), $P<0.05$ as well as total fat mass and osteocalcin ($r=-0.45$), b-CrossLaps ($r=-0.41$) and magnesium levels ($r=-0.43$), $P<0.05$ in patients before surgery.
Conclusion
Changes of bone and mineral parameters in PHPT can lead to metabolic disorders. Remission of the parathyroid pathology is suspected to improve carbohydrate and purine balance but further studies are required to clarify this statement.

DOI: 10.1530/endoabs.81.EP133

EP134

«Hungry bone» syndrome in delay diagnosed primary hyperparathyroidism with fibrocystic osteitis: A case report

Karina Pogosian[1], Lubov Yanevskaya[1], Arina Mikhailova[1], Alisa Semenova[2], Daria Ryzhkova[3], Lidia Belousova[1], Uliana Tsoy[1] & Tatiana Karonova[1]
[1]Almazov National Medical Research Center, Endocrinology, St. Petersburg, Russian Federation; [2]Pavlov First Saint Petersburg State Medical University, Saint Petersburg, Russian Federation; [3]Almazov National Medical Research Center, Nuclear Medicine and Theranostics, St. Petersburg, Russian Federation.

Background
Fibrocystic osteitis is rare PHPT manifestation. Poor management and delay in diagnosis of fibrocystic osteitis may lead to reduced quality of life and also provoke severe postoperative hypocalcemia – «hungry bone» syndrome.
Clinical case
We present a case of 66-years-old Caucasian woman, with history of urulithiasis/nephrocalcinosis (CKD stage 4), two pathological fractures, and fibrocystic osteitis. In Jan 2021 MRI was performed due to increasing bone and joint pain, unsteady gait and showed multiple vertebral lesions in L3 and L4. Since the diagnosis was not established CT was performed, it revealed bone resorption sites in Th12, L2 – L5, sacrum, and left ileum. These changes were considered to be multiple myeloma signs, but bone marrow trephine biopsy and monoclonal antibody assay did not support this diagnosis. L3 trephine biopsy suggested the giant-cell tumor. Zoledronic acid (4 mg/28 days) therapy was started and undertook whithin 4 months. Later PHPT was suspected. Subsequently iPTH level was 2306.9 pg/ml (15.0–68.3), serum Ca^{++} level – 2.17 mmol/l (1.11–1.29), serum total Ca – 3.86 mmol/l (2.15–2.65), 25(OH)D – 10.80 ng/ml (9.40–59.10). Within the adenoma localization neck ultrasound was performed, although it didn't show any lesions. CT and ^{11}C-methionine PET/CT neck and thorax scans revealed two lesions presumed to be ectopic parathyroid adenomas (3.0x2.1x4.8 cm and 0.8x0.5x0.9 cm). Loop diuretics, rehydration, and cholecalciferol (2000 IU/daily) therapy was started. Parathyroidectomy was performed shortly due to increasing hypercalciemia, both lesions were confirmed to be adenomas. From the third day postoperatively low serum Ca^{++} was detected 0.85 mmol/l in terms of normal iPTH level (45.83 pg/ml), as the patient was having seizures, muscle pain, hallucinations, fatigue, and bradycardia. This condition was evaluated as a «hungry bone» syndrome in terms of prolonged course of fibrocystic osteitis. IV calcium gluconate (16.8 g/daily) and oral calcium carbonate/citrate (5 g/daily), cholecalciferol (4000 IU/daily) and alfacalcidol (4 μg/daily) were used to cope with hypocalcemia. Fourteen-day therapy and replacing alfacalcidol with calcirliol (2 μg/daily) allowed to withdraw IV calcium and reduce oral calcium supplementation.
Conclusion. Delayed diagnosis of long-term hypercalcemia, high iPTH level, unsubstituted 25(OH)D deficiency, and the use of bisphosphonates in high doses

caused development of "hungry bones" syndrome in early postoperative period. Severe hypocalcemia required prescription of active and native forms of vitamin D, oral calcium supplements and IV calcium therapy.

DOI: 10.1530/endoabs.81.EP134

EP135

Abstract Withdrawn

DOI: 10.1530/endoabs.81.EP135

EP136

Quality of life improvement as a valuable outcome of parathyroidectomy in patients with symptomatic and asymptomatic primary hyperparathyroidism

Tatiana Nikitina, Dmitry Buzanakov, Inna Gladkova, Vladimir Rusakov, Roman Chernikov, Yulia Karelina, Sergey Efremov & Tatiana Ionova
Saint-Petersburg State University Hospital, Saint Petersburg, Russian Federation.

Background
Comprehensive evaluation of the effect of surgery in patients with primary hyperparathyroidism (PHPT) and monitoring of patient's well-being after treatment including assessment of patient-reported outcomes is worthwhile.
AIM
We aimed to assess changes in quality of life (QoL) and symptoms in patients with symptomatic and asymptomatic PHPT after surgery (parathyroidectomy, PTX).
Materials and methods.
Adult patients with PHPT who were referred for PTX were included in the single-center prospective observational real-world study. Patients filled out generic and specific questionnaires, namely SF-36 and PHPQoL, for QoL assessment and symptom checklist for assessment of presence and severity of their symptoms prior to surgery and 3, 12 months after PTX. Statistical analysis included Student's t-test or Wilcoxon's non-parametric test, the generalized estimating equations (GEE) method, correlation analysis, and $\chi 2$ test.
Results
In total 72 patients (mean age (S.D.) – 52 years (10.4), 97% female) with symptomatic (68%) and asymptomatic (32%) PHPT were enrolled in the study. Moderate/severe hypercalcemia was observed in 34.7% patients. Before PTX patients with PHPT experienced significantly decreased role functioning, physical and social functioning, and vitality as compared to healthy controls ($P<0.05$). Mean PHPQoL score was 53.7 (IQR: 42.2–64.1). Half of the patients experienced moderate-to-severe symptoms such as weakness, fatigue, cognitive impairment, changes in mood, as well as joint and bone pain. In 3 and 12 months after surgery, improvement in both physical and psychological components of QoL in PHPT patients was shown. Significant changes were observed for the total PHPQoL score as well as for role, physical, emotional and social functioning and vitality by SF-36 (GEE, $P<0.05$). Positive QoL changes were demonstrated for patients with both symptomatic and asymptomatic PHPT, but they were more pronounced in the first ones. QoL improvement was not associated with baseline Ca level or type of PHPT (χ^2, $P>0.05$), but correlated with baseline QoL: the lower baseline QoL the higher QoL improvement after PTX ($r=-0.376$, $P<0.05$). Significant decrease in PHPT-associated symptoms such as weakness, fatigue, loss of concentration and mood changes was found within 12 months after PTX (GEE, $P<0.05$); it was more pronounced in symptomatic PHPT.
Conclusion
PTX leads to pronounced positive QoL changes in PHPT patients. The results obtained demonstrate that QoL improvement is a valuable outcome of surgery both in patients with symptomatic and asymptomatic PHPT. Positive effect of PTX from patient's perspective confirms the value of QoL assessment to measure the degree of recovery at long term follow-up.

DOI: 10.1530/endoabs.81.EP136

EP137

Glomerular filtration rate 12 months after parathyroidectomy in patients with primary hyperparathyroidism

Alina Elfimova[1], Anna Eremkina[1], Olga Rebrova[1,2], Elena Kovaleva[1], Anastasia Miliutina[3,4] & Natalia Mokrysheva[5]
[1]Endocrinology Research Center, Department of parathyroid disease, Moscow, Russian Federation; [2]Pirogov Russian National Research Medical University, Department of Medical Cybernetics and Informatics, Moscow, Russian Federation; [3]Endocrinology Research Center, Department of Edemiology of Endocrinopathy, Moscow, Russian Federation; [4]Pirogov Russian National Research Medical University, Moscow, Russian Federation; [5]Endocrinology Research Center, Director, Moscow, Russian Federation.

Background
In some patients with primary hyperparathyroidism (PHPT), glomerular filtration rate (GFR) demonstrate decrease after parathyroidectomy (PTE). GFR may decrease immediately after surgery due to general anesthesia, but after a month not all patients restore kidney function; a decreased GFR is also observed after 1–2 years after surgery.
Aim
To find the pre-surgical factors of GFR decrease after PTE.
Methods
Patients with PHPT who underwent selective PTE in 1993–2010 (50% of the patients) or 2017–2020 at the Endocrinology Research Center were included. Twenty-two variables were analysed. PTH, calcium total, phosphorus were measured prior to surgery (5 days – 4 years before surgery) and administration of drugs affecting calcium-phosphorus metabolism – cinacalcet, denosumab or bisphosphonates (either as monotherapy or as a part of combination therapy). 25(OH)D, alkaline phosphatase (AP), osteocalcin, c-terminal telopeptide of type 1 collagen (CTX-1), GFR, urea, triglycerides, uric acid, dual-energy X-ray absorptiometry and clinical characteristics were measured on 4–365 days before surgery. GFR was also estimated at 12 months after surgery.
Results
206 patients were included, aged 57 [47; 62] years, 19 (9%) male and 187 (91%) female. On 12 months after surgery 56 of them (27%) progressed to more severe stage of CKD (group 1), and 150 remained at the same stage of CKD (group 2): in the group 1 there were 25 (45%) patients with CKD C2, 17 (30%) with CKD C3a, 8 (14%) with CKD C3b, 6 (11%) with CKD C4, in the group 2 there were 65 (43%) patients without CKD, 63 (42%) with CKD C2, 13 (9%) with CKD C3a, 7 (5%) with CKD C3b, and 2 (1%) with CKD C5. There were no differences in sex, age, BMI, frequency of renal colic and stones, initial stages of CKD, initial GFR, frequency of bone fractures and osteoporosis between the groups. There were also no differences in phosphorus–calcium metabolism (total calcium, ionized calcium, and phosphorus), lipid metabolism (total cholesterol, LDL and HDL cholesterol, triglycerides), PTH, uric acid, urea, osteocalcin and CTX-1. AP was higher in group 1 (309.0 vs 190.3 IU/l, $P<0.001$, U-test).
Conclusions
Groups with decreased and stable GFR significantly differ by bone remodeling marker AP, but not in clinical manifestations of bone disorder. Moreover, groups were comparable in terms of GFR, uric acid and renal complications (renal colic and stones, CKD).

DOI: 10.1530/endoabs.81.EP137

EP138

A comparison study of sublingual spray versus peroral capsules and oil in vitamin d supplementation

Sintija Sausa[1,2], Marija Aleksejeva[1], Ilva Trapina[3] & Valdis Pirags[1,2]
[1]University of Latvia, Faculty of Medicine, Riga, Latvia; [2]Pauls Stradinš Clinical University Hospital, Internal Medicine, Rīga, Latvia; [3]University of Latvia, Genomics and Bioinformatics, Institute of Biology, RIga, Latvia.

Background
Vitamin D is a vital hormone for calcium metabolism, bone and muscle health, and immune responses. Vitamin D deficiency affects entire Latvian population.
Aim
To compare the effectiveness of different forms of vitamin D.
Materials and methods
In a prospective, open-label, randomized study in the Jaunliepaja Primary Health Care Centre, data from 98 vitamin D deficient volunteers over one month at initiation of substitution with 4000 IU (100 mcg) Colecalciferol was analyzed. The efficacy of the peroral oil, lanolin-derived microemulsion sublingual spray and peroral capsules dissolved in sunflower oil was evaluated by comparing patient data with age, BMI, renal function.
Results
Among 98 volunteers with total 25(OH) D vitamin levels below 30 ng/ml, mean 18.30 ± 7.01 ng/ ml, and BMI below 35 kg/m^2, mean age 39.34 ± 13.01 years, 60.2% were female. After one month of intervention, the increase in vitamin D in all groups was 13.21 ± 11.82 ng/ml (95% CI, $P=5.72\times10^{-6}$). In oil group 14.98 ± 13.58, using capsules 11.06 ± 7.13 and in spray group 9.97 ± 7.73 ng/ml accordingly. In the capsule group, an inversely related – slower increase in vitamin D was observed in the elderly (-0.36, $P=4.53\times10^{-2}$) and in participants with a higher body mass index (BMI) (-0.40, $P=2.30\times10^{-2}$),

but the spray group higher increase in vitamin D levels was in participants with a higher glomerular filtration rate (GFR) (0.37, $P=2.93\times10^{-2}$).
Conclusions
An increase in vitamin D levels was observed in all groups after one month of supplementation, and the formulation did not statistically significantly affect the overall outcome. There was at least one respondent with negative vitamin D dynamics in each group. In the capsule group, the changes in vitamin D were statistically significantly inversely related to the respondent's age and BMI – the younger the person, the more pronounced the increase in vitamin D, similarly, the lower the BMI, the higher the increase in vitamin D. In the spray group, a statistically significant correlation was found between the increase in vitamin D and higher GFR.
Declaration of interest
The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research project.
Funding
Pharm&med Ltd.
Keywords: Vitamin D, overweight, age, renal function.
DOI: 10.1530/endoabs.81.EP138

EP139

«Physician to physician» telemedicine consultations in parathyroid pathology: experience of quaternary endocrinological medical center

Anna Gorbacheva, Maria Fadeyeva, Anna Eremkina & Natalia Mokrysheva
Endocrinology Research Center, Parathyroid disorders, Moscow, Russian Federation.

Introducton
Telemedicine consultations (TMC) are a useful tool for ensuring communication between medical specialists, especially in a large country and in the era of COVID-19. It is important to study the needs and possibilities of TMC for various diseases, in particular, for the pathology of the parathyroid glands.
Materials and methods
TMC between regional health specialists and Endocrinology Research Centre (Moscow, Russian Federation) were conducted in 2019–2021 via All-Russian Center for Disaster Medicine «Zashchita».
Results
In 2019 1221 TMC were held in our center, 859 (70%) – for adult patients. In 2020 there were 1248 TMC, in 2021 – 3005 TMC, among them there were 1077 (86%) and 1622 (54%) TMC for adults, respectively. A high prevalence of parathyroid disorders in TMC was noticed (Table 1).

Table 1 Parathyroid disorders in nosological structure of "physician to physician" (P2P) TMC.

	2019	2020	2021
Total TMC count	1221	1248	3005
Number of TMC for adults	859	1077	1622
Number of TMC for parathyroid disorders/% regarding the number of consultations for adults	100 (11,6%)	121 (11,2%)	187 (11,5%)
Among them (according to ICD-10):			
E89.2 (Postprocedural hypoparathyroidism)	9	9	26
E21.0 (Primary hyperparathyroidism)	56	75	111
E21.1 (Secondary hyperparathyroidism)	20	13	18
E21.2 (Other hyperparathyroidism)	3	1	8
E21.3 (Hyperparathyroidism, unspecified)	12	21	18
E21.4 (Other specified *disorders of parathyroid gland)	0	0	3
21.5 (Disorder of parathyroid gland, unspecified)	0	2	3
Hospitalization recommended/% regarding the number of consultations for parathyroid disorders	43 (43%)	61 (50,4%)	121 (64,7%)

Conclusion
The relatively high proportion of parathyroid gland pathology in the structure of P2P TMC may indicate a relatively low awareness of doctors in the regions of Russian Federation about these diseases. At the same time, a high percentage of recommended hospitalizations indicates that such patients need high-tech treatment in a specialized center, which leads to their referral to a fourth-level facility. Further analysis is needed to determine the role of P2P TMC in routing of patients with parathyroid disorders.
DOI: 10.1530/endoabs.81.EP139

EP140

Practical approach for hypocalcemia in infants: earlier diagnosis, earlier management

Abeer Alassaf
University of Jordan, Pediatric Department, Amman, Jordan.

Background
Hypocalcemia is a serious condition that occurs at any age with various etiologies according to various age groups. Hypocalcemia in infant is an emergency condition and the exact etiology should be identified as early as possible to ensure early appropriate management.
Methods
We are presenting 3 cases for infants who presented with seizures caused by hypocalcemia.
Case 1: A 3-month-old male infant presented with apnea and up rolling of eyes. He was full term with normal birth weight. He had poor weight gain, deep-seated eyes, long philtrum and small hands.
Case 2: An 11-day-old male neonate, presented with left-sided focal seizure. He was full term with normal birth weight. He was breast-fed with no vitamin D supplementation. Physical exam was unremarkable.
Case 3: A 6-day-old female neonate who presented with bilateral upper and lower limb clonic seizure. She was full term with normal birth weight. Her physical exam was normal.
Critical sample was sent at the time of hypocalcemia for the three patients. They received intravenous calcium gluconate during admission then switched to oral calcium.
Results
Laboratory work up for case 1 showed hypocalcemia, hyperphosphatemia and absent parathyroid hormone level in blood. Based on his dysmorphic features and laboratory work up, Sanjad Sakati syndrome was suspected which was confirmed by genetic testing. He is currently on daily oral calcium supplement and alfacalcidiol. For Case 2, patient had hypocalcemia, normal blood phosphorus level and very low vitamin D level. Vitamin D level was done for his mother and it was low. He was discharged on oral calcium and vitamin D. Calcium supplement was stopped after 1 week and he continued on vitamin D till last follow up. Case 3 had hypocalcemia, normal blood phosphorus level, low parathyroid hormone and low magnesium level. She was treated during admission in addition to intravenous calcium gluconate, with intravenous magnesium sulfate. She was discharged on calcium and magnesium supplement which were decreased gradually till stopped after few months. Magnesium deficiency which was the cause of her hypocalcemia was transient with no obvious cause.
Conclusion
Physicians should be aware of the precise approach for investigating the etiology of hypocalcemia in infants, in order to establish an early diagnosis and an early appropriate management, through taking full history and full physical exam and performing the appropriate investigations.
DOI: 10.1530/endoabs.81.EP140

EP141

Mediastinal parathyroid lipoadenoma as a cause of primary hyperparathyroidism

Jesus Manuel Cornejo Dominguez, Alvaro Vidal Suarez, Isabel Maria Mateo Gavira, Maria del Mar Roca Rodriguez & Isabel Maria Torres Barea
Hospital Universitario Puerta del Mar, Cádiz, Spain.

Introduction
The parathyroid gland is made up of principal cells and oxyphilic cells, surrounded by stroma, whose main component is adipose tissue, which accounts for 25% of the content of the parathyroid in adults. In parathyroid adenomas, prominent parathyroid cellularity can be observed, with a very marked decrease in

the stroma. Parathyroid lipoadenoma is a rare variant of parathyroid adenoma, characterized by hyperfunctioning parathyroid cells in an abundant fatty stroma. Case reports.
We present a case of a 76-year-old woman with a history of high blood pressure and a previous diagnosis of non-toxic multinodular goiter without follow-up. During an outpatient study due to weakness and incipient cognitive disorders, severe hypercalcemia of 18.3 mg/dl with creatinine of 2.3 mg/dl was detected, for which she was admitted for treatment and study. In previous tests, a progressive increase in calcium was observed that had not been studied, with at least 6 years of evolution, with levels of 15 mg/dl the previous year. During admission, she showed parathyroid hormone (PTH) figures of 2,310.7 pg/ml (NV: 15–68), 25-OH-vitamin D of 12 ng/ml and TSH 0.12 IU/ml, with normal FT4. Cervical ultrasound revealed a multinodular goiter. In the 99mTc-sestamibi SPECT scintigraphy with a heterogeneous uptake of the radiotracer. Cervicothoracic CT revealed a right paratracheal mass with well-defined borders, with solid and fat densities, and dimensions of 5 × 5 × 8 cm, with no other lesions. A biopsy of the mass was performed, obtaining a whitish-brown sample consisting of adipose tissue and tissue with benign characteristics, with a low proliferative index (Ki67 of 1%), confirming its parathyroid origin with immunohistochemical techniques (positivity for the expression of panCK, PAX8 and chromogranin, and negative for PLAP, TTF1 and thyroglobulin). All this compatible with parathyroid lipoadenoma. Before surgical treatment, we started treatment with cinacalcet 30 mg/day, zoledronic acid and fluid therapy. The patient underwent total thyroidectomy and resection of the mediastinal mass. Intraoperative PTH was determined with progressive reduction (basal: 609.8 pg/ml; 5': 240 pg/ml; 10': 155.6 pg/ml; 20': 132.6 pg/ml). The mediastinal surgical specimen, 91 g and 9 × 5 × 3.5 cm, had a nodular appearance with a smooth, yellowish surface, covered by a fibrous capsule. The definitive histological study confirmed nodular thyroid hyperplasia and mediastinal parathyroid lipoadenoma. At hospital discharge, the patient presented calcium 9.34 mg/dl and was undergoing outpatient treatment with LT4 and calcium and vitamin D supplements

DOI: 10.1530/endoabs.81.EP141

EP142

Brown Tumors as a first sign of secondary hyperparathyroidism

Maria Boudina, Chrysanthi Zouli, Eleana Zisimopoulou, Aimilia Fotiadou, Mariana Stamati, George Christantoniou, Chrysanthi Balodimou & Alexandra Chrisoulidou
"Theagenio" Cancer Hospital of Thessaloniki, Endocrinology, Thessaloniki, Greece.

Aim
Brown tumors are a very rare and serious complication of sustained undiagnosed secondary hyperparathyroidism. Diagnosis and differential diagnosis are made by combining clinical, biochemical, radiological and pathological findings. We present the case of a male with chronic renal disease and multiple bone damage.
A 58-year-old male was referred to the endocrine clinic because of lower back and pleural pain. He was an obese smoker with a heavy medical history of hypertension, Stage III chronic kidney disease, obstructive pulmonary disease, heart failure and atrial fibrillation. His past medical history included hyperthyroidism and a large retrosternal goiter. The patient underwent a Thorax CT, which revealed extrapulmonary masses infiltrating the thoracic cage and the ribs. The masses were considered at first to be metastatic and the patient underwent further imaging of the abdomen and cerebrum, as for staging. However, no possible primary lesion was illustrated and the patient was referred for a biopsy. The laboratory tests showed total calcium: 9,2 mg/dl (8,4–10,2), albumin: 4,1 mg/dl (3,5–5), phosphorus: 2,38 mg/dl (2,7–4,5), Parathyroid hormone: 1184 pg/ml (15–65), mild Vitamin D deficiency of 17,3 ng/ml and elevated levels of alkaline phosphate: 595 mg/dl (33–122). Histology confirmed the presence of brown tumors. The patient received supplementation with calcium and vitamin D analogs, as well as cinacalcet, and there was a significant improvement in his laboratory results: calcium 8,3 mg/dl, albumin 3,9 mg/dl, PTH 274 pg/ml, ALP 776 mg/dl and vit D 38 ng/ml. A Thorax CT six months after the diagnosis showed a decrease in the multiple bone lesions and further improvement in his laboratory tests.
Conclusions
Secondary hyperparathyroidism is a common complication of end stage renal disease. Rarely, when undiagnosed and left untreated it can lead to the formation of brown tumors, as a result of osteoclastic activity, fibroblast proliferation and bone resorption. Differential diagnosis should be made from giant cell tumors and metastatic disease.
References
Multilevel brown tumors of the spine in a patient with severe secondary hyperparathyroidism. A case report and review of the literature. Salamone D, Muresan S, Muresan M, Neagoe R.Ann Ital Chir. 2016 Mar 31;87
A brown tumor secondary to hyperparathyroidism in the maxilla, skull, scapula, and femora. Alison Psaila, MDa, Luca Conti, MDb, Alexander P. Azzopardi, BChD, PhDc, and David V. Coppini, MD PROC 2021;34(1):163–165

DOI: 10.1530/endoabs.81.EP142

EP143

Bilateral neck exploration is comparable to preoperative visualization methods in searching for parathyroid adenomas on the neck

Dmitrii Buzanakov[1,2], Arseny Semenov[1,2], Ilya Sleptsov[1,2], Roman Chernikov[1], Konstantin Novokshonov[1], Yuliya Karelina[1], Anna Uspenskaya[1], Nataliya Gorskaya[1], Svetlana Alekseyeva[1], Nataliya Timofeyeva[1], Igor Chinchuk[1], Elisey Fedorov[1], Yuriy Malyugov[1], Dina Rebrova[1], Shamil Shikhmagomedov[1], Ilya Sablin[1], Timur Dzhumatov[2], Mikhail Lyubimov[1], Alexander Pushkaruk[1], Kseniya Gerasimova[1], Anna Zolotukho[2] & Alexander Bubnov[1]
[1]Saint Petersburg State University Hospital, Saint Petersburg, Russian Federation; [2]Saint Petersburg State University, Faculty of Medicine, Saint Petersburg, Russian Federation.

Background
Undetected multiglandular disease (MGD) is a leading cause of persistent primary hyperparathyroidism after surgical treatment. There is still a number of clinically significant parathyroid adenomas that remain unseen preoperatively.
Materials and methods
A retrospective cohort study was conducted in order to reveal factors associated with risk of MGD. 810 cases of pHPT patients who had received primary surgical treatment at SPBU Hospital in 2017–2018 were included. All the patients had at least one preoperative visualization study (neck ultrasound performed by a surgeon) before the operation. In 537 cases two studies (additional 4D CT or MIBI scan) were performed and 164 cases had all three studies. A surgeon was free to choose whether perform bilateral neck exploration or not. Data analysis was performed in R.
Results. Number of patients with at least one adenoma that was not localized preoperatively with no less than two studies performed was 46 (26 single adenomas and 20 complementary). In 30 cases BNE was performed resulting in finding an unseen adenoma in 27 cases (90%). US, CT and MIBI sensitivity values were found to be 83.5%, 92.3% and 75.1% respectively. MGD rate accounted for 6.17% (50 cases). 43 cases of persistent disease after surgery were reported, 25 of them were caused by MGD. Negative predictive value of MGD for different combinations of studies with concordant results (US + MIBI, US + CT and US + CT + MIBI) did not differ significantly and was 96.95%, 97.4% and 97.7% respectively. Logistic regression model was performed, showing that independent negative US, negative CT or negative MIBI were not statistically significant in predicting risk of MGD, as well as age and body mass index.
Conclusion. Bilateral neck exploration added to a routine parathyroidectomy is helpful for discovering an unsuspected MGD case.

DOI: 10.1530/endoabs.81.EP143

EP144

Serum calcium, magnesium and phosphorus levels in patients with coronavirus disease 2019: an analysis of their relationship with poor outcome and mortality

Juan Jose Diez[1], Pedro Iglesias[1], Agustín García[2], Ignacio Martín Casasempere[3] & Francisco A Bernabéu-Andréu[4]
[1]Hospital Universitario Puerta de Hierro Majadahonda, Department of Endocrinology, Majadahonda, Spain; [2]Hospital Universitario Puerta de Hierro Majadahonda, Department of Admission and Clinical Documentation, Majadahonda, Spain; [3]Consejería de Sanidad de la Comunidad de Madrid, Madrid, Spain; [4]Hospital Universitario Puerta de Hierro Majadahonda, Department of Biochemistry, Majadahonda, Spain.

Purpose
To assess the impact of serum corrected calcium (CorrCa), magnesium (Mg) and phosphorus (P) levels at hospital admission on SARS-CoV-2 infection outcome.
Methods
In this retrospective study, all adult patients with laboratory-confirmed COVID-19 hospitalized in Hospital Universitario Puerta de Hierro Madadahonda during 2020 were included. Demographic, clinical and laboratory data were registered and related to the prognosis of the disease. Poor outcome was considered in patients who presented need for mechanical ventilation, intensive care unit (ICU) admission, or in-hospital mortality.

Results
Of a total of 2,473 patients (956 females) aged (mean ± s.d.) 63.4 ± 15.9 years were studied. Median (IQR) hospitalization time was 7(4–13) days. During admission, 169 patients (6.8%) required mechanical ventilation, 205 (8.3%) were admitted to the ICU, and 270 (10.9%) died. Composite variable of poor outcome, defined as need for mechanical ventilation, ICU admission or death, was present in 434 (17.5%) patients. In univariate analysis, the need for mechanical ventilation was positively to related to Mg levels (OR 8.37, confidence interval [CI] 3.62-19.33; $P < 0.0001$). ICU admission was related to CorrCa (OR 0.49, CI 0.25–0.99) and Mg levels (OR 5.81, CI 2.74–12.35; $P < 0.0001$). In-hospital mortality was related to CorrCa (OR 1.73, 95% CI 1.14–2.64; $P = 0.011$) and the composite variable of poor outcome was only related to Mg (OR 2.68, 95% CI 1.54–4.68; $P = 0.001$). However, in multivariate analysis CorrCa was significantly related to the need for mechanical ventilation (OR 0.19, 95% CI 0.05–0.72; $P = 0.014$) and ICU admission (OR 0.25; 95% CI 0.09–0.66; $P = 0.005$), but not with in-hospital mortality or the composite variable of poor outcome. We found no relationship between poor outcome or mortality and serum levels of Mg or P in the multivariate analysis.
Conclusion
These results suggest that CorrCa can be used as a simple and reliable marker of poor outcome in patients with COVID-19, although not to predict the risk of in-hospital mortality.

DOI: 10.1530/endoabs.81.EP144

EP145

Autosomal dominant hypocalcaemia type 1 with intact PTH and relative hypocalciuria.

Razan Ali Rashid[1], Richard Quinton[1] & Ashwin Joshi[2]
[1]Royal Victoria Infirmary, Newcastle upon Tyne Hospitals NHS Foundation Trust, Department of Endocrinology and Diabetes, Newcastle upon Tyne, UK; [2]Sunderland Royal Hospital, South Tyneside and Sunderland NHS Foundation Trust, Department of Endocrinology Diabetes and Metabolic Medicine, Sunderland, UK.

Autosomal Dominant Hypocalcaemia (ADH) type 1 is caused by activating mutations of the calcium-sensing receptor (CaSR) gene. Although a rare condition, the exact prevalence is uncertain as patients are asymptomatic and, historically, were sometimes diagnosed with hypoparathyroidism (HPT) due insensitivity of earlier PTH assays and failure to check urinary calcium. The consequences of an erroneous diagnosis of HPT in patients with ADH can be profound, as treatment with calcium salts or activated vitamin D characteristically result in more severe hypercalciuria and nephrocalcinosis. A 28-year-old female was referred with hypocalcaemia, extreme tiredness and generalised muscle aches that persisted despite correction of hypovitaminosis D. She had no paresthesia symptoms of tetany or muscle spasms, but suffered from intermittent restless legs at night. There was no history of recurrent urinary tract infections or kidney disease. She had a normal childhood with no significant past medical history. There were no significant medical or genetic conditions in the family, except for type II diabetes. She gave birth to a healthy girl 5 years ago with no complications. She had gastric banding for obesity a year ago and recovered well from the surgery with no complications. She is not on regular medications. On examination, she was clinically euthyroid, with positive Chvostek's but negative Trousseau's signs. Other systems were unremarkable. Height was 1.69 m. Her kidney ultrasound showed no renal calculi. Genetic analysis of the patient identified a heterozygous autosomal dominant CASR variant: c.2497G > T (p.Val833Phe) diagnosing her with Autosomal Dominant Hypocalcaemia Type 1 (ADH). This gene variant has not been identified in the gnomAD population database yet. In conclusion, hypocalcaemia needs to be investigated as we now have better assays to detect low normal PTH levels. Misdiagnosing ADH type 1 with hypocalcaemia or HPT increases the risk of nephrocalcinosis and hypercalciuria in those patients.

Laboratory analysis (Table 1):

Parameter	Results	Normal Range
Corrected calcium level	1.92 mmol/l	2.20–2.60 mmol/l
Magnesium	0.81 mmol/l	0.7–1.20 mmol/l
Phosphate	1.45 mmol/l	0.80–1.50 mmol/l
Alkaline phosphatase	81 u/l	30–130 u/l
Potassium	5.1 mmol/l	3.50–5.30 mmol/l
Creatinine	104 umol/l	45–85 umol/l
Vitamin D	57.6 ng/l	
TSH:	1.00 mIU/l	0.30–4.50 mIU/l
Calcium Fractional Excretion	1.38%	
Urinary Calcium/Creatinine	0.22 mmol/umol	
PTH	4.1 pmol	1.10–6.90 pmol
Tissue transglutaminase antibody	Negative	

DOI: 10.1530/endoabs.81.EP145

EP146

Quality of life in chronic hypoparathyroidism on conventional treatment

Nikolay Gins[1], Alina Elfimova[2], Elena Kovaleva[2], Anna Eremkina[2] & Natalia Mokrysheva[3]
[1]Endocrinology Research Centre, Department of Epidemiology of Endocrinopathy, Moscow, Russian Federation; [2]Endocrinology Research Centre, Department of Parathyroid Disorders, Moscow, Russian Federation; [3]Endocrinology Research Centre, Director, Moscow, Russian Federation.

Introduction
Reduced health-related quality of life (HRQoL) is common in patients with hypoparathyroidism (HypoPT) treated conventionally with calcium and active vitamin D supplements.
Aim
we studied the HRQoL in patients with chronic HypoPT estimated with the 36-Item Short-Form Health Survey (SF-36) and multidimensional fatigue inventory (MFI-20).
Methods
64 patients with chronic HypoPT (women/men – 57/7, median age 47[36;59] years) participated in the study. The median duration of the disease was 4 years [3;9]. SF-36 is a 36-item QOL questionnaire with response alternative scores 1–6 for each item. A scoring algorithm transforms the raw score to a score from 0 to 100, where a high score indicates better HRQoL. MFI-20 has an even proportion of positively and negatively worded items that are rated on a 5-point Likert scale. Subscale scores are calculated as the sum of item ratings and a total fatigue score – as the sum of subscale scores. Higher scores indicate a higher level of fatigue.
Results
we didn't find any associations between the SF-36 and MFI-20 scores of and serum calcium levels. However, HypoPT patients with magnesium (Mg) level under 0,7 mmol/l had significantly higher SF-36 scores such as PF ($P = 0.0131$); BP ($P = 0.0034$); RE ($P = 0.0376$); PH ($P = 0.0042$). We found a negative correlation between the number of tablets and SF-36 PF score ($P = 0.0133$; $r = -0.31$). Median of tablets' number in patients with Mg < 0.7 mmol/l is 6[5;10] vs median of tablets' number 7[5;10] in patients with Mg ≥ 0.7 mmol/l. But the difference isn't significant. Duration of HypoPT had a positive correlation with SF-36 scores VT($P = 0.0083$; $r = 0.33$), MH($P = 0.2594$; $r = 0.04$) and negative correlations with some MFI-20 scores – general fatigue ($P = 0.015$; $r = -0.31$), reduced activity ($P = 0.0336$; $r = -0.27$) and reduced motivation ($P = 0.0088$; $r = -0.33$). These results may be related to the phenomenon of adaptation to chronic diseases such as HypoPT. In general, the presence of HypoPT complications had a positive correlation with SF-36 scores VT($P = 0.0496$; $r = 0.25$), SF($P = 0.0013$; $r = 0.39$) and negative correlation with reduced activity ($P = 0.0204$; $r = -0.29$). These results also can be explained by better examination and thus better awareness in patients with chronic HypoPT, especially if they already have at least one complication.
Conclusion
further studies with better instruments for assessing HRQoL are required. Patients with HypoPT often can use a lot of medications and should follow the strict rules of their taking, which can significantly affect the HRQoL. Of course, doctors want to improve all mineral disturbances, but therapy should be personalized and clearly discussed with the patients.

DOI: 10.1530/endoabs.81.EP146

EP147

25-hydroxyvitamin D, parathyroid hormone and bone turnover markers in patients with addison disease

Dhoha Ben Salah, Khouloud Boujelben[1], Abdelmouhaymen MISSAOUI[1], Mouna Elleuch[1], Mnif Fatma[1], Mouna Mnif[1], Nadia Charfi[1], NABILA REKIK MAJDOUB[1], Faten Haj Kacem Akid[1] & Mohamed Abid
Hedi Chaker Hospital, Department of Endocrinology, Diabetology, Sfax, Tunisia.

Introduction
Patients with Addison disease require lifelong glucocorticoid replacement treatment and it is recommended that glucocortiocoid therapy should be monitored in these patients to avoid over replacement and minimize long-term consequences of bone loss. The present study was carried out with the aim of evaluating bone turnover markers in patients with Addison disease.
Patients and methods
A cross sectional study including 50 patients who are followed for Addison disease, at the department of Endocrinology at Hedi Chaker hospital, sfax-Tunisia. Biochemical markers of bone metabolism (calcium, phosphorus, alkaline phosphatases, vitamin D and parathyroid hormone (PTH)) were measured and the average values were retrospectively analyzed.
Results
There were 40 females and 10 males. The average age of patients was 49,5 ± 13,9 years (18–78 years). The majority (70%) were aged between 40 and 50 years old. Average duration of the disease was 13,9 ± 8,7 years (5–35 years). Approximately 42,5% of females were menopausal. Two-thirds (66%) of patients were not physically active. All patients took no calcium oral supplementation nor oestrogen replacement. Only four patients received Vitamin D oral supplementation. Mean serum levels of calcium and phosphorus were 2,29 ± 0,13 mmol/l (1,9–2,55 mmol/l) and 1,10 ± 0,18 mmol/l (0,8–1,66 mmol/l),respectively. Hypocalcemia was observed in 9 (18%) patients after a mean duration of Addison disease of 11,9 ± 7,1 years (4–26 years) and a mean cumulative hydrocortisone dose of 317,7 ± 211,7 mg (75–702 mg). No significant statistically differences were found between hypocalcemia with regard to age, duration of glucocorticoid replacement or glucocorticoid dose. Mean alkaline phosphatase was 77,2 ± 28,5 IU/l (15–190 IU/l). Patients presenting an increased alkaline phosphatase level (18%) received higher cumulative hydrocortisone dose but without statistical difference (413,4 ± 348 mg versus 365,5 ± 271 mg; $P = 0,7$). Mean vitamin D level was 22,28 ± 14,14 ng/ml (5,6–78,6 ng/ml).Hypovitaminosis D was observed in 33 (66%) patients. Mean PTH level was 51,79 ± 23,84 pg/ml (16,36–139 pg/ml).An elevated PTH level was observed in 10 (20%) patients who had all vitamin D deficiency.
Conclusion
Long-term glucocorticoid replacement therapy in patients with Addison disease is associated with an increased risk of fractures and osteoporosis, which is not only identified by bone mineral density. Other markers as bone turnover markers may be useful. Markers of bone resorption seem to be higher in patients with Addison disease, particularly those who present hypovitaminosis D.

DOI: 10.1530/endoabs.81.EP147

EP148

Pregnancy and lactation induced osteoporosis – a social media based survey

Naama Peltz-sinvani[1,2], Sophia Ish-Shalom[3], Iris Vered[1,2] & Liana Tripto-Shkolnik[1,2]
[1]Sheba Medical Center, Division of Endocrinology, Diabetes and Metabolism, Ramat Gan, Israel; [2]Sackler School of Medicine, Tel Aviv University, Tel Aviv-Yafo, Israel; [3]Elisha Hospital, Haifa, Israel.

Background
Pregnancy and lactation induced osteoporosis (PLO) presenting as spinal fractures in late pregnancy or early postpartum period is a rare condition. The risk factors and pathophysiology are still incompletely understood. The impact of the disorder on the young mother's quality of life can be profound, further aggravated by a delay in diagnosis and treatment that often occurs.
Aim
To delineate clinical parameters related to fractures in a group of women with PLO, and to compare risk factors and osteoporosis-related quality of life with a control group.
Methods
Participants of a social media (WhatsApp) group for women with PLO were offered a questionnaire, including a specific osteoporosis-related quality of life section (MINI OQLQ). Mothers of young children in parent WhatsApp groups were approached to serve as a random control.
Results
Twenty-four patients with PLO and 43 healthy controls (36.9 ± 4.8 vs 38.8 ± 4.3 y.o, $P = 0.11$) were included in the study. Fifty percent of patients suffered from fractures of more than 5 vertebrae, 25% of 4 and 25% had 3 or less vertebrae involved, 85.7% of the fractures were a-traumatic. Nineteen percent of the fractures occurred during pregnancy and others, during early postpartum period. Diagnosis was delayed for more than 16 weeks in 41.8% of women. Bone mineral density test was performed in all participants in the PLO group and 62.5% were treated with teriparatide. A significantly lower proportion of women in the PLO group engaged in physical activity over 2 h/week during pregnancy (37.5 vs. 86.3%, $P < 0.05$) and more PLO patients were treated with low-molecular-weight-heparin during pregnancy, although the difference was of borderline significance ($P = 0.06$). No difference was observed in smoking, periods of amenorrhea, lactation, or family history of fractures between the groups. Seventy-one percent of the PLO patients expressed fear of fractures and 58.3% fear of falls compared to none and 2.3%, respectively ($P < 0.01$) of the controls.
Conclusions
PLO-related spinal fractures involve multiple vertebrae in the majority of the affected women, and the diagnosis is delayed in many. Less physical activity might pose a risk. Most of PLO patients in our cohort were treated with teriparatide. PLO patients reported a significant impairment of quality of life. Multidisciplinary effort should be exerted to early identification and treatment of this severe condition.

DOI: 10.1530/endoabs.81.EP148

EP149

Bone mineral density in patients with addison disease versus congenital adrenal hyperplasia

Mariana Lavrador, Bárbara Filipa Araújo, Ana Carreira, Sandra Paiva, Luísa Barros & Isabel Paiva
Centro Hospitalar e Universitário de Coimbra, Endocrinology, Coimbra, Portugal.

Introduction
The treatment of Primary Adrenal Insufficiency involves the chronic use of glucocorticoids. The balance between the dose needed to supply the cortisol deficit and the possible consequences of overtreatment is a challenge. In patients with Addison disease (AD), androgens deficiency is an additional factor for osteoporosis.
Objective
To evaluate if there are differences in bone mineral density (BMD) in patients with Addison's disease versus congenital adrenal hyperplasia (CAH) – classic form.
Methods
We included patients with a diagnosis of Addison's disease or CAH, with follow-up in a tertiary center. Patient's characteristics and cumulative doses of glucocorticoid (in hydrocortisone converted doses) were recorded and calculated by body surface area (HC/BSA). BMD was evaluated by dual-energy X-ray absorptiometry (DXA), at lumbar spine, femoral neck, and distal radius. Excluded patients with secondary causes of osteoporosis.
Results
27 patients were included: 16 with AD and 11 with CAH. Sex and age distribution were similar between groups. Patients with Addison had a lower BMI (26.34 ± 4.17 vs 31.47 ± 6.4, $P = 0.030$), and shorter disease duration (17,75 ± 12.27 vs 31.63 ± 11.47, $P = 0.007$). Daily doses of HC/BSA were similar between groups (15.91 ± 4.48 for AD vs 11.22 ± 4.17, $P = 0.061$), but cumulative yearly doses of HC/BSA were higher in patients with Addison (5672 ± 1621 vs 3480 ± 1885, $P = 0.027$). Lumbar T-score was significantly inferior in patients with Addison (−2.00 ± 1.20, vs −0.69 ± 0.93, $P = 0.022$), with no differences in femoral or radius T-score between groups. There was a non-significant correlation between lumbar T-score and cumulative yearly doses of HC/BSA ($r = -0.321$, $P = 0.208$).
Conclusion
The significantly difference found in lumbar T-score between AD and CAH my be explained by the higher cumulative yearly dose of HC/BSA of the AD group which is associated to high risk of BMD reduction. Also, the AD group had lower BMI, which is known to be a protective factor against bone mineral loss. Androgen deficiency, typical of Addison disease, is also a reasonable explanation for this discrepancy, since androgens are known to increase bone formation markers.

DOI: 10.1530/endoabs.81.EP149

EP150

SuperJump training in eumenorrheic women and gut peptides: a randomized controlled study about the mechanism of action on bone and glucose homeostasis

Alessandra Amato[1], Sonya Vasto[2], Patrizia Proia[1] & Sara Baldassano[2,3]
[1]University of Palermo, Department of Psychology, Educational Science and Human Movement, Palermo, Italy; [2]Università degli Studi di Palermo, Department of Biological, Chemical and Pharmaceutical Sciences and Technologies, Palermo, Italy; [3]Edificio 16 – Aula S1, Department of Biological, Chemical and Pharmaceutical Sciences and Technologies, Palermo, Italy.

The role played by physical activity in promoting bone health is now widely recognized. Physical activity limits and slows down the physiological demineralization that occurs over the years and plays an important role in the prevention of osteoporosis. SuperJump, a high-impact training activity performed on a mini-trampoline characterized by alternating between aerobic and anaerobic exercises, has been shown to be able to generate a substantial osteogenic response and increase bone balance and strength in eumenorrheic women. In this study it was analyzed whether gastrointestinal peptides play a role in the regulation of bone metabolism and their impact on glucose homeostasis.

Methods

Using a randomized controlled study design, participants were assigned either to the intervention group performing SuperJump activity for 20 weeks or to the control group, that did not undertake any intervention. Blood samples were collected at baseline and at the end of the study and compared within and between the groups for markers of bone metabolism (CTX, osteocalcin, PTH, Vitamin D, albumin adjusted calcium) gut peptides (GLP-1, GIP, GLP-2, PYY, ghrelin) markers of glucose metabolism (glucose, insulin, insulin resistance, β-cell function, insulin sensitivity).

Results

After 20 weeks of SuperJump activity, CTX and PTH was reduced, GLP-1 and GIP levels were significantly increased while levels of GLP-2, PYY and ghrelin did not change. Moreover, SuperJump activity significantly reduced fasting insulin, glucose, insulin resistance and increased insulin sensitivity but did not affect beta cell function.

Conclusion

The results of the study show that 20 weeks of SuperJump was highly effective in improving bone and glucose homeostasis in eumenorrheic women and suggests that GLP-1, and GIP are involved in the mechanism of action.

DOI: 10.1530/endoabs.81.EP150

EP151

Sex differences of the reaction of undercarboxylated osteocalcin to hypoglycaemia

Hana Pospisilova, Michaela Duškova, Lucie Kolátorová, Hana Jandíková & Luboslav Stárka
Institute of Endocrinology, Prague, Czech Republic.

In recent years, there has been increasing evidence for the hypothesis of bones as endocrine organs. Osteocalcin, long considered just a marker of new bone formation, is now seen as the first hormone produced by bones, and seems to be associated with regulating glucose metabolism and reproduction. The aim of this work was to monitor changes of osteocalcin in reaction to hypoglycaemia, and determine if there are differences in such reactions between the sexes. The study included 61 healthy probands with physiological calciophosphate metabolism (30 men and 31 women). We applied to each of them an insulin tolerance test, and then monitored levels of undercarboxylated osteocalcin and reactions to hypoglycaemia at regular time intervals. We found differences in the reaction to hypoglycaemia between the sexes. In men there was a significant decline in undercarboxylated osteocalcin between the 30 and 40 min ($P < 0.0015$), which reflects a reaction to a glycemic decline between 25 and 30 min, followed by reversal. Low undercarboxylated osteocalcin in men lasted up to 90 min, after which they returned to levels before the test. In women we did not find any significant changes in undercarboxylated osteocalcin levels. Changes in undercarboxylated osteocalcin induced by hypoglycaemia indicate a relationship between bones and glucose metabolism. There was an interesting difference between the sexes. However, a definitive conclusion about the role of osteocalcin in human metabolism will require numerous future studies. Acknowledgements: This study was supported by the Ministry of Health of the Czech Republic (MZ ČR – RVO; Endokrinologický ústav – EÚ, 00023761).

DOI: 10.1530/endoabs.81.EP151

EP152

Teriparatide for hypoparathyroidism after bariatric surgery

Ettore Maggio[1], Cesare Morgante[2], Vittoria Ramunno[2], Andrea Corsello[2], Gianluca Cera[2], Alfredo Pontecorvi[2] & Salvatore Maria Corsello[2,3]
[1]Fondazione Policlinico Universitario Agostino Gemelli IRCCS Università Cattolica del Sacro Cuore, Unit of Endocrinology and Diabetes, Rome, Italy; [1]Fondazione Policlinico Universitario Agostino Gemelli IRCCS Università Cattolica del Sacro Cuore, Unit of Endocrinology and Diabetes, Rome, Italy; [3]Saint Camillus International University of Health Sciences, UniCamillus, Rome, Italy.

Background

Hypoparathyroidism is an endocrine disorder characterized by hypocalcemia due to low levels of parathyroid hormone (PTH). Activated vitamin D (calcitriol) and calcium supplementation may be difficult in patients with malabsorption, as calcium requires an acid environment to dissolve. In this setting, subcutaneous administration of PTH analogues may be effective in reducing the dosage of oral calcium and vitamin D supplementation.

Case report

A 36-year-old woman with a history of sleeve gastrectomy and Single Anastomosis Duodeno-Ileal switch was diagnosed with papillary thyroid carcinoma and referred to total thyroidectomy. After surgery, she presented paresthesia, undetectable PTH, calcium 6.5 mg/dl and TSH was normal, so an oral regimen of calcium carbonate 1 gr tid and calcitriol 0.5 mcg tid was started without resolution. She came several times both to our Endocrinology Unit and to the emergency department due to symptomatic hypocalcemia. Therefore, oral treatment was gradually increased up to calcium carbonate 9 gr and calcitriol 4 mcg per day, and then intravenous calcitriol and calcium gluconate infusion was started. However, this did not allow complete resolution of hypocalcemia and the patient experienced some discomfort mainly due to gastrointestinal symptoms. Symptoms began to worsen after several weeks. At this moment, in Italy, RDNA PTH (1–84) is not refunded by the national health service. For that, after patient's consent, treatment with rhPTH (1–34 – teriparatide) analogue 20 mcg/day was started with no adverse reaction. Soon, we were able to significantly reduce the dosage of calcium carbonate to 2 gr and calcitriol 2.5 mcg/day. After fifty days of this treatment calcium was 8.5 mg/dl. Recently the dose of teriparatide was titrated to 40 mcg/day, with further reduction of oral treatment, and the patient has not had any symptoms related to hypocalcemia.

Conclusion

First-line of treatment in hypoparathyroidism is activated calcitriol and calcium supplementation maintain low-normal calcium levels, to prevent hypocalcemia and avoid hypercalcemia and renal calcification. Gastric bypass or duodenal resection can increase the risk of hypocalcemia, as they cause malabsorption. As alternative options intravenous calcium, calcitriol infusion and rhPTH should be considered to maintain normal calcium levels. Even when the patient is stabilized, episodes of hypocalcemia may occur, so careful monitoring is still required. To date, this is the second reported case of the use of a PTH analogue to treat hypoparathyroidism with good calcium control in a patient who underwent bariatric surgery.

DOI: 10.1530/endoabs.81.EP152

EP153

The parathyroid carcinoma manifesting during pregnancy

Daria Sazonova[1], Ekaterina Bibik[2], Anna Gorbacheva[2], Anna Eremkina[2] & Natalia Mokrysheva[1]
[1]Endocrinology Research Centre, Moscow, Russian Federation; [2]Endocrinology Research Centre, Department of Parathyroid Pathology and Mineral Disorders, Moscow, Russian Federation.

Background

Parathyroid carcinoma (PC) is a rare cause of primary hyperparathyroidism (PHPT) and extremely rare endocrine malignancy during pregnancy. Different maternal and fetal/neonatal complications of PHPT occur in 67 and 80% of untreated cases respectively, probably more due to severe hypercalcemia.The diagnostic and therapeutic approaches are limited in pregnant women and require individual risk-benefit assessment.

Aim

We present a case of PC manifested during pregnancy when delayed treatment led to severe complications.

Clinical case

Young woman suffered from urolithiasis since the age of 19. Moreover, she had a history of multiple low-energy bone fractures of limbs. At the age of 35 lab tests showed high PTH (55,51 pmol/l (NR 1,6–6,9)) and hypercalcemia (total calcium 3,28 mmol/l), US detected a tumor of the left inferior parathyroid gland

33x25x18 mm (PG). So, PHPT was diagnosed at 29 week of gestation. Given severe hypercalcemia and gestational age parathyroidectomy was recommended but the patient refused the surgery as well as cinacalcet therapy. Cesarean section was performed at 38 week of pregnancy without any complications. The woman breastfed for 1,5 years. During this period, the patient had low-energy fractures of left humerus that required osteosynthesis. 2 years after delivery exam showed albumin-adjusted calcium 2.9 mmol/l, PTH 1044 pg/ml (15–65), 24-hours urinary calcium 13.3 mmol. US, CT scan, 99mTc-sestamibi scintigraphy confirmed tumor of the left inferior PG. The patient had bilateral nephrolithiasis, significant BMD reduction (Z-score radius −5.9 S.D.), also osteitis fibrosa cystica and vertebrae fractures (Th8-9,12) were verified. The parathyroidectomy was carried out, PTH and total calcium decreased to 50.1 pg/ml and 2.18 mmol/l respectively on the fifth day after surgery, oral calcium supplementation and alfacalcidol were prescribed. Morphological examination revealed PC, pT1NxM0.

Conclusion

Parathyroidectomy is a preferable treatment for patients with symptomatic PHPT in the second trimester of pregnancy. Severe hypercalcemia accompanied with high PTH and large tumor size are suspicious for PC. Mutation of CDC73 should be examined to assess the prognosis in patients with confirmed PC.

DOI: 10.1530/endoabs.81.EP153

EP154

Clinical outcomes of COVID-19 infection in rare bone and mineral disorders

Ana Luisa Priego Zurita[1], Jillian Bryce[2], Maria-Luisa Brandi[3], Simona Glasberg[4], Alberto M Pereira[1], Luca Sangiorgi[5], Camilla Schalin-Jantti[6], Erica van den Akker[7], Faisal Ahmed[1,2,8] & Natasha Appelman-Dijkstra[1]

[1]Leiden University Medical Centre, Department of Medicine, Division of Endocrinology, Leiden, Netherlands; [2]University of Glasgow, Office for rare Conditions, Glasgow, UK; [3]Fondazione Italiana Ricerca Sulle Malattie Dell'Osso (F.I.R.M.O. Foundation), Florence, Italy; [4]Hebrew University, Neuroendocrine Unit, Enets Center of Excellence, Department of Endocrinology and Metabolism, Hadassah Medical Organization and Faculty of Medicine, Jerusalem, Israel; [5]Irccs Istituto Ortopedico Rizzoli, Department of Rare Skeletal Disorders, Bologna, Italy; [6]University of Helsinki and Helsinki University Hospital, Division of Endocrinology, Abdominal Center, Helsinki, Finland; [7]Erasmus Mc – Sophia Children's Hospital, University Medical center Rotterdam,, Division of Pediatric Endocrinology, Department 0f Pediatrics, Rotterdam, Netherlands; [8]University of glasgow, Developmental Endocrinology Research Group, Royal Hospital for Children, Glasgow, UK.

Background

The European Registries for Rare Endocrine Conditions and the European Registries for Rare Bone and Mineral Conditions were created in collaboration with the European Reference Networks for Rare Endocrine and Bone Disorders (Endo-ERN and ERN BOND). Following the onset of the COVID-19 pandemic in 2020, the registries, together with the ESE RD Committee, have collected the occurrence of confirmed and suspected cases of COVID-19 in patients with rare endocrine and bone conditions via the electronic reporting system (e-REC), a tool that does not collect personal identifiable information.

Aim

To collect clinical outcome data of patients with rare bone and mineral disorders affected by COVID-19.

Methods

Between May 2020 and May 2021, 11 cases of COVID-19 in patients with a preexisting mineral condition and 8 in patients with a preexisting bone condition were reported. Reporters were invited to complete a secure online questionnaire. The questionnaire was completed in 15/19 cases (79%) from four centres in three countries. Of 19 cases, 18(95%) were confirmed by a test. Vaccination status was reported only for one case of mineral conditions (1/19), who had received the vaccine.

Results

Of 7 mineral cases, 3 had hypophosphatemia (42%), 3 hypoparathyroidism (42%) and 1 primary hyperparathyroidism (14%). The median age at the time of infection was 39 (range 4,52). Of 7 cases 6 were confirmed by a test (86%). The most prevalent symptoms were fever 5/7 (71%), cough 3/7 (43%), fatigue 3/7 (43%), loss of taste and smell 3/7 (43%), muscle pain 3/7 (43%), runny nose 2/7 (28%), headache 2/7 (28%) and shortness of breath 2/7 (28%). One patient was asymptomatic. Comorbidities were reported in 4/7 (57%): hypertension 2/7 (28%), obesity 1/7 (14%), asthma 1/7 (14%). None required hospital admission and complete remission occurred in all cases. Of 8 bone cases 5 had fibrous dysplasia of bone (62%), 2/8 (25%) had a bone dysplasia with increased bone density and 1/7 (13%) had osteogenesis imperfecta. The median age at the time of the COVID-19 infection was 35 (range 16,69). The most prevalent symptoms were cough 6/8 (75%), fever 4/8 (50%), and shortness of breath 2/8 (25%). Two patients were asymptomatic (25%). Comorbidities were reported in 3/8 (38%): obesity 2/7 (25%) and asthma 1/8 (13%). None required hospital admission and complete remission occurred in 100% of cases.

Conclusion

The results of this survey suggest good clinical outcomes in patients with rare bone and mineral disorders experiencing a COVID-19 infection.

DOI: 10.1530/endoabs.81.EP154

EP155

Prevalence of anemia in patients with primary hyperparathyroidism: a single-center observational study

Anna Gorbacheva, Anastasia Miliutina, Alina Elfimova, Anna Eremkina & Natalia Mokrysheva

Endocrinology Research Center, Moscow, Russian Federation.

Background

The combination of primary hyperparathyroidism (PHPT) with anemia was first described in 1931. It remains unclear whether PHPT is the direct cause of anemia, or it develops as a PHPT's complication. The etiology of anemia in PHPT could be multifactorial, including iron deficiency, renal failure as well as bone marrow fibrosis.

Aim

To assess the prevalence of anemia in patients with PHPT admitted to the Department of Parathyroid Glands Pathology of the Endocrinology Research Centre from January 2017 to August 2020.

Materials and Methods

The study included patients with PHPT over 18 years old. A single-center observational one-stage one-sample uncontrolled study was carried out. We analyzed laboratory and instrumental data obtained during inpatient examination in accordance with the standards of medical care. Statistical analysis was performed using Statistica 13 (StatSoft, USA) and SPSS (IBM, USA) software.

Results

The study included 327 patients with PHPT, 28(9%) men and 299(91%) women. The median age was 59 years [51;66]. 26 patients (8%) with anemia were identified. Significant differences between patients with and without anemia were found only in the GFR. Comparison of patients with and without anemia didn't reveal any significant differences in the incidence of PHPT's complications. Significant differences in serum hemoglobin concentration and average hemoglobin concentration in erythrocytes were revealed between patients with and without vertebrae fractures. In the group of patients without compression fractures these parameters were higher ($p < 0.001$ for both). In the subgroup of patients with total calcium >3 mmol/l and iPTH >3 normal values, the incidence of anemia reached 21% (95% CI: 10%;35%). Within this subgroup we revealed tendencies to higher levels of iPTH, ionized calcium and osteocalcin in patients with anemia.

Conclusion

We did not find any correlations between hypercalcemia, iPTH levels and the presence of anemia in the general group. However, in the subgroup of patients with severe hypercalcemia, there was a relationship between the iPTH, ionized calcium and the incidence of anemia. In patients with PHPT and vertebral fractures, significantly lower concentrations of blood hemoglobin and hemoglobin in erythrocytes were observed.

DOI: 10.1530/endoabs.81.EP155

EP156

Late diagnosis of life-threatening hypocalcemia in a patient with hypoparathyroidism after hemithyroidectomy: A case report

Sona Maghakyan[1], Anna Vardanyan[1], Ara Ghazaryan[2] & Elena Aghajanova[3,4]

[1]Yerevan State Medical University, Endocrinology, Yerevan, Armenia; [2]Mikaelyan Institute of Surgery, Medical Director, Yerevan, Armenia; [3]Yerevan State Medical University, Head of YSMU Department of Endocrinology; [4]Muratsan University Hospital, Head of Endocrinology Clinic of "Muratsan" University Hospital Complex, Armenia.

Introduction

Hypocalcemia is defined as a decreased level of calcium in the blood. The presentation of hypocalcemia varies widely, from asymptomatic to life-threatening. The most common cause of chronic hypocalcemia is postsurgical hypoparathyroidism. This may occur after removal of all parathyroid tissue

during thyroidectomy and radical neck dissection for malignancies or after inadvertent interruption of the blood supply to the parathyroid glands during head and neck surgery. Here we report the case of an elderly patient with hypoparathyroidism after hemithyroidectomy who developed clinical manifestations of severe hypocalcemia and her life was saved through a tracheostomy.
Case Presentation
A 72-year-old woman was admitted to Mikaelyan University hospital with shortness of breath. She spoke with difficulty, in syllables. The patient's general condition was extremely heavy and she was admitted in ICU department. She had a history of hemithyroidectomy 30 years ago. The patient had a disorder of consciousness, perioral paresthesia and tingling of the fingers during these years. For this, she was started treatment with calcium 1–3 g/daily, vitamin D3 5000U daily for 10 years and L-thyroxin 25 mcg for 5 years. She had a history of acute respiratory infection 1 month before admission. On admission, examination revealed Ps = 122 bpm, BP = 160/85 mmHg, T = 36.5 °C, SpO_2 95% (15 liter/min O_2+), BMI = 27.5 kg/m^2. Trousseau and Chvostek signs were positive. Electrocardiogram revealed a prolonged QTc interval. The patient received first medical aid with oxygen, dexamethasone, euphyllin. After the results of blood chemistry, which showed low serum corrected calcium level (1.80 mmol/l), calcium gluconate 10% 10 ml IV was added to the treatment. Unfortunately, the patient's condition didn't improved on treatment and she even could not be intubated because of laryngospasm, that's why tracheostomy was performed. Endocrine examinations showed: 25(OH)D-39.66 ng/ml (n 30−70), parathormone-6.54 pg/ml (n 15−65), TSH-0.939 uIU/ml (n 0.3−4.5), FT4-15.07 pg/ml (n 8.9−17.2). She was diagnosed with postoperative hypoparathyroidism. She continued treatment with calcium gluconate, dexamethasone, L-thyroxine and started treatment with calcitriol 0.25 mcg. The patient improved on this treatment; the tracheostomy was removed after 2 weeks. She was discharged in good general health condition and was advised to continue L-thyroxine, calcitriol therapy with the same dose, calcium 1 g/daily and check serum corrected calcium level in 1 week.
Conclusion
This case report showed that severe hypoparathyroidism can develop even after hemithyroidectomy and lead to life-threatening hypocalcemia requiring emergency procedures. Screening programs for patients with thyroidectomy could help to prevent these life-threatening complications.

DOI: 10.1530/endoabs.81.EP156

EP157

Vitamin D and bone metabolism in Graves' disease. A prospective study

Selwan Khamisi[1], Martin Lundquist[2], Annica Rasmusson[3], Britt Eden Engstrom[2], F Anders Karlsson[2] & Östen Ljunggren[2]
[1]Uppsala University Hospital, Uppsala, Sweden, Department of Endocrinology and Diabetes, Uppsala, Sweden; [2]Akademiska Sjukhuset, Sweden; [3]Institutionen för Medicinska Vetenskaper, Sweden.

Objective
Vitamin D and osteoporosis in Graves' disease (GD) have previously been examined in cross-sectional studies with partly divergent results. Here, we prospectively studied vitamin D metabolism and bone health in patients with newly diagnosed GD.
Methods
Thirty consecutive patients with *de novo* overt thyrotoxicosis diagnosed with GD were included. None of the patients at diagnosis were treated with vitamin D supplementation or anti osteoporotic drugs. All patients were initially treated with antithyroid drugs. Blood samplings were performed at baseline and at 6 weeks, 3, 6, 12 and 24 months after treatment start. Serum levels of 25OHD3, 1,25OH2D3, calcium, parathyroid hormone (PTH), and C-terminal telopeptides of Type I collagen (CTX-I) were analyzed. Bone mineral density (BMD) was measured at baseline, and after one and two years after treatment initiation.
Results
At diagnosis patients with GD did not have vitamin D deficiency. There were no significant correlations between levels of 25OHD3 and thyrotoxicosis. Upon treatment of the thyrotoxicosis, serum calcium transiently fell, and PTH and 1,25OH2D3 increased. 25OHD3 fell within the normal range and stabilized at 6 months. CTX-I fell over 12 months, BMD increased significantly up to 2 years, $P = 0.002$, < 0.001 and 0.005 in spine, left total hip and left femoral neck respectively.
Conclusion
The present data underline that thyrotoxicosis negatively impacts bone health and demonstrate fine-tuned dynamics in bone and vitamin D metabolism. Upon treatment, bone health improved over a follow-up period of 24 months despite rising PTH. Increased conversion of 25OHD3 to 1,25OH2D3 occur during treatment of GD.

DOI: 10.1530/endoabs.81.EP157

EP158

Milk-alkali syndrome in a patient with chronic hypoparathyroidism

Catarina Cidade-Rodrigues, Catarina Chaves, Filipe Cunha, Mariana Martinho & Margarida Almeida
Centro Hospitalar do Tamega e Sousa, Endocrinology, Penafiel, Portugal.

Introduction
Milk-alkali syndrome is defined by the triad hypercalcemia, metabolic alkalosis and renal impairment, due to intake of calcium salts and absorbable alkali. It is the 3rd leading cause of hypercalcemia but often underdiagnosed. Patients with chronic hypoparathyroidism after total thyroidectomy have increased risk for this potentially life-threatening complication and its epidemiology is unclear. We present a case of milk-alkali syndrome in a patient with chronic hypoparathyroidism.
Case report
Female, 60 years-old. Chronic hypoparathyroidism and hypothyroidism after total thyroidectomy due to non-toxic multinodular goiter 2 years ago. Rheumatoid arthritis, chronic kidney disease and inferior limb deep vein thrombosis. Brown-Sequard syndrome 1 year ago due to cervical spine hematoma and submitted to vertebral laminectomy. Medication: levothyroxine 100 ug, calcitriol 0.25 ug id, calcium carbonate/cholecalciferol 1500 mg/400 UI 2id, acenocoumarol, *methotrexate,* and methylprednisolone 4 mg bid. She presented with nausea, vomiting and polydipsia for 4 days. She was dehydrated, BP 139/74 mmHg, HR 78 bpm, SatO2 99% (room air), temperature 36.4°C. Normal cardiopulmonary auscultation. No signs of acute abdomen and no peripheral oedema. Arterial blood gas analysis: pH 7.49, pCO2 59 mmHg, pO2 79 mmHg, HCO3− 38.6 mmol/l, iCa^{2+} 1.70 mmol/l. ECG: 57 bpm. Venous blood analysis: creatinine 2.5 mg/dl, urea 89 mg/dl, sodium 142 mmol/l, potassium 3.1 mmol/l, corrected total calcium 14.4 mg/dl, magnesium 2.3 mg/dl, phosphate 3.7 mg/dl, PTH <4 pg/ml, 25-hidroxicholecalciferol 5 nmol/l, TSH 0.81 uUI/ml, T4L 1.22 ng/dl, CRP 6 mg/dl, leukocyte count 10690/uL. Kidney ultrasound: non-obstructive bilateral echogenic foci. She was diagnosed with milk-alkali syndrome. Calcium and vitamin D supplements were suspended and started treatment with intravenous isotonic saline and potassium chloride, maintaining a good urine output. Calcium and creatinine levels improved progressively. Calcium carbonate/cholecalciferol 1500 mg/400 UI 2id and calcitriol 0.25 ug one every other day were restarted and she was discharged 4 days after. At the follow-up, she was asymptomatic with a corrected total calcium 8.7 mg/dl, phosphate 4.0 mg/dl and creatinine 1.37 mg/dl.
Discussion
In people exposed to large doses of calcium and alkali, normal kidney function and calcitriol suppression help maintain calcium and acid–base balance. However, once hypercalcemia develops, it perpetuates metabolic alkalosis, which itself decreases renal calcium excretion. Risk factors are older-age, chronic kidney disease, pregnancy and medication. Potential triggers are dehydration, volume depletion, infection, diets rich in pH-basic foods and altered medication dose. Our patient had chronic kidney disease, so when exposed to volume depletion and dehydration secondary to vomiting, she was unable to excrete excessive calcium. Additionally, the inability to decrease calcium absorption, due to exogenous calcitriol, in response to increased serum calcium levels might have aggravated hypercalcemia.

DOI: 10.1530/endoabs.81.EP158

EP159

Long term treatment with teriparatide in hypoparathyroidism

Antonio Spada, Daniela Bosco & Assunta Santonati
San Giovanni Addolorata Hospital, Endocrinology, Roma, Italy.

Hypoparathyroidism is, in Italy, an orphan disease because the hormonal replacement therapy is possible only with teriparatide (fragment 1–34 of of human parathyroid hormone). Otherwise the patients use oral calcium and calcitriol. This scheme of therapy obtained correct plasmatic calcium and phosphate levels, correct urinary excretion of calcium and phosphate, adequate quality of life – QoL only in a little percentage of patients. Especially kidney stones, intra-renal calcifications, chronic kidney disease are too frequent during this "conventional" therapy. Recently, Italian Agency of drug approved the use of recombinant human parathyroid hormone (rhPTH) for chronic hypoparathyroidism, but only on payment. Long-term studies on rhPTH(1–84) replacement therapy, up to 6 years, demonstrated prolonged efficacy of this drug, with persistent normal plasmatic and urinary levels of calcium and phosphate, reduced renal complications, high QoL. We have given teriparatide at the started dose of 20 mcg twice, to four hypoparathyroid patients (all women, post-surgical, after an unsuccessful period of "conventional" therapy characterized by frequent accesses in emergency for hypolcalcemic crisis notwithstanding high levels of oral calcium and calcitriol) for six (one patient) or eight years (three patients), monitoring

plasmatic and urinary biochemical levels, renal ultrasounds, femoral and lumbar densitometry, questionnarie for QoL. All patients quickly obtained increased plasmatic calcium levels, despite reduction or interruption of calcium and calcitriol supplementation; no one had hypocalcemic crisis: three of them normalized plasmatic calcium levels and one had to stop teriparatide for hypercalcaemia. One patient had persistent low values of serum calcium (even though higher than in conventional therapy), but without hypocalcemic crisis and a persistent well-being feeling. Plasmatic phosphate levels decreased up to normal, as urinary excretion of calcium and phosphate. No other biochemical parameter was significantly modified. No patient developed urinary complications. No-one is in therapy with bone active drugs for osteoporosis. We also administered, at baseline, at 6 and 24 months and at the end of study, the RAND 36-Item Short Form (SF-36) Health Survey, covering eight domains of physical and mental health, to evaluate their perception of QoL before and during therapy with teriparatide. Data showed a significant improvement in the mean scores of all eight domains, especially during the first two years of therapy. We can conclude that the treatment with teriparatide in post-surgical hypoparathyroidism is effective and safe in improving mental and physical health of patients, also in a prolonged period of therapy.

DOI: 10.1530/endoabs.81.EP159

EP160

Clinical evidence for the benefits of burosumab therapy in two adult cases of X-Linked Hypophosphatemia

Elisa Dinoi[1], Laura Pierotti[1], Laura Mazoni[1], Simona Borsari[1], Elena Pardi[1], Filomena Cetani[2] & Claudio Marcocci[1]
[1]University of Pisa, Department of Clinical and Experimental Medicine, Pisa, Italy; [2]University Hospital of Pisa, Endocrine 2 Unit, Pisa, Italy.

X-linked hypophosphatemia (XLH), representing about 80% of hypophosphatemic rickets, is an X-linked dominant disease due to inactivating mutations in the *PHEX* gene (located at Xp22.1) resulting in an excessive secretion of the phosphaturic hormone fibroblast growth factor 23 (FGF23). The effects are renal phosphate wasting and reduced active vitamin D synthesis leading to rickets, osteomalacia, bone deformities, odontomalacia, frequent dental abscesses and disproportionate short stature. Conventional therapy, based on phosphate and/or active vitamin D supplementation, heals the active radiological lesions of rickets and improves statural growth but doesn't prevent the clinical manifestations of the disease and is associated to potential side effects such as nephrolithiasis, nephrocalcinosis and hyperparathyroidism. Since 2018 burosumab, a fully humanized monoclonal antibody against FGF-23, has been authorized for patients affected by XLH on the basis of promising results from different clinical trials in adults and children. However, all studies include severely affected patients and very few data on the effects of burosumab in everyday setting are available. We present the response to one-year treatment with burosumab injected subcutaneously at 1 mg/kg every four weeks in two patients belonging to the same family namely patient 1 (mother, aged 54 years) and patient 2 (son, aged 19 years), with a genetically confirmed diagnosis of XLH, due to a splice site mutation in the PHEX gene. Of note, patient 2 was on conventional therapy with oral phosphate and calcitriol which was suspended one week before the beginning of burosumab. Both patients had bone deformities, such as varus knee and scoliosis. Patient 1 had undergone multiple orthopedic interventions during childhood and suffered from limb stiffness and severe arthralgias with functional limitations. Patient 2 was in general good conditions but developed recurrent dental abscesses. In both patients burosumab led to rapid normalization of phosphate levels and increase of tubular reabsorption of phosphate (TRP) and TmP/GFR. Serum PTH and bone alkaline phosphatase (BAP) levels were not significantly modified during treatment. Burosumab was well-tolerated, with overall adverse events of mild severity, such as transient nausea, diarrhea, skin lesions, muscle cramps and arthralgia. In patient 2, only one episode of dental abscess occurred during burosumab treatment. BPI and WOMAC questionnaires, assessing the severity of pain, stiffness and physical functioning respectively, were administrated at each visits showing a great improvement of scores. In conclusion, in our patients burosumab has been proven to be effective and safe allowing a significant improvement in quality of life.

DOI: 10.1530/endoabs.81.EP160

EP161

Abstract Withdrawn

DOI: 10.1530/endoabs.81.EP161

EP162

Hypophosphatemia in patients with primary hyperparathyroidism

Alessandro Amodeo[1], Giorgia Dito[2], Gregorio Guabello[3], Matteo Longhi[3] & Sabrina Corbetta[4]
[1]Endocrinology and Diabetology Service, IRCCS Istituto Ortopedico Galeazzi, Department of of Biotechnology and Translational Medicine, University of Milan, Milan, Italy; [2]Endocrinology and Diabetology Service, IRCCS Istituto Ortopedico Galeazzi, Milan, Italy; [3]Rheumatology Unit, IRCCS Istituto Ortopedico Galeazzi, Milan, Italy.

Osteoporosis management increased determination of serum calcium (Ca) levels, and detection of hypercalcemia in the set of out patients. Serum phosphate (P) levels are less frequently measured in osteometabolic patients. Primary hyperparathyroidism (PHPT) is the most common cause of hypophosphatemia. However, hypophosphatemia receives poor attention during the PHPT diagnostic work up, and also data in literature are scanty. We retrospectively reviewed the clinical records from 3 different series of PHPT patients: a first surgical series (group 1; all patients underwent successful parathyroidectomy), a second series from a Hospital setting with Emergency Department (group 2), and a third series of out-patients referred for osteoporosis management (group 3). In group 1, serum P levels were measured in 74 [13%; 13 males, 61 females; 58.0 (49.0,67.3) years, median (range IQ)] out 567 surgically confirmed PHPT patients, confirming that it is often neglected. Group 2 included 115 PHPT patients, 22 males, 93 females, aged 65.5 (56.0, 74.0) years. Group 3, included 88 PHPT patients, 13 males, 75 females, aged 66.0 (59.0, 75.0) years. Group 1 patients were younger than those in group 2 ($P=0.003$) and group 3 ($P=0.0005$ by ANOVA). Serum phosphate levels were lower in Group 1 patients [2.4 (2.1, 2.8) mg/dl] with respect to levels in Group 2 [2.7 (2.3, 3.0) mg/dl, $P=0.016$] and group 3 [2.7 (2.4, 3.0) mg/dl, $P=009$ by ANOVA] patients. Considering the whole series of 277 patients, hypophosphatemia (<3.0 mg/dl) was detected in 209 (75%) patients. Serum P levels were lower in males than females. Hypophosphatemia was mild (2.1–3.0 mg/dl) in 171 patients (62%), moderate (2.0–1.1 mg/dl) in 37 (13%), while severe hypophosphatemia (<1.0 mg/dl) was not registered in any patients. As expected, hypophosphatemic PHPT patients showed lower serum total calcium, higher PTH levels, than normophosphatemic patients. Any difference in age, serum creatinine levels, ionized calcium levels, serum 25hydroxyvitamin D (25OHD), 24 h urine calcium excretion corrected for body weight, prevalence of kidney stones, bone mineral density at lumbar and femur sites as well as number of fragility fractures could be detected. Indeed, a positive correlation emerged between serum 25OHD and P levels ($r=0.176$, $P=0.015$ by Spearman correlation). In conclusions, our data supported recently published data on hypophosphatemia in PHPT patients, confirming the relationship with a more severe PHPT phenotype. Determination of serum P levels concomitantly with serum calcium, PTH, 25OHD, and creatinine helps clinicians in the diagnosis of PHPT and in estimation of its severity.

DOI: 10.1530/endoabs.81.EP162

EP163

Primary hyperparathyroidism: what is the impact on bone ?

Lamiae Zarraa, Soumiya Berrabeh, Yousra Laalaoua, Siham ROUF & Hanane Latrech
Endocrinology-Diabetology and Nutrition Department Chu Mohamed VI, Laboratory of Epidemiology, Clinical Research and Public Health, Faculty of Medicine and Pharmacy Mohammed Premier University Oujda, Oujda, Morocco.

Key words: Primary hyperparathyroidism-PTH level –osteoporosis-osteolytic bone lesions-brown tumor

Introduction

Primary hyperparathyroidism is a frequent pathology responsible for an alteration of the phosphocalcic metabolism at the origin of numerous complications, in particular osseous. The objective of this work is to evaluate the bone impact of primary hyperparathyroidism in our series.

Matériel et méthodes

Retrospective descriptive and analytical study, including 44 patients followed for primary hyperparathyroidism over a period spanning 6 years from 2015 to 2021. Data were collected from medical records and analyzed by SPSS-V21 software.

Material and methods

The mean age was 55 ± 11 years, with a clear female predominance with a sex ratio M/F = 0.29 which 80% of the women were menopausal. Eighty-one percent of the cases had hypercalcemia with 36% of the cases presenting with malignant hypercalcemia.The assessment of the bone consequences of primary hyperparathyroidism showed osteoporosis in 58.6% of the cases with osteopenia in 24%. A pathological fracture revealed primary hyperparathyroidism in one case or in

2.3% of cases. The bone CT scan showed osteolytic bone lesions in 51.5% of the cases, the most of them were diffuse, brown tumors in 18.2% of the cases, most often of multiple locations, affecting the maxillomandibular region, pelvis (iliac bone and ischium), scapula and femoral neck respectively. Primary hyperpathyroidism was complicated by fibrocystic osteitis in one case, i.e. 2.3% of our series. Vitamin D deficiency was noted in all patients, with a deficiency in 61.4% of cases. six point eight percent of cases in our series ($n=3$) were complicated by Hungry bone syndrome and 3 cases (6.8%) by definitive hypoparathyroidism. The relationship between the level of bio-intact PTH 1–84 and the occurrence of bone complications found: a statically significant association with the occurrence of brown tumor and osteolytic bone lesions and with Hungry bone syndrome, while no statically significant correlation with osteoporosis and bio-intact PTH 1–84 level.
Discussion–conclusion
Although primary hyperparathyroidism is a benign endocrinopathy, it remains a serious condition because of its complications, particularly bone complications, as shown by the results of our work in our series, which is in agreement with the literature. Early and adequate management can improve the prognosis of its complications.

DOI: 10.1530/endoabs.81.EP163

EP164

The clinical presentation of primary hyperparathyroidism during the Covid-19 pandemic

Elena Castellano, Giorgio Borretta, Micaela Pellegrino, Francesco Tassone, Andrea Craparo, Claudia Baffoni & Laura Gianotti
Santa Croce and Carle Hospital, Department of Endocrinology, Diabetes and Metabolism, Cuneo, Italy.

Background
In the last decades, the clinical profile of PHPT in Western Countries has changed from a highly symptomatic to a largely asymptomatic disease. However, a substantial stability in its clinical features has been reported in the last two decades. The usual management, including time to diagnosis and treatment, of PHPT during the Covid-19 pandemic has been changed and likely slowed down. Whether further changes in the clinical presentation of PHPT have occurred during the Covid-19 pandemic is currently unknown.
Patients
A retrospective survey was conducted in our series of 150 well-characterized consecutive PHPT patients, who were admitted to our Hospital between January 2012 and December 2021. Patients were initially subdivided according to the date of PHPT diagnosis in 2 consecutive 5-year period ($n=79$ and 71, respectively). The more recent group was then split into 2 subgroups before and after the Covid-19 Pandemic (i.e. 2017–2019, $n=45$; 2020–2021, $n=26$).
Results
In the last five-year period an increased rate of post menopausal women ($P=0.011$) and of patients with osteoporosis at any site ($P=0.007$) was found among PHPT patients compared to those in the previous five-year period. Furthermore a non significant reduction of "mild asymptomatic" patients was observed. After subdividing the last five-year period based on the pandemic, the increased rate of post menopausal women was confirmed in the Covid-19 period compared to the remaining ones ($P=0.022$). In addition, the number of criteria for surgery met by asymptomatic PHPT patients has become statistically higher in the pandemic period than in preceding periods ($P=0.017$).
Conclusions
During the Covid-19 pandemic, when surgery for benign diseases and hospital visits have been restricted, only minor changes in the PHPT clinical presentation have occurred. An increased rate of postmenopausal women with osteoporosis was diagnosed with PHPT.

DOI: 10.1530/endoabs.81.EP164

EP165

Reduced bone mineral density in primary adrenal insufficiency: consequences of long-term treatment

Bárbara Filipa Araújo, Mariana Lavrador, Cátia Araújo, Mafalda Ferreira, Luisa Barros, Sandra Paiva & Isabel Paiva
Centro Hospitalar e Universitário de Coimbra, Endocrinology Department, Portugal.

Introduction
The effects of long-term replacement therapy of primary adrenal insufficiency (PAI) are still a matter of debate. Glucocorticoid (GC) replacement regimens do not completely mimic the endogenous hormonal production and their monitoring is sometimes difficult. Therefore, some patients are exposed to mild GC excess with potential complications, such as hypertension, diabetes, and skeletal fragility. Data on bone mineral density (BMD) in PAI is still scarce and controversial.
Objective
To evaluate the impact of long-term GC treatment on BMD, in patients with PAI.
Methods
We conducted a retrospective cohort study of patients with a diagnosis of PAI, followed-up between 2011 and 2021. Patients with other causes of osteoporosis were excluded. BMD was evaluated by dual-energy X-ray absorptiometry (DXA). Doses of the various glucocorticoids were converted to hydrocortisone (HC) equivalents. We calculated cumulative doses of HC (annual and lifetime), divided by corresponding body area (mg/m2), until the date of DXA.
Results
47 patients with PAI were included, 29 with autoimmune origin (63%), 11 with congenital adrenal hyperplasia (CAH) (23.9%), 4 from tuberculosis (8.7%), 1 from x-ALD and 1 from spontaneous bilateral bleeding (2.2%). Mean age 51.3 ± 14.3 years, 57.5% females, disease duration 24.6 ± 15.5 years. Mean daily HC dose was 16.6 ± 4.3 mg/m^2 and mean cumulative lifetime dose was 154 ± 139 g/m^2. 43 patients were under mineralocorticoid (91.5%). Osteoporosis was present in 35.7% of patients. There was an inverse correlation between cumulative lifetime GC dose and lumbar ($r=-0{,}435$, $P=0{,}030$) or femoral T-scores ($r=-0.437$, $P=0.030$); and between cumulative annual dose and lumbar T-score ($r=-0.458$, $P=0.025$). Patients with osteoporosis (any T-score ≤ -2.5) had a higher cumulative lifetime HC dose ($P=0.027$), and a logistic regression model revealed that this association was independent of sex, PAI etiology, and treatment with mineralocorticoids ($P=0.048$). There was no association between T-score and type of GC replacement. There was a correlation between lumbar T-score and age ($r=-0.460$, $P=0.016$), but there was no relationship between BMD and disease duration.
Conclusion
In this study, there was an inverse linear relationship between glucocorticoid cumulative dose and bone mineral density at lumbar spine, which is in line with the known preferential action of GC on trabecular bone. Mild GC excess for some periods of life may have a greater impact in BMD reduction than disease duration. Our results reinforce the need for close monitoring of GC replacement therapy in patients with PAI.

DOI: 10.1530/endoabs.81.EP165

EP166

Endocrinopaties in thalassemia patients

ÖZGE ÖZER[1], Goknur Yorulmaz[1], Müfide Okay Ozgeyik[2], Hava Usküdar Teke[3] & Eren Gunduz[3,3]
[1]Eskisehir Osmangazi University, Department of Endocrinology and Metabolism, Esogu, Turkey; [2]Eskisehir City Hospital, Department of Hematology, Eskisehir, Turkey; [3]Eskisehir Osmangazi University, Department of Hematology, Eskisehir, Turkey.

Objectives
Disorders concerning the endocrine system may be seen in patients with transfusion-dependent thalassemia major.It is thought that iron accumulated in the organs,especially with transfusion,causes this.In our study,we tried to reveal a relationship by comparing the iron parameters of these patients with various endocrine parameters.
Methods
Our study is a retrospective study.The data of 18 thalassemia major patients who applied to Osmangazi University Endocrinology and Hematology departments were collected from medical records.Parametres are sex,age,iron parameters,H-ba1c,fasting glucose,fructosamine,lipid profile,thyroid function tests, anterior pituitary hormone panel, parathormone (PTH), 25-OH vitamin D level.
Results
18 patients with thalassemia major were analyzed. 8(44.4%) were male and 10 (55.6%)were female.The mean age was 36.94 ± 10.86 years and the age range was between 20 and 54 years. All of the patients received blood transfusion once a month and were followed up with iron chelation therapy. The fructosamine levels of 6 patients were also above the normal value. GH and IGF-1 levels of the patients were in the normal range. The 25 OH vitamin D level of 11 patients was below 30 ng/ml. Osteoporosis was detected in 9 patients. Seven of these patients (7/9) were evaluated as secondary osteoporosis. Endocrine parameters of the patients were compared with iron parameters. There was a positive relationship between transferrin saturation and 25-OH vitamin D,a negative relationship between iron and PTH, and a negative relationship between ferritin and FSH,LH. Thyroid function tests were normal in 9 patients (50%), primary hypothyroidism was found in 8 patients (44.4%), and hyperthyroidism with graves diagnosis was

detected in 1 patient. There was no thyromegaly in thyroid USG. Autoimmunity was only present in the patient diagnosed with graves.
Conclusions
Evaluation of endocrinopathies in thalassemia patients should be done regularly to detect and treat endocrine complications. It may be appropriate to screen these patients at least once a year in this respect. The role of pituitary hormones in the routine follow-up of thalassemia patients is still controversial. Larger prospective studies are needed. Collaborative multicenter studies should be considered to reach more precise information.
Keywords
Thalassemia, endocrinopathy, ferritin, iron, transfusion
DOI: 10.1530/endoabs.81.EP166

EP167

Classical complications of primary hyperparathyroidism

Lamiae Zarraa, Yousra Laalaoua, Soumiya Berrabeh, Siham ROUF & Hanane Latrech
Endocrinology-Diabetology and Nutrition Department CHU MOHAMED VI, Laboratory of Epidemiology, Clinical Research and Public Health, Faculty of Medicine and Pharmacy Mohammed Premier University Oujda, Oujda, Morocco.

Key words
Primary hyperparathyroidsm-Bone complications-Renal complications and digestive complications.
Introduction
Primary hyperparathyroidism is a frequent endocrinopathy whose diagnosis is biological and linked to an inappropriate secretion of parathyroid hormone (PTH), wich leads to an altered phosphocalcic metabolism that can be responsible for numerous complications. The aim of this work is to evaluate the classical complications of primary hyperparathyroidism in our series: bone, digestive and renal.
Material and methods
Retrospective descriptive and analytical study including 44 patients followed for primary hyperparathyroidism between 2015 and 2021. Only classical complications (bone, kidney and digestive) were noticed in this work. Data were collected from medical records and analyzed by SPSS-V21 software.
Results
The mean age was 55 ± 11 years, with a clear predominance of women in 77.3% of whom 80% were postmenopausal. 81% of the cases had hypercalcemia, including 36% with malignant hypercalcemia ($n=13$). The diagnosis of primary hyperparathyroidism was revealed by complications in 25% of cases ($n=11$).The impact assessementof hyperparathyroidism showed a remarkable effect on the skeletal system with osteoporosis in 60.7% of the cases, osteolytic bone lesions in 18% ($n=8$), the majority of which were of diffuse localization, and brown tumors in 13.6% of the cases ($n=6$), Fibrocystic osteitis was observed in 2 cases (4.5% of our series) and a pathological fracture in one patient. On the renal level, renal lithiasis complicating primary hyperparathyroidism in 31.8% ($n=14$) which 78.5% of the cases were bilateral ($n=11$) and complicated by nephrocalcinosis in 2 cases or 5.7%. Alteration of renal function was noted in 11.6% ($n=5$ and GFR: 30–60 ml/min). The digestive complications were mainly represented by acute pancreatitis in 3 patients (6.8%) and chronic calcifying pancreatitis in one case. On postoperative, Hungry bone syndrome complicated 6.81% of the cases or 3 cases in our series. On postoperative, Hungry bone syndrome complicated 6.81% of the cases or 3 cases in our series. The relationship between the bio-intact PTH 1–84 level and the occurrence of complications finds: a statically significant association with the occurrence of brown tumor as well as a statically significant correlation with osteolytic bone lesions, while no significant correlation with the occurrence of renal lithiasis, osteoporosis and pancreatitis and PTH level.
Discussion–Conclusion
Primary hyperparathyroidism is an endocrinopathy that is usually benign but remains a serious condition because of its bone, kidney and digestive complications.
DOI: 10.1530/endoabs.81.EP167

EP168

Hypercalcemia in sarcoidosis unmasked by treatment with Vitamin D

Helmine Kejem[1], Scott Williams[1,2,2], Emmanuel George[1], Yee Ho Chiu[1] & Upendram Srinivas Shankar[1]
[1]Wirral University Teaching Hospital, St Helens, UK; [2]Wirral University Teaching Hospital NHS Foundation Trust (WUTH), Birkenhead, UK.

We present the case history of a 62 year old male, who was recently diagnosed with sarcoidosis which was confirmed on biopsy of a calf nodule. CT scan revealed pulmonary involvement. Our patient had low vitamin D 12 nmol/l (nr 50–100) and initial adjusted calcium was 2.48 mmol/l (2.13–2.63). DEXA bone density scan revealed osteopenia. He was commenced on loading dose of colecalciferol 40,000 units weekly and received 3 doses. He presented 1 month later with polydipsia, polyuria, bone pains and lethargy. Adjusted calcium went up to 3.69 mmol/l and PTH was low at 0.39 pmol/l (1.1–6.0). At this point vitamin D was 94 nmol/l (50–100) and serum creatinine 156 umol/l (59–104) with baseline creatinine being normal at 76 umol/l. Adjusted calcium remained elevated at 3.5 mmol/l, despite treatment with intravenous pamidronate 60 mg. Our patient received oral prednisolone 40 mg/day and is currently on a tapering dose of prednisolone. The adjusted calcium normalised to 2.35 mmol/l in 15 days.
Discussion
Our case history highlights the importance of replacing vitamin D in patients with sarcoidosis with caution. Alveolar macrophages produces 1-alpha hydroxylase which converts 25-hydroxyvitamin D3 to 1, 25-dihydroxyvitamin D3. Vitamin D replacement results in avidly available, 25-hydroxyvitamin D3 to the macrophages in sarcoid granulomata, leading to excess production of 1,25 dihydroxy vitamin D3, which causes intestinal absorption of calcium and bone resorption leading to raised calcium levels. Another point our case history highlights is the role of corticosteroids in the treatment of hypercalcaemia due to sarcoidosis. Corticosteroids reduce gastrointestinal calcium absorption and inhibit osteoclast function, and are particularly effective in sarcoidosis because of their effects on vitamin D metabolism, as they are potent inhibitors of macrophage 1-alpha hydroxylase.
DOI: 10.1530/endoabs.81.EP168

EP169

Expanding the phenotype of Familial hypocalciuric hypercalcemia type 3

Lior Baraf[1,2], Noa Averbuch[3,4,5], Lior Carmon[2,6], Auryan Szalat[7,8], Rivka Sukenik-Halevy[5,9] & Merav Fraenkel[1,2]
[1]Soroka University Medical Center, Endocrinology, Be'er Sheva, Israel; [2]Ben Gurion University of the Negev, Faculty of Health, Be'er Sheva, Israel; [3]Schneider Children's Medical Center in Israel, The Jesse Z and Sara Lea Shafer Institute for Endocrinology and Diabetes, National Center for Childhood Diabetes, Petah Tikva, Israel; [4]Beilinson Hospital Rabin Medical Center, Recanati Genetic Institute, Petah Tikva, Israel; [5]Tel Aviv University, Sackler Faculty of Medicine, Tel Aviv-Yafo, Israel; [6]Soroka Medical Center, Pediatric Endocrinology, Be'er Sheva, Israel; [7]Hadassah Medical Organization, Osteoporosis Center, Endocrinology Diabetes and Metabolism Service; [8]The Hebrew University of Jerusalem, Faculty of Medicine, Jerusalem, Israel; [9]Meir Medical Center, Genetics Institute, Kefar Sava, Israel.

Introduction
Familial hypocalciuric hypercalcemia (FHH) is a rare mostly asymptomatic genetic disorder affecting the calcium sensing receptor (CaSR) and its associated proteins with autosomal dominant inheritance. Mutation in AP2S1 gene is responsible for FHH3.
Aim
Expand the phenotype of FHH type 3.
Methods
Clinical and biochemical characterization of a patient with *de-novo* FHH3 mutation.
Results
S.Z, A 30-year-old man was hospitalized for recurrent pancreatitis. His medical history included chronic hypercalcemia in the range of 11.7–13.3 mg/dl attributed to his prior clinical diagnosis of FHH. Abdominal imaging and lipid profile were unremarkable. The working diagnosis was of hypercalcemia-related acute pancreatitis. He was treated conservatively with resolution of symptoms and normalization of serum amylase and lipase. A multi-gene panel that was performed (INVITAE) revealed a heterozygous mutation in the *AP2S1* gene-p.Arg15Leu. His parents and two siblings were normocalcemic. A second genetic panel for pancreatitis related genes was negative. DXA bone mineral density revealed Z score of -2.3 at LS and -2.9 at FN and TH – a typical finding in FHH3 patients. Cinacalcet at a dose of 120 mg daily was well tolerated and normalized calcium levels with no episodes of pancreatitis within 26 months of follow-up. His three-year-old son is followed for speech delay and was found to be hypercalcemic; he carries the same AP2S1 mutation.

Conclusions
We describe a family with a de novo mutation in the AP2S1 gene presenting with recurrent pancreatitis, low bone mass and speech delay thus expanding the phenotype of FHH3.

DOI: 10.1530/endoabs.81.EP169

EP170

Vitamin D levels in relationship to thrombotic markers in severe Sars-CoV-2 infection

Ifigenia Kostoglou-Athanassiou[1], Lambros Athanassiou[2], Sofia Nikolakopoulou[3], Alexandra Konstantinou[3], Olga Mascha[4], Charilaos Samaras[3] & Panagiotis Athanassiou[5]
[1]Asclepeion Hospital, Voula, Department of Endocrinology, Athens, Greece; [2]Asclepeion Hospital, Voula, Department of Rheumatology, Athens, Greece; [3]Asclepeion Hospital, Voula, Covid-19 Department, Athens, Greece; [4]Asclepeion Hospital, Voula, Department of Biochemistry, Athens, Greece; [5]St. Paul's Hospital, Department of Rheumatology, Thessaloniki, Greece.

Introduction
Severe infection from the SARS-CoV-2 virus is associated with various manifestations, including hematological manifestations. Thrombotic events or a tendency to develop thrombotic events also characterize severe COVID-19 disease and may be related to fatalities. Vitamin D is known to have immunomodulating properties and to enhance the body defense system against invading pathogens and to have immunostimulatory properties as far as the innate immune response is concerned.
Aim
The aim of the study was to measure $25(OH)D_3$ levels in patients hospitalized for severe COVID-19 infection and to investigate the relationship between $25(OH)D_3$ levels and ferritin levels and d-dimer levels in this cohort.
Methods. In a cohort of 42 patients hospitalized for severe infection from the SARS-CoV-2 virus 25(OH)D3 levels were measured. In the same cohort ferritin levels and d-dimer levels were also measured. Observations were also performed in a control group.
Results
$25(OH)D_3$ levels were 8.08 ± 1.48 ng/ml (mean $\pm$ S.E.M.) and they were inversely related to ferritin levels, correlation coefficient -0.15, $P=0.001$, linear regression analysis and to d-dimer levels, correlation coefficient -0.34, $P<0.001$, linear regression analysis.
Conclusions
Severe infection from the SARS-CoV-2 virus is related to a tendency for the development of thrombotic events. D-dimer levels are measured and followed in these patients. Ferritin levels are also increased in severe SARS-CoV-2 infection and may be related to adverse outcome. We showed that vitamin D levels are low in hospitalized patients with severe SARS-CoV-2 infection and are inversely related to ferritin and d-dimer levels. It may thus be proposed that vitamin D is an inverse index of severity in the context of SARS-CoV-2 infection.

DOI: 10.1530/endoabs.81.EP170

EP171

A sporadic case of pseudohypoparathyroidism type Ib and fahr's syndrome

Cátia Araújo, Mafalda Martins Ferreira, Bárbara Filipa Araújo, Mariana Lavrador, Carla Baptista, Margarida Bastos & Isabel Paiva
Centro Hospitalar Universitário de Coimbra, Serviço de Endocrinologia, Diabetes e Metabolismo, Coimbra, Portugal.

Introduction
Pseudohypoparathyroidism is a heterogeneous disease characterized by hypocalcemia, hyperphosphatemia and parathyroid hormone resistance. The distinct pseudohypoparathyroidism types are distinguished by physical features, the coexistence of other hormone resistances and genetic defects. Pseudohypoparathyroidism type Ib is more often associated with sporadic cases, unlike others types.
Clinical Case
Male, born in France, diagnosed with pseudohypoparathyroidism during childhood. There was a history of fatigue, gait disorder and delayed eruption of teeth. Laboratory investigation revealed serum hypocalcemia, hyperphosphatemia and elevated serum PTH levels. No family history of phosphocalcium metabolism disorder. He was treated with oral calcium and cholecalciferol. At the age of 9, he starts living in Portugal. Physical examination showed no features of Albright Hereditary Osteodystrophy. Laboratory results showed normal thyroid function and no evidence of other hormone resistances. He started treatment with calcitriol also in addition to oral calcium and cholecalciferol. Over the years, the goal to an adequate calcium-phosphate level was difficult to obtain in this patient due to poor treatment adherence. At 34 years old, urinary calculi was detected on renal ultrasonography. 7 years later, head computerized tomography revealed extensive calcifications at the level of the cerebellar hemispheres, lenticular nuclei, corona radiata, centra semiovale and subcortical level, suggestive of Fahr's syndrome. He was referred to a geneticist and the molecular genetic result revealed a GNAS gene methylation defect specifically in 20q13.32 region performed by MS-MLPA analysis. STX16 deletion was not detectable. This result confirms the diagnosis of pseudohypoparathyroidism type Ib caused by a paternal uniparental disomy of the long arm of chromosome 20.
Conclusions
The molecular investigation is not essential for the therapeutic approach. In this patient, the identification of a methylation defect in a region of *GNAS* gene was useful for the classification of pseudohypoparathyroidism and allowed us to evaluate this case as a sporadic event, therefore without specific risk for the patient's offspring. The present case also serves to emphasize the importance of treatment adherence that may prevent acute and chronic complications of hypocalcemia.

DOI: 10.1530/endoabs.81.EP171

EP172

Acute hypercalcemic crisis in an elderly with granulomatous disease

Leo Tiu Jr & Maria Leonora Capellan
Makati Medical Center, Section of Endocrinology, Diabetes and Metabolism, Makati City, Philippines.

Background
Tuberculosis rarely leads to clinically significant hypercalcemia. However, elderly patients remain predisposed due to advanced age, multiple comorbidities and polypharmacy.
Clinical Case
An 81-year-old female presented with 1 month history of bilateral weak hand grip and sluggish mastication. She was initially managed as progressive Parkinson's Disease. After 3 weeks, she was now reported to have episodes of fall from imbalance. After few days, there was noted increased sleeping time, decreased verbal output, response lag and slurred speech. There were no pulmonary symptoms or febrile episodes. Her medical history includes hypertension, Diabetes Mellitus, previous CVD infarct, Chronic Kidney Disease, recovered Moderate COVID-19 infection and pulmonary tuberculosis that was diagnosed 30 years ago. Outpatient evaluation revealed severe hypercalcemia (15.36 mg/dl). Upon admission, Calcium (500 mg/day) and Vitamin D (1500 IU/day) supplements were discontinued. She was started on vigorous intravenous hydration and diuresis with Furosemide. Calcitonin nasal spray was administered for 2 days. Cranial CT scan showed absence of acute infarction or intracranial hemorrhage. On the 3rd hospital stay, serum calcium was still elevated (11.99 mg/dl) but decreased from baseline. Other blood tests results showed elevated 25(OH)D 119.72 ng/ml (>30 ng/ml), normal PTH 15.84 pg/dl ($<$ 67.90 pg/dl), magnesium 2.41 mg/dl (1.6–2.6 mg/dl) and phosphorous 3.6 mg/dl (2.29–4.79 mg/dl). Hence, PTH-independent causes were evaluated with high suspicion of Vitamin D intoxication. Chest imaging showed a thick walled cavitary mass with adjacent consolidation and surrounding centrilobular nodule in a tree-in-bud configuration in the right upper lobe suggestive of an infectious process. On the 10th hospital stay, CT guided biopsy of the right upper lung mass was done. Histopathology showed lung tissues with fibrosis, focal necrosis, and chronic inflammation. MTB GeneXpert was positive consistent with Tuberculosis for which she was started on Anti-Koch's medications to be completed for 6 months. An elevated Serum $1,25(OH)_2D$ could have supported extrarenal 1α hydroxylation in granulomatous disease but was not readily available. On the 12th hospital stay, due to persistent hypercalcemia (11.72 mg/dl), she was started on Prednisone 10 mg/day which was up titrated to 20 mg/day after 3 days of initiation then down titrated weekly. She was discharged in a stable condition. Normocalcemia was documented upon follow up with subsequent improvement in the patient's sensorium.
Conclusion
Granulomatous disorders as the etiology of hypercalcemia should be suspected in the setting of hypervitaminosis D and low-normal or low parathyroid hormone level. Hypercalcemic crisis is an infrequent endocrine emergency that portends excellent outcomes with prompt diagnosis and management.

DOI: 10.1530/endoabs.81.EP172

EP173

Palovarotene for the treatment of fibrodysplasia ossificans progressiva: methodology of the phase III open-label PIVOINE rollover trial

Alexander Artyomenko[1], Aude Houchard[2] & Azzeddine Zemam[2]
[1]Ipsen, Slough, UK; [2]Ipsen, Boulogne-Billancourt, France.

Objectives
Fibrodysplasia ossificans progressiva (FOP) is an ultra-rare genetic disorder characterized by heterotopic ossification (HO) and progressive restriction of mobility. To date, no approved disease-modifying treatments for FOP exist, but interim phase III trial (NCT03312634) results suggest marked efficacy for palovarotene (PVO).[1] Here, we describe methodology of the PIVOINE trial (NCT05027802) designed to allow treatment continuity and further evaluation of PVO safety and efficacy.
Methods
Patients will receive 5 mg PVO daily, or the parent study completion dose, for a maximum of 3 years; during flare-ups, patients will receive 20 mg daily for 4 weeks, then 10 mg daily for 8 weeks. Enrollment criteria: completion of a parent study (end of study/treatment visit of NCT03312634 or NCT02279095/NCT02979769), ≥14 years old, full skeletal maturity if aged <18 years or deemed to be final adult height. PIVOINE aims to enroll 61 patients; recruitment has not begun. Outcomes are presented in Table.
Summary
Results from PIVOINE, estimated to end in November 2024, will allow further evaluation of PVO in FOP.
References
1. Pignolo R *et al*. ASBMR 2020;35(Suppl 1):16–17.
Funding
Sponsored by Ipsen.

Table: Trial outcomes

Primary
Incidence of treatment-emergent adverse events[a]
Secondary[b]
Cumulative Analogue Joint Involvement Scale (CAJIS) total score[c]
Use of aids, assistive devices and adaptations[c]
FOP-Physical Function Questionnaire percentage of worst score (total score; upper extremities/mobility sub-scores)[c]
Frequency of healthcare utilization
Observed/percentage predicted:[c]
Forced vital capacity (FVC)
Forced expiratory volume in 1 second (FEV_1)
Diffusion capacity of the lung for carbon monoxide (DLCO)
Absolute/percentage predicted:[c]
FEV_1/FVC ratio
Patient Reported Outcomes Measurement Information System (PROMIS) Global Health Scale physical and mental function scores[c]
Number of investigator-reported flare-ups, outcomes and duration[c]
Percentage of patients with new bone growth

[a]Collected continuously over trial period; [b]Collected every 6 months over trial period; [c]Raw values and change from inclusion visit.

DOI: 10.1530/endoabs.81.EP173

EP174

McCune Albright syndrome – a clinician's challenge and a multi-disciplinary approach: case report

Mădălina Elena Iftimie[1], Iulia Florentina Burcea[1,2], Mihnea-Nicolae Moise[3], Rareş-Ştefan Deculescu[3], Larisa Budulucă[1] & Catalina Poiana[1,2]
[1]C.I. Parhon National Institute of Endocrinology, Bucureşti, Romania; [2]Carol Davila University of Medicine and Pharmacy, Bucureşti, Romania; [3]Elias University Emergency Hospital, Bucureşti, Romania.

Introduction
McCune-Albright syndrome is a rare, heterogenous disorder, consisting of at least two of the following three features: polyostotic fibrous dysplasia, café-au-lait skin pigmentation and autonomous endocrine hyperfunction. We present the case of a patient with an atypical presentation of McCune Albright syndrome (MAS) and severe fibrous dysplasia lesions.
Case report:
An 18-year-old girl diagnosed with MAS (at the age of four) was referred to our clinic for a first endocrine evaluation. She had a history of allergodermia and recurrent wheezing from an early age (8 months and 1.8 years respectively), with the subsequent development of a limp (2.5 years old). She had attained menarche at 3.3 years of age (currently having normal spontaneous menses) and had multiple pathologic fractures during childhood, the first being a proximal femoral shaft fracture (4 years old), for which she underwent 2 surgeries, resulting in shortening of the left leg. Prior X-ray imaging and CT scans showed left coxa vara, tibial bowing, cortical thinning, and multiple sclerotic and lytic lesions suggesting polyostotic fibrous dysplasia (confirmed by left femur biopsy). On physical examination, she had hyperpigmented macules with irregular margins, leg length discrepancy, macrocephaly with clover shaped skull and facial asymmetry. Her height was 165 cm, within her target height range (172.5+/−10 cm). Laboratory data revealed normal calcium, phosphorus and parathyroid hormone levels, vitamin D deficiency, very high alkaline phosphatase levels (15.6×upper limit of normal, ULN) and elevated bone turnover markers. Insulin-like growth factor 1 was within the normal range, but she had unsuppressed growth hormone (GH) levels following 75 g oral glucose load (nadir GH 1.72 ng/ml) and elevated random GH (10.56 ng/ml). Prolactin levels were slightly elevated (1.29×ULN). Pituitary imaging found a sellar mass of 5/7/6.7 mm. Thyroid ultrasonography showed several micronodules, with normal thyroid function. No other endocrinopathies were found. Antiresorptive agents such as bisphosphonates (pamidronate) or anti-RANKL antibody (denosumab) are taken into consideration as therapeutic options.
Conclusion
Diagnosis of MAS is usually established on clinical grounds, but the presenting signs and symptoms are highly variable. Although GH and prolactin excess are common (21%)[1], the clinical expression can be 'whispering', as in our case. As all MAS features have a varied time of presentation, early referral to an endocrinologist and meticulous follow-up and management is essential.
References
Christoforidis A et al, McCune-Albright syndrome: growth hormone and prolactin hypersecretion.J Pediatr Endocrinol Metab. 2006; 19 Suppl 2:623–625

DOI: 10.1530/endoabs.81.EP174

EP175

Differences between atypical parathyroid adenomas and parathyroid adenomas in patients with primary hyperparathyroidism

Ensar Aydemir, Coskun Ates, Yasemin Aydoğan Ünsal, Erhan Hocaoglu, Filiz Mercan Saridas, Soner Cander, Ozen OZ GUL, Canan Ersoy & Erdinc Erturk
Uludag University Medical School, Bursa, Turkey.

Background
Atypical parathyroid adenoma (APA) is a rare disease that can be challenging to distinguish from benign parathyroid adenoma. APA shows some laboratory and histopathological features with parathyroid cancer. This study attempts to compare clinical, laboratory, radiologic and histopathological characteristics in APA and parathyroid adenoma (PA).
Methods
This was a retrospective study was based on the database of eighty-two subjects who underwent surgery for primary hyperparathyroidism at a tertiary referral center between 2010 and 2021. Forty-one patients with APA matched by age and gender to controls with PA. Clinical, laboratory, radiologic and characteristics were obtained from the hospital database.
Results
Forty-five (54.8%) of primary hyperparathyroidism (PHPT) patients were symptomatic, 36 (90%) had nephrolithiasis, 6 (15%) had fracture and 3 (7.5%) had hypercalcaemic crisis. APA patients present with significantly inceased serum calcium, parathormone (PTH) and alkalen phosphatase levels ($P<.001$, all). No significant difference was observed in the results of bone mineral density (BMD), T-scores and Z-scores. The size of adenoma was significantly greater in APA group (24 (8.8–70) mm vs. 12 (3.8–32) mm, $P=0.005$).
Conclusion
Our study revealed that increased preoperative serum calcium, parathormone, alkalen phosphatase concentrations and parathyroid adenoma size on ultrasound may have predicted the atypical parathyroid adenoma.

DOI: 10.1530/endoabs.81.EP175

EP176

PTH 1–34 delivery via insulin pump in a patient with severe post-operative hypoparathyroidism

Elisa Dinoi[1], Laura Mazoni[1], Laura Pierotti[1], Matteo Apicella[1], Claudio Marcocci[1] & Filomena Cetani[2]
[1]University of Pisa, Department of Clinical and Experimental Medicine, Pisa, Italy; [2]University of Pisa, Endocrine 2 Unit, Pisa, Italy.

Hypoparathyroidism (HypoPT) is the only hormone deficiency syndrome whose standard treatment is not based on the replacement of the missing hormone. Although most cases of postsurgical HypoPT can be effectively managed with the conventional use of oral calcium and active vitamin D (SOC therapy), some patients require very high doses and develop complications such as hypercalciuria, renal stones, nephrocalcinosis and ectopic calcifications. In the last few years, recombinant human PTH (rhPTH) has become an appealing option for patients affected by chronic HypoPT who are refractory to SOC therapy. Winer et al have adapted an insulin pump delivery system to treat patients with a continuous infusion of rhPTH (1–34) (teriparatide). We describe the case of a 33-years old woman who was referred to our Clinic for severe chronic HypoPT after total thyroidectomy for multinodular goiter. Despite being on therapy with high doses of oral calcium and active vitamin D, she reported muscle spasms, cramps and perioral paresthesia on a daily basis and was frequently admitted to the Emergency Room to be treated with intravenous calcium infusion. At our evaluation, we confirmed a severe hypocalcemia (7.5 mg/dl), hyperphoshatemia (5.2 mg/dl) and hypercalciuria (388 mg/24 h). The abdomen ultrasound showed the presence of medullary nephrocalcinosis and right microlithiasis. After using teriparatide 20 mcg twice-daily injection without success, we decided to treat the patient with a continuous subcutaneous perfusion of rhPTH (1–34) by using an insulin pump. rhPTH (1–34) (Terrosa®, 20 μg/80 μL) was diluted with distilled water and the patient start continuous administration of subcutaneous rhPTH (1–34) via a Medtronic® pump with a rate of 0.8 UI/h (equivalent to 11 mcg of teriparatide/day). The patient was monitored by daily clinical evaluation (symptoms and Chvostek and Trousseau signs) and assessment of serum calcium and ionized calcium levels. Moreover, we assessed the patient's quality of life by using the SF-36 questionnaire at baseline and at 6 months. The daily dose was progressively uptitrated until 22 mcg/day and the SOC therapy was gradually reduced until discontinuation. At the last evaluation (9 months) serum calcium was 9.5 mg/dl, serum phosphate was 3.3 mg/dl and 24 h urine calcium was 100 mg/24 h. Abdomen ultrasound did not show the nephrolithiasis. The SF-36 test showed a significant improvement of the scores. In conclusion, the continuous infusion of rhPTH (1–34) in our patient was the only treatment option able to restore long-term calcium homeostasis and improve the quality of life.

DOI: 10.1530/endoabs.81.EP176

EP177

Identification of GATA3 pathogenic variants in two patients with hypoparathyroidism, deafness and renal dysplasia (HDR) syndrome

Elisa Dinoi[1], Laura Pierotti[1], Laura Mazoni[1], Simona Borsari[1], Matteo Apicella[1], Fulvia Baldinotti[2], Maria Adelaide Caligo[2], Claudio Marcocci[1] & Filomena Cetani[3]
[1]University of Pisa, Department of Clinical and Experimental Medicine, Pisa, Italy; [2]University Hospital of Pisa, Laboratory of Molecular Genetics, Pisa, Italy; [3]University of Pisa, Endocrine 2 Unit, Pisa, Italy.

Hypoparathyroidism, deafness and renal dysplasia (HDR) syndrome, also known as Barakat syndrome, is a rare autosomal dominant disease characterized by the triad of hypoparathyroidism (H), deafness (D) and renal abnormalities (R). Its genetic cause is known to be the haploinsufficiency of the zinc finger transcription factor *GATA3*. This disorder exhibits a great clinical variability and an age-dependent penetrance of each feature. The most frequent manifestation is sensorineural deafness, usually diagnosed during childhood. Symptomatic or asymptomatic hypoparathyroidism affects about 90% of patients. Kidney abnormalities, such as renal cysts, are less common. We report two cases of HDR syndrome due to pathogenic variants in exon 3 of the *GATA3* gene. Subject 1 was a 17-years-old boy who was referred to our Department in 2018 for hypocalcemia incidentally detected at routine blood tests. At physical examination Trousseau and Chvostek signs were positive and laboratory evaluation confirmed a severe hypocalcemia (ionized calcium 0.62 mmol/l, n.v. 1.13–1.32), hyperphosphatemia (8.8 mg/dl) with undetectable PTH levels (< 4 pg/ml, n.v. 8–40). At abdomen ultrasound and magnetic resonance multiple renal cysts were detected. Subject 2 was a 16-years-old boy who was referred to our Department in 2005 for hypocalcemia complicated by epileptic seizure. His past clinical history was remarkable for right nephrectomy at 4 months of age for multicystic renal disease. At our first evaluation physical examination was normal and blood tests showed low ionized calcium (0.99 mmol/l, n.v. 1.13–1.32) with undetectable PTH levels (< 10 pg/ml, n.v. 15–75). Computed tomography displayed multiple cerebral calcifications and the audiometric evaluation revealed the presence of bilateral mild sensorineural hearing loss in both patients. On the basis of clinical and biochemical data, HDR syndrome was suspected and genetic analysis of the *GATA3* gene revealed the presence of a pathogenetic variant in exon 3, c.404dupC in subject 1, but not in his parents and sister, and c.431dupG in subject 2. These frameshift variants produce a premature stop codon resulting in the synthesis of a non-functional truncated protein (p.Ala136GlyfsTer168 and p.His145ProfsTer159, respectively). A good control of H is achieved in both patient by using rhPTH in subject 1 and oral calcium and active vitamin D in subject 2. HDR syndrome, although rare, is one of the genetic causes of H and must be excluded in all patients with idiophatic H, particularly if young. A correct diagnosis is important for the early detection of other features of the syndrome and for genetic counseling.

DOI: 10.1530/endoabs.81.EP177

EP178

Sickle cell disease and hyperparathyroidism: case report

Maysam JRIDI, Sabrine Mekni, Adel Meriem, Imen Rojbi, Ibtissem Ben Nacef, Nadia Mchirgui & Karima Khiari
Hospital Charles Nicolle, Tunis, Tunisia.

Introduction
Primary hyperparathyroidism (pHPT) is a common endocrine disorder usually diagnosed by the presence of elevated serum calcium levels with inappropriate normal or increased parathyroid hormone (PTH) serum levels. This condition has been reported in few cases of patients with sickle cell disease (SCD), a multisystem disorder with acute and chronic complications.
Observation
We report a case of a 63-year-old Tunisian woman with a history of homozygous sickle cell disease (SS phenotype), high blood pressure and atrial fibrillation, referred to the emergency department for hypercalcemia 3.68 mmol/l (*n*:2.25–2.6) with electrocardiogram (ECG) abnormalities. After hydration, a decrease of calcium level 2.82 mmol/l and normalized ECG, she was admitted to the endocrinology ward. Physical examination showed a centimetric basal cervical mass. Blood tests showed: hypophosphatemia 0.73 mmol/l (*n*: 0.78–1.52), an elevated parathyroid hormone level 1479 pg/ml (*n*: 26.5–96.5) and a moderate decrease in kidney function (creatinine clearance = 44 ml/min). Urinary cast showed no hypercalciuria. This case was compatible with pHPT. Hypercalcemia was treated with oral route and intravenous hyper hydration along with bisphosphonate perfusions. Ultrasonography of the neck revealed a mass at the left inferior parathyroid lobe of 17 × 14 mm and the Sestamibi scan showed a 15 mm single left parathyroid adenoma. Renal echography revealed no nephrolithiasis albeit an aspect of chronic renal disease. Bone densitometry revealed osteoporosis (T scores of −3.5, −2.5 in lumbar spine and left hip respectively). Then the patient underwent an excision of the parathyroid adenoma. The histological analysis showed pseudo adenomatous parathyroid hyperplasia.
Discussion
Some explanations for the association of SCD with pHPT have been delineated in the literature, such as vitamin D deficiency, high levels of EPO du to chronic hemolysis which could stimulate the parathyroid glands and increased growth factors and fibroblastic growth factor which seem to promote parathyroid cells proliferation
Conclusion
If we consider pHPT to be a complication of SCD, calcium levels should be routinely checked, keeping in mind the fatality of hypercalcemia complication adding to that the threatening complications of SCD. Further research is required to underpin the association of SCD with pHPT.

DOI: 10.1530/endoabs.81.EP178

EP179

Primary hyperparathyroidism revealed by a brown tumor: a case report

Gorgi Khaoula, Kamel Farah, Echchad Lamya, Rifai Kaoutar, Iraqi Hinde & Gharbi Mohamed El Hassan
Ibn Sina University Hospital, Endocrinology and Metabolic Diseases, Rabat, Morocco.

Introduction
Brown tumors are osteolytic lesions rarely revealing hyperparathyroidism. They result from abnormalities of bone metabolism. They usually occur in the terminal stage of hyperparathyroidism. We report the case of a patient with hyperparathyroidism revealed by a brown tumor.
Case
A 39-year-old female patient with no notable medical history who presented for 1 year a mandibular swelling progressively increasing in size after a dental extraction without other associated signs. A phosphocalcic assessment was requested, coming back in favor of a primary hyperparathyroidism: high level of calcemia at 132 mg/l, a low phosphoremia at 17 mg/l and an elevated parathormonemia 9 times above the normal. A biopsy of the mass was performed, which anatomopathological examination was in favor of a reparative giant cell granuloma, hence the diagnosis of brown tumor. Cervical ultrasound revealed a 3–4 cm parathyroid adenoma and scintigraphy confirmed the parathyroid origin. The patient underwent parathyroidectomy and the histological study was in favor of an atypical parathyroid adenoma. The evolution was marked by a normalization of the phosphocalcic balance.
Discussion and conclusion
Brown tumors are rarely revealing bone manifestations of primary PTH.Their discovery requires exploration of the parathyroid glands, which are most often the site of an adenoma. Excision of the parathyroid adenoma remains the reference treatment for this condition.

DOI: 10.1530/endoabs.81.EP179

EP180

Primary hyperparathyroidism revealed by acute pancreatitis: a case report

Gorgi Khaoula, Kamel Farah, Khamel Ghita, Echchad Lamya, Rifai Kaoutar, Iraqi Hinde & Gharbi Mohamed El Hassan
Ibn Sina University Hospital, Endocrinology and Metabolic Diseases, Rabat, Morocco.

Introduction
Primary hyperparathyroidism (PPH) can be complicated by pancreatitis. The frequency of association of primary hyperparathyroidism with pancreatitis is rare, varying between 1.5% and 7%. We report the case of a patient with hyperparathyroidism revealed by acute pancreatitis.
Case
A 78-year-old patient, without any particular history, who consulted the emergency room for an acute digestive picture with abdominal pain and bilious vomiting, an abdominal CT scan was ordered showing stage D pancreatitis. After eliminating other classical causes of pancreatitis with a normal triglyceride level. The etiological research revealed a profile of primary hyperparathyroidism: PTH: 392 pg/ml or 9×normal, hypercalcemia: 141 mg/l (85–105), hypophosphatemia 19 mg/l (20–45). Cervical ultrasound and cervico-thoracic MRI confirmed the parathyroid localization by showing a paratrachial formation dte in front of the post edge of the inf pole of the thyroid lobe dte measuring 17×15×23 mm. The workup for hypercalcemia was unremarkable. The patient was rehydrated and given furosemide, and when her blood calcium level did not improve, she was given a bisphosphonate infusion. After the normalization of the calcemia the patient underwent a parathyroidectomy with good clinical and biological evolution.
Discussion and conclusion
The association between HPTP and pancreatitis is rare, however, the pathophysiology of this association is still unknown. Experimental data support a direct or indirect role of hypercalcemia via activation of pancreatic proteases. Acute pancreatitis may be indicative of HPTP, which should be systematically investigated in all acute pancreatitis, in the absence of an obvious cause.

DOI: 10.1530/endoabs.81.EP180

EP181

Small and foudroyant parathyroid carcinoma with lung metastasis and no local invasion at diagnosis

Daniel Grigorie, Mircea Ghemigian, Dumitru Ioachim, Cristina Florescu & Alina Sucaliuc
National Institute of Endocrinology, Bucharest, Romania.

Parathyroid carcinoma (PC) rarely presents with metastasis at diagnosis and usually in patients also having gross local invasion.
Case presentation
We report the case of a 51-year-old postmenopausal woman presenting at our institution in June 2019 with symptomatic hypercalcemia (fatigue, polyuria, constipation and bone pain), but with a surprisingly good general condition. She had been treated with bisphosphonates for osteoporosis (DXA: LS T score −4.2 s.d., Z score −3.6 s.d.; FN T score −2.4 s.d., Z score −1.7 s.d.) for 2 years, having a variable hypercalcemia up to 12.6 mg/dl, but undiagnosed for primary hyperparathyroidism (PHPT). She had no family history of parathyroid disease or endocrine neoplasia. Initial laboratory findings revealed marked hypercalcemia (17.5 mg/dl), very high PTH levels (1561 pg/ml) and turnover (CTX 4.58 ng/ml) and normal kidney function, which led to the suspicion of PC. Neck ultrasound showed a hypoechoic tumor with slightly irregular margins, Ø max 1.5 cm, in the position of right superior parathyroid gland. The tumor was surgically removed and three other parathyroids were identified in canonical location and of normal appearance, with no gross invasion. As the preliminary pathology report revealed characteristic features of PC, a total thyroidectomy was performed, and a small normal parathyroid gland was found adjacent to the initial tumor. After tumor removal, her PTH levels decreased by 65%, from 1561 pg/ml to 560 pg/ml (Ca 11.34 mg/dl) and then increased fast, at the the same rate as preoperatively: 39% in 3 weeks preop vs 39% in 1 mo postop; and progressively reached 1684 pg/ml after 3 mo. A MIBI scan including the mediastinum was negative and a FDG−PET CT showed increased metabolic activity in a 10 mm nodule, in the right para aortic mediastinal pleura, the descending colon and skeleton. A bone scan showed homogenous symmetrical uptake throughout the skeleton and X-rays were normal. A CT scan confirmed a mediastinal nodule measuring 11/7/13 mm, tangent to the right antero-lateral face of the ascending aorta and bilateral pulmonary micronodules. Total serum Ca was variably controlled (9.1 mg/dl to 15 mg/dl) with pamidronate and then denosumab (60−120 mg). The surgery performed abroad confirmed that the mediastinal nodule was a metastasis of PC. Eventually, the hypercalcemia became resistant to denosumab (6 mo postop) and the patient died due to a hypercalcemic crisis (20 mg/dl).
Conclusion
This is a rare case of a small and very aggressive parathyroid carcinoma with lung metastasis at diagnosis although with no local invasion.

DOI: 10.1530/endoabs.81.EP181

EP182

Aberrant promoter methylation, expression and function of RASSF1A gene in a series of Italian parathyroid tumors

Chiara Verdelli[1], Fabrizio Federico Pio[2], Giulia Stefania Tavanti[1,3], Paola Maroni[4], Annamaria Morotti[5], Vito Guarnieri[6], Elena Pardi[7], Filomena Cetani[8], Alfredo Scillitani[9], Riccardo Maggiore[10], Valentina Vaira[11], Lucia Anna Muscarella[2] & Sabrina Corbetta[12]
[1]Laboratory of Experimental Endocrinology, IRCCS Istituto Ortopedico Galeazzi, Milano, Italy; [2]Laboratory of Oncology, IRCCS Casa Sollievo della Sofferenza, San Giovanni Rotondo (FG), Italy; [3], Department of Biomedical, Surgical and Dental Sciences, University of Milan, Milano, Italy; [4]Laboratory of experimental Biochemistry & Molecular Biology, IRCCS Istituto Ortopedico Galeazzi, Milano, Italy; [5]Department of Pathophysiology and Transplantation, University of Milan, Milan, Milan, Italy; [6]Division of Medical Genetics, IRCCS Casa Sollievo della Sofferenza, San Giovanni Rotondo (FG), Italy; [7]Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy; [8]Endocrine Unit, University Hospital of Pisa, Pisa, Italy; [9]Endocrinology Unit, IRCCS Ospedale Casa Sollievo della Sofferenza, San Giovanni Rotondo (FG), Italy; [10]Endocrine Surgery, IRCCS Ospedale San Raffaele, Milan, Italy; [11]Division of Pathology, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Department of Pathophysiology and Organ Transplantation, University of Milan, Milan, Italy; [12]Endocrinology and Diabetology Service, IRCCS Istituto Ortopedico Galeazzi, Department of Biomedical, Surgical and Dental Sciences, University of Milan, Milano, Italy.

Aberrant epigenetic features occurring in parathyroid tumors involve DNA methylation, histone methylation, and non-coding RNAs. RASSF1A and APC were frequently downregulated in human cancers. Here, we investigated *RASSF1A* and *APC* methylation status in a series of parathyroid tumors from Italian patients with primary hyperparathyroidism (PAds, $n=80$), confirming *RASSF1A* and *APC* promoter methylation as a hallmark of sporadic parathyroid adenomas. Morever, we extended the analysis in parathyroid carcinomas (PCas, $n=9$), which displayed *RASSF1A* promoter methylation, while *APC* promoter was methylated only in 2 samples. In PAds, *RASSF1A* promoter methylation levels positively correlated with the methylation levels of *APC* promoter, suggesting a common methylation process for both genes. We focused the attention on the oncosuppressor RASSF1A. Our results showed that *RASSF1A* transcripts were significantly reduced in PAds ($n=35$) when compared with normal parathyroid glands (PaNs; $n=3$), though *RASSF1A* mRNA levels and levels of *RASSF1A* promoter methylation did not correlate. At protein level, RASSF1A was detectable by immunohistochemistry in the cytoplasm of cells in PaNs ($n=3$) and in the rim of PaN surrounding parathyroid adenomas, while cells in PAds ($n=11$) showed weakly positive citoplasmic staining. PCas ($n=6$) were definitely negative both at cytoplasmic and nucelar levels. Furthermore, we investigated 2 potential epigenetic modifiers involved in *RASSF1A* promoter methylation: the methylatransferase DNMT1 and the antisense lncRNA *RASSF1-AS1*. DNMT1 methylates both *RASSF1A* and *APC* gene promoters. We found that DNMT activity, investigated in PAds nuclear extracts ($n=16$), was inversely correlated with RASSF1A protein levels ($r^2=0.400$, $P=0.009$), supporting the involvement of deregulated DNMT activity in the aberrant *RASSF1A* promoter methylation. *RASSF1-AS1* (alias *ANRASSF1*) was implicated in a locus-specific mechanism for the *RASSF1A* epigenetic repression, mediated by Polycomb Repressive Complex 2 (PRC2), reinforcing RASSF1A long-term epigenetic silencing. In PAds, *ANRASSF1* levels positively correlated with expression levels of *RASSF1A* ($r=0.788$, $P=0.0001$). Similarly, *RASSF1A* promoter methylation negatively correlated with *ANRASSF1A* mRNA levels ($r=-0.366$, $P=0.031$). These findings exclude *ANRASSF1* in the methylation process of the *RASSF1A* promoter in PAds. Finally, using HEK293A cells transiently transfected with human CASR as experimental model (CASR-HEK293A), we investigated the effects of *RASSF1A* gene silencing on pERK/ERK levels stimulated by the CASR agonist R568. Efficient *RASSF1A* silencing increased basal pERK/ERK levels and blunted the pERK/ERK increase induced by CASR activation, suggesting that loss of RASSF1A may contribute to the parathyroid cell desensitization towards extracellular calcium concentrations observed in parathyroid tumors.
In conclusion, *RASSF1A* and *APC* promoter methylation is a hallmark of parathyroid adenomas.

DOI: 10.1530/endoabs.81.EP182

EP183

Prediction of 25-hydroxy vitamin D status by serum alkaline phosphatase (ALP) value.

Ishara Ranathunga, J P Naveenkumar, Manilka Sumanatilleke & Noel Somasundaram
NHSL, Colombo, Sri Lanka.

Background and Objectives
The low vitamin D status in an individual leads to a compensatory increase in serum parathyroid hormone (PTH) level giving rise to secondary hyperparathyroidism. The elevated PTH will conserve calcium excretion from the kidneys in the expense of excreting phosphate. Thus, serum calcium levels tend to remain normal until the latter stages of vitamin D deficiency. PTH action on the bone to reabsorb more calcium from the bone lead to elevation of bone alkaline phosphatase (ALP) in the serum. Nevertheless, population screening for vitamin D deficiency in asymptomatic individuals is currently not recommended. ALP measurement as a screening test to detect vitamin D deficiency is a relatively inexpensive test that can be performed easily. We have studied the relationship between the ALP, calcium, phosphate and PTH level to the vitamin D status of patients attending the NHSL.
Methods
A descriptive cross sectional study was conducted from March/ 2019 to March/ 2020 at the Endocrinology Unit of the National Hospital of Sri Lanka. Consecutive sampling was done recruiting all patients who have had vitamin D assessment as part of the routine medical care. Interviewer administered questionnaire was used collect data. Vitamin D sufficiency, insufficiency and deficiency was defined on levels of >50 ng/ml, 20–50 ng/ml, <20 ng/ml respectively. Pearson correlation analysis was used to determine the effects of vitamin D status on various blood parameters including serum total calcium, serum phosphate, ALP and PTH level. Receiver operating characteristic (ROC) curves were used to determine the optimal ALP level to predict vitamin D deficiency.
Results
153 subjects who meets the inclusion and exclusion criteria were recruited in to the study over a period of one year. The population mean age was 52.1 (S.D. $\pm$ 14.38) years and ranged from 18 to 89 years. Out of the whole population 58.8% had vitamin D deficiency while 31.4% suffered from vitamin D insufficiency. Only 9.8% had normal vitamin D levels. ALP level was significantly related to vitamin D deficiency ($P<0.05$). At ALP cutoff value of 72.5 U/L the vitamin D deficiency could be predicted with 76% sensitivity and 80% specificity. ALP cutoff 43 U/L predicts vitamin D deficiency at a 100% sensitivity and 20% specificity.
Conclusions
The population screening for vitamin D deficiency is not a cost effective intervention. A more cheaper and feasible ALP assessment at a cutoff value of 72.5 U/L can predict vitamin D deficiency at a significantly higher specificity and sensitivity.

DOI: 10.1530/endoabs.81.EP183

EP184

The short test with active metabolites of vitamin D in differential diagnosis between primary normocalcemic and secondary hyperparathyroidism for inpatient treatment

Elena Karaseva[1], Anna Eremkina[1], Alina Elfimova[1], Anna Gorbacheva[1], Ekaterina Bibik[1], Elena Kovaleva[1] & Natalia Mokrysheva[2]
[1]Endocrinology Research Center, Department of Parathyroid Disease, Moscow, Russian Federation; [2]Endocrinology Research Center, Director, Moscow, Russian Federation.

Objective
Normocalcemic primary hyperparathyroidism (PHPT) is a phenotype of PHPT characterized by normal serum calcium and persistently increased parathyroid hormone (PTH) after exclusion of secondary causes of PTH elevation.
The aim
of this study was to investigate the capability of the short test with active metabolites of vitamin D for differential diagnosis between normocalcemic PHPT and secondary hyperparathyroidism (SHPT) for inpatient treatment.
Material and methods
We included 90 hospitalized patients with normal albumin-adjusted calcium ($Ca_{adj.}$) and elevated PTH levels (84 women, 6 men, median age 60 years). Ca_{adj}, PTH, creatinine, eGFR, daily calciuria were evaluated before and PTH, $Ca_{adj.}$, creatinine, eGFR 3–5 days after taking 1 mcg of alfacalcidol or calcitriol. Data is presented by medians and interquartile ranges (Median, (25;75)).
Results
According to baseline and dynamic biochemical evaluation patients were divided into 3 groups: group 1 ($n=32$) – patients with elevated or within the upper limit PTH ($n=4$) who reached hypercalcemia ($Ca_{adj.}>2.55$ mmol/l); group 2 ($n=14$) – patients with normalization of PTH and normal Ca_{adj}; group 3 ($n=44$) patients with elevated PTH and normal $Ca_{adj.}$. In group 1, baseline $Ca_{adj.}$ was 2.52 mmol/l (2.50; 2.54), PTH 101.1 pg/ml (81.9; 138.0), after short test – 2.61 mmol/l (2.58; 2.64), and 92.3 pg/ml (71.2; 119.5) respectively, regarded as PHPT. Among them 19 patients underwent surgery with histological confirmation of diagnosis, 2 patients are waiting for surgery, 11 patients with asymptomatic form are under dynamic observation. In group 2, baseline $Ca_{adj.}$ was 2.34 mmol/l (2.31; 2.44), PTH 81.1 pg /ml (72.9; 95.7) vs 2.40 mmol/l (2.33; 2.51) and 54.53 pg/ml (40.7; 63.6) respectively after short test regarded as SHPT. Groups with PHPT and SHPT significantly differed from each other in Ca_{adj} and daily calciuria ($P<0.05$) but not in PTH, eGFR. 44 patients from group 3 did not show significant changes thus differential diagnosis was continued on an outpatient basis.
Conclusion
The study showed significant changes in calcium and PTH levels during the short test in 46/90 patients. Stable normocalcemia and normalization of PTH allows confirming SHPT while elevated or within the upper limit PTH levels with hypercalcemia – PHPT.

DOI: 10.1530/endoabs.81.EP184

EP185

Evaluation of response to alendronate treatment on osteoporosis using cathepsin K and other biomarkers

Roxana Novac[1], Popescu Costin-Ioan[2] & Cotirlet Valentin-Adrian[3]
[1]Emergency Hospital, Moineşti, Romania; [2]Institute of Biochemistry of the Romanian Academy, Bucureşti, Romania; [3]Vasile Alecsandri University of Bacău – Mărăşeşti Campus, Bacău, Romania.

Background
Osteoporosis has been an excruciating disease for many years now. Although various treatments are available, there is an unmet need for disease prognosis, early disease diagnosis and prediction of treatment efficacy. New biomarkers are crucial for the diagnosis or prognosis of a disease as well as for monitoring treatment efficacy and improve decision making. Cathepsin K is a cysteine protease that cleaves collagen type I, the major type of collagen found in bone, so it is useful to measure to assess the function and number of osteoclasts. The aim of the current study was to evaluate the fluctuation of cathepsin K, phosphorus, 25 HO vitamin D, alkaline phosphatase and PTH before and after 6 and 12 months of treatment with alendronate.
Methods
We conducted a longitudinal study with a cohort of 28 female patients with osteoporosis and 15 healthy controls. All subjects were menopaused, non-diabetic, non-obese, without secondary osteoporosis. All patients were treated with alendronate and calcium and vitamin D supplements. Serum samples were collected longitudinally before treatment, at 6 and 12 months post treatment initiation and the levels of cathepsin K, phosphorus, 25 HO vitamin D, alkaline phosphatase and PTH were measured.. Basal serum cathepsin K levels were also compared to premenopausal women without osteoporosis ($n=15$).
Results
We observed that serum cathepsin K levels were higher in premenopausal women with osteoporosis (9746.07 +/− 1824 RFU/ml) compared with healthy premenopausal women (7747.33 +/− 762.67 RFU/ml; $P<0.01$). Also, serum cathepsin K decreases gradually after alendronate treatment (5.09% at 6 months, and 7,17% at 12 months, $P<0.05$). We also found a positive association of cathepsin K and phosphorus and alkaline phosphatase and a negative association with 25 HO vitamin D.
Conclusion
We conclude that serum cathepsin K may serve as an additional biomarker for bone metabolism and alendronate treatment monitoring besides phosphorus and alkaline phosphatase. The role of Cathepsin K as a risk biomarker marker in premenopausal women without osteoporosis is also discussed.

DOI: 10.1530/endoabs.81.EP185

EP186

Bone tissue metabolism in children with dystrophic form of congenital epidermolysis bullosa before and during therapy with cholecalciferol.

Irina Pronina[1], Svetlana Makarova[1], Nikolay Murashkin[2], Elena Semikina[3] & Tamara Chumbadze[1]
[1]National Medical Research Center of Children's Health of the Russian Federation Ministry of Health, Department of Preventive Pediatrics, Moscow, Russian Federation; [2]National Medical Research Center of Children's Health of the Russian Federation Ministry of Health, Department of Dermatology, Moscow, Russian Federation; [3]National Medical Research Center of Children's Health of the Russian Federation Ministry of Health, Clinical Diagnostic Laboratory with a group of express diagnostics, Moscow, Russian Federation.

Introduction
Malnutrition, deficiency of micro- and macronutrients, including calcium and vitamin D are typical for children with dystrophic form of congenital epidermolysis bullosa (DEB). Thereby, there is a slowdown in osteogenesis and in stimulation of osteoclast activity, bone tissue resorption, which leads to increased bone fragility and low-traumatic fractures.
Aim of the study
To evaluate markers of bone tissue metabolism and phosphorus-calcium metabolism in children with DEB before and during therapy with cholecalciferol.
Methods and materials
71 children with DEB were included (39 girls (55%), 32 boys (45%)), the median age was 8.5 years [3.67; 11.92] and 5.75 years [3.13; 10.46]. All patients were examined before the therapy with cholecalciferol, and 6 months after. Dual X-ray absorptiometry was used to assess bone tissue density. Vitamin D, total calcium, phosphorus, N-terminal propeptide of procollagen type I (P1NP), osteocalcin (OS) and carboxyterminal cross-linked telopeptide of collagen type I (CTX) levels were determined.
Results
A high frequency of insufficiency (20–30 ng/ml) – 22.5%, deficiency (10–20 ng/ml) – 31% and deep deficiency (< 10 ng/ml) – 9.9% of vitamin D, as well as hypocalcemia total calcium (< 2.2 mmol/l) – 39.4% was identified. BMD decrease to osteopenia level was identified in 33.8%, osteoporosis – in 19.7% of children. In patients with hypocalcemia (Me total calcium 2.13 mmol/l [2.1; 2.16]), OS and CTX was significantly lower than in patients with normal calcium (Me OS 53.16 ng/ml [32.86; 64.61] vs 73.61 ng/ml [44.43; 111.9], $P=0.001$; Me CTx 1.22 ng/ml ml [0.93; 1.38] vs 1.49 ng/ml [1.2; 1.83], $P=0.015$). P1NP levels did not differ in patients with hypocalcemia and normal calcium ($P=0.617$). In children with hypocalcemia there was a lower BMD ($P=0.004$). The median daily dose of colecalciferol was 1100 IU in boys [1000; 2250] and 2000 IU [1000; 3000] in girls. After 6 months of the therapy normalization of 25(OH)D level in 62% of children. Statistically decreased levels of P1NP (409.15 ng/ml [156.1; 695] after the treatment vs. 436.65 ng/ml [196.1; 864] before the treatment, $P<0.001$), phosphorus (1.51 mmol/ l [1.3; 1.68] vs 1.58 mmol/l [1.45; 1.67], $P=0.012$) were detected. As well as BMD decrease severity (Z-score −1.3SD [−2.3; −0.2] vs −1.5 s.d. [−2.2; −0.4], $P=0.024$), with simultaneous OS growth 70.1 [56.3; 96.04] vs 65.17 [42.86; 85.4], $P<0.001$.
Conclusion
On cholecalciferol supplementation, we observed bone tissue metabolism markers positive dynamics and BMD increase. Further research in this field with the optimal medicine dose is needed.

Keywords
congenital epidermolysis bullosa, vitamin D, hypocalcemia, osteoporosis.
DOI: 10.1530/endoabs.81.EP186

EP187

A special case of type Ib pseudohypoparathyroidism

Kadiri Chaimae & Amhager Samah
Hôpital Cheikh Zayd, Pediatric, Rabat, Morocco.

Introduction
Pseudohypoparathyroidism type Ib are genetic diseases with transmission maternal, defined by a resistance to the action of the parathormone without resistance to the TSH. Clinical manifestations are variable and depend on the severity of hypocalcaemia. We report the case of a patient presenting with type Ib pseudohypoparathyoidia.
Observation
This is a 9-year-old child admitted for care and exploration of a severe hypocalcaemia. The patient has been followed for unlabeled laryngeal stridor since birth. We note childhood obesity. He has episodes of spasm repetitive pedal carpe with vomiting. The clinical examination demonstrates a moon faces with macroglossia. The phosphocalcic balance shows a severe hypocalcaemia at 56 mg/l with elevated phosphoremia and hypocalciuria. The parathormone dosage was high (160.6 pg/ml) with normal TSH (1.27 uIU/ml). Brain CT finds Fahr's syndrome. X-ray of the hands finds a slight brachymetacarpy of the fourth ray. The genetic study highlights evidence of pseudohypoparathyroidism in non-transmissible somatic mosaicism. The patient received vitamin-calcium supplementation with a good clinical and biological evolution.
Discussion
Pseudohypoparathyroidism is a pathology that is sometimes difficult to diagnose, generally evoke in front of any hypocalcaemia with hyperphosphatemia and PTH high. This observation underlines the interest of thinking about pseudohypoparathyroidism in children in front of spasms in order to allow an adapted treatment allowing avoiding the occurrence of severe hypocalcaemia threatening the vital prognosis and the impact on child growth.

DOI: 10.1530/endoabs.81.EP187

EP188

Chronic bone pain revealing a parathyroid adenoma

Kadiri Chaimae & Lachkar Hassan
Hôpital Cheikh Zayd, Endocrinology, Rabat, Morocco.

Introduction
Primary hyperparathyroidism is an endocrinopathy characterized by the excessive secretion of parathyroid hormone, most commonly associated with parathyroid adenoma. The osteoarticular manifestations of hyperparathyroidism are currently exceptional. The diagnosis is most often established at the asymptomatic stage by measuring calcium levels and parathyroid hormone.
Observation
We report the case of a 67-year-old patient with a history of partially calcified right parietal meningioma, and who consulted for diffuse mechanical bone pain. A phosphocalcic balance is carried out objectifying a hypercalcemia corrected to 117 mg/l with a normal phosphoremia at 29 mg/l, a normal vitamin D and a parathyroid hormone elevated to 115 g/l. A subtraction parathyroid scintigraphy with MiBi-99mTc/Pertechnetate revealed a right lower polar parathyroid adenoma measuring 5×4×6 mm, oval, regular, hypoechoic and heterogeneous. Ablation of the parathyroid adenoma was performed in our patient with simple operative consequences and good progress.

Discussion and conclusion
Bone manifestations have become rare in hyperparathyroidism. They are characterized mainly by mechanical polyarthralgia, bone swelling or even pathological fractures. The positive diagnosis is based biologically on confirmed hypercalcemia with elevated PTH and morphologically on parathyroid scintigraphy at TC 99 m which allows visualization of the parathyroid adenoma. The treatment is surgical.

DOI: 10.1530/endoabs.81.EP188

EP189

Bilateral pathologic fracture of the femur in brown tumor İnduced parathyroid carcinoma

Filiz Mercan Sarıdaş, Ensar Aydemir, Coskun Ates, Erhan Hocaoğlu, Soner Cander, Ozen Oz Gul, Canan Ersoy & Erdinc Erturk
Bursa Uludag University, Endocrinology and Metabolism, Bursa, Turkey.

Introduction
Brown tumor refers to the skeletal change that develops as one of the complications of hyperparathyroidism, in which cystic and fibrous changes occur in the bone. It occurs in approximately 10−20% of patients with primary hyperparathyroidism. Parathyroid cancer is a rare cause of primary hyperparathyroidism and accounts for approximately 1% of cases. In some cases, hyperparathyroidism may be asymptomatic until it becomes a pathological fracture and may be the first sign of a malignant tumor. Here, we report a case of parathyroid carcinoma presenting with bilateral femoral fracture because of its rarity.
Case
A 56-year-old male patient presented with pain and limitation of movement in both thighs after falling in the bathroom. It was learned that he had difficulty in walking and pain in the legs for 6 months in his history, and he did not have an additional disease or medication. X rays showed the fractures in both femurs and left olecranon and findings consistent with multiple (bilateral femur, tibia, fibula and right radius and ulna) Brown tumors were found in the bones. Blood investigations showed raised levels of serum calcium, with highly raised levels of serum parathyroid hormone (PTH). After neck ultrasonography and parathyroid scintigraphy, an appearance compatible with parathyroid adenoma was found in the inferior of the right thyroid lobe, and parathyroidectomy was performed, but postoperative PTH elevations continued. Thereupon, the patient was evaluated with neck tomography and parathyroid scintigraphy for the second time, and he was reoperated when another focus was detected in the upper mediastinum at the level of the angulus venosus in the isthmus inferior of the thyroid gland. The operative pathology resulted as parathyroid carcinoma. The patient who developed postoperative hungry bone syndrome was operated for bilateral femoral fracture after calcium normalization was achieved.
Conclusion
The main treatment for parathyroid carcinoma is surgery. In the presence of fracture, it is recommended to perform parathyroidectomy first and then orthopedic treatment. In the presence of osteolytic lesion and high serum calcium in patients presenting with pathological fracture, Brown tumor related to parathyroid carcinoma should be kept in mind in the differential diagnosis.
Keywords
Hyperparathyroidism, brown tumor, femur, pathological fracture.
DOI: 10.1530/endoabs.81.EP189

EP190

Giant cells and a hungry bone: a diagnostic and therapeutic challenge.

Rashmi Nanjundaswamy[1,2], Sunil Navalgund[1], Govindarajan Mallarajapatna[1], Srimant Srinivas Bindiganavile[1] & Hema Venkataraman[1]
[1]Apollo Hospitals Bangalore, Bengaluru, India; [2]Apollo Sugar Clinics, Bengaluru, India.

Introduction
Brown tumours (BT) are a recognised complication of severe prolonged untreated hyperparathyroidism (HPT). BT can mimic bone metastases and giant cell tumors (GCT). Hungry bone syndrome (HBS) is a severe and prolonged, postoperative hypocalcemia following parathyroidectomy. BT are a risk factor for HBS. We report the case of a young lady with BT masquerading as a GCT,from a tertiary centre in India.
Case study
A 25 year lady presented with pathological fractures of humerus,tibia and inabilty to weight bear. MRI in primary care, showed multiple hyperintense (T2 imaging) expansile lytic lesions over humerus,pelvis and femur with compression fracture of vertebrae. FNAC was suggestive of giant cell tumour. PET-CT confirmed hypermetabolic multifocal expansile bone lesions with fractures and osteoporotic vertebrae with no evidence of primary malignancy, raising a differential diagnosis of brown tumours. Biochemistry revealed elevated calcium (S.Ca 11.9 mg/dl, normal range (NR) 8.8–10.6), Alkaline phosphatase(304 IU/L,(NR 53–141)). Parathyroid hormone(PTH) was elevated: PTH 486 pg/ml (NR 10.0 −65 pg/ml) with severe Vitamin D deficiency: 6.5 ng/ml(NR 30–100 ng/ml),low phosphorous 1.7 mg/dl(NR 2.5–4.5 mg/dl). A diagnosis of primary HPT with brown tumours was made.PETCT, contrast enhanced CT and targeted ultrasound failed to localize a parathyroid adenoma. Sestamibi scan showed faint uptake at the right superior parathyroid. Preoperatively a loading dose of 300,000 units of Intramuscular and 200 units of oral cholecalciferol was given. Consent for targeted parathyroidectomy and possible full neck exploration was taken. Right superior parathyroid gland of 1.6×1.2 cm was excised, which was thin and flat (probably the reason for missing on CT/ultrasound). Significant decrease in intraoperative PTH level (628.1–35.5 pg/ml) was observed. Intra-operative frozen section confirmed parathyroid adenoma.Post procedure she developed HBS (mean calcium 7.9 mg/dl) remaining asymptomatic. She required escalating dose of oral calcium upto 15 g of elemental calcium and 4 mg calcitriol with intermittent intravenous calcium and magnesium supplements. Proton pump inhibitors (PPI) were with-held. Post discharge calcium remained stable around 9 mg/dl with above dose of calcium and calcitriol. Pathological fractures are being managed conservatively.
Conclusion
BT is an important differential diagnosis for lytic expansile bone lesions with giant cell morphology on histology. BT often resolves with HPT treatment. Early diagnosis aviods complex surgical intervention.BT increases risk of post-operative HBS. Pre-operative loading of Vitamin D may have reduced duration and severity of HBS. However more evidence is needed to support this approach. Correction of Hypomagnesemia and withholding PPI aids optimal absorption of oral calcium.

DOI: 10.1530/endoabs.81.EP190

EP191

Primary hyperparathyroidism in the setting of previous roux-en-Y gastric bypass: a case report

Lavinia Monte, Dario Tuccinardi, Rocky Strollo, Silvia Briganti, Donatella Rausa, Paolo Pozzilli, Nicola Napoli & Silvia Manfrini
Campus Bio-Medico University of Rome, Unit of Endocrinology and Diabetes Department of Medicine, Rome, Italy.

Introduction
Primary hyperparathyroidism (PHPT) after roux-en-Y gastric bypass (RYGB) is poorly described. The diagnosis can be difficult as secondary hyperparathyroidism(SHPT) commonly occurs in patients after RYGB due to calcium hypoabsorption and vitamin D deficiency.
Observation
We present the case of a 50-year-old female with a history of normocalcemic hyperparathyroidism and nephrolithiasis. In 2005 the patient had undergone RYGB. During the first visit, an iso-hypoechoic nodule below the right inferior pole of the thyroid gland with a maximum size of 47 mm and internal vascularization was detected. Her biochemistry revealed a PTH of 930 pmol/l (18–80 pmol/l), normal levels of total calcium and phosphorus, mild hypoalbuminemia, adjusted calcium of 9.8 mg/dl, hypercalciuria, 25-OH vitamin D levels of 6.4 mcg/l (>30 mcg/l). She was initially treated with 100 000 IU of Vitamin D3 intramuscularly once a month, but calcifediol, a hydroxylated form of vitamin D, was later prescribed due to the patient's discomfort with the intramuscular injection. Further investigations demonstrated decreased bone density at the hip and distal radius and a single image suggestive for parathyroid adenoma detected by SestaMIBI scintigraphy. The patient underwent parathyroidectomy, and she was discharged with calcium carbonate and calcitriol therapy, but a few days later, she accessed our A&E for hypocalcemia. The hungry bone syndrome was excluded due to her normal phosphorus and magnesium. Histology confirmed a parathyroid adenoma with a maximum diameter of 5 cm. The patient was treated with a single 10% calcium gluconate vial, and subsequently, we preferred to start with calcium citrate supplementation, which is absorbed more efficiently than calcium carbonate. Calcitriol and a protein supplement to treat the persistent patient's hypoalbuminemia were added. After that, no more severe hypocalcemia episodes occurred, her serum calcium and vitamin D level remained within normal range, PTH levels dropped until 135 pmol/l, and a gradual reduction of the oral supplementation doses was made.

Conclusion
PHPT after RYGB is a rare condition, and concomitant SHPT can make diagnosis and follow-up difficult and predispose patients to more severe postoperative hypocalcemia.

DOI: 10.1530/endoabs.81.EP191

EP192

Fahr Syndrome secondary to pseudohypoparathyroidism.

Tea Shehu, Violeta Hoxha, Dorina Ylli & Agron Ylli
University of Medicine, Mother Teresa Hospital Center, Endocrinology, Tirana, Albania.

Background
Fahr's Syndrome, also known as striopallidodentate calcinosis is a rare form of neurological disorder characterized by abnormal calcified deposits in basal ganglia, cerebellar and cerebral cortex. Its prevalence goes from 2 to 12.5%. Etiology of this disorder is very wide and involves endocrinopathy, mitochondrial myopathies dermatological abnormalities, infectious disease or may be idiopathic. We present a case of a patient with diffuse brain calcifications due to pseudohypoparathyroidism probably type 1b.
Case description
We present a case of a 37 years old man who presented in the Emergency Unit with epileptic generalized tonic-clonic seizure. He was known to suffer from epilepsy since 4 months of age but head CT was performed for the first time during this hospitalisation and difuse bilateral brain calcifications were noticed. The patient has short stature with round face and brachydactyly of 4th metacarp. He also showed intellectual disability.Biochemical analysis showed hypocalcemia (6.1 mg/dl) with low/normal Vit D levels (29.8 ng/ml) and high PTH levels (152.1 ng/l). Hepatic and renal function were normal. Other electrolytes were also normal. Anterior hypophysis hormones were in their normal range. Because of hipocalcemia with high PTH levels and normal vit D, magnesium levels and renal function, diagnosis of pseudohypoparathyroidism was made. Lack of other hormone resistances, and clinical appearance suggests pseudohypoparathyroidism type 1b. The patient was treated with IV calcium and Vit D3 firstly and then with calcitriol 0.25/daily. On follow up levels of serum ionized calcium and 24 h calcinuria were improved.
Conclusions
Fahr's Disease is a rare, neurological complication of chronic pseudohypoparathyroidism. In most cases the diagnose is clinical-radiological with diffuse brain calcifications. It is suggested that PTH plays a protective role against calcifications in the brain. The mechanism is not fully explained but it is emphasized the importance of PTH receptor 2, found in brain cells and mitochondrial superoxides. After confirming pseudohypoparathyroidism, the patients should start treatment with cholecalciferol or ergocalciferol (firstly to fill the depots) and calcium supplements. Because PTH is required for the renal conversion of calcidiol to calcitriol (active metabolite) calcitriol is often the treatment of choice.
Key words
calcium, PTH, hypoparathyroidism, pseudohypoparathyroidism, brain calcifications.

DOI: 10.1530/endoabs.81.EP192

EP193

Late hypocalcaemia complicating the management of papillary thyroid carcinoma

Ihssane Abidi, Kaoutar Rifai, Iraqi Hinde & Mohamedelhassan Gharbi
University Mohammed 5 Rabat, Endocrinologie, Rabat, Morocco.

Introduction
COVID-19 is a pandemic related to SARS-COV-2 virus infection. It is most often manifested by an influenza-like syndrome with other symptoms that are more specific such as loss of smell and taste.
Its severity is highly variable, ranging from asymptomatic to severe or prolonged forms.
We report the case of a 47-year-old female patient, who is being followed for hypoparathyroidism, who developed severe and persistent cramps after the COVID-19 vaccine.
Observation
This is a 47-year-old female patient with a history of high-risk papillary thyroid carcinoma since 2018, operated and irradiated. Her surgery was complicated by supplementary hypoparathyroidism. Her blood calcium was well controlled and she was asymptomatic since her supplementation with Alfacalcidol and calcium. She received the first dose of astrazeneca in July 2021, after 4 h she developed persistent painful cramps in her extremities. Her clinical examination did not reveal any signs of hypocalcaemia and the biological dosage was 84 mg/l. As the cramps persisted, we started her on calcium and magnesium. The clinical evolution was good after 6 h and there was no recurrence.
Discussion
COVID-19 vaccines are as well tolerated in neuromuscular patients as in the general population (1). Hypoparathyroidism is not a neuromuscular disease, but it can be caused by hypocalcaemia, which is the cause of the neuromuscular manifestations. Campesium can be seen with COVID-19 vaccines, and is generally benign and transient. The particularity of our observation is that the cramps were severe and incapacitating with the need for intravenous calcium treatment and monitoring, adding the hypoparathyroid terrain which posed a problem of differential diagnosis.
Conclusion
The vaccine against COVID-19 has become an unavoidable necessity in the face of the pandemic population. It certainly has short and long term side effects. Fragile patients must be monitored to avoid complications, particularly neuromuscular ones.
References
(1) NEUROMUSCULAR DISEASES AND COVID-19 VACCINATION, Recommendations of the filnemus rare diseases health sector, Version 1.0 of 4 January 2021.

DOI: 10.1530/endoabs.81.EP193

EP194

Vitamin D deficiency in the type 2 diabetic population of Northern Gran Canaria Island: Still highly prevalent but supplementation is on the rise

Alba Hernandez-Lazaro, Ricardo de Leon-Durango, Agnieszka Kuzior, Carmen Acosta-Calero, Claudia Arnas-Leon, Maria del Sol Sanchez-Bacaicoa, Debora Garcia-Alamo, Marta Martin-Perez, Paula Gonzalez-Diaz & Francisco Javier Martinez Martin
Hospital Universitario de Gran Canaria Dr. Negrín, Spain.

Introduction
Vitamin D deficiency is associated with higher risk of severe COVID-19, and type 2 diabetic patients are a vulnerable group**.** We described an alarming rate of vitamin D deficiency (around 80.0% with plasma calcifediol <30 ng/ml) in unsupplemented type 2 diabetes patients during the 2020 spring lockdown and the following winter in Northern Gran Canaria. There is an increasing awareness of this problem, both in family physicians and the general population, and the use of vitamin D supplements is rising.
Objectives
To assess the prevalence of vitamin D deficiency in type 2 diabetic patients from Northern Gran Canaria during the late autumn-early winter period (November 2021 to January 2022), and its relationship with vitamin D supplementation.
Methods
Plasma calcifediol levels were sampled in an unselected type 2 diabetic population, and recorded anonymously along with age, gender and vitamin D supplementation status. All included patients gave their informed consent.
Results
Data were obtained from 217 consecutive patients; only 2 ($<1\%$) were excluded due to lack of consent.129 were female (59.4%), mean age was 58.6 ± 13.9 years. 138 (60.8%) were taking vitamin D supplements. Mean plasma calcifediol was 35.7 ± 14.9 ng/ml; but it was lower than recommended ($<$ 30 ng/ml) in 85 (39.2%) of the patients, deficient ($<$ 20 ng/ml) in 35 (16.1%) and severely deficient (<12 ng/ml) in 8 (3.7%). In vitamin D supplemented patients, mean calcifediol was 43.2 ± 11.6 ng/ml, with 20 patients (14.5%) <30 ng/ml, 6 (4.3%) <20 ng/ml, none $<$ 12 ng/ml and 1 (0.7%) $>$ 80 ng/ml. In unsupplemented patients, mean calcifediol was 22.7 ± 9.3 ng/ml, with 65 (82.2%) $<$ 30 ng/ml, 29 (36.7%) $<$ 20 ng/ml and 8 (10.1%) <12 ng/ml). Plasma calcifediol was significantly higher in supplemented patients (mean difference 20.5 ± 5.9 ng/ml, unpaired t-test, $P < 0.0001$) and the proportions of low, deficient and severely deficient patients were significantly lower (Fisher's exact test, $P < 0.0001$, $P < 0.0001$ and $P = 0.0002$, respectively).
Conclusions
The prevalence of vitamin D deficiency during the late autumn-early winter months in our unsupplemented type 2 diabetic population remains extremely high. However, the use of supplements is increasing, about 60% of our patients at present (45% in our previous survey 1 year ago). In supplemented patients vitamin D status is satisfactory with 4% deficient, none severely deficient and $<$ 1% above the recommended level.

DOI: 10.1530/endoabs.81.EP194

EP195

Management of denosumab discontinuation in a patient with osteonecrosis of the jaw and coexisting primary hyperparathyroidism

Matteo Malagrinò, Elisabetta Belardinelli, Paola Altieri, Uberto Pagotto & Guido Zavatta
Division of Endocrinology and Diabetes Prevention and Care, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Department of Medical and Surgical Sciences (DIMEC), Alma Mater Studiorum University of Bologna, Bologna, Italy.

Context
Patients with primary hyperparathyroidism (PHPT) may be treated with denosumab due to coexisting osteoporosis. Few studies have been conducted in this population.
Case presentation
An 84-year-old woman was seen in the outpatient clinic in March 2018 due to calcium levels at the upper limit of reference range (10,2 mg/dl) associated with elevated levels of PTH (112 pg/ml) and sufficient 25(OH)Vit D (24 ng/ml) levels, findings consistent with mild PHPT. Her past medical history included: osteoporosis with vertebral fractures (T11 and T12 vertebral bodies) since 2009, hystero-annexectomy in 1973, quadrantectomy for breast carcinoma in 2009, bowel resection for adenocarcinoma in 2008, prior ischemic stroke, prior gastric ulcer treated with gastrectomy and current jejunum ulcer. The patient had been on Alendronate 70 mg weekly since 2008 and taking 1100 IU of vitamin D3, and furosemide 25 mg/day. Patient's biochemistries were rechecked after three months: PTH was 61 pg/ml (12–88 pg/ml), serum Ca 11.3 mg/dl, serum phosphate 2.6 mg/dl, CTX 0.809 ng/ml. Due to age and comorbidities, the patient was not a good candidate for parathyroid surgery. Alendronate was stopped and denosumab 60 mg q6m was prescribed, the patient being evaluated every six months. In December 2020, a 2-cm area of active osteonecrosis appeared in the right mandibular region. Denosumab was promptly interrupted. To avoid potential rebound hypercalcemia the patient was immediately switched to cinacalcet at an initial dose of 30 mg per day, then increased at 60 mg per day after a few months, while checking serum calcium levels every 3 to 6 months, with safe control of serum calcium, PTH and overall symptoms.
Discussion
Denosumab is effective in improving BMD, lowering bone turnover and serum calcium in patients with PHPT, nonetheless, because of its mechanism of action, its discontinuation has been associated with rebound clinical fractures. Currently, limited data are available on the best management of patients discontinuing denosumab, although it is recommended to continue anti-osteoporotic treatment with oral or intravenous bisphosphonates. For our patient we could not consider these options due to coexisting active osteonecrosis. The patient had also two previous vertebral fractures. Hypercalcemia was managed with cinacalcet, and the patient has not sustained any fractures as of January 2022.
Conclusion
We suggest prompt cinacalcet use to manage potential rebound hypercalcemia following denosumab discontinuation in patients with PHPT, although these patients will remain at risk of rebound fractures.

DOI: 10.1530/endoabs.81.EP195

EP196

Impact of COVID-19 pandemic on waiting time from referral to definitive surgery in primary hyperparathyroidism: a large tertiary centre experience

Razan Ali Rashid[1], Jason Ramsingh[2], Richard Bliss[2], Peter Truran[2] & Yaasir Mamoojee[1]
[1]The Newcastle upon Tyne Hospitals, Department of Endocrinology, Newcastle upon Tyne, UK; [2]The Newcastle upon Tyne Hospitals, Department of Endocrine Surgery, Newcastle upon Tyne, UK.

Background
The COVID-19 pandemic has resulted in widespread disruption to delivery of emergency and elective care in the last 2 years. Nevertheless, healthcare systems have quickly readapted to accelerate use of novel pathways for delivering clinical services. We reviewed the impact of COVID-19 pandemic on our time from community referral to definitive surgery in patients with Primary Hyperparathyroidism (PHPT).
Methods
We retrospectively reviewed the waiting times from General Practice (GP) referral to parathyroid surgery through our pathway which includes initial Endocrinology review before referral for surgical review. Data was collected before COVID19 pandemic (2019) and compared with data during the pandemic (2020–2021). Results are reported as mean for continuous variables. The Mann Whitney U test was used for comparing continuous variables between groups. A P value of <0.05 was considered statistically significant.
Results
28 patients were included in the pandemic cohort and 37 patients were in the pre-pandemic cohort. Time from GP referral to Endocrinology review was 60 days in the pandemic cohort (vs. 91 days in the pre-pandemic cohort, $P=0.03$). Time from first Endocrinology review to referral for surgery was 26 days in the pandemic cohort, compared to 341 days in the pre-pandemic cohort ($P<0.01$). There was no statistical difference in waiting times from surgical referral to surgical clinic review and thence to surgery between the pandemic and pre-pandemic cohort (54 days vs. 73 days and 181 days vs. 156 days, respectively). Overall, time from GP referral to definitive surgery was lower in the pandemic cohort at 314 days compared to 651 days in the pre-pandemic cohort ($P<0.01$), with the most impact on this reduced waiting time being from GP referral to surgical referral by Endocrinology (84 days vs. 422 days, $P<0.01$). There was no difference in our surgical pathway from time of referral for surgery to date of surgery in both cohorts (239 days v.s 229 days, $P=0.85$).
Conclusion
Our waiting times from GP referral to definitive surgery in patients with PHPT are surprisingly lower during the COVID-19 pandemic when compared to pre-pandemic times. These improved waiting times can be attributed to innovative pathways and judicious use of resources by both the Endocrinology and Surgical teams in our tertiary centre.

DOI: 10.1530/endoabs.81.EP196

EP197

Correlation between vitamin D levels and severity of COVID 19 disease. Argentine Experience

María Laura García[1], Ana Paula Lisdero[1], Evangelina Giacoia[2], Franco López[3], Mauro Cruceño[2], Valeria Pollini[4], Marcia Esposito[5], Mariana Scarabino[6], Susana Bacigaluppi[7] & Aizhar Giselle Mumbach[7]
[1]Sanatorio Méndez, Endocrinology, Buenos Aires, Argentina; [2]Hospital Posadas, Endocrinology, Argentina; [2]Hospital Posadas, Endocrinology, Argentina; [4]Hospital Morón, Argentina; [5]Sanatorio Anchorena, Argentina; [6]Sanatorio Méndez, Internal Medicine, Argentina; [7]Sanatorio Méndez, Endocrinology, Argentina.

Objective
Vitamin D (VD) plays a role in immune response. Recent data shows that low levels of VD could worsen COVID-19 outcomes. This study aimed to establish an association between VD levels among COVID-19 patients with clinical outcomes and inflammatory markers.
Methods
Prospective multicentric cohort study. Consecutively recruitment. Patients were grouped according admission status and level of VD [sufficient >30 ng/ml (VDS), insufficient 20–30 ng/ml (VDI), deficient <20 ng/ml (VDD)]. The variables evaluated were age, gender, oxygen mask requirement (O2r), mechanical ventilation (MV), pre-existing comorbidities, inflammatory markers, severity of COVID-19 measured by News Score.
Results
363 patients were recruited (age 53 ± 16), 59% male, 88% from total were hospitalized, whose VD levels were significantly lower than ambulatories (19 ± 11 vs. 24.3 ± 14 ng/ml P:0.006). The amount between groups was VDS (15%), VDI (27%), VDD (58%).VD levels correlated negatively with hospitalization days and evolution time (P:0.045-P:0.043). Severity of COVID-19 adjusted by comorbidities was linked to a lower VD status (P: <0.001) Also an association with pronation requirement among patients with lower VD levels (P: 0.008) was observed. O2r risk was elevated among VDI (OR 2.9 95%CI 1.3–7) and VDD (OR 3 95%CI 1.4–6),multiplying the odds in 2.6 and 3.7 in presence of 1 or more comorbidities with a higher need of ICU in VDD groups (OR 4.8 95%CI 1.2–20). A negative relation between VD levels, basal ferritin and LDH was described (P:0.018 and P:0.045).
Conclusion
Among COVID-19 hospitalized VD level was significantly lower than ambulatory patients. There is an association between low VD with a worse course of disease needing more days of hospitalization, thus lengthening the time of sickness. VDI and VDD group had severe forms of COVID-19. VDD presented a higher risk for ICU attention. Further studies are needed to emphasize the importance of adequate levels of VD to improve COVID-19 outcomes.

DOI: 10.1530/endoabs.81.EP197

EP198

From chronic hypomagnesemia with secondary hypoparathyroidism to basal ganglia calcification

Irine Lomtadze[1], Maka Mania[2], Tamari Khutsishvili[3] & Nino Eloshvili[4]
[1]Aversi Clinic, Endocrinology, Tbilisi, Georgia; [2]Aversi Clinic, Neurology, Tbilisi, Georgia; [3]Research Institute of Clinical Medicine, Todua Clinic, Endocrinology, Tbilisi, Georgia; [4]New Hospitals, Endocrinology, Tbilisi, Georgia.

As it is known, hypomagnesemia leads to decreased synthesis of Parathyroid hormone (PTH) and can cause PTH resistance. Chronic hypoparathyroidism itself may lead to basal ganglia calcification. We report a 58 years old male, who has suffered from convulsions for over 10 years, with a history of alcohol abuse (more than 25 units of alcohol/week). During this period there have been frequent aware convulsions, resembling to tetany, typical for hypocalcemia. Hypocalcemia and hypomagnesemia had been detected several times. Symptoms usually resolved by administration of Calcium and Magnesium. Patient used to stop taking supplements and continued alcohol abuse as soon as symptoms ameliorated.At the age of 58 patient had 3 tonic-clonic seizures with loss of consciousness, different from previous convulsions. The laboratory investigations showed severe hypocalcemia, hypomagnesemia, very low level of PTH and hyperphosphatemia (ionized Ca_0,60 mmol/l (1.15–1.29), Mg_0.56 mmol/l (0.66–1.07), PTH_2.5 pkg/ml (15–65), Phos_1.54 mmol/l (0.81–1.45), 25(OH)D_24.0 ng/ml. Electroencephalogram showed epileptiform activity (less common to hypocalcemia) and brain CT showed basal ganglia calcification, which may be manifestation of longstanding hypoparathyroidism. According to those findings, patient was diagnosed with structural generalized epilepsy. We believe it is a complication of longstanding hypomagnesemia with secondary hypoparathyroidism. Anticonvulsant (CBZ 200 mg TID) was added to prescription. Main cause of hypomagnesemia seems to be alcohol abuse, but other factors may also exist.
I/v correction of hypocalcemia and hypomagnesemia was followed by oral Magnesium orotate (Mg _ 32.8 mg) two times a day, Calcium Carbonate (Ca _ 500 mg.) three times a day, and Calcitriol 0.5 mcg/daily. Calcitriol was discontinued in several days after Calcium correction. On follow up visit (6–7 weeks later) elevation of PTH level was found _ PTH 10.49 ng/l (12–50), Ca _1.12 mmol/l (1.12–1.32), Mg_ 1.66 mg/dl (1.6–2.6). No more seizures were noted. Non managed chronic hypomagnesemia with secondary longstanding hypoparathyroidism might lead to basal ganglia calcification, followed by development of epilepsy. In our case, it is not till clear, if hypomagnesemia is the only cause of hypoparathyroidism or not, because PTH level still stays below of reference range. However, it is clear, that administration of magnesium increased PTH secretion and decreased severity of hypoparathyroidism. We keep on observing.
Conclusion
Serum Magnesium level (as well as Calcium level) should be measured in all patients with seizures. Early diagnosis and management of hypomagnesemia with secondary hypoparathyroidism may prevent long-term irreversible neurologic complications.

DOI: 10.1530/endoabs.81.EP198

EP199

When to expect a positive parathyroid hormone washout in primary hyperparathyroidism – a single center experience

Mirna Mustapic[1], Jelena Andric[1], Ana Majic[1], Ozana Jaksic[2], Lovorka Derek[3], Tajana Stoos Veić[4] & Vlatka Pandzic Jaksic[1]
[1]Dubrava University Hospital, Department of Endocrinology, Zagreb, Croatia; [2]University of Zagreb, School of Medicine, Zagreb, Croatia; [3]Dubrava University Hospital, Department of Laboratory Diagnostics, Zagreb, Croatia; [4]Dubrava University Hospital, Department of Pathology and Clinical Cytology, Zagreb, Croatia.

Parathyroid localization by fine needle aspiration and parathyroid hormone (PTH) washout measurement is not a widely accepted method because of possible alterations in parathyroid histology. However, when performed with technical competence this easily available method has been praised to be an immediate confirmation of enlarged parathyroid glands found on ultrasound. We retrospectively reviewed primary hyperparathyroidism (PHPT) patients with previously performed PTH washout in pathologically confirmed parathyroid adenoma or hyperplasia. Their biochemical and anthropometric data, the size and location of analyzed parathyroid glands and concordant thyroid sonographic features were collected. Among 48 included patients, PTH washout measurement was available for 51 operated glands. In only 5 cases PTH washout level was lower than patient's serum PTH value. In this analysis we applied a stringent criterion: the ratio between the PTH washout level and serum PTH (PTH W/S) ≥ 2 was considered unequivocally positive. The sample was divided in two groups: 39 cases with positive PTH W/S and remaining 12 cases that did not reach this cutoff. In the comparison between investigated groups there was no difference in serum and urine calcium or PTH elevation. Body mass index, the upper or lower location of parathyroid glands and the presence of concomitant thyroid nodules or ultrasound features of diffuse thyroid disease were not different between groups. The volume and the maximal diameter of enlarged parathyroid glands measured by ultrasound were significantly larger in the group with positive PTH W/S ($P < 0.05$), while the minimal parathyroid diameter was not different between groups. For parathyroids that have a volume lower than 0.145 ml the odds ratio for not obtaining positive PTH W/S was 8.75 (CI 1.47–56.67). Adverse events or later surgical and pathological complications related to PTH washout procedure were not reported. While location, concomitant thyroid disease and patient obesity did not show a significant role in obtaining a positive PTH washout, the size of diseased glands remains the biggest challenge in parathyroid localization. It has significant impact on the accuracy of almost all available imaging methods. Considering that small size might be also associated with multigland PHPT, optimal diagnostic steps should be carefully planned. Doubts about the safety of parathyroid fine needle aspiration need to be finally solved with further analysis in large series of histological specimens.

DOI: 10.1530/endoabs.81.EP199

EP200

Management of hypocalcemia after thyroidectomy

Ben Arfi Tayssir, El Abed Wed, Akrout Ines & Gnaba Khalil
Ibn El Jazzar Teaching Hospital of Kairouan, ENT Department, Kairaoun, Tunisia.

Introduction
Hypocalcemia is a well-known complication of total thyroidectomy. Usually, it's a reversible and a transitory complication. However, it requires a regular check-up.
Objective
The aim of this study is to determine the epidemiological and the therapeutic characteristics of hypocalcemia after total thyroidectomy.
Methods
This is a retrospective study about 106 cases of total thyroidectomy that operated between the year of 2010 and 2019 in the ENT department in Kairouan.
Results
The average age was 44.11 [22–76 years] with a sex ratio of 0.1. The determination of serum calcium is done systematically at day 2 or 3 after surgery; earlier on if the hypocalcemia was symptomatic.The incident usually occurs 3 days after surgery. Postoperative hypocalcemia was found in 36 patients (33.9%). Symptoms were found in 20 patients (55.5%): 18 of them presented with paresthesia of the extremities (90%). And the other 2 patients presented with tetany (10%). All patients presented with hypocalcemia were given calcium gluconate and vitamin D orally. The IV supplementation was only given in 22.2% of the symptomatic patients.The treatment took about 2 months on average. And only 6 patients developed definitive hypocalcemia. The multinodular goiter was the most found pathology in the cases of postoperative hypocalcemia (72%). In second place comes the Grave's disease (16%). And in third place, cancer. In our study, 6 patients had total thyroidectomy with lymph node dissection. 4 of them, developed postoperative hypocalcemia.
Conclusion
Hypocalcemia is a frequent complication of total thyroidectomy, needing both, clinical and biological surveillance. Temporary oral supplementation usually does the trick.

DOI: 10.1530/endoabs.81.EP200

EP201

Chronic asymptomatic hypocalcemia following thyroid surgery

Mohamed Gharbi, Sabrine Mekni, Imen Rojbi, Youssef Lakhoua, Nadia Mchirgui, Ibtissem Ben Nacef & Karima Khiari
Hospital Charles Nicolle, Tunis, Tunisia

Introduction
Postoperative hypoparathyroidism is a frequent complication of total thyroidectomy that must be detected and treated. The resulting hypocalcemia is quite severe and usually occurs in the first few days or weeks after surgery.Herein, we describe a case of chronic asymptomatic hypocalcemia related to postoperative hypoparathyroidism diagnosed years after total thyroidectomy.
Observation
We report the case of a 61 year old woman, who had a total thyroidectomy in 1997 for papillary carcinoma and was lost to follow up after surgery. She was referred to the endocrinology department (24 years later) to explore asymptomatic hypocalcemia (1.47 mmol/l) discovered incidentally in a biological check-up. She had no family or personal history of autoimmune disease. Physical examination showed no abnormalities but the electrocardiogram suggested prolongation of the Q-T interval. The patient was treated with i.v. infusion of calcium gluconate. Laboratory tests revealed, a controlling serum calcium: 1.65 mmol/l (55 mg/l), phosphate: 2.56 mmol/l (80 mg/l), PTH levels: 12 pg/ml. Further exploration showed long-term complications of hypoparathyroidism: a Fahr's syndrome on the CT scan of the brain, dental anomalies, bilateral sub capsular cataract but no renal calcifications. The diagnosis of chronic hypocalcemia secondary to postoperative hyoparathyroidism was retained. She was put on calcium gluconate and alfacalcidol.
Conclusion
This case present a rare presentation of chronic asymptomatic hypocalcemia diagnosed 24 years after thyroid surgery and probably due to postoperative hypoparathyroidism.

DOI: 10.1530/endoabs.81.EP201

EP202

Artificial intelligence technology for the early diagnosis of osteoporosis in cushing syndrome

Margaret McBride
Lancaster University, School of Medicine & Health Sciences, Bailrigg, United Kingdom

In Cushing syndrome (CS), glucocorticoid-induced osteoporosis is suggested to be the main reason for drug-induced osteoporosis. This health condition creates weaknesses in bones which are then easily fractured.Studies estimate that osteoporosis is under diagnosed in the UK by around *50%*, and according to the International Osteoporosis Foundation 2021, osteoporosis is a major healthcare burden in Europe with 4.3 million fragility fractures and healthcare costs more than 56billion euros annually. Primary prevention rates are very low, and most patients only receive a Dual-Energy X-ray Absorptiometry (DEXA), scan following a first or second fracture. Osteoporosis is one of the most common comorbidities in CS patients.A recent Doctor of Philosophy (PhD) survey of CS members of a support group found 30 (*42%*) of the female members and 1 male member (*6.6%*), had been diagnosed with this condition. Only 12 of them initially had a DEXA scan to confirm their osteoporosis, and *23.8%* reported that they had found an improvement in their condition after being prescribed medical therapy.However, the length of waiting time for a DEXA scan was between 8 months to 2 years. Over *70%* of the women and *40%* of the men in the survey reported bone pain, proximal muscle weakness, and mobility disabilities, and this had impacted on their social, personal, and working lives.The findings from recent clinical trials have shown that by using advanced physics modelling and Artificial Intelligence (AI), methods, accurate measure of bone mineral density from standard digital x-ray (DXR), images, example wrist and hip, can be achieved. This means for the first time, patients who undergo skeletal imaging can be opportunistically assessed for osteoporosis.Interestingly, in this PhD study, *33.3%* ($n=24$), of the other members including males, were referred for skeletal x-ray examinations mainly due to fractures which occurred following their CS diagnosis.AI technology could revolutionize the way in which the early onset of osteoporosis is identified and subsequently lead to earlier treatment and improved quality of life. Additional benefits being a reduction in the socioeconomic cost of long-term treatment for fractures and unnecessary radiation doses to patients. The recommendation from the PhD study being, that more research using AI technology is required and could become an integral part of the diagnostic workup for endocrine patients, thus avoiding the wait for a DEXA scan, as DXR equipment is more readily available.

DOI: 10.1530/endoabs.81.EP202

EP203

A comparison of bone densitometry and mineral disorders in hemodialysis patients due to diabetics and non diabetics patients

Ramy Ben Tekaya[1], Haifa Hachfi[1], Mouna Brahem[1], Zahra Sfar[1], Olfa Jomaa[1], Zohra Atii[2] & Mouhamed Younes[1]
[1]University Hospital Tahar Sfar, Rheumatology Department, Mahdia, Tunisia; [2]University Hospital Tahar Sfar, Nephrology Department, Mahdia, Tunisia

Introduction
The chronic kidney disease (CKD) is associated to various bone and mineral disorders.Many studies showed that diabetics influence the bone and mineral metabolism
Aim
To investigate the bone disorder in CKD and the effect of diabetes on bone mineral density.
Methods
This is a cross sectional study conducted in rheumatology department of Taher Sfar university hospital in mahdia, Tunisia. The study involved 61 patients with chronic hemodialysis. They were invited to participate and were included after signing informed consent until the calculated sample size was reached. Patients were asked to undergo a hip and lumbar (L2-L4) densitometry by DXA to measure bone mineral density (BMD).
Results
The studied group of 61 patients was 26 females (42,6%) and 35 males (57.4%), there mean age was 53.9 [17-83] years, with mean dialysis duration 6,1 years. The mean onset age of hemodialysis therapy was 44.7+/- 15.4 years. It was diabetic nephropathy in 25 cases (41%) vascular nephropathy in 15 cases and tubulointerstitial nephropathy in 21 cases (34,4). 23 patients (37,7%) had osteoporosis using the WHO criteria (T-score $<$ -2,5), 26 patients (42,6%) had osteopenia and 12 patients had normal BMD. The mean bone mineral density of lumbar in diabetics patients and non-diabetics patients -1,72 vs -1,43 ($P<0{,}005$). The mean bone mineral density of the hip in diabetics patients and non-diabetics patients -1,83 vs -1,21 ($P<0{,}005$).
Conclusion
Our study showed that chronic kidney disease has an important impact on bone and mineral metabolism. Second our study showed that diabetes can worsen patient bone mineral density.

DOI: 10.1530/endoabs.81.EP203

EP204

Abstract Withdrawn

DOI: 10.1530/endoabs.81.EP204

EP205

Regional Migratory Osteoporosis- An under-diagnosed entity

Ashutosh Kapoor & Laxmi Manohar Rao Balmuri
Manchester University NHS FT, United Kingdom

Introduction
Regional Migratory Osteoporosis (RMO) is a rare condition, characterised by a self-limiting migratory arthralgia, which generally tends to involve the lower limbs. The arthralgia is usually, not associated with any history of trauma. Radiologically, Magnetic Resonance Imaging (MRI) is the investigation of choice. Bone Marrow Oedema (BMO) with subchondral sparing are the usual findings in patients with RMO. This condition is usually under diagnosed due to the complexity and lack of classical features.
Case details
We report the case of a 59-year-old gentleman, who presented to his General Practitioner (GP) with traumatic Right second toe pain, accompanied by significant deterioration in Quality-of-life (QOL). On X-Ray, there was no evidence of acute fractures. The symptoms at the time, were managed with analgesia and strapping.Subsequently, a year later, he incurred symptoms of pain and stiffness in the Right third and fourth toes, which was not preceded by a history of trauma. On this occasion, there was involvement of the Right hip as well. In total, at this point his QOL was severely impacted over the course of the last 18 months.He was then referred to the Tertiary sports and exercise specialist, for expert input. An MRI scan detected bone and soft tissue oedema centred on the second and third metatarsal heads involving the surrounding muscles,

subcutaneous tissues and proximal and perhaps the middle phalanges. Mild plantar bone marrow oedema seen of the fourth metatarsal head.The appearances were highly suggestive of RMO, which instigated a referral to Metabolic bone services.A battery of investigations showed normal renal functions, Adjusted Calcium levels, Thyroid status and Vitamin D levels. Extended screening for Coeliac disease, Testosterone deficiency, Multiple Myeloma and Hyperparathyroidism were normal.
Management
A discussion in the Metabolic Bone Multi-Disciplinary setting advised repeat MRI and treatment with Bisphosphonates. The repeat MRI confirmed appearances in keeping with Transient BMO syndrome.Treatment with Intravenous Zoledronate alleviated his symptoms significantly and shortened recovery time, with Improvement in QOL.
Discussion
Till this date, the aetiology of RMO remains unclear. The key to diagnosis lies in a thorough clinical history supplemented by radiological findings. The radiology of RMO resembles Transient Osteoporosis of the Hip (TOH) and thus, the history of migratory arthralgia is key in distinguishing between both entities.Treatment options generally involve repletion of Vitamin D and Calcium levels, where appropriate. Bisphosphonates have been shown to improve symptoms and shorten recovery time.

DOI: 10.1530/endoabs.81.EP205

EP206

Osteoporosis in patients with Addison's disease: Incidence and predictive factors

Dhoha Ben Salah, Khouloud Boujelben, Asma Zargni, Faten Haj Kacem Akid, Ameni Salah, Mnif Fatma, Mouna Mnif, Nadia Charfi, Nabila Rekik Majdoub, Mouna Elleuch & Mohamed Abid
Hedi Chaker Hospital, Diabetology and Endocrinology Department, Sfax, Tunisia

Introduction
Because of a long-term glucocorticoid replacement over many years, patients with Addison disease may have an increased occurrence of osteoporosis. Furthermore, the prevalence of osteoporosis in patients with Addison disease may also be increased because of premature menopause associated autoimmune endocrinopathies and hypovitaminosis D.The objective of this study is to assess the incidence and risk factors for osteoporosis among patients with Addison disease.
Patients and methods
A cross-sectional study including 50 patients with Addison disease who had been receiving glucocorticoid replacement therapy for at least 5 years.Bone mineral density of the lumbar spine and both femoral necks was measured on osteodensitometry. The incidence of osteoporosis and its potential predictive factors were analyzed.
Results
Our study included 40 females and 10 males with a mean age of 49,5 ± 13,9 years (18-78 years). Average age at diagnosis was 35,5 ± 14,6 years (0-70 years). All patients were on hydrocortisone replacement, taking mean daily dose of 27,4 ± 6,7 mg (15-42,1 mg) corresponding to 0,388 ± 0,128 mg/kg.Mean cumulative hydrocortisone dose was 374,636 ± 283,821 mg (60 – 1184, 94 mg). No patient received antiresorptive therapy (oestrogen substitution therapy, bisphosphonates) .Low bone mineral density was observed in 24 (48%) patients, 12 (24%) of whom had osteoporosis. No osteoporotic fracture was observed.Patients who developed osteoporosis were significantly older than those with normal bone mineral density were ($P = 0{,}018$). Menopause was a significant predictor of incident osteoporosis ($P = 0{,}006$). Furthermore, osteoporosis was significantly more prevalent among females ($P = 0{,}046$).No statistically significant association was found between osteoporosis and Addison disease duration neither the body mass index.Daily and cumulative hydrocortisone dose were higher in patients with osteoporosis than those with normal osteodensitometry (26,5 ± 8,3 mg/day vs 25,6 ± 6,3 mg/day; 462,2 ± 373,2 mg vs 344,6 ± 245,5 mg) but without statistical significance.
Conclusion
Identification of predictive factors of osteoporosis in patients with Addison disease is useful in the management of long –term glucocorticoid therapy's bone impact. Then, further studies are needed to better analyze these factors and control bone mineral density during the course of Addison disease.

DOI: 10.1530/endoabs.81.EP206

EP207

rhPTH(1-84) treatment-induced increased bone turnover in a young woman with postsurgical hypoparathyroidism

Foteini Adamidou[1], Paraskevi Komzia[1], Gesthimani Mintziori[2] & Marina Kita[1]
[1]Ippokration General Hospital, Department of Endocrinology, Thessaloniki, Greece; [2]Aristotle University of Thessaloniki, 1st Department of Obstetrics and Endocrinology, Thessaloniki, Greece

Introduction
rhPTH(1-84) replacement is the treatment of choice in adults with hypoparathyroidism not adequately controlled on standard therapy. Although increased bone turnover markers have consistently been reported in trials of safety and efficacy, marked elevations coupled with significant symptoms have been rare. We describe a case of increased treatment-induced bone turnover, necessitating significant therapeutic adjustments and monitoring.
Case report
A 26-year-old female suffered with severe hypoparathyroidism for 10 years, following total thyroidectomy and incidental parathyroidectomy (three glands) for papillary thyroid cancer (pT1N0). Laboratory values on calcium carbonate 4gr daily, alfacalcidol 3 mg daily, magnesium aspartate 60 mg bid and thyroxine 137 mg/d were as follows: TSH 0.33μIU/ml (0.27-4.7), thyroglobulin <0.1ng/ml (<1), anti-TG negative, corrected calcium 6.5 mg/dl (8.4-10.1), phosphate 6.6 mg/dl (2.7-4.5), Mg 1.61 mg/dl (1.6-2.6), Cr 0.7 mg/dl, ALP 55IU/l (23-104), PTH 5.1 pg/ml (15-65), 25(OH)D 34.9 ng/ml (20-50), $1,25(OH)_2D3$ 29 pg/ml (18-80). Kidney ultrasound revealed nephrocalcinosis bilaterally and 24h urinary calcium was 539.7 mg/24h (<250 mg/24h).Following referral, rhPTH(1-84) 50 mg daily was started and titrated to 100 mg daily within 6 months. The patient discontinued alfacalcidol and remained on 500 mg calcium carbonate and 1000IU cholecalciferol daily, with excellent response.Within a week on 100 mg/d the patient reported severe bone pain in the knee joints and back, paralleled with successive increase in serum ALP at 163IU/l, 221IU/l and 611IU/l (range 23-104IU/l) and bone markers: CTx 1.59ng/ml (0.04-0.6ng/ml), P1NP 623ng/ml (15-60 ng/ml) and osteocalcin 157ng/ml (5.4-59.1ng/ml). Liver function tests and liver ultrasound were normal. rhPTH(1-84) was reduced to 50 mg daily with gradual improvement in bone pain, but with immediate relapse of hypoparathyroid symptoms and worsened biochemical control. ALP levels normalized within 10 weeks to the upper normal range [113IU/l (46-116IU/l)]. Subsequently the dose was up titrated to 75 mg/d, together with calcium carbonate 500 mg bid, magnesium 60 mg bid and alfacalcidol 1 mg/d. She has remained stable clinically and biochemically for the past 6 months. ALP values increased again but are maintained within 10%ULN.
Conclusions
Elevation of bone turnover markers are anticipated by rhPTH(1-84) mechanism of action. However, they remain within normal range in the long term. The etiology for marked symptomatic increase in bone turnover in a minority of patients affecting treatment tolerability is unknown.
References
1) Mannstadt M *et al*, *J Clin Endocrinol Metab.* 2019;104(11):5136-51472)
2) Mannstadt M *et al*, *Lancet Diabetes Endocrinol.* 2013;1(4):275-2833)
3) Rubin M *et al*, *J Clin Endocrinol Metab.* 2016; 101(7): 2742-27504)
4) Tay YD *et al*, *J Clin Endocrinol Metab*. 2019; 1;104(11):5601-5610.

DOI: 10.1530/endoabs.81.EP207

EP208

Patient with mediastinal mass and hypercalcemia

Katarina Mlekus Kozamernik[1,2], Barbara Salobir[1,2], Marko Hočevar[1,3] & Tomaž Kocjan[1,2]
[1]Faculty of Medicine, University of Ljubljana, Slovenia; [2]University Medical Center Ljubljana, Slovenia; [3]Institute of Oncology Ljubljana, Slovenia

Introduction
Hypercalcemia is mostly caused by primary hyperparathyroidism and malignancy. Parathyromatosis is a rare condition characterized by multiple nodules of hyperfunctioning parathyroid tissue scattered throughout the neck and superior mediastinum, which can present a diagnostic and therapeutic challenge.
Case report
A 56-year-old woman visited the ER due to chest pain, left-sided neck edema, and hematoma. The day before, she experienced left-sided neck pain and dysphagia. Her other complaints were recent weight loss and fatigue. Due to chest pain and high D-dimer level, CT pulmonary angiography was ordered, which showed a large heterogeneous soft tissue formation extending from the left side of the neck over the upper thoracic aperture and over the posterior mediastinum to just above

the esophageal hiatus. The patient was admitted to Respiratory Medicine, where hypercalcemia (serum calcium 3.18 mmol/l; ref. 2.1-2.6 mmol/l) was found. At first, it was thought to be paraneoplastic, and an ultrasound-guided fine-needle aspiration biopsy of the mediastinal formation was performed, which was not diagnostic. FDG PET/CT two weeks after admission revealed a significant shrinkage of the mediastinal formation that showed low metabolic activity. Nothing abnormal was detected elsewhere. Finally, the patient was diagnosed with parathyroid hormone-dependent hypercalcemia (PTH 225 ng/l; ref. 10-65 ng/l) and transferred to Endocrinology. After parenteral hydration and introduction of a calcimimetic, serum calcium level fell to 2.68 mmol/l. Marked hypercalciuria (17 mmol (680 mg)/24 h was found, however, nephrocalcinosis or nephrolithiasis on ultrasound were absent. Bone mineral density was in the range of osteoporosis (T-scores: lumbar spine -2.5 SD, femoral neck -2.6 SD, one-third radius -4.5 SD) with increased bone turnover (bone-specific ALP 59.1 µg/l; ref. 5.5-27.1 µg/l, CTX 3.976 µg/l; ref. 0.142-1.351 µg/l, PINP 50.0 µg/l; ref. 27.7 – 127.6 µg/l). 18F-choline PET/CT showed hyperfunctioning parathyroid tissue at the lower part and behind the left thyroid lobe. A metabolically active process around the esophagus extending caudally to Th3 level was also present. Surgery revealed extensive parathyromatosis at the lower part of the left thyroid lobe and in the neck adipose tissue. Histopathology confirmed extensive parathyromatosis. A surgical cure was not possible, and the patient continued treatment of persistent primary hyperparathyroidism with a calcimimetic. Cholecalciferol supplementation and zoledronate were given for osteoporosis.
Conclusion
We present a patient with mediastinal mass and hypercalcemia, which was first thought to be paraneoplastic. Further diagnostic workup revealed a rare case of spontaneous rupture and hemorrhage of a parathyroid adenoma with subsequent surgically incurable parathyromatosis.

DOI: 10.1530/endoabs.81.EP208

EP209

Complications of a rare condition, untreated due to difficult living conditions

Lea Slahor & Henzen Christoph
Luzerner Kantonsspital, Division of Endocrinology/Diabetes, Lucerne, Switzerland

Introduction
Pseudohypoparathyroidism is a rare disorder characterized by end-organ resistance to parathyroid hormone, caused by molecular defects of the PTH receptor. Resulting chronic hypocalcemia and hyperphosphatemia require lifelong treatment with active vitamin D metabolites and monitoring, representing a challenge especially in difficult living conditions.
Case report
A 19-year-old woman presented to our clinic with carpopedal spasms and tetany. Living in Switzerland since 5 years as a refugee from Eritrea, she reported having been treated with "pills" because of an undefined condition diagnosed in her early infancy. Her treatment was inevitably stopped when fleeing her native country and medical reports were not available. Clinical examination was unremarkable (61 kg, 164 cm, BMI 22.7 kg/m^2), normal pubertal development and menstrual history. Her parents and the four siblings were asymptomatic. Laboratory tests showed hypocalcemia of 1.59 mmol/l, serum albumin-corrected calcium 1.35 mmol/l [reference range 2.15-2.55], with an elevated parathyroid hormone (PTH) of 389 pg/ml [reference range 15-65], accompanied by hyperphosphatemia of 1.94 mmol/l [reference range 0.87-1.45] and vitamin D deficiency (25-OH-vitamin D3 17 nmol/l [$<$50]). Renal function, magnesium- and TSH-levels were normal. Hypercalciuria was absent. Brain MRI revealed severe calcification of basal ganglia. Molecular genetic analysis showed reduced methylation at the GNAS gene locus, which, in combination with the unremarkable clinical phenotype, pointed to pseudohypoparathyroidism type 1 B. Treatment with calcium carbonate, cholecalciferol and calcitriol was started and symptoms resolved with correction of serum calcium.
Comment and conclusion
Pseudohypoparathyroidism type 1 B is defined by predominantly renal resistance to parathyroid hormone, resulting in hypocalcemia and hyperphosphatemia with elevated PTH, caused by molecular defects (sporadic or inherited) at the GNAS locus of PTH receptor, a G-protein–coupled receptor (Gsα). As various endocrine receptors depend on stimulatory G-protein-coupled transduction, other hormonal resistance (TSH, gonadotropins, GHRH) can result, typically found in different subtypes in the heterogenous group of pseudohypoparathyroidism disorders. The hormone resistance syndromes, in combination with specific somatic features (round facies, heterotrophic subcutaneous ossifications, brachydactyly) and development abnormalities, were first described by F. Albright in 1942, therefore known as Albright hereditary osteodystrophy. Although a rare disease (estimated prevalence: 0.79/100'000), pseudohypoparathyroidism must be suspected in symptomatic hypocalcemia with elevated PTH. Our case report highlights the importance of correct diagnosis, medical treatment and patient information to avoid potentially fatal consequences. Unfortunately, this was delayed for several years in our patient due to difficult living conditions as a refugee and asylum seeker.

DOI: 10.1530/endoabs.81.EP209

EP210

Hypercalcaemia induced acute pancreatitis

Mona Abouzaid & Sony Anthony
North Tees and Hartlepool NHS Foundation Trust, Department of Diabetes & Endocrinology, Stockton on Tees, United Kingdom

Introduction
Milk-alkali syndrome (MAS) consists of hypercalcemia, renal failure, and metabolic alkalosis as a result of ingestion of large amounts of calcium and absorbable alkali. Daily elemental calcium intake of no more than 2 g is considered safe. However, even doses lower than 2 g daily may result in hypercalcemia if additional predisposing factors are present. Vulnerable patients because of vomiting, diuretic use, and deviant eating habits. In these susceptible patient groups, supplementing calcium in a form that contains no absorbable alkali is probably a safer.
Case Presentation
We report a case of a 70 -year-old woman presented in September 2021 with sever lower abdominal pain and confusion. She was diagnosed with acute pancreatitis precipitated by hypercalcemia. Her past medical history of hypertension, gastroesophageal reflux disease. Her regular medications are Atorvastatin and Ramipril. Her husband stated that she has been taking over the counter Deflatine tablets "like sweets" for at least 2 years as an antacid (Deflatine or Rennie tablets contain calcium carbonate and magnesium carbonate). On admission she was found to have very high serum adjusted calcium at 4 mmol/l (2.20 – 2.60), acute kidney injury with EGFR of 15 (her base line EGFR prior to admission was 45) and significantly high lipase and amylase. Her parathyroid hormone PTH level was on the low side at 1 pmol/l (1.3 - 7.3). 25 OH total vitamin D level was 42 nmol/l. CT chest, abdomen and pelvis confirmed the diagnosis of acute pancreatitis, there was no evidence of malignancy or gall stones. She recovered very well with hydration and supportive treatment. Her calcium level normalized after stopping of Deflatine tablets and remained normal up to date.
Conclusion
MAS is believed to be the third most common cause of in-hospital hypercalcemia, after hyperparathyroidism and malignant neoplasms. Hypercalcemia can be severe and, in our patient, caused acute pancreatitis. Renal failure is generally reversible, but impairment in renal function may persist in some cases. Treatment is supportive and involves hydration and withdrawal of the offending agents. Physicians and the public need to be aware of the potential adverse effects of ingesting excessive amounts of calcium carbonate.

DOI: 10.1530/endoabs.81.EP210

EP211

Acute confusional state as presenting feature in severe para-neoplastic hypercalcemia

Uzair Akbar Ali, Ghazanfar Iqbal Rana & Summan Jannat
St. Luke's General Hospital, Kilkenny, Ireland

Background
Hypercalcemia is a common clinical problem. Severe hypercalcemia or hypercalcemic crisis is an endocrine emergency and can be life threatening if left untreated. The condition has high mortality and requires immediate therapeutic interventions and diagnostics. A rapid rise to the calcium levels can result in the impaired function of organ systems including central nervous system. Hypercalcemia is mainly (more than 90%) caused by primary hyperparathyroidism or malignant conditions.
Clinical case
A 63-year-old man with background history of alcohol abuse presented to our institution with acute confusional state. Collateral history revealed that he was wandering in the streets. He was found pleasantly confused and disorientated by local police who brought him to the hospital. His physical examination revealed a Glasgow coma scale (GCS) score of 13/15 with no obvious localizing signs or

neurological deficit. Initial investigations showed alcohol levels of less than 10 mg/dl, negative toxicology screen, unremarkable CT brain with normal blood glucose and serum amylase levels. He had decreased urinary output of 15-20 ml/hr with normal renal function but raised calcium levels of 3.72 mmol/l (2.20-2.60) and low phosphate levels of 0.77 mmol/l (0.8-1.5).He was treated as hypercalcemic crisis with intravenous fluids and given intravenous bisphosphonate (zolendronic acid 4 mg) in critical care unit. His calcium levels started decreasing with the treatment and his conscious level significantly improved. The diagnostics included low PTH levels with value of 6.7 pg/ml (15-65) and CT of thorax, abdomen and pelvis which revealed a left renal lesion of 15 x 12 cm^2 infiltrating into anterior and posterior perinephric soft tissue.He was referred to urology department for further investigations. Histopathology of renal biopsy specimen showed renal cell carcinoma and graded as advanced renal cancer (Stage IIIc). Unfortunately, due to his baseline status and compliance issues he was not deemed a candidate for surgery or systemic therapy and advised consideration for palliative approach.

Conclusion

The case illustrates the need to carefully review the differentials of hypercalcemia and consider immediate treatment interventions in situations of severe hypercalcemia or hypercalcemic crisis. Renal cell carcinoma should be considered as possible causative in hypercalcemia of unknown underlying pathology.

Key words: hypercalcemia, hyperparathyroidism, cancer

DOI: 10.1530/endoabs.81.EP211

EP212

A rare case of Pseudohypoparathyroidism

Natia Shonia & Nino Zavrashvili
Tbilisi Institute of Medicine, Endocrinology, Tbilisi, Georgia

Background

Pseudohypoparathyroidism includes a genotypically diverse group of syndromes of primary resistance to hormones whose actions are mediated by cyclic adenosine 3': 5'-monophosphate, in most cases caused by mutations and/or epigenetic changes at the complex GNAS locus on chromosome 20q13.3.Renal resistance to PTH leads to impaired formation of 1,25(OH)2D, the fully active form of vitamin D, and reduces expression of sodium-dependent phosphate transporters in the renal tubules, leading to hypocalcemia and hyperphosphatemia, with elevated serum PTH levels.Patients with PTHT clinically manifest with tetany seizures, soft tissue calcifications and many congenital malformations.Early diagnosis and vitamin D3 or calcium treatment seem to be the most important for patient's condition.

Case

We describe a case of possible sporadic pseudohypoparathyroidism type II, confirmed hashimoto thyroiditis, iron deficiency anemia, chronic erosive gastritis. 28 year old Caucasian female visited our clinic with complaints of frequent hospitalizations due to seizures and tetany since December 11, 2021. Patient was hospitalized at least 4 times and required Ca infusions. Patient complained of mild, intermittent and self-limited paresthesias, persistent asthenia, tachycardia, arrhythmia since early years. She had been diagnosed at the age of 6 with hypocalcemia and possible pseudohypaparathyroidism, but diagnosis was not verified by genetic test. Initial lab investigation showed elevated PTH- 334.3 (15-65) pg/ml, hypocalcemia (iCa-0.73 (1.15-1.29) mmol/l) hyperphosphatemia (*P*-2.03 (N0.81-1.45) mmol/l), hypocalciuria (<0,2 mmol/l (N2,5-7,5), decreased bone mineral density on Dexa Scan - T score L2=-2.4. Combined calcium and calcitriol supplementation was commenced, with symptomatic and laboratory improvement. Couple days after initiating Ca supplements and calcitriol, we achieved laboratory and clinical improvement (Ca-1.93 (2.15-2.5) mmol/l, p-1.85 (0.81-1.45) mmol/l (18.01.2022), Mg- 0.65 mmol/l (0.6-1.07)).Molecular identification is ordered and will be presented.

Conclusion

With initiated treatment, we hope for complete resolution of patient's complaints and attaining symptomatic remission. A careful follow-up is needed to avoid complications and recurrence. Once correction of hypocalcemia and hyperphosphatemia is achieved, with no reported complications and recurrence, a good prognosis is anticipated, comparable to the general population.

DOI: 10.1530/endoabs.81.EP212

EP213

Primary hyperparathyroidism – experience of a single center

Ana Rita Elvas, Joana Couto, Raquel G. Martins, Jacinta Santos, Teresa Martins & Fernando Rodrigues
Portuguese Oncology Institute of Coimbra, Department of Endocrinology, Coimbra, Portugal

Introduction

Primary hyperparathyroidism (pHPT) is the most common cause of hypercalcemia in the outpatient setting and is a frequent endocrine disorder. Large cohort studies of pHPT patients in the Portuguese population are scarce.

Aim

To characterize patients with pHPT followed at a tertiary center.

Material and Methods

Retrospective analysis of clinical records of patients with pHPT followed in our hospital from 2003 to 2021.

Results

A total of 177 patients were included, 82.5% were female. The mean age was 61±13.6 years. In 79.6% of the cases, hypercalcemia was detected in a routine analysis. Some patients had complaints of muscle and/or bone pain (33.3%), asthenia (27.6%) and polydipsia and polyuria (15.5%). 124 (80%) patients had DXA scan done out of which 37.4% had osteoporosis and 28.5% had osteopenia. History of fragility fractures was seen in 9.4% of the patients; nephrolithiasis was present in 37.5%; hypercalciuria (>400 mg/24h) in 17.1% and renal function impairment in 7.0%. At diagnosis, the mean ionized calcium, total calcium, phosphate, parathormone and 25-OH D levels were 1.44±0.17 mmol/l; 11.52±1.20 mg/dl; 2.71±0,62 mmol/l; 333.90±891.80 pg/ml and 20.61±10.ng/dl, respectively. 14 (7.9%) patients presented normocalcemic pHPT. Neck ultrasound and sestamibi scan detected parathyroid disease in 53.7% and 81.5% of the cases. 111 patients (62.7%) underwent surgical treatment, only two patients with pHPT normocalcemic. Pathological examination revealed a parathyroid adenoma (PT) in 65.5%, atypical adenoma 5.4%, hyperplasia 14.5%, carcinoma 9.0% and no parathyroid tissue in 6.3% of the patients. Right inferior parathyroid gland was the most common site of PT. A >50% decline of PTH 10-15 minutes after gland excision was observed in 80.8% of the patients. Post-operative transient and permanent hypocalcemia was observed in 52.4% and 8.5% of the cases. After PT surgery, the cure rate was 84.8%. Persistence and recurrence disease rates were 9.9% and 3.6% respectively. Hereditary forms of hyperparathyroidism were present in 11 patients: MEN-1 in 4 (2.3%) patients and MEN2A in 7 (4.0%). Somatic CDC73 mutations were found in 3 patients with PT carcinoma.

Conclusion

To the best of our knowledge this is the largest cohort of patients with pHPT in Portugal. Despite the diagnosis being mostly incidental with most patients presenting mild hypercalcemia, some were found to have evidence of skeletal and renal manifestations of the disease.

DOI: 10.1530/endoabs.81.EP213

EP214

Risk factors associated with bone loss in patients with Addison disease

Dhoha Ben Salah, Khouloud Boujelben, AbdelMouhaymen Missaoui, Mouna Elleuch, Mnif Fatma, Mouna Mmnif, Nadia Charfi, Nabila Rekik Majdoub, Faten Haj Kacem Akid & Mohamed Abid
Hedi Chaker Hospital, Sfax-Tunisia, Department of Endocrinology, Diabetology

Introduction

Even at physiological doses, glucocorticoid replacement therapy may lead to deleterious outcomes on bone mineral density (BMD).The aim of our study was to investigate the BMD in Tunisian patients with Addison disease and to identify the risk factors associated with its decline.

Patients and methods

The study included 50 patients diagnosed with primary adrenal disease (Addison disease). BMD was assessed by the dual -energy -X-ray absopitometry. Predictive factors of reduced BMD were analyzed.

Results

The mean age of patients was 49,5±13,9 years and 40 patients were female;42,5% menopausal. Disease duration was 13,9±8,7 years.). All patients were on hydrocortisone replacement, taking daily 27,4±6,7 mg (15-42,1 mg) corresponding to 0,388±0,128 mg/kg. Hypovitaminosis D was observed in 66% of patients. Twenty percent of patients had a higher than normal level of parathyroid hormone (PTH).The BMD was significantly reduced in 48% of patients. Three patients presenting congenital adrenal hyperplasia had normal

BMD.A significant higher incidence of reduced BMD was observed among menopausal women ($P=0,049$). Moreover, a higher mean PTH level was found in patients with decreased BMD but without statistically significant difference ($56\pm21,8$ pg/ml vs $48,1\pm25,4$ pg/ml;$P=0,1$).A lower mean vitamin D level was also found among those patients ($19\pm10,2$ ng/ml vs $25,2\pm16$ ng/ml).Cumulative hydrocortisone dose was higher among patients with reduced BMD compared to those with normal BMD, without statistical significance ($408,9\pm324$ mg vs $338,9\pm236$ mg;$P=0,7$).No significant correlation was identified between decreased BMD and duration of glucocorticoid substitution.
Conclusion
Bone loss is frequent in patients with Addison disease taking long-term glucocorticoid therapy and related to many factors affecting bone remodeling such as hydrocortisone dose and vitamin D deficiency. It seems imperative to ensure long-term follow-up of changes in BMD in patients with Addison disease.

DOI: 10.1530/endoabs.81.EP214

EP215

Pregnancy and lactation-associated osteoporosis

Zvezdana Jemuovic, Marina Nikolic Djurovic, Sandra Pekic Djurdjevic, Dragana Miljic, Marko Stojanovic, Mirjana Doknic, Ana Petakov & Milan Petakov
Clinic for Endocrinology, Diabetes and Diseases of Metabolism, University Clinical Center of Serbia, Department of Neuroendocrinology, Belgrade, Serbia

Introduction
Pregnancy and lactation-associated osteoporosis (PLO) is a rare condition in which women have fragile fractures associated with significant reduction of BMD during pregnancy or postpartum period.
Case report
A 37-year-old female patient was admitted at our Clinic for further investigation of aetiology of osteoporosis in July 2019. Soon after delivery in February 2019 patient had felt left hip and foot pain as well as sharp intensive pain (intensity 9/10) in thoracic spine with propagation anteriorly into intercostal spaces. Pain was increased during body position changes, and was alleviated with ibuprofen intake. She also complained on morning stiffness. MRI of thoracic spine was performed in June and it showed irregularly decreased height of thoracic vertebrae 7 and 8, which seemed as compressive fractures. Osteodensitometry showed osteoporosis with total T-score of spine -2.8 (L3 -3.1), Z-score -2.6(L3 -3.0) and osteopenia of the hip with T-score of neck of the femur -1.1, Z-score -1.1. Trabecular bone score indicated preserved microarchitecture of bones. On admission she complained of malaise, cold hands and feet, tingling in legs and dry mouth with occasional problem swallowing solids and liquids. First menstrual period after the delivery was in July and it is also when she stopped breast-feeding. In the previous years she had a spontaneous miscarriage and 3 tries of insemination. During 1st trimester she was on progesterone therapy. She had an operation of myoma in 2015. Her family history is positive for CVD, DM, and lung carcinoma. Patient is a smoker (did not stop during the pregnancy). Full laboratory workup showed normal calcium and PTH levels, with vitamin D insufficiency. Thyroid hormones, FSH, LH, prolactin, testosterone, and cortisol were within normal reference range as well as electrophoresis of proteins, tumour markers, Bence-Jones protein. Vertebral fracture assessment indicated crush fracture of L4. After all workup, we concluded that this is a case of pregnancy and lactation -associated osteoporosis and we advised vitamin D 2000IU, calcium-carbonate 1000 mg. In December 2019, she received a first dose of zolendronic acid. On a first check-up 6 months later, X-ray of thoracic spine was performed and it showed new pathological fractures of toracic vertebra 9 and 11 so she received 2nd dose of zolendronic acid. Third dose was applied in December 2021. Next osteodensitometry is scheduled for March 2022.
Conclusion
PLO is a rare condition and it should be considered as differential diagnosis in patients with back pain during or after pregnancy.

DOI: 10.1530/endoabs.81.EP215

EP216

Association of primary hyperparathyroidism and papillary thyroid Cancer: a case report

Gorgi Khaoula, Mhamdi Zineb, Lamya Echchad, Rifai Kaoutar, Iraqi Hinde & Gharbi Mohamed El Hassan
Ibn Sina University Hospital, Endocrinology and Metabolic Diseases, Rabat, Morocco

Introduction
Primary hyperparathyroidism is a common pathology. The association of papillary thyroid carcinoma and primary hyperparathyroidism has been reported in 2.3–4.3% of patients operated on for primary hyperparathyroidism.We report the case of a patient with papillary thyroid carcinoma revealed by primary hyperparathyroidism
Observation
53-year-old patient admitted for management of primary hyperparathyroidism. A cervical ultrasound revealed a right subthyroid tissue nodule suggestive of a parathyroid adenoma associated with a multiheteronodular goiter classified as eutirads 3-5. The cervical scan shows 2 lobar nodules, upper and lower right. Thyroid scintigraphy confirmed the upper and lower right parathyroid originthe patient benefited from an upper and lower adenomectomy + total thyroidecto-my.The anatomopathological study was in favor of a parathyroid adenoma associated with a papillary thyroid carcinoma
Discussion &Conclusion
The coexistence of papillary thyroid carcinoma and hyperparathyroidism is thought to be rare. The mechanisms underlying this association have not been established. A possible hypothesis is suggested for this relationship based on shared embryological origin and genes, high parathyroid hormone, low 1,25 hydroxy vitamin D, hypercalcemia resulting in high levels of angiogenic growth factors.The presence of these two diseases can complicate patient management due to untreated hypercalcemia, unrecognized thyroid cancer and need for second surgery if not screened for both diseases carefully

DOI: 10.1530/endoabs.81.EP216

EP217

Abstract Withdrawn

DOI: 10.1530/endoabs.81.EP217

EP218

Results of denosumab used in postmenopausal women

Yana Navmenova[1], Elena Makhlina[2], Tamara Moskvicheva[1], Nelli Chernova[1] & Irina Savasteeva[1]
[1]SI «The Republican Research Center for Radiation Medicine and Human Ecology», Gomel, Belarus, Endocrinology, Gomel, Belarus; [2]Gomel State Medical University, Internal Medicine No. 1 with courses in Endocrinology and Hematology, Gomel, Belarus

The aim of the study was to assess the effectiveness of postmenopausal osteoporosis (PMOP) therapy with denosumab.Patients and methods 32 postmenopausal women with established PMOP for a period of 24 months or more received denosumab 60 mg subcutaneously once every 6 months combined with calcium and vitamin D. A quantitative assessment of bone mineral density (BMD) was carried out before treatment, after 12 and 24 months of observation, using dual-energy X-ray absorptiometry of the lumbar spine (LI – IV) and femoral neck (FN) on the right and left. Changes in the severity of pain were assessed using a visual analogue scale (VAS), the severity of the pain syndrome was assessed before treatment, after 12 and 24 months of observation.Statistical processing was carried out using the SPSS 23.0 software package.
Results and Discussion
The average age of women included into the study was 61.76 (59.35; 68.47) years. The average age at the onset of menopause was 47.52 (43.13; 49.83) years, the average duration of menopause at the time of the study was 12.64 (10.10; 21.62) years.The median values of the T-score in LI-IV before, after 12 and 24 months of treatment were, respectively: «-»2,5/«-»2.1/«-»1.85 ($P<0,0001$).The median values of the T-score in the FN on the right before and after 12 months of treatment were "-"1.9/"-"1.7 ($P=0.07$); The median values of the T-score in the FN on the left before and after 12 months of treatment were "-"1.9/"-"1.5 ($P=0.04$).The median values of the T-score in the FN on the right before and after 24 months of treatment were "-"1.9/"-"1.5 ($P=0.012$); The median values of the T-score in the FN on the left before and after 24 months of treatment were "-"1.9/"-"1.4 ($P=0.01$).The median values of pain severity according to VAS before, after 12 and 24 months of treatment were 5.5/4/2 points, respectively ($P<0.0001$).After 24 months of using denosumab, the mineralization indices of all the studied localizations significantly improved in comparison with the initial data.

Conclusions
Therapy with denosumab 60 mg subcutaneously 2 times a year with an interval of 6 months for 24 months in combination with calcium and vitamin D made it possible to significantly increase the BMD of the lumbar spine and significantly reduce the severity of pain syndrome according to VAS.

DOI: 10.1530/endoabs.81.EP218

EP219

Is obesity detrimental to postmenopausal bone health?

Radina Dimitrova[1], Mila Boyadzhieva[1], Kiril Hristozov[1] & Yana Bocheva[2]
[1]MU Varna, Second Department of Internal Medicine, Varna, Bulgaria; [2]MU Varna, Department of Clinical Laboratory, Varna, Bulgaria

Introduction
Despite available evidence for a relationship between bone health and obesity, the results of clinical trials remain conflicting. Thus, we conducted a cross-sectional study to analyze possible associations between waist circumference (WC), body mass index (BMI) and body weight (BW) with bone health in postmenopausal women.
Materials and Methods
The study included 84 women from Northeastern Bulgaria. Their mean age was 60.54 ± 7.07 years, and their mean duration of menopause was 11.45 ± 6.62 years. Bone health was assessed by dual-energy X-ray absorptiometry (DEXA), analysis of bone metabolic markers and fracture risk calculation.
Results
According to BMI 31% of the subjects were with normal weight, 50% were overweight and 20% were obese. In 82% of the women WC was over 80 cm. Significant positive correlations of bone mineral density (BMD) with **WC** (L1-L4 $r=0.264$; $P=0.015$, Femoral Neck $r=0.338$; $P=0.002$, Total Neck $r=0.393$; $P < 0.001$), **BMI** (L1-L4 $r=0.295$; $P=0.006$, Femoral Neck $r=0.223$; $P=0.042$, Total Neck $r=0.330$; $P=0.002$) and **BW** (L1-L4 $r=0.446$; P 0.001, Femoral Neck $r=0.409$; P 0.001, Total Neck $r=0.457$; P 0.001) were found. However, after BW adjustment the correlations of BMD with WC and BMI became insignificant. Moreover, a negative association was found between Femoral Neck BMD and BMI after BW adjustment ($r=-0.260$; $P=0.018$). On the other hand, the positive relationship between BMD and BW remained significant after WC and BMI adjustment. In addition, WC was inversely related to osteocalcin ($r=-0.217$; $P=0.048$) and Beta CrossLaps ($r=-0.226$; $P=0.039$). Nevertheless, a positive relationship was found between WC and pyrilinks D/creatinuria ratio ($r=0.277$; $P=0.011$), but it was associated with higher eGFR in obesity. Furthermore, higher BW was noted as a significant negative predictor of the 10-year risk of major osteoporotic fracture (MOF) ($\beta=-0.730$, P0.001) and hip fracture (HF) ($\beta=-0.730$, P0.001), but positive associations were found between BMI and the both fracture risks (for MOF $\beta=0.532$, $P=0.009$; for HF ($\beta=0.441$, $P=0.026$).
Conclusion
We assumed that obesity might be detrimental to postmenopausal bone health, as it was associated with lower BMD, lower bone turnover and higher fracture risks.

DOI: 10.1530/endoabs.81.EP219

EP220

Endocrine disorders and osteoporosis: case series

Meriem Adel, Sabrine Mekni, Maysam Jridi, Imen Rojbi, Youssef Lakhoua, Nadia Mchirgui, Ibtissem Ben Nacef & Karima Khiari
Charles Nicolle Hospital, Endocrinology, Tunis, Tunisia

Introduction
Homeostasis of calcium and phosphor influence bone metabolism. They depend on several hormones, including parathyroid hormone, thyroid and sexual hormones. Low bone mass seems a common issue in endocrine disorders. The aim of this study is to identify the different endocrine disorders in patients with low bone mass.
Methods
Retrospective study collecting the medical files of patients followed in the endocrinology department of Charles Nicolle Hospital between the years 2018 and 2021. The exclusion criteria are: patients followed for a systemic disease or rheumatic disease and patients who received corticosteroid therapy.
Results
We have studied 50 consecutive patients (14 males, 36 females, sex ratio 0.38, aged 8-88 years). Postmenopausal women represented 56% of the study population.We measured bone mineral density (BMD) at the hip: 70% of patients had osteoporosis (36% males, 64% females) and 30% had osteopenia (12% males, 88% females). The average of T score was -2,78 (min -6; max 0.8) for the spine and -2,09 (min -4,7;max 0,7) for the femur neck with a significant correlation between them. 44% of patients were at a risk of fracture and 2% had a pathological fracture. According to the type of endocrinopathy: 62% of patients had hyperparathyroidism (63,3% osteoporosis; 36.7% osteopenia), 12% had hypogonadotropic hypogonadism (85,7% osteoporosis; 14,3% osteopenia), 10% had hyperthyroidism, 8% had primary ovarian insufficiency (25% osteoporosis; 75% osteopenia) and 2% had hyperadrenocorticism (50% osteoporosis; 50% osteopenia).
Conclusion
Additional studies are needed to further understand the endocrine secondary osteoporosis in order to establish evidence based guidelines about its diagnosis, evaluation, treatment and follow up.

DOI: 10.1530/endoabs.81.EP220

EP221

IPN60130 for the treatment of fibrodysplasia ossificans progressiva: methodology of the randomized, double-blind, placebo-controlled phase II FALKON trial

Negar Karimian[1], Christine Powell[2] & Fei Shih[2]
[1]Ipsen, Montreal, Canada; [2]Ipsen, Cambridge, MA, United States

Objectives
Fibrodysplasia ossificans progressiva (FOP) is an ultra-rare genetic disorder caused by activin receptor-like kinase-2/activin A receptor type 1 (*ALK2/ACVR1*) mutation and characterized by heterotopic ossification (HO) inducing progressive restriction of mobility. IPN60130 is a selective ALK2/ACVR1 inhibitor being investigated for the treatment of FOP.[1] Here, we describe methodology of the FALKON trial (NCT05039515) designed to compare efficacy and safety of IPN60130 with placebo in patients with FOP.
Methods
Patients will be randomized to oral placebo, or low or high dose IPN60130 for 12 months; patients receiving placebo will then transition to IPN60130 for 12 months. Enrollment criteria include: ≧5 years old, clinical FOP diagnosis with disease-causing mutation, and either a flare-up, new HO or joint ankylosis, or increase in Cumulative Analogue Joint Involvement Scale (CAJIS) score in the prior year. Recruitment is ongoing to enroll 90 patients. The primary efficacy outcome will be annualized change from Baseline in HO volume to Month 12, assessed by low-dose whole-body computed tomography (CT). Secondary efficacy outcomes are presented in the **Table**. Safety will be assessed via adverse event (AE) and serious AE incidence over 25 months. Patients aged ≧15 years will be eligible for a sub-study assessing HO by [^{18}F]NaF positron emission tomography-CTT.

Table 1 Secondary efficacy outcomes

Timeframe, months[a]	Outcome	Comparison
12	CfB in volume of new HO lesions[b] CfB in number of HO lesions[b] Flare-up rate; number of flare-up days Number of body regions with new HO CfB in pain intensity Proportion of patients with new HO	IPN60130 vs placebo
24	CfB in HO volume[b]	IPN60130 vs placebo and untreated natural history study (NCT02322255) participants

[a]From Baseline up to the month given; [b]Assessed by low-dose whole-body computed tomography. CfB: change from Baseline; HO: heterotopic ossification.

Summary
Results from FALKON, estimated to complete in August 2025, will allow evaluation of the efficacy and safety of IPN60130 in patients with FOP.
References
1. Davis A *et al*. J Bone Miner Res 2019;34(Suppl 1):290
Funding
Sponsored by Ipsen

DOI: 10.1530/endoabs.81.EP221

EP222

Brown tumour of the mandible as the first manifestation of primary hyperparathyroidism: a case report

Ana Majic[1], Maja Cigrovski Berkovic[1], Ivan Zajc[2] & Ivan Salaric[2]
[1]Clinical Hospital Dubrava, Department of Endocrinology, Diabetes, Metabolic Diseases and Clinical Pharmacology, Zagreb, Croatia; [2]Clinical Hospital Dubrava, Department of Oral Surgery, Zagreb, Croatia

Introduction
Brown tumour is a rare, benign, tumour-like lesion of bones.The presence of brown tumour is a rare complication of uncontrolled primary, secondary or tertiary hyperparathyroidism.Brown tumours can be solitary or multifocal and are most commonly located in ribs, clavicles, pelvic girdle, extremities and facial bones (maxilla, mandible, and hard palate).A diagnosis of brown tumour in hyperparathyroidism is established by evaluation of serum calcium, phosphorus and parathyroid hormone levels. Very often a histologic diagnosis of a giant cell tumour is made in case of brown tumour.Treatment of these lesions is often directed to the management of the underlying hyperparathyroidism, which frequently results in regression and resolution of the lesion without surgical intervention. However, surgical treatment may be required in refractory cases or in large symptomatic lesions.
Case presentation
A 67-year-old male was referred to an oral surgeon for a right mandible mass and bleeding that was present for approximately one year. The patient's past medical history was significant for recurrent nephrolithiasis.An incisional biopsy of the mass was performed and histologic examination suggested giant cell granuloma. Despite the histologic diagnosis, the experienced oral surgeon suspected brown tumour in hyperparathyroidism. The patient was referred to an endocrinologist and additional evaluation was performed.A laboratory examination showed hypercalcemia: total calcium level of 2.94 mmol/l (normal range: 2.14 – 2.53), ionized calcium level of 1.61 mmol/l (normal range: 1.18 – 1.32), hypophosphatemia: 0.66 mmol/l (normal range 0.79 – 1.42) and a high PTH level: 44.02 pmol/l (normal range: 1.59 – 7.24).The patient's renal function was normal and kidney ultrasound revealed mild bilateral nephrocalcinosis without nephrolithiasis. Bone density test revealed osteoporosis.Neck ultrasound revealed an enlarged parathyroid gland and Tc-99 m MIBI SPECT/CT imaging of the neck and mediastinum showed pathological radiopharmacology uptake posterior of the left thyroid lobe compatible with a parathyroid adenoma.The patient underwent left inferior parathyroidectomy and the pathological findings confirmed the diagnosis of parathyroid adenoma.After one-year follow-up, serum calcium, phosphorus and PTH levels were normal. The excision of the remaining exophytic mandible mass was carried out by an oral surgeon due to slow bone healing.
Conclusion
Brown tumour can be the first manifestation of uncontrolled primary hyperparathyroidism, often misdiagnosed as a giant cell tumour. It is an important differential diagnosis in the evaluation of patients with osteolytic bone lesions, with serum calcium, phosphorus and parathyroid hormone measurements being helpful and widely available diagnostic tools.

DOI: 10.1530/endoabs.81.EP222

EP223

Malignant hypercalcemia showing parathyroid adenoma in a patient with renal impairment

Tizgha Mohamed[1,2]
[1]Faculty of Medicine Mohamed Maherzi, Medicine, Algier, Algeria; [2]El Djazair, Medicine, El Djazair, Algeria

Introduction
hyperparathyroidism is usually diagnosed at a pauci or asymptomatic stage. However, in rare cases, the diagnosis is made at the stage of major threatening hypercalcemia. This diagnostic delay may be responsible for complications such as chronic end stage renal disease (CRRD).
Observation
we report the case of a 64-year-old patient referred to the endocrinology department for primary hyperparathyroidism, with no particular family history and a personal history of type 2 diabetes mellitus known for 14 years, high blood pressure and renal lithiasis performed 14 years ago (without etiologic exploration) . Hyperparathyroidism was discovered following a review commissioned by the nephrologist for the exploration of malignant hypercalcemia. The clinical examination revealed major signs of hypercalcemia and a large cervical nodule. Biology: PTH >560 pg/ml twice with serum calcium >130 mg/l, renal balance: clearance at 24 ml/min. This CKD has long been considered secondary to diabetic nephropathy while it was strongly in favor of interstitial nephropathy due to chronic hypercalcemia due to the absence of diabetic retinopathy. Cervical ultrasonography: 45 mm parathyroid macro-nodule. The patient received hyperhydration and injectable biphosphonates 30 times (Bondronate: the only one listed in the CRI) before referring him to surgery.
Discussion
malignant hypercalcemia is a sign of severity in primary hyperparathyroidism, hence the value of screening for asymptomatic forms to avoid life-threatening complications

DOI: 10.1530/endoabs.81.EP223

EP224

A pathological fracture of the femur and multiple pelvic osteolytic lesions mimicking bone metastases as the first presentation of Primary Hyperparathyroidism

Haris Khan[1], Maimoona Nawaz[2], Cuong Dang[1] & Isha Malik[1]
[1]North Manchester General Hospital, Crumpsall, United Kingdom; [2]Fairfield General Hospital, Manchester, United Kingdom

Introduction
Pathological fractures are uncommon in young patients and raise concern about malignancy. Brown tumour (osteitis fibrosa cystica) is a rare benign resorptive bone lesion reported in approximately 3% of patients with primary hyperparathyroidism (PHPT). These have become uncommon in contemporary practice and have the potential to be misdiagnosed because of radiological similarities to other bone diseases especially malignancy.We present a case where the first presentation of PHPT was a fracture of the left femur with multiple pelvic lesions masquerading as a metastatic malignancy.
Case Report
A 47-year-old male patient presented to the emergency department with sudden sharp pain in his left hip. He was unable to weight bear. He had been suffering from chronic hip pain for the last few weeks. On examination, he had no active movement in the left hip. X-ray showed left superior pubic rami fracture. An MRI scan revealed a left neck of femur fracture with multiple osteolytic lesions in the pelvis. A differential diagnosis of metastases was suggested. He was subsequently diagnosed to have PHPT confirmed by high serum calcium, 3.28 mmol/l (2.10-2.60), serum phosphate 0.73 mmol/l (0.8-1.45), PTH 162.7 pmol/l (1.2-6.9), and Vitamin D 26.7 nmol/l (>50). A parathyroid sestamibi scan revealed a large right posterior inferior adenoma measuring $41\times15\times13$ millimeters. His pelvic lesions and fractures were attributed to Brown tumour secondary to PHPT. He had a left intramedullary nail inserted for left hip repair. His parathyroid adenoma was excised following correction of vitamin D levels. He was transferred to the high dependency unit in anticipation of 'hungry bone syndrome' post-surgery. His calcium level dropped to 1.67 mmol/liter. It was treated with intravenous calcium and activated vitamin D (alfacalcidol). He recovered well and subsequent imaging showed good healing of the fractures and mobility returned to normal.
Conclusion
Brown tumours are rare diagnostic findings in developed countries due to routine monitoring of calcium levels and early detection of PHPT.The presentation of pathological fracture as the first presentation of PHPT as in our case is exceedingly rare. It highlights that once a diagnosis of pathological fracture is made, metabolic bone diseases (such as PHPT and osteomalacia) should be investigated. Brown tumours should be in the differentials of patients presenting with bone tumours, to avoid unnecessary invasive investigations.A timely good outcome in this patient was achieved by collaboration between endocrinologists, endocrine and orthopaedic surgeons, and intensive care.

DOI: 10.1530/endoabs.81.EP224

EP225

Intrathyroidal parathyroid adenoma: a rare localization

Rihab Laamouri[1,2], Raccolta Niculina[2], Stahl Ninon[1], Lerintiu Felix[2], Caro Lopez Rita[2] & Smagala Agnès[2]
[1]University of Medicine of Strasbourg, Strasbourg, France; [2]Hospital Louis Pasteur, Colmar, France

Primary hyperparathyroidism is a frequent endocrine disorder but intrathyroidal parathyroid adenoma is extremely rare. Combining cervical ultrasound and MIBI scintigraphy allows localizing most parathyroid adenomas. Because intrathyroidal parathyroid adenomas mimic thyroid nodules the diagnosis can be challenging, requiring eventually the realization of a fine-needle cyto-puncture. We report here a case of an intrathyroidal parathyroid adenoma diagnosed via a combination of cervical ultrasound, cyto-puncture and MIBI scintigraphy.A 47-year old female was addressed by her GP for diarrhea and asthenia associated with a 3.3 mmol/l hypercalcemia. Biologic assessment confirmed hypercalcemia associated with hypophosphatemia and elevated PTH, confirming primary hyperparathyroidism. The patient did not present ECG modifications. Abdominal ultrasound did not find renal lithiasis and osteopenia was found on DXA. Hypercalcemia was managed with iv hydration, bisphosphonate iv perfusion and Cinacalcet oral treatment. Cervical ultrasound did not find any parathyroid adenoma but showed a 24x18x15 mm, regular, smooth border, hypoechoic EUTIRADS 4 inferior nodule in the right lobe. Scintigraphy concluded to a MIBI focal uptake behind the lower part of the right thyroid lobe. A cyto-puncture of the thyroid nodule was performed and concluded to the presence of parathyroid tissue. The patient underwent right lobectomy. Pathological analysis confirmed an intrathyroidal parathyroid adenoma.Intrathyroidal parathyroid adenoma remains a rare entity. Different case reports and studies confirm the most common ultrasound features being a solid hypoechoic nodule, smooth and regular shaped, like the adenoma presented by our patient. One feature that is extremely characteristic for the intrathyroidal parathyroid adenoma is the presence of a hyperechoic line on the ventral surface of the adenoma, feature that was not identified for our patient. Nevertheless, as these intrathyroidal adenomas mimic suspicious thyroid nodules, cyto-puncture is frequently performed before any surgery and helps confirm the diagnosis, as in our case.

DOI: 10.1530/endoabs.81.EP225

EP226

Osteitis fibrosa cytica as index presentation of severe vitamin D deficiency

Mohammad Jeeyavudeen[1], Anca Oniscu[2], Matthew Hicks[3] & Ganesh Arunagirinathan[1]
[1]Edinburgh Centre for Endocrinology & Diabetes, Western General Hospital, Edinburgh, United Kingdom; [2]Department of Pathology, Royal Infirmary Of Edinburgh, Edinburgh, United Kingdom; [3]Department of General Medicine, Western General Hospital, Edinburgh, United Kingdom

Introduction
Osteitis fibrosa cystica (OFC) or brown tumour is a non-neoplastic fibrocystic expansile lytic bone lesion caused due to excess parathormone (PTH). Brown tumour is classically known to occur in severe primary or secondary hyperparathyroidism due to end-stage renal failure with very high PTH level. OFC presenting as a mass due to nutritional vitamin D deficiency (NVD) is exceedingly rare.
Case presentation
47-year-old Caucasian gentleman presented with symptoms of generalised bone pain, particularly in the back and right knee progressing over two years with declining mobility but denied tingling, numbness or spasm. He is a strict vegetarian by choice with a significant past history of Vitamin B12 deficiency anaemia. Clinical examination revealed profound kyphoscoliosis causing 19 cm height loss and a warm tender 6 cm swelling arising from the lateral aspect of proximal right tibia. He had diffuse tenderness in the pelvis and lumbar spines and exhibited positive Gower's sign. Serum bone profile is shown belowImaging studies confirmed a cavitating lesion in the tibia and several areas of lytic lesion at other bony sites. In view of radiological suspicion of malignancy, biopsy of the tibial lesion was performed which showed extensive bone remodelling with areas of cellular and focally haemorrhagic stroma rich in osteoclast giant cells consistent with brown tumour. He was treated with high dose intramuscular Ergocalciferol and went on to develop hungry bone syndrome, requiring parenteral calcium infusion.

	Patient's value	Normal range
Adjusted calcium	2.24	2.2- 2.6 mmol/l
Phosphate	0.61	0.8-1.4 mmol/l
Alkaline phosphatase	1988	40-125 U/l
PTH	85	1.6-6.9 pmol/l
25(OH) Vitamin D3 $^{\Psi}$	<14	50-170 nmol/l
eGFR*	>60	
Myeloma and coeliac screen	Negative	

Ψ- 25 hydroxy vitamin D3, *-estimated glomerular filtration rate

Discussion
NVD induced brown tumours are extremely rare in the developed world due to fortification of food,. Hence only a handful of cases are reported in high risk individuals with poor dietary intake, malabsorption disorders and poor exposure to sunlight due to dressing habit. This gentleman was house-bound and completely lacked vitamin D containing foods in his diet for several years leading to this unusual presentation. Radiologically, OFC can be challenging to distinguish from primary bone tumor. Bone biopsy remains the gold standard for diagnosis. The mainstay of treatment is medical with correction of vitamin D and calcium supplementation during the acute phase to prevent hungry bone syndrome. Thorough education and long-term maintenance with Vitamin D supplements should be pursued in high risk individuals.

DOI: 10.1530/endoabs.81.EP226

EP227

Non-functioning parathyroid cystic tumour: a diagnostic and therapeutic challenge

Moncef Sellami, Wadii Thabet, Malek Mnejja, Bouthaina Hammami, Souha Kallel & Ilhem Charfeddine
Habib Bourguiba Hospital, University of Sfax, Otorhinolaryngology, Tunisia

Introduction
Parathyroid cysts (PCs) are uncommon lesions. They represent less than 0.5% of parathyroid lesions. Cysts are divided into two groups, functional and non-functional, in relation to their hormonal characteristics. Non-functioning ones make up 80 – 90% of PCs.We discussed three cases of non-functioning parathyroid cysts that we surgically excised.
Methods
We report 3 cases of non-functioning PCs treated in our department.
Results
Our series included 1 man and 2 women. The median age was 35 years [22 years – 45 years]. Patients presented a neck lump in the lower anterior neck. Dysphagia was noted in 2 cases. Clinical examination showed a soft, non-tender and well-limited anterior neck mass that move on swallowing. The mass had a median approximate size of 3 cm.Ultrasonography of the neck revealed a cystic lesion behind the left lobe of the thyroid gland in 1 patient and a right cystic thyroid nodule in 2 cases.Fine-needle aspiration (FNA) with detection of parathyroid hormone (PTH) in the cyst fluid was performed in one patient and the intracystic PTH level was high (355 ng/l). Recurrence was noted 1 month after the cyst aspiration. Serum calcium and PTH levels were normal in all patients.All patients underwent surgical treatment: surgical excision of the cystic mass in one case and right lobectomy in 2 cases. Histologic exam confirmed the diagnosis in all cases. PC was intrathyroidal in 2 cases.After median follow-up of 25 months [12 months - 41 months], no recurrence was noted.
Conclusion
Parathyroid cysts are extremely rare lesions. Our cases were nonfunctional parathyroid cystic lesions. FNA with detection of PTH in the cyst fluid (regardless of the level) is an important tool and confirmed the diagnosis in one patient in our study. Three therapeutic options are indicated: cyst aspiration, sclerotherapy and surgery.

DOI: 10.1530/endoabs.81.EP227

EP228

Pseudohypoparathyroidism type I-b: a rare entity

Eugénia Silva, Rute Ferreira, Bernardo Marques, Francisco Sousa Santos & João Manuel Sequeira Duarte
Hospital Egas Moniz, Endocrinology, Lisboa, Portugal

Introduction
Pseudohypoparathyroidism (PHP) is a rare disorder characterized by parathormone (PTH) resistance, caused primarily by genetic defects involving the alpha-subunit of the stimulatory G protein. Biochemical and molecular analysis classify pseudohypoparathyroidism into types I-a, I-b, I-c and 2. We report a case of PHP I-b in an adolescent presenting with a neurological disorder.
Case Report
11 years old female patient, with no relevant personal or family history, referred to a Neurology appointment for paroxysmal episodes of dystonia of the feet. She had hypocalcemia (corrected serum calcium 6.4 (8.6-10) mg/dl), hyperphosphatemia (serum phosphate 8.6 (2.5-4.5) mg/dl), elevated parathormone (PTH 438 (15-65)pg/ml); low urinary calcium (<9 mg/24H), normal D vitamin (1,25-diOH-calciferol and 25-OH-calciferol), magnesium and kidney function. Thyroid function showed TSH 7,21, uU/ml (0.4-4.6), free T4 11,1 pmol/l (12-22) and negative thyroid antibodies (TPO, TG). The laboratory results were suggestive of PTH resistance and partial TSH resistance. Supplementation with calcitriol, calcium carbonate and levothyroxine was initiated. No typical features of Albright hereditary osteodystrophy (AHO) were observed. A cerebral computed tomography scan revealed bilateral symmetrical calcifications of the cranial base nuclei involving the lenticular nucleus, globus pallidus, posteroexternal aspect of the thalamus and the cerebellar nuclei, especially dentate nucleus, suggestive of Fahr syndrome. Renal ultrasound revealed nephrolithiasis; thyroid ultrasound showed no alterations. Oftalmologic evaluation excluded cataracts. Genetic study was requested revealing a maternally inherited 3-kb *STX16* deletion, with loss of methylation restricted to the *GNAS* exon A/B, cause of autosomal dominant PHP I-b. Currently, the patient shows little compliance to therapy, despite the risks, and remains with asymptomatic hypocalcemia.
Conclusion
PHP I-b is most often a sporadic disorder, but sex-linked autosomal dominant inheritance has been reported. Patients with PHP I-b show, occasionally, thyroid stimulating hormone (TSH) resistance and typically lack of Albright hereditary osteodystrophy features.

DOI: 10.1530/endoabs.81.EP228

EP229

Multifactorial causes of secondary osteoporosis: a case report

Delfina Indira Fortes & Ana Paula Barbosa
Hospital Santa Maria, Endocrinology, Lisboa, Portugal

Introduction
Osteoporosis is a metabolic bone disease, characterized by reduction and changes in the bone mass quantity and quality, leading to an increased risk of fractures. It can be divided in primary (postmenopausal or senile), secondary and idiopathic. In the presence of osteoporotic fractures, particularly in men before the age of 65, it is essential to investigate the presence of secondary causes in order to establish an etiological therapy.
Case Report
A 62-year-old man was referred to an outpatient consultation for fractured osteoporosis after suffering spontaneous rib fractures during a coughing episode. He had history of arterial hypertension, diabetes mellitus, smoking, depressive disorder and an adrenal nodule under surveillance for 9 years. He was chronically medicated with metformin, enalapril, lercanidipine, nebivolol, hydrochlorothiazide, atorvastatin and fluoxetine.Physical examination revealed a mildly Cushingoid phenotype and deformation of the left tibia without local inflammatory signs. The analytical evaluation reveled bone alkaline phosphatase 97.6 ($n<$ 22.9 µg/l), serum cortisol 22.8 µg/dl and after 1 mg of dexamethasone 4.5 µg/dl, urinary cortisol 388 µg/24 h ($n<$ 213.7), ACTH 8.7 (N: 7 – 63 pg/ml), hemoglobin A1c 8.1%, calcium 9.3 mg/dl, phosphorus 3.7 mg/dl, Vitamin D 10 ng/ml and PTHi 117 (N: 12-65 pg/ml).DXA revealed T-scores -1.6 CL and -1.5 CF, while bone scintigraphy showed uptake of 3 right posterior rib arches (C8,9,10) and homogeneous uptake of the proximal two-thirds of the left tibia and distal extremity of the left femur. MRI confirmed the diagnosis of Paget's Bone Disease of the left tibia and femur.Adrenal MRI revealed a dimensional increase (from 12 to 27 mm) of the right adrenal nodule. Treatment with zoledronic acid associated with calcium and vitamin D supplementation was initiated, as well as optimization of antidiabetic therapy with empagliflozin. He underwent laparoscopic right adrenalectomy, and histology revealed nodular hyperplasia of the adrenal cortex.
Discussion and Conclusions
In the reported case, the patient had several risk factors for low bone mass and fragility fractures, namely diabetes mellitus, functional hypercortisolemia, secondary hyperparathyroidism, Paget's bone disease and smoking. A multifactorial therapeutic approach was essential in order to reduce its high fracture risk.

DOI: 10.1530/endoabs.81.EP229

EP230

Association between musculoskeletal manifestations in hemodialysis patients and depression

Ramy Ben Tekaya[1], Haifa Hachfi[1], Mouna Brahem[1], Olfa Jomaa[1], Amal Hariz[1], Zohra Atti[2] & Mouhamed Younes[1]
[1]University Hospital Tahar Sfar, Rheumatology Department, Mahdia, Tunisia; [2]University Hospital Tahar Sfar, Nephrology Department, Mahdia, Tunisia

Introduction
Musculoskeletal pain is a major problem for hemodialysis patients. So, we have to control it, to ameliorate their life quality.
Aim
The purpose of this study was to evaluate the prevalence musculoskeletal symptoms and their relation with chronic hemodialysis.
Methods
This is a cross sectional study conducted in rheumatology department of Taher Sfar university hospital in mahdia, Tunisia. The study involved 61 patients with chronic hemodialysis. They were invited to participate and were included after signing informed consent until the calculated sample size was reached. Clinical and demographic characteristics were recorded, as well as years of hemodialysis duration. We asked the patients HAD score, and DN4.
Results
61 patients were included 26 females (42,6%) and 35 males (57.4%). The mean age of the study group was 53.9 [17-83]. The mean age of onset of nephropathy was 44.7+/- 15.4 years, the medium duration of dialysis: 6,1 years. Musculoskeletal manifestation was noted in 49 (80,3%) patients, the bone pain was noted in 32 patients (52,5%) 20 patients (32,8%) had diffuse bone pain, 34 (55,7%) patients had myalgia, 24 patients (39,3%) had muscular weakness, 14,3% had neuropathic pain, 3 patients (4,9%) have jobs, 12 patients (19,7%) are retired, 46 patients (75,4%) are unemployed. The mean HAD score was 17,88 and 33 patients (54,1%) with HAD score over 19. The mean duration of dialysis in symptomatic patients and asymptomatic patients 7,01 years vs 3,24 years ($P<$0,005). The mean HAD score of symptomatic patients and asymptomatic patients 18,81 vs 14,04 ($P<$0,005).
Conclusions
Our study shows the important damage of chronic kidney disease on the musculoskeletal system that can affect patients' quality of life and professional life. That's why mineral and bone disorders in advanced CKD should be well managed.

DOI: 10.1530/endoabs.81.EP230

EP231

Association between serum magnesium levels and physical performance tests in patients with primary osteoporosis

Daniela Ioana Iulia Greere[1,2], Gabriela Voicu[3], Dana Alice Manda[4] & Cătălina Poiană[1,2]
[1]"C.I. Parhon" National Institute of Endocrinology, Pituitary and Neuroendocrine Disorders, Bucharest, Romania; [2]"Carol Davila" University of Medicine and Pharmacy, Discipline - Endocrinology - National Institute of Endocrinology C.I. Parhon and Clinical Base Carol Davila Central Military Emergency University Hospital, Bucharest, Romania; [3]"C.I. Parhon" National Institute Of Endocrinology, Radiology and Imaging, Bucharest, Romania; [4]"C.I. Parhon" National Institute Of Endocrinology, Research, Bucharest, Romania

Introduction
Osteoporosis is the most frequent metabolic bone disease worldwide affecting primarily the senior population. The associated bone loss in combination with a decline in physical performance lead to increased incidence of falls and fragility fractures. Thus, improving physical performance is key to preventing osteoporotic fractures.

Methods
A total of 140 participants were inrolled in a cross-sectional study. Secondary causes of osteoporosis were excluded. All participants underwent dual x-ray absorptiometry analysis and lateral spine radiography (which resulted in 105 subjects being diagnosed with primary osteoporosis and 35 subjects with osteopenia or normal bone density). Each subject underwent several physical performance tests. Blood samples were obtained to perform biochemical and hormonal assessment.
Results
Statistically significant correlations were found between serum magnesium levels and 4-m Gait Speed values in patients suffering from osteoporosis with or without fragility fracture ($P=0{,}004$, $r=0{,}272$). Linear regression showed a negative statistically significant correlation between serum magnesium levels and Timed Up and Go Test ($P=0{,}034$, $r=-0{,}207$) in the osteoporosis subgroup. None of these correlations applied to subjects with osteopenia or normal bone density. All subjects except one had serum magnesium levels within the reference range.
Conclusion
Serum magnesium levels correlate with pysical performance tests in patients suffering from primary osteoporosis. In the setting of hypomagnesemia being known to be associated with poor physical performance, the results of this study suggest more research is needed to establish whether magnesium supplementation should be an adjunct to osteoporosis therapies.

DOI: 10.1530/endoabs.81.EP231

EP232

Hypoparathyroidism: about 61 cases

Mnif Fatma, Asma Zargni, Kawthar El ARBI, Mouna Elleuch, Raida Trigui, Nadia Charfi, Mouna Mnif, Nabila Rekik Majdoub, Faten Haj Kacem Akid & Mohamed Abid
Hedi Chaker Hospital, Diabetology and Endocrinology Department, Sfax, Tunisia

Introduction
Hypoparathyroidism (HPT) is an often under-diagnosed condition. It is imperative to diagnose it at an early stage and to initiate prompt treatment given the evolving potential of the disease.The aim of our study is to describe the epidemiological, clinical and paraclinical features of HPT.
Patients and Methods
This is a retrospective study of 61 observations of HPT collected at the endocrinology department during a 12-year period.
Results
The mean age of our patients at the time of diagnosis was 41 years and 6 months (extremes ranging from 13 to 80 years). HPT was more frequent in the age group 21-30 years. A clear female predominance was observed with a sex ratio of 4.5. The circumstances of discovery were mainly paresthesias (65%) and muscle cramps (62%). The majority of our patients (90%) had hypocalcemia with an average blood calcium level of 1.65 mmol/l (normal range 2.2-2.6 mmol/l). Hypophosphatemia was found in 52% of cases, and hypocalciuria in 80%. Low PTH was found in 72% of cases with a mean level of 9.48 pg/ml. Cervical surgery was responsible for a postoperative HPT in 74% of cases. However, 16% of the cases were idiopathic PTH. Autoimmune origin was observed in 3 cases (5%).
Discussion-conclusion
HPT is a rare and often asymptomatic disease, hence the interest of the calcemia analysis in front of even minor clinical signs.

DOI: 10.1530/endoabs.81.EP232

EP233

Persistent hypophosphataemia due to gastrointestinal losses

Rahat Tauni[1,2,3], Nida Ali[1] & Amjad Khan[1]
[1]St Albans City Hospital, United Kingdom; [2]Hemel Hempstead General Hospital, United Kingdom; [3]Watford General Hospital, United Kingdom

A 49-year-old lady was referred to the endocrine clinic for hypophosphataemia. Apart from tiredness, she had no other symptoms. Past medical history was significant for bronchiectasis, obstructive sleeps apnoea, caudaequina syndrome, migraine and anxiety. She had frequent hospitalisations due to bronchiectasis exacerbations requiring systemic steroids. Usual medications included azithromycin, gabapentin, omeprazole, antacids, laxatives, carbocisteine, fluoxetine, montelukast, propranolol and inhaled formoterol and budesonide. She drank at least 16 pints of milk every week, did not drink alcohol in excess and stopped smoking two years ago. Examination was unremarkable with negative Chvostek sign, no proximal myopathy and no evidence of endocrine disease. Body mass index was raised in the overweight range. Phosphate levels were persistently low for the last two years, with the lowest recorded at 0.15 mmol/l during hospital admissionrequiring intravenous phosphate replacement. Calcium and other bone biochemistry were normal. 25-hydroxy Vitamin D level was 61 nmol/l and she was commenced on oral cholecalciferol 1000 IU/day. Urine tests did not suggest renal potassium loss. She was maintained on oral phosphate replacement on outpatient basis as she was not keen to stop PPI and antacids. Phosphate is a molecular element critical to normal cellular function. Intestines, kidneys and bones are important in phosphate homoeostasis. Hypophosphataemia is caused by inadequate phosphate intake, reduced intestinal absorption, increased renal excretion, phosphate shift from extracellular to intracellular space or a combination of above mechanisms. In our case, hypophosphataemiawas thought to be caused by PPI and antacids, frequent use of steroids, frequent hospital admissions, and intermittent under-nutrition and feeding (‘fast and feast’). Severe and/or symptomatic cases need intravenous replacement as generalised muscular weakness, rhambdomyolysis and acute kidney injury are potential complications. Mild cases may not present with any symptoms but it is important to explore the cause and replace phosphate orally as prolonged hypophosphatemia can lead to osteoporosis or osteomalacia due to reduced bone mineralisation and there are no contraindications of oral phosphate replacement.

DOI: 10.1530/endoabs.81.EP233

EP234

Clinical, biological and evolutionary comparison of postsurgical hypoparathyroidism and non-postsurgical hypoparathyroidism

Siddiqa Soomauroo, Fatma Mnif, Mohamed Abdellahi Mohamed Ahmed, Faten Haj Kacem Akid, Nadia Charfi, Mouna Mnif & Mohamed Abid
Hedi Chaker University Hospital, Department of Endocrinology, Sfax, Tunisia

Introduction
Hypoparathyroidism (HPTH) is an uncommon condition resulting in the production of insufficient amounts of parathyroid hormone (PTH) by the parathyroid glands consequently affecting the calcium phosphate balance. The most frequent etiology of HPTH is the damage to or removal of the parathyroid glands due to a surgery for another condition. Other causes, including autoimmunity and genetic disorders may be responsible for HPTH. Our aim is to compare the different clinical, biological and evolutive aspects of postsurgical HPTH to non-surgical HPTH.
Patients and methods
It is a retrospective study that collected data from 61 patients diagnosed with hypoparathyroidism that were hospitalized in the Department of Endocrinology, Hedi Chaker University Hospital, Sfax over 12 years.
Results
The most common etiology of HPTH was postsurgical HPTH found in 45 cases (74%), including 40 women and 5 men. The mean age of the patients that underwent surgery was 41.5 years. A clear female predominance with a sex ratio (F/M) of 8. The type of intervention was total thyroidectomy in 29 cases, subtotal thyroidectomy in 11 cases and parathyroidectomy in 7 cases. The diagnosis of HPTH was made within the first few days post-intervention. The mean serum calcium level within the first week of surgery was 1.8 mmol/l (extremes: 1.24-2.38 mmol/l). The hypocalcaemia was symptomatic in 29 cases. In 31 cases, the patients required urgent treatment with intravenous calcium salts as well as oral calcium supplementation. Transient HPTH was observed in 3 patients with a mean recovery time of 2.5 months whereas as permanent HPTH was found in 34 patients. Only the presence of clinical signs of hypocalcaemia within the first week post-intervention was significantly correlated as a predictive risk factor for permanent HPTH. More trophic and psychic disorders were found in non-postsurgical HPTH whereas there was no significant difference in serum calcium levels. A more favorable clinical outcome under calcium supplementation therapy in postsurgical HPTH than in non-postsurgical HPTH.
Conclusion
HPTH is a rare affection which results from an absence or reduced secretion of PTH form parathyroid glands resulting in the inability to maintain extracellular calcium homeostasis. One of the most common causes either of transient or permanent HPTH remains post-thyroid surgery. Serum calcium dosage within the first days of thyroid or parathyroid surgery is primordial as well as monitoring the

patients for clinical symptoms so as to detect hypocalcaemia and treat it effectively and accordingly.

DOI: 10.1530/endoabs.81.EP234

EP235

Association between primary hyperparathyroidism with severe bone disease and osteomalacia: A case report.

Hager Khiari[1], Imen Rojbi[1], Houaida Smadhi[2], Sabrine Mekni[1], Youssef Lakhoua[1], Ibtissem Ben Nacef[1] & Karima Khiari[1]
[1]Charles Nicolle Hospital, Endocrinology, Tunis, Tunisia; [2]Beja Hospital, Endocrinology, Beja, Tunisia

Introduction
Primary hyperparathyroidism is associated with multiple complications: severe bone disease is one of them. Osteomalacia is by definition a metabolic bone disease characterized by a softening of the bones. We herein report a rare case of an association between primary hyperparathyroidism with osteitis fibrosa cystica and osteomalacia caused by a severe vitamin D deficiency.
Observation
A 37-year old woman was referred for investigation of weakness and loss of autonomy. She complained of generalized muscular and bone pain, height and weight loss for 1 year. On physical examination, she had waddling gait and hourglass chest deformity. X-ray examination showed looser zones at the pelvis, osteopenia and an aspect of osteitis fibrosa cystica. Computed tomography showed a brown tumor at the right ilium. The patient was diagnosed with primary hyperparathyroidism based on increased serum calcium 2.7 mmol/l (normal range: 2.20-2.60), increased parathormone concentration 2504 pg/ml (normal range: 15-72) and a low serum phosphate 0,67 mmol/l (normal range:0.80-1.45). The urinary calcium was 0.08 mmol/kg/24h. Renal ultrasonography showed a bilateral nephrolithiasis and BMD showed osteoporosis with a high fracture risk: lumbar T-score -5.3 and Hip T-score -4. The diagnosis of osteomalacia was based on clinical and radiological presentation, low 25-OH vitamin D 3.28 ng/ml and elevated phosphatase alkaline 4590 UI/l (normal range <240). Cervical ultrasonography showed a 25x17 mm hypoechoic mass below the left lobe of the thyroid. Parathyroid scintigraphy confirmed increased uptake in the topography of left inferior parathyroid gland. The patient received vitamin D and calcium supplementation and therefore underwent a left lower parathyroidectomy. Postoperative pathology confirmed the diagnosis of parathyroid adenoma. The intraoperative serum PTH concentration was 106 pg/ml. She had hypocalcemia on the third day after surgery: the serum calcium concentration was 1.9 mmol/l. She recovered well after calcium supplementation and was discharged 1 week after surgery.
Conclusion
This case report illustrates a rare case of a severe bone disease caused by an association of a chronic primary hyperparathyroidism and osteomalacia. Prevention, diagnosis and treatment of vitamin D deficiency and the early diagnosis of primary hyperparathyroidism are very important.
Key words
Primary hyperparathyroidism-bone disease-osteomalacia-vitamin D deficiency-case report

DOI: 10.1530/endoabs.81.EP235

EP236

Sporadic multiple-gland disease in primary hyperparathyroidism

Sirine Ayedi[1], Wadii Thabet[1], Mohamed Amine Chaabouni[1], Manel Mallouli[2], Malek Mnejja[1] & Ilhem Charfeddine[1]
[1]Habib Bourguiba Hospital, University of Sfax, Otorhinolaryngology, Tunisia; [2]Habib Bourguiba Hospital, University of Sfax, Pathology, Tunisia

Introduction
In 80–90% of cases, the cause of sporadic primary hyperparathyroidism is adenoma of one parathyroid gland. Multiple-gland disease (MGD) is defined in patients with more than one pathological parathyroid gland. The frequency of occurrence of MGD is from 7% to 33%.Our aim is to report a case of primary hyperparathyroidism with MGD and to describe its diagnostic and therapeutic features.
Case Report
A 55-year-old man presented with 1-year history of bone pain and asthenia. He had history of diabetes and hypertension. He had not been suffering from pathological fractures, nephrolithiasis or gastropathy. No familial history of multiple endocrine neoplasia syndrome was noted. Physical exam showed a 2-cm left anterior neck mass.The laboratory workup revealed: serum calcium level was 3.05 mmol/l, serum phosphate level was 0.99 mmol/l, and serum PTH level was 127 ng/l. Ultrasonography of the neck revealed a 26-mm parathyroid nodule behind the left lobe of the thyroid gland and another one behind the right lobe, measuring 15 mm. A 99 m technetium (99 mTc) sestamibi scan has been performed: it showed an inferior right parathyroid adenoma with doubt on another left adenoma.The patient underwent superior and inferior right parathyroidectomy and left inferior parathyroidectomy. The intra-operative examination suggested parathyroid adenomas. The postoperative course was uneventful. The level of serum PTH (43 ng/l) and serum calcium (2.45 mml/l) were normalized after the surgery. Histological exam confirmed the diagnosis of MGD: adenoma of the right superior parathyroid gland, pseudo adenomatous hyperplasia of the right inferior parathyroid gland and hyperplasia of the left inferior parathyroid gland.No recurrence was noted after 1 year of follow-up.
Conclusion
Identifying preoperatively patients at risk for MGD remains challenging. Intraoperative decisions are important for achieving acceptable cure rates and long-term follow-up is mandatory in such patients. Patients with MGD have an increased risk of complications at surgery and for persistence and recurrence after surgery.

DOI: 10.1530/endoabs.81.EP236

EP237

Particularities of primary hyperparathyroidism in multiple endocrine neoplasia type 1: Tunisian data

Mnif Fatma[1], Kawthar El Arbi[1], Yosra Lajmi[2], Asma Zargni[1], Dhoha Ben Salah[1], Oumeyma Trimeche[1], Mouna Elleuch[1], Nadia Charfi[1], Mouna Mnif[1], Nabila Rekik Majdoub[1], Faten Haj Kacem Akid[1], Hassen Kammoun[2], Fatma Abdelhédi[2] & Mohamed Abid[1]
[1]Hedi Chaker Hospital, Department of Endocrinology, Sfax, Tunisia; [2]Hedi Chaker Hospital, Department of Medical Genetics, Sfax, Tunisia

Introduction
Multiple endocrine neoplasia type 1 (MEN1) is an inherited syndrome characterized mainly by the association of: Primary hyperparathyroidism (PHP), gastro-entero-pancreatic tumors (GEP) and pituitary tumors. The aim of our work is to specify the particularities of PHP in MEN1 among Tunisian population.
Patients & Methods
It is a retrospective descriptive study of 7 cases of MEN1, including 3 familial cases, during a 28-year period.
Results
The mean age at diagnosis of our patients was 36 years with a female predominance (Sex-Ratio = 1.3). PHP was the most frequent initial manifestation in MEN1 (5 cases) and it was present in all cases (7 cases). Four patients were asymptomatic at the time of diagnosis. PHP was complicated by urinary lithiasis in 3 cases and osteoporosis in 3 cases, which was severe in 2 cases. Surgical treatment was considered in six cases. This consisted of parathyroid adenoma removal in 4 cases and subtotal parathyroidectomy in two cases. The anatomopathological study concluded to multiple adenomas in 3 cases. A therapeutic failure with persistent hypercalcemia was observed in 2 cases. The genetic study was done in 4 patients. It showed the presence of a novel mutation, not previously described in the literature, of the MEN1 gene at exon 4 in three cases.
Conclusion
Our work illustrates the particularities of PHP in MEN1 and subsequently confirms the results of the literature.

DOI: 10.1530/endoabs.81.EP237

EP238

Primary hyperparathyroidism and rheumatoid arthritis

Lambros Athanassiou[1], Ifigenia Kostoglou-Athanassiou[2], Maria Mavroudi[3], Pavlos Tsakiridis[3], Nikolaos Koukosias[3] & Panagiotis Athanassiou[3]
[1]Asclepeion Hospital, Voula, Department of Rheumatology, Athens, Greece; [2]Asclepeion Hospital, Voula, Department of Endocrinology, Athens, Greece; [3]St. Paul's Hospital, Department of Rheumatology, Thessaloniki, Greece

Rheumatoid arthritis is a systemic autoimmune inflammatory disease characterized by severe pain, if left untreated. Primary hyperparathyroidism is a systemic disorder characterized by disordered calcium metabolism leading to increased serum calcium and PTH levels. Primary hyperparathyroidism may be due to the presence of a parathyroid adenoma or parathyroid hyperplasia. The aim was to present a cohort of patients with rheumatoid arthritis who presented with primary hyperparathyroidism.A cohort of patients with rheumatoid arthritis is presented. Three patients with active rheumatoid arthritis are described. Patients were female, aged 58, 65 and 67 years old. They had seropositive rheumatoid arthritis, anti-CCP positive, rheumatoid factor positive and had severe pain on treatment with methotrexate and corticosteroids. During laboratory evaluation increased calcium levels were observed along with increased PTH levels.In further evaluation an ultrasonogram revealed the presence of a parathyroid adenoma adjacent to the thyroid in two of the patients, while in the other scintigraphy with 99 mTc-SESTAMIBI was performed which revealed an adenoma beneath the left lobe of the thyroid gland. Surgical removal of the parathyroid adenomas was planned. For the management of rheumatoid arthritis biologic therapy was introduced.Primary hyperparathyroidism in the context of rheumatoid arthritis is rare. If diagnosed it may require surgical removal of the parathyroid adenoma as increased calcium levels may aggravate pain in the setting of systemic inflammation. The diagnosis of primary hyperparathyroidism in the setting of rheumatoid arthritis may be due to routine screening for calcium levels on biochemical evaluation in modern times.

DOI: 10.1530/endoabs.81.EP238

EP239

How we managed malignant hypercalcemia in a hyperparathyroid in heart failure in the emergency room

Ali Halouache, Errahali Yassine, Chakdoufi Sanae, Isouani Jad & Guerboub Anas
Hopital Militaire d'Instruction Mohammed V, Endocrinology, and Metabolic Diseases, Rabat, Morocco

Introduction
We report a case of malignant hypercalcemia complicated by acute pancreatitis, in a patient whose cardiac insufficiency obliged us to use an unconventional therapeutic means: calcimimetics
Case Report
Mrs. Halima, 74 years old, had a history of arterial hypertension complicated by ischemic heart disease at the stage of heart failure. She consulted the emergency room for typical pancreatic pain, the biological workup found a lipasemia at 30 times normal and acute renal failure, the abdominal CT scan was in favor of an acute pancreatitis stage E of Balthazaar.The etiological investigation found malignant hypercalcemia (140 mg/l) secondary to primary hyperparathyroidism (PTH: 679 pg/ml).the patient was put on fasting, with analgesic treatmentFor hypercalcemia, hyperhydration was not possible in the presence of decompensated cardiac insufficiency, and biphosphonates were contraindicated in the presence of kidney failureFaced with the reduced therapeutic choices, our attitude was to prescribe cinacalcet at a progressive dose: 30 mg per day then 60 mg per day, the calcemia went in two days from 140 mg/l to 120 mg/l then to 100 mg/l, as regards the adverse effects; our patient presented only one episode of vomiting the first day.After stabilization, she benefited from a localization check-up which revealed a parathyroid nodule, and the evolution was favorable after surgical removal.
Discussion
Cinacalcet is an oral calcimimetic that mimic the effects of calcium on the calcium receptors of the parathyroid cell. It lowers blood calcium and reduces PTH concentration.[1] Initially used in hyper parathyroid hypercalcemia associated with end-stage renal disease is actually FDA approved to treat secondary HPT in patients with parathyroid carcinoma (2011) [2], and hypercalcemia in patients with primary HPT who are unable to undergo Para thyroidectomy.but its use in malignant hypercalcemia in emergency situations has not been recommended, in some cases, and when the classical treatment of hypercalcemia is not possible, as in our patient's case, calcimimetics, and in particular cinacalcet, can be the most effective therapeutic option to save the patient
Conclusion
we suggest that the use of this therapeutic class may be useful in urgent situations in patients with cardiac or kidney failure when hyper hydration is not possible[1] Wada M., and Nagano N.: Control of parathyroid cell growth by calcimimetics. Nephrol Dial Transplant 2003; 18: pp. iii13-iii17[2] Silverberg S.J. *et al*: Cinacalcet hydrochloride reduces the serum calcium concentration in inoperable parathyroid carcinoma. J Clin Endocrinol Metab 2007; 92: pp. 3803-3808

DOI: 10.1530/endoabs.81.EP239

EP240

Post covid 19 vaccine cramps in a patient followed for hypoparathyroidism: who is to charge?

Ihssane Abidi, Kaoutar Rifai, Iraqi Hinde & Mohamedelhassan Gharbi
University Mohammed 5 Rabat, Endocrinologie, Rabat, Morocco

Introduction
COVID-19 is a pandemic related to SARS-COV-2 virus infection. It is most often manifested by an influenza-like syndrome with other symptoms that are more specific such as loss of smell and taste.Its severity is highly variable, ranging from asymptomatic to severe or prolonged forms.We report the case of a 47-year-old female patient, who is being followed for hypoparathyroidism, who developed severe and persistent cramps after the COVID-19 vaccine.
Observation
This is a 47-year-old female patient with a history of high-risk papillary thyroid carcinoma since 2018, operated and irradiated. Her surgery was complicated by supplementary hypoparathyroidism. Her blood calcium was well controlled and she was asymptomatic since her supplementation with Alfacalcidol and calcium.She received the first dose of astrazeneca in July 2021, after 4 hours she developed persistent painful cramps in her extremities. Her clinical examination did not reveal any signs of hypocalcaemia and the biological dosage was 84 mg/l.As the cramps persisted, we started her on calcium and magnesium. The clinical evolution was good after 6 hours and there was no recurrence.
Discussion
COVID-19 vaccines are as well tolerated in neuromuscular patients as in the general population (1). Hypoparathyroidism is not a neuromuscular disease, but it can be caused by hypocalcaemia, which is the cause of the neuromuscular manifestations.Campesium can be seen with COVID-19 vaccines, and is generally benign and transient.The particularity of our observation is that the cramps were severe and incapacitating with the need for intravenous calcium treatment and monitoring, adding the hypoparathyroid terrain which posed a problem of differential diagnosis.
Conclusion
The vaccine against COVID-19 has become an unavoidable necessity in the face of the pandemic population. It certainly has short and long term side effects. Fragile patients must be monitored to avoid complications, particularly neuromuscular ones.
References
• (1) NEUROMUSCULAR DISEASES AND COVID-19 VACCINATION, Recommendations of the filnemus rare diseases health sector, Version 1.0 of 4 January 2021.

DOI: 10.1530/endoabs.81.EP240

EP241

Pseudohypoparathyroidism discovered in adulthood

Chayma Besrour, Rojbi Imen, Mekni Sabrine, Majdoub Marwa, Lakhoua Youssef, Ben Nacef Ibtissem & Khiari Karima
Hospital Charles Nicolle, Endocrinology, Tunis, Tunisia

Introduction
Pseudohypoparathyroidism (PHP) is a part of a very rare heterogeneous group of endocrine disorders. It is caused by alterations in the PTH receptor, which is encoded by the GNAS1 gene inducing target tissue resistance to PTH. Pseudohypoparathyroidism typically gets discovered during early childhood, rare are the cases discovered in adulthood.
Observation
Herein the case of a 35-year-old man, descendant of a non-consanguineous marriage, with a medical history of bilateral cataract surgery at the age of 33 years-old, who consulted the emergency department for an epileptic seizure then he was transferred after discovering a severe hypocalcemia with Fahr's syndrome at the CT-Scan.The patient didn't present neither cramps or paresthesia. Chvostek

and Trousseau signs were negative. He had a short stature (Height 153 cm vs Target height 180 cm), dental hypoplasia and soft tissue calcifications on the dorsal part of the hands confirmed by the X-Ray imaging. The patient was in sinus tachycardia at 115 bpm with a non-prolonged corrected QT interval (353 ms). The biology showed a low corrected calcium level at 1.94 mmol/l, an elevated level of phosphorus (1.89 mmol/l), a high level of PTH (170 pg/ml) and a normal renal function (creatinine 60µmol/l), in favor of the diagnosis of PHP. The patient was treated with the association of calcium (6g/day) and alphacalcidol (2µg/day), and the corrected calcium level when he was discharged was at 2.14 mmol/l.
Conclusion
In PHP the target tissue is resistant to PTH, resulting in hypocalcemia and hyperphosphatemia. Five different types of PHP, each with specific features, have been described. The best-known type of PHP is type 1a, where biochemical disruptions are combined with a phenotype called Albright's hereditary osteodystrophy (AHO), including short stature, round face, brachymetacarpia, and subcutaneous ossifications. But the diagnosis of certainty in our case remains genetic.

DOI: 10.1530/endoabs.81.EP241

EP242

Primary vs tertriary hyperparathyroidism in a patient with medullary nefrocalcinosis and chronic renal failure

Tea Shehu, Violeta Hoxha, Dorina Ylli, Adishah Çerma & Agron Ylli
University of Medicine, Mother Teresa Hospital Center, Endocrinology, Tirana, Albania

Background
Nephrocalcinosis is characterized by the deposition of calcium products in kidney parenchyma and tubules. It may cause acute or chronic kidney injury or be incidentally detected radiographically in a patient with normal kidney function. Most patients with nephrocalcinosis do not progress to end-stage kidney disease, but with certain underlying conditions, may be associated with progressive kidney dysfunction.
Methods
The patient was diagnosed with primary hiperparathyroidism on the basis of blood analysis, biochemical analysis, schintigraphy, calcium levels and parathyroid hormone (PTH).
Case presentation
A 70 year old female patient came to the Emergency Unit with fatigue, diffuse abdominal pain, vomiting, diarrhea and decrease in the amount of urination. Laboratory analysis revealed hyperkalemia, hyponatremia, high azotemia (266 mg/dl) and creatinemia (7.2 mg/dl), high uricemia and phosphatemia. PTH = 832 g/d (high), 25-hidroxyVit D = 8.3 mg/dl (low), total Ca = 9 mg/dl(normal). Cell blood count showed normocromic normocytic anemia. Diuresis was 1 liter/24 - hours (low) and diagnosis of acute renal failure was made. Hemodyalisis was started and after first session dhe patient was hospitalized to nephrology department. The patient was well known for a 20 years of recidivant renal calculosis and has had three interventions of renal calculus, which ended successfully. She suffered from chronic renal failure as well. Levels of calcium and PTH raised progressively from 2016 to 2021. Actual abdominal echography showed calculus and multiple cysts. Parathyroid schintigraphy showed hyperfixation of 99 mTc MIBI 20 mCi that leads to the conclusion of parathyroid adenoma. During hospitalization the patient underwent hemodyalisis. She was planned for three and half gland parathyroidectomy.
Conclusion
Medullary nephrocalcinosis is a well known manifestation of primary hyperparathyroidism. When this happens, hyperplasia of parathyroid gland also occur and if primary hyperparathyroidism wasn't diagnosed, tertiary hyperparathyroidism can develop and differential diagnosis become very difficult. In our case, nephrocalcinosis is a strong evidence of primary hyperparathyroidism and correlates with schintigraphy, but raising values of PTH during years also suggests secondary hyperparathyroidism due to chronic renal failure. In this scenario tertiary hyperparathyroidism can also happen. Treatment of choice is three and a half parathyroidectomy wich is a definitive solution for adenoma (primary vs tertiary), and calcium lowering therapy even in the background of parathyroid hyperplasia.
Keywords
Medullary nephrocalcinosis, primary hyperthyroidism, parathyroid adenoma, calcium, PTH, kidney, parathyroid glands, calcul, chronic renal faiure.

DOI: 10.1530/endoabs.81.EP242

EP243

Paralytic sciatica revealing hyperparathyroidism: a case report

M'ballou Camara, Sana Rafi, Ghizlane EL Mghari & Nawal EL Ansari
CHU Mohammed VI, Endocrinology, Diabetes, Metabolic Diseases and Nutrition, Marrakech, Morocco

Introducing
Primary hyperparathyroidism (HPT1) is a frequent endocrinopathy. Diagnosed incidentally or in front of a urinary or bone symptomatology, we report a case of primary hyperparathyroidism in the mode of revelation makes the originality "a paralyzing sciatica".
Observation
The patient was 44 years old and was undergoing neurosurgery for chronic low back pain that was resistant to etiological treatment. In view of the persistent and hyperalgesic nature of the disease, a detailed radiological work-up was carried out: CT scan of the spine with multiple somatic lesions in the lumbosacral region and in the iliac wings. The diagnosis of multiple myeloma was ruled out and on the phosphocalcic workup: primary hyperparathyroidism was diagnosed (with parathyroid hormone (PTH) elevated to 1033 pg/ml, hypercalcemia at 116 mg/l compared to albuminemia at 36 g/l, high calciuria at 392 mg/24h, low phosphorus level at 12 g/l with total protein at 76 g/l);A cervico-thoraco-abdomino-pelvic CT scan showed a left parathyroid nodule measuring 3.6 cm with thyroid nodules classified as TIRADS 2, 3, and 4, the patient benefited from a total thyroidectomy with excision of the parathyroid nodule, on anatomopathological examination: aspect of a parathyroid adenoma subsequently substituted in calcium and vitamin D
Discussion
Primary hyperparathyroidism results from an increased secretion of parathyroid hormone (PTH), associated with hypercalcemia, most often related to a parathyroid adenoma, hyperplasia of the parathyroid glands and parathyroid carcinoma are very exceptional. The classic presentation associating fibrocystic osteitis, chondrocalcinosis, nephrocalcinosis, renal colic, and the digestive and neuropsychic clinical signs of hypercalcemia is less and less frequently encountered in Western countries, but remains frequent in some countries. The diagnosis of severity and the etiological diagnosis allow the indications and the modalities of surgical treatment to be determined; any symptomatic form (bone, kidney or hypercalcemia-related signs) constitutes an indication for surgery. Minimally invasive parathyroidectomy is the first-line treatment for most patients.
Conclusion
The presence of diffuse cervical and lower extremity polyarthralgia may not be due to osteoarthritis alone. This deserves a thorough investigation such as a blood calcium and PTH measurement

DOI: 10.1530/endoabs.81.EP243

EP244

Symptoms alleviation of primary hyperparathyroidism intensified by COVID-19 pandemic effects using a balanced diet: a case report

Narges Kashanivahid[1], Hadi Tabesh[1] & Hamid Bazrafshan[2]
[1]Department of Life Science Engineering, Faculty of New Sciences and Technologies, University of Tehran, Tehran, Iran; [2]LMU Klinikum, Ludwig Maximilian University of Munich, Munich, Germany

Introduction
Hyperparathyroidism happens when one or more of parathyroid glands secret excessive parathyroid hormone, causing calcium levels in blood to rise. A diagnosis may be missed or delayed because there are no symptoms or they are vague, like depression, tiredness, losing your appetite in addition to hypercalcaemia symptoms e.g. vomiting, bone and joint pain, dehydration, hypertension, etc. Surgery to remove the parathyroid gland is usually the only way of treating primary hyperparathyroidism. Patients who are unable to have surgery, cinacalcet tablet may help control the condition while being sure to have a healthy and balanced diet.
Method
A 57 years old female patient with 115 kg weight and 160 cm height and a history of osteoarthritis, osteoporosis, joint pain and inability of movement in addition to depression was referred to our endocrinology clinic. Since COVID-19 pandemic, she had to leave her job as a teacher and staying at home. This situation dramatically deteriorated her mental health and intensified weight gain procedure. Considering her history and laboratory examination results, especially high plasma level of calcium, hyperparathyroidism was diagnosed. Nevertheless, no

medicine was prescribed for her. Analyzing her routine nutrition, we found that her daily liquid intake was very low ca. 2 glasses, accompanied by irregular meals with almost no snack. Instead, an intense diet of 1500 kcal per day with high citrate, magnesium and B-complex and low calcium and high liquid consumption was designed in order to change her nutrition style for 6 months. The diet was planned to balance her meals with 3 main meals and 3 snacks in the meantime. She was recommended to consume more citrus and lemons and no spinach to prevent renal calculi formation. Her health condition was monitored every week by our dietitian staff.
Results
After one month of this intense diet, the patient lost 5 kg of her weight. She reported a kind of lightheadedness feeling, amelioration of joint's pain while she could walk 10 minutes at home each day. By 6 months follow up, she reported a remarkable improvement of her QOL and losing 12 kg of the weight, no more joint pains and no renal problem.
Conclusion
Although the effects of COVID-19 pandemic especially staying at home could worsen the symptoms of primary hyperparathyroidism and hypercalcaemia, a healthy and balanced diet seems to highly ameliorate these symptoms without the need of any medicine and prevent the surgery to remove the parathyroid gland.

DOI: 10.1530/endoabs.81.EP244

EP245

A recurrent hypercalcemia after subtotal parathyroidectomy revealing a Munchhausen syndrome

Elyes Kamoun[1,2], Ibtissem Ben Nacef[1,2], Sabrine Mekni[1,2], Youssef Lakhoua[1], Nadia Mchirgui[1,2], Imen Rojbi[1,2] & Karima Khiari[1,2]
[1]Hospital Charles Nicolle, Endocrinology Department, Tunis, Tunisia; [2]Faculté de Médecine de Tunis, Tunis, Tunisia

Introduction
Primary hyperparathyroidism is the most common manifestation of multiple endocrine neoplasia (MEN) type 1, with a frequent involvement of all the parathyroids. In cases where the four glands weren't resected, a close monitoring should be performed for an early diagnosis of recurrence. Elevated calcium levels with elevated parathormone (PTH) levels in this context makes the physician suspect an adenoma or a hyperplasia of the remaining parathyroid. We herein describe the case of a suspected recurrent hyperparathyroidism which revealed a Munchhausen syndrome.
Observation
We report the case of a 34-year-old man carrying a heterozygous missense mutation of the third exon of the MEN1 gene. He didn't have gastric nor intestinal tumors. He had two infracentimetric nodules in the tail of the pancreas, with a negative hormonal screening. He had a two millimeters pituitary nodule with normal prolactin and IGF1 levels. For the adrenal tumors, there was a non-functional micronodular hyperplasia. There was no thymic nor bronchopulmonary tumor. The patient presented four years ago a hypercalcemia at 3 mmol/l with elevated PTH levels at 400 pg/ml, and he was operated on with resection of three parathyroid gland containing each an adenoma; the fourth parathyroid gland wasn't found during surgery. During four years, calcium and PTH levels were normal, with the last normal control respectively at 2,5 mmol/l and 84,5 pg/ml (26,5-96,5), all in favor of a remission. During follow-up, he presented an asthenia and tachycardia with elevated calcium levels at 3,26 mmol/l and PTH at 68,5. In this context, a recurrent hyperparathyroidism was suspected, but cervical ultrasound, computed tomography and parathyroid scintigraphy didn't find any abnormal or functional gland. The lability of the calcemia and the excessive concern for his disease made us suspected a facticious hypercalcemia, confirmed when he presented a severe hypercalcemia at 4,28 mmol/l, low PTH at 3 pg/ml and elevated vitamin D at 267 ng/ml (>60ng/ml) with the presence in his belongings of calcium-containing pills and ampoules and activated vitamin D. After treatment with intravenous saline and glucocorticoids, his calcemia reached 2,64 mmol/l. He was referred for psychiatric management, confirming the Munchhausen syndrome, with a calcemia level controlled at 2,62 mmol/l.
Conclusion
Hypercalcemia was rarely reported in association of Munchhausen syndrome. In our patient, the calcium and active vitamin D used to treat a member of his family for post-operative hypoparathyroidism and his knowledge of his disease allowed him to use hypercalcemia as a self-inflicted symptom.

DOI: 10.1530/endoabs.81.EP245

Diabetes, Obesity, Metabolism and Nutrition

EP246

Association between interleukin-6 and renal function in patients with diabetes mellitus

Volha Vasilkova[1], Tatsiana Mokhort[2], Ivan Pchelin[3] & Yana Borovets[1]
[1]Gomel State Medical University, Endocrinology, Homiel, Belarus; [2]Belarusian State Medical University, Minsk, Belarus; [3]Saint Petersburg State University, Saint Petersburg, Russian Federation

Background and Aims
to assess the relationship between level of interleukin-6 (IL-6) and the renal function in patients with diabetes mellitus (DM).
Method
A total of 416 patients with DM, aged 34 to 75 years, were examined. Control group included 60 healthy patients the same age/All patients underwent standard clinical and laboratory examination, with an assessment of the levels of natriuretic peptides (BNP, proBNP) and level of IL-6. Renal function was assessed based on the levels of serum creatinine, cystatin C, eGFR, which was calculated according to the CKD-EPI formula, and albuminuria, which was assessed as albumin/creatinine ratio. Statistical data analysis was performed using smSTATA 14.2 for Mac (2018).
Results
The levels of IL-6 in patients with DM were higher than in control group (3,14 [1,7;9,1] vs. 1,5 [1,5;1,7] mg/ml). The level of IL-6 increased with GFR decreasing from 1.7 [1.5; 1.9] mg/ml in CKD 1 to 11.4 [8.9; 32.1] mg/ml in CKD 5 and significantly different between all groups. At the same time, IL-6 values in patients with CKD 1 were also significantly higher compared to the control group (1.7 [1.5; 1.9] mg/ml vs. 1.5 [1.5; 1.7], at $p<0.001$). IL-6 significantly correlated with cystatin C ($r=0.71$, $p<0.001$). A strong negative correlation was also observed between IL-6 and eGFR ($r=-0.73$, $p<0.001$). Multiple linear regression analysis revealed a significant association of creatinine and IL-6 ($ß=0.29$, $p<0.001$). To find the optimal cut-off threshold for reducing eGFR, a classification analysis using ROC curves was used. At the level of IL-6=2.6 mg/ml, the sensitivity and specificity were 76.7% and 73.9%.
Conclusion
IL-6 might be an independent predictor of decreased renal function in patients with diabetes. Further study of the role of pro-inflammatory cytokines in the development of renal impairments will make it possible to finally decode the mechanisms of their pathogenesis, which will further allow us to understand their complex effect on the body and obtain information for the development of new effective and safe specific medicines.

DOI: 10.1530/endoabs.81.EP246

EP247

COVID-19 triggered inborn errors of metabolism in adults: a case report of mitochondrial fatty acid β-oxidation disorder

Viacheslav Serebrennikov[1] & Kseniya Serebrennikova[2]
[1]The Vishnevsky 3rd Central Military Clinic Hospital, Endocrinology department, Krasnogorsk, Russian Federation; [2]A.N. Bach Institute of Biochemistry, Research Center of Biotechnology, Russian Academy of Sciences, Moscow, Russian Federation

Introduction
Autosomal recessively inherited disorders in the metabolism of mitochondrial fatty acid β-oxidation (FAO) constitute a group of rare diseases with different clinical manifestations and prognosis depending on the type of enzyme deficiency. Hypoketotic hypoglycemia is common to all these types of disorders and is associated with increased consumption of glucose and impaired synthesis of ketone bodies from fatty acids during the fasting periods, infection, or prolonged physical exertion. The analysis of acylcarnitines using tandem mass spectrometry is the gold standard diagnosis of FAO disorders; however, it can be supplemented by the determination of acylglycines, organic acids and other metabolites to clarify the type of enzyme deficiency. The study aims to discuss a clinical case of genetic FAO disorder, first diagnosed after coronavirus disease (COVID-19) as a trigger for the development of clinical signs of the disease.
Case report
A previously healthy 18-year-old male patient was admitted to the intensive care unit in a hypoglycemic coma with a blood glucose level of 1.8 mmol/l. Upon examination, COVID-19 with moderate bilateral pneumonia was diagnosed. Biochemical investigations showed the significantly elevated levels of creatine phosphokinase, liver enzymes, creatinine and urea. After clinical stabilization and

resolution of SARS-CoV-2 infection the renal biomarkers, liver enzymes and creatine phosphokinase were normalized, and the patient was transferred to the endocrinology department for further examination. After exclusion of insulin-producing tumors, adrenal insufficiency and other common causes of hypoglycemia, a fasting test was performed. Decreasing the glucose level to 3.4 mmol/l, insulin to 5.5 IU/l and C-peptide to 0.7 ng/ml, accompanied by severe headache, nausea and recurrent vomiting in the patient, led to the decision to stop fasting after 28 hours. In cases of suspected congenital metabolic disorders, the profiles of acylcarnitine in plasma and organic acid in urine during a period of fasting were measured. Elevated levels of plasma acylcarnitines and increased excretion of ethylmalonic, glutaric and isovaleric acids indicated multiple deficiency of acylcoenzyme A dehydrogenase.
Conclusions
Along with the risk of a severe course of COVID-19 in individuals with metabolic dysfunction, COVID-19 can be a trigger for the initial detection of rare inherited metabolic disorders. This study describes for the first time a clinical case of a newly diagnosed multiple deficiency of acylcoenzyme A dehydrogenase in an adult during the development of SARS-CoV-2 infection.

DOI: 10.1530/endoabs.81.EP247

EP248

Correlation between pulse wave velocity and cardiovascular risk in type 2 diabetes

Chayma Besrour[1], Rojbi Imen[1], Ben Ahmed Habib[2], Mekni Sabrine[1], Mchirgui Nadia[1], Ben Nacef Ibtissem[1] & Khiari Karima[1]
[1]Hospital Charles Nicolle, Endocrinology, Tunis, Tunisia; [2]Hospital Charles Nicolle, Cardiology, Tunis, Tunisia

Introduction
Diabetes increases the risk of high blood pressure, atherosclerosis, coronary heart disease and stroke. Therefore, People with diabetes have an increased cardiovascular risk. Arterial stiffness is a marker of cardiovascular risk and has been shown to have an independent prognostic effect on cardiovascular disease. The aim of this study was to examine the relationship between cardiovascular risk and arterial stiffness in type 2 diabetes.
Methods
We conducted a prospective study including 249 diabetic patients without macroangipathic complications, between July 2020 and May 2021. Using a SphygmoCor®XCEL device, we measured arterial stiffness directly by the carotid to femoral pulse wave velocity (cfPWV).
Results
The mean age of the study population was 57.53 ± 9.34 years (139 women and 110 men). The mean duration of the disease was 10.2 years.Our population were divided into two groups; high cardi-vascular risk 27.3% and very high cardio-vascular risk 72.7%.CfPWV $>$ 10 m/s was found in 77.9% of the patients with high cardio-vascular risk and in 95% of the patients with a very high cardio-vascular risk.In the first group, cfPWV was at 11.92 ± 2.08 m/s VS 14.29 ± 2.79 m/s in the second group ($P < 0.001$).
Conclusion
Arterial stiffness is often increased in type 2 diabetics. Moreover, it has been shown that it may predict cardiovascular events in asymptomatic individuals. Therefore, its evaluation in a high-risk population such as the diabetics, must be a routine in our daily practice.

DOI: 10.1530/endoabs.81.EP248

EP249

Evaluation of pulse wave velocity in type 2 diabetes

Chayma Besrour[1], Rojbi Imen[1], Ben Ahmed Habib[2], Mekni Sabrine[1], Mchirgui Nadia[1], Ben Nacef Ibtissem[1] & Khiari Karima[1]
[1]Hospital Charles Nicolle, Endocrinology, Tunis, Tunisia; [2]Hospital Charles Nicolle, Cardiology, Tunis, Tunisia

Introduction
Type 2 diabetes is an insidious and progressive disease; accounting for about 90% of all diabetes cases worldwide. Atherosclerosis is a common pathology in diabetes that involves a combination of fatty degeneration (atherosis) and stiffening of the arterial vessels (sclerosis), and the best tool to evaluate the arterial stiffness is the pulse wave velocity. The aim of this study is to evaluate the arterial stiffness in type 2 diabetic patients.
Methods
We conducted a prospective study including 249 diabetic patients without macroangipathic complications, between July 2020 and May 2021. Using a SphygmoCor®XCEL device, we measured arterial stiffness directly by the carotid to femoral pulse wave velocity (cfPWV).
Results
The mean age of the study population was 57.53 ± 9.34 years (139 women and 110 men). The mean duration of the disease was 10.2 years. The mean body mass index was at 29.31 ± 4.98 kg/m^2 and the prevalence of obesity was at 41%.High blood pressure and dyslipidemia were present in 54.2% and 98.4% of patients. Microangiopathic complications were found in 58.2% of the patients. Only 24.5% of the patients had a controlled diabetes. Arterial stiffness defined as cfPWV $>$ 10 m/s was present in 91.2% of the patients. And the mean cfPWV was at 13.64 ± 2.82 m/s.
Conclusion
Arterial stiffness is often increased in type 2 diabetes. It is currently considered an essential link in the development of atherosclerosis and represents a new marker of cardiovascular risk. Carotid-femoral pulse wave velocity is the "gold-standard" method for assessing arterial stiffness in both populations; diabetics and the general population.

DOI: 10.1530/endoabs.81.EP249

EP250

Diabetes Mellitus and COVID-19: Is there a bidirectional relationship?

Ajili Rihab, Mlouki Imen, Ayed Souha, Naimi Arij, Karchoud Syrine, Ouerghi Nawres, Sfar Nouha & El Mhamdi Sana
University Hospital Tahar Sfar Mahdia, Department of Preventive and Community Medicine, Mahdia, Tunisia

Introduction
Diabetes mellitus is a well-known risk factor for worse clinical outcomes in patients with Coronavirus Disease 2019 (COVID-19). However, the relationship between these two entities seems to be bidirectional. The aim of this study was to identify the relationship between diabetes and COVID-19.
Methods
We conducted a prospective study including all patients admitted at the COVID-19 departments of The University Hospital Taher Sfar (Tunisia), between November 2020 and December 2021. We used "The RAPID CORE CASE REPORT FORM" developed by the World Health Organization.
Results
A total of 422 patients were included with a mean age of 59.8 ± 14.7 years (53.2% were females). The type 2 diabetes mellitus (T2DM) was present in 32.5% of cases. During hospitalization, 62.5% patients with T2DM presented a poor glycemic controlwith a mean rate of blood glucose level of 12.7 ± 9 mmol/l and a mean rate of hemoglobin A1c of 8.4 ± 2.5%.Hyperglycemic complications among patients with T2DM included diabetic ketoacidosis and hyperosmolar hyperglycemic syndrome in 48.5% and 12.1% of cases respectively. A quarter of non-diabetic patients affected by COVID-19 was diagnosed with new-onset diabetes.Our survey showed a significantly higher death rate among patients with T2DM ($P = 0.015$).
Discussion and Conclusion
The ongoing pandemic of COVID-19 has significantly affected blood glucose control in patients with T2DM. The results of this effects can be classified into direct effects by the viral infection and indirect effects especially by the use of treatments for the COVID-19 infection like corticosteroids, which affect glucose homeostasis and can also induce diabetes. Furthermore, diabetes is a risk factor for worse outcomes and even death in patients with COVID-19.

DOI: 10.1530/endoabs.81.EP250

EP251

Canagliflozin and liraglutide effect on myocardial damage in diabetic rats with experimental myocardial infarction

Natalya Timkina[1,2], Anna Simanenkova[1,2], Anzhelika Shimshilashvili[1], Valeria Timofeeva[1], Alena Chernikova[1], Sarkis Minasian[1,2] & Michael Galagudza[1,2]
[1]National Medical Research Center. VA Almazov, Clinical Endocrinology Laboratory, Sankt-Peterburg, Russian Federation; [2]Pavlov First State Medical University of St. Petersburg, Sankt-Peterburg, Russian Federation

Background
Cardiovascular events are the major cause of mortality among patients with type 2 diabetes mellitus (DM2). Menopause in women additionally increases cardiovascular risk. Despite myocardial infarction (MI) treatment approach in diabetic patients is not specific, some glucose-lowering drugs could have cardioprotective properties. In general, most glucagon-like peptide-1 receptor agonists (GLP-1Ra) and sodium-glucose co-transporter-2 inhibitors (SGLT-2i) have cardiovascular advantages. Particularly, liraglutide (LIRA), semaglutide, empagliflozin, canagliflozin (CANA), dapagliflozin decrease MI incidence. However, SGLT-2i and GLP-1Ra influence on MI manifestations, damage volume and severity in patients with DM2 remains the subject for further investigation. Moreover the cardiotropic properties of these drugs in menopause diabetic subjects undergoing MI is even less studied.
Aim
To evaluate the effect of CANA in comparison with LIRA on myocardial damage area in menopause type 2 diabetic rats in experimental MI.
Materials and methods
Female Wistar rats were subjected to bilateral ovariectomy on order to induce menopause. DM2 was modelled by high-fat diet and streptozotocin 60 mg/kg + nicotinamide 230 mg/kg injection. Rats in control group were fed with standard chow. The following groups were formed: "DM + M" (ovariectomized (menopause) rats with DM2, $n=5$), "DM + M + CANA" (ovariectomized rats with DM2 treated with CANA 25 mg/kg for 8 weeks, $n=5$), "DM + M + LIRA" (ovariectomized rats with DM2 treated with LIRA 0,06 mg/kg for 8 weeks, $n=4$), "CRL" (females without any procedures, $n=5$). After 16 weeks of treatment transient global myocardial 30-min ischemia of isolated heart was modelled in all rats. Myocardium necrosis area was evaluated after 90 min of reperfusion.
Results
Necrosis area was significantly larger in "DM + M" group (42.00 (34.00; 70.00) % of total heart area) in comparison to "CRL" group (33.00 (22.60; 40.00) %, $P=0.003$). Both LIRA and CANA administration led to decrease of myocardial damage area (31.67 (15.50; 46.00) % and 31.75 (24.00; 59.00) %, respectively) in comparison with "DM + M" (42.00 (34.00; 70.00) %) group (significantly for LIRA, $P=0.009$ and statistical tendency for CANA, $P=0.07$). Importantly, there was no significant difference in myocardial damage area between "DM + M + CANA" and "DM + M + LIRA" groups, $P=0.2$. Glucose control was similarly satisfactory in both treatment groups.
Conclusions
Both LIRA and CANA similarly decrease heart necrosis area in menopause diabetic rats with myocardial infarction.

DOI: 10.1530/endoabs.81.EP251

EP252

Comparative analysis of characteristics of pregnant women with pathological oral glucose tolerance test vs negative oral glucose tolerance test in a trimester of 2019

Víctor José Simón Frapolli[1], José Ignacio Martínez Montoro[1], María José Picón César[1], Carolina Gutiérrez Repiso[1,2], María Suárez Arana[3], Francisco José Tinahones Madueño[1,2] & María Molina Vega[1]
[1]Hospital Universitario Virgen de la Victoria, Endocrinology and Nutrition Clinical Management Unit, Málaga, Spain; [2]CIBER Fisiopatología de la Obesidad y Nutrición-CIBEROBN; [3]Hospital Regional Universitario de Málaga, Gynecology and Obstetrics Clinical Management Unit, Málaga, Spain

Introduction
Gestational diabetes mellitus (GDM) is the metabolic disorder most frequently associated with pregnancy, presenting important maternal and fetal implications. Strict glycemic control through lifestyle measures and/or pharmacotherapy is essential to achieve adequate obstetric-perinatal results. The objective of this study is to compare baseline characteristics and perinatal results in patients diagnosed with GDM after performing oral glucose tolerance test (OGTT) vs patients with negative OGTT, in a trimester of 2019.
Materials and method
Retrospective observational study comparing baseline clinical-laboratory characteristics and obstetric-perinatal results of 258 women referred to our center during the September-October-November trimester of 2019 due to a positive O'Sullivan test to perform the confirmatory test with 100-g OGTT.
Results
Exposed in Table 1. Of the 258 OGTT performed, 217 were negative and 41 were positive (16% positive). Among the most relevant findings, the BMI before pregnancy of the 41 women diagnosed with GDM was 29.08 ± 5.82 kg/m^2 compared to 27.64 ± 7.03 kg/m^2 in the 217 with negative OGTT ($P=0.046$). Weight gain during pregnancy was significantly lower in the group with GDM ($P=0.001$): 6.79 ± 5.3 kg vs 10.33 ± 5.26 kg. Of the 41 women diagnosed with GDM, 11 received treatment with insulin, 1 with metformin and 29 with dietary measures. No differences were found in obstetric or perinatal outcomes in both groups.
Conclusion
Through diagnosis and treatment of GDM, perinatal and obstetric results achieved were similar to those of women without GDM. Although women diagnosed with GDM started with higher BMI values, they presented significantly less weight gain during pregnancy than those with negative OGTT, after undergoing a specific treatment

Table

	Pathological OGTT ($n=41$)	Negative OGTT ($n=217$)	p
Previous BMI (kg/m^2)	29,08 ± 5,82	27,64 ± 7,03	0,046
History of GDM ($n=111$)	4	8	0,142
History of DM ($n=224$)	14	46	0,075
Weight gain (kg)	6,79 ± 5,3	10,33 ± 5,26	0,001
Treatment with insulin	11		
Treatment with metformin	1		
Treatment with diet	29		
Birth gestational age (weeks)	38,95 ± 1,61	38,76 ± 1,87	0,748
Prematurity ($n=228$)	2	18	0,902
Newborn weight	3258 ± 449	3258 ± 579	0,906
Newborn height	50,2 ± 1,95	49,8 ± 2,44	0,630
Births ($n=224$): eutocic; instrumental, cesarean	19; 5; 11	109; 22; 58	0,889
Fetal percentile	53,52 ± 27,92 ($n=34$)	54,86 ± 30,36 ($n=183$)	0,773
Neonatal hypoglycemia; neonatal jaundice; distress	2 ($n=35$); 3 ($n=41$); 0 ($n=35$)	2 ($n=178$); 9 ($n=217$); 14 ($n=179$)	0,130; 0,634; 0,580
Neonatal admission; neonatal ICU admission; deaths	4 ($n=35$); 0 ($n=35$); 0 ($n=34$)	14 ($n=179$); 8 ($n=177$); 2 ($n=179$)	0,336; 0,230; 0,706
Dystocia	1 ($n=35$)	1 ($n=177$)	0,304

DOI: 10.1530/endoabs.81.EP252

EP253

PSMA6 and KEAP1 genes methylation in patients with type 1 diabetes and diabetic retinopathy

Deimante Kardonaite[1], Rasa Verkauskiene[1], Lina Radzeviciene[1], Laura Daugintyte-Petrusiene[2], Vilma Jurate Balciuniene[3], Jelizaveta Sokolovska[4] & Natalia Paramonova[5]
[1]Institute of Endocrinology, Kaunas, Lithuania; [2], Department of Endocrinology, Kaunas, Lithuania; [3], Department of Ophthalmology,

Kaunas, Lithuania; [4]Faculty of Medicine, Rīga, Latvia; [5]Institute of Biology, Rīga, Latvia

Background
Diabetic retinopathy (DR) is one of the most common complications resulting from uncontrolled diabetes mellitus (DM). DR is the leading cause of blindness and low vision. DR is usually diagnosed at an advanced stage, so despite the individual treatment, it is only possible to slow down the progression of DR. Therefore, new potential biomarkers are needed for an earlier DR prognosis to prevent the development of DR. According to the latest studies, ubiquitin-proteasome system (UPS) dysfunction is associated with an increased risk of developing DR. UPS is the main protein quality control system which is responsible for recognition and degradation of damaged proteins. DNA methylation has been linked to a variety of pathological conditions such as tumorigenesis. However, the role of epigenetic modifications of UPS and UPS related genes in the pathogenesis of DR is poorly understood. The aim of this study was to analyze UPS (*PSMA6)* an UPS related (*KEAP1*) genes methylation levels in samples of DR patients and to identify their association with patients' clinical data.
Materials and methods
120 blood samples, taken from patients with the diagnosis of DM and DR, were analyzed. DNA was extracted by salting out method from peripheral blood tissue leukocytes. *PSMA6* and *KEAP1* genes methylation level was determined by RT–PCR analysis with SYTO 9 fluorescent dye using OneStep qMethyl™ kit. Associations of *PSMA6* and *KEAP1* genes methylation level and the patients' gender, age, duration of DM and the stage of DR were analyzed.
Results
PSMA6 gene methylation levels were higher in the group of patients with non-proliferative DR (NPDR) compared to patients with proliferative DR (PDR) ($P<0.01$). Increased *KEAP1* gene methylation level was observed in the group of patients with DM compared to patients with NPDR and PDR ($P<0.001$). Increased levels of *KEAP1* gene methylation were observed in patients with shorter duration of DM (*P*0.001). In different groups of DR severity, the methylation level of the *KEAP1* gene was the lowest in the group of patients with more advanced stage of DR – PDR, and the highest in the group of patients without DR (*P*0.001).
Conclusions
KEAP1 gene could be used as a prognostic biomarker for determining the severity of DR or as a risk factor for the development of DR.

DOI: 10.1530/endoabs.81.EP253

EP254

Effects of semaglutide on glycemic control and weight loss in a patient with Prader-Willi Syndrome: a case report

Elena Sani[1], Giuliana Da Prato[1], Maria Grazia Zenti[1], Andrea Bordugo[2], Maddalena Trombetta[1] & Enzo Bonora[1]
[1]University of Verona and Azienda Ospedaliera Universitaria Integrata of Verona, Division of Endocrinology, Diabetes and Metabolism, Verona, Italy; [2]Azienda Ospedaliera Universitaria Integrata, Verona, Italy, Inherited Metabolic Diseases Unit and Regional Centre for Newborn Screening, Diagnosis and Treatment of Inherited Metabolic Diseases and Congenital Endocrine Diseases, Verona, Italy

Background
Prader-Willi syndrome (PWS) is the most frequent genetic cause of obesity and is often complicated by glucose metabolism alterations. Conventional therapies prescribed in type 2 diabetes mellitus (T2DM), like oral hypoglycemic agents and insulin, frequently failed to achieve adequate glycemic control in patients with PWS. Beneficial effects of the glucagon like peptide-1 receptor agonists (GLP1RAs) exenatide and liraglutide have been reported for the management of T2DM in PWS, but no data are currently available on the use of semaglutide, belonging to the same class of drugs, in this particular population.
Case presentation
We report for the first time the use of semaglutide 1 mg per week in an adult patient with genetically confirmed PWS complicated by poor controlled diabetes and severe obesity. At baseline his HbA1c was 11.1%, body weight 99.5 kg, BMI 37.5 kg/m2. He was on a multi-injection insulin therapy, with a total daily insulin dose of 180 IU, in addition to metformin 3000 mg/day. After 6 months of semaglutide treatment, his weight had fallen to 93.9 kg (-5.6 kg, BMI 39.1 kg/m2) and HbA1c had dropped to 7.7% (-3.4%). After 12 months, his weight had plateaued at 94.3 kg (-5.2 kg, BMI 39.3 kg/m2) and HbA1c further improved until 7.2% (- 3.9%). As assessed by bioimpedentiometry, there was also a notable decrease in fat mass (-4.9 kg), without significant changes in lean mass, and a progressive reduction in insulin requirements up to 140 IU (-40 IU/day). The patient well tolerated the therapy and no adverse events were reported. Interestingly, our patient had previously tried liraglutide therapy in adjunction to metformin and insulin therapy reporting no substantial efficacy.
Conclusions
The beneficial effects of semaglutide on glycemic control and weight reduction provide a promising treatment for diabetes and obesity in PWS. This treatment could also be successfully used in combination with insulin, to reduce the dosage of the latter and to avoid weight gain frequently related to its use, and could be even considered in those patients who have already tried a treatment period with liraglutide or other GLP1RAs with no substantial efficacy. Further studies are required to confirm the efficacy and safety of semaglutide in patients with PWS.

DOI: 10.1530/endoabs.81.EP254

EP255

Central nervous system condition in children with diabetes mellitus type I

Nataliia Nikolaeva, Olga Gumeniuk, Yuriy Chernenkov & Nina Bolotova
Saratov State Medical University, Saratov, Russian Federation

Diabetes mellitus is a metabolic disease that is accompanied by brain injury manifested as cognitive, emotional and vascular impairment.
Purpose
To study prevalence and degree of disorders of central nervous system in children with diabetes mellitus type I (TIDM).
Objects and methods
Examination of nervous system in 100 children - age 7-18 yrs [9.0-17.8] with TIDM was provided. The control group consisted of healthy children ($n=30$). The condition of central nervous system was determined on the basis of cognitive and emotional function tests; studying of cerebral circulation was performed using extracranial Doppler study according to standard techniques. The degree of compensation of diabetes was estimated according to criteria ISPAD Consensus Guidelines (2018).
Results
Optimal level (HbA1c $<7.0\%$) of compensation was revealed in 62% of children (group I) and nonoptimal in 38% of children (group II). Decrease of cognitive functions, disturbance of emotional sphere and deterioration of cerebral circulation was established in 12 children (19%) in group I and 16 patients (42%) in group II ($P=0.02$). The performed correlation analysis revealed association of cognitive, emotional dysfunction and cerebral circulation disorders with the $HbA1_c$ level ($r=-0.41$; –0.5 and –0.47 accordingly, *P* 0,001).
Conclusions
Diabetic children with nonoptimal $HbA1_c$ level frequently cognitive, emotional and cerebral circulation disorders (42%). Prevalence of cognitive, emotional and cerebral circulation increased parallel to $HbA1_c$ level.

DOI: 10.1530/endoabs.81.EP255

EP256

Association of sarcopenia with peripheral nerve functions in type 2 diabetes mellitus patients in East India: A prospective cross sectional study.

Kishore Behera[1], Subarna Mohapatra[2], Nibedita Priyadarsini[2], Pranati Nanda[2] & Ananda Srinivasan[3]
[1]AIIMS BHUBANESWAR, Endocrinology & Metabolism, Khordha, India; [2]AIIMS BHUBANESWAR, Physiology, Khordha, India; [3]AIIMS BHUBANESWAR, Pharmacology, Khordha, India

Background
Diabetic peripheral neuropathy (DPN) is considered to be the risk factor for the development of sarcopenia. Various previous studies showed the correlation between DPN and muscle disorders, but the study regarding the association between sarcopenia and nerve conduction parameters in diabetic peripheral neuropathy is limited.
Aim
This study was planned to detect the association between sarcopenia with peripheral nerve functions in type 2 diabetes mellitus (T2DM) patients.

Methods
A total of 174 participants aged ≧ 45 years were included in the study. Out of 174, group-1 58, were age and gender matched healthy volunteers (28 males and 30 females); group-2,56 were T2DM without neuropathy (30 males and 26 females); group-3, 60 were T2DM with neuropathy (30 males and 30 females). The mean age of the T2DM subjects was 47.5±7.7(range 42-68 years, mean HbA1c of 7.4%. All the participants underwent peripheral nerve function tests by nerve conduction studies and sarcopenia was evaluated according to the Asian Working Group for Sarcopenia (AWGS) criteria using prediction equation.
Results
According to ASMI cut-off [ALM/height 2: <7.0 kg/m2 (men) <5.4 kg/m2(women)], T2DM with neuropathy had sarcopenia of 67%, T2DM without neuropathy prevalence of sarcopenia was 46%. There was a statistically significant difference in sarcopenia between DM with and without neuropathy ($P<0.002$). All the patients with T2DM with neuropathy are having reduced handgrip strength in contrast to 94% without neuropathy. In addition, there was a significant correlation between ASMI and nerve conduction parameters found in men but in women, significance was found between right common peroneal latency.
Discussion
The prevalence of diabetic neuropathy detected by using nerve conduction studies in our population was 33%. Based on the Sarc-Calf questionnaire score > 11 was about 63% of patients with neuropathy and 29.6% of patients without neuropathy are diagnosed with sarcopenia. Skeletal Muscle mass was compared between the three groups and it was found that there was a statistically significant difference between the groups with ASMI, Handgrip strength, and Sarcopenia calf score (*P*-value <0.05) in males but not in females except for sarcopenic calf score.
Conclusion
The prevalence of sarcopenia in T2DM patients with neuropathy is higher in comparison to those without neuropathy. Therefore, regular screening for skeletal muscle mass and strength may be performed in T2DM patient with DPN.g
Keywords
Diabetic peripheral neuropathy; sarcopenia; Appendicular skeletal muscle mass index(ASMI); Sarc-Calf questionnaire score.

DOI: 10.1530/endoabs.81.EP256

EP257

Subclinical left ventricular dysfunction in patients with obesity and chronic obstructive pulmonary disease

Elena Klester, Karolina Klester & Oksana Stefanovskaya
Altai State Medical University, Therapy and Endocrinology, Barnaul, Russian Federation

The purpose of the work
to compare the changes in the global longitudinal strain of the left ventricle in obese patients with and without COPD.
Material and methods of research
group I consisted of obese patients without COPD ($n=50$; 21 - males, mean age - 48.8±9.1 years). Group II – 40 patients with obesity and COPD, comparable in age, gender. Group III – 37 patients with COPD without obesity, comparable in age, gender and risk group of COPD, group A was in 7, group B – in 16, group C – in 5, group D – in 9 patients (GOLD, 2021).
Exclusion criteria
secondary forms of obesity, persons with a BMI <18 kg/m2. BMI, waist circumference, hip circumference, their ratio, visceral obesity index (VAI) and percentage of adipose tissue content according to Deurenberg, cardiometabolic risk on the CMDS scale, fat-free mass index (FFMI) and appendicular skeletal muscle mass index (ASMI) were evaluated. All patients in remission underwent standard echocardiography (EchoCG) with estimated global LV strain in the longitudinal direction (Global Longitudinal strain-GLS) using the "AFI" option.
Results
unlike conventional echocardiographic parameters, speckle-tracking echocardiography revealed a significant deterioration in global LV strain in the II group compared to the I group (-14.4%±2.4% vs. -16.3%±1.8%, $P=0.04$). At the regional level, LV apical septum tension was reduced in I group ($P=0.003$) in the presence of metabolically unhealthy obesity. Patients of group I and III have a deterioration of GLS that correlated with the severity of COPD ($P=0.02$), the visceral obesity index VAI and a decrease in the appendicular lean mass index.After adjustment for clinical and echocardiographic characteristics, MUHO in patients was independently associated with changes in GLS (95% confidence interval was from 0.98 to 2.11, *P*0.001).
Conclusion
the deterioration of global LV longitudinal strain is determined in 66% of patients in the presence of metabolically unhealthy obesity (vs 26% without obesity, p< 0.001). The negative dynamics of GLS is associated with the severity of COPD, visceral obesity and low muscle mass.

DOI: 10.1530/endoabs.81.EP257

EP258

The effect of mimic-mir-21/au@ nanosystem on browning activation: a possible therapeutic tool against obesity

Said Lhamyani[1], Adriana-Mariel Gentile[1], Rosa María Giráldez Pérez[2], Elia Grueso[3], María Mengual Mesa[4], Enrique Estepa[1], Gabriel Olveira[1,5], Francisco-José Tinahones[6,7] & Rajaa El Bekay[1,7]
[1]Instituto de Investigación Biomédica de Málaga (IBIMA), Unidad de Gestión Clínica Intercentros de Endocrinología y Nutrición, Hospital Regional Universitario de Málaga, MÁLAGA, Spain; [2]2Universidad de Córdoba, Facultad de Ciencia., Departamento de Biología Celular. Fisiología e Inmunología, CÓRDOBA, Spain; [3]Universidad de Sevilla. Facultad de Química, Departamento de Química Física, SEVILLA, Spain; [4]Instituto de Investigación Biomédica de Málaga (IBIMA), Universidad de Málaga, MÁLAGA, Spain; [5]Centro de Investigación Biomédica en Red de Diabetes y Enfermedades Metabólicas Asociadas CB07/08/0019 (CIBERDEM), Instituto de Salud Carlos III, MÁLAGA, Spain; [6]Instituto de Investigación Biomédica de Málaga (IBIMA), Unidad de Gestión Clínica Intercentros de Endocrinología y Nutrición, Hospital Clínico Virgen de la Victoria, MÁLAGA, Spain; [7]Centro de Investigación Biomédica en Red de Obesidad (CIBERobn), Instituto de Salud Carlos III, MÁLAGA, Spain

Background and aim
Obesity is a chronic disease associated with a positive energy balance leading to lipotoxicity, which contributes to the onset of obesity-associated metabolic disorders such as type 2 diabetes and insulin resistance. It's well known that thermogenesis in brown adipose tissue (BAT) and "browning" of white AT (WAT) increase energy expenditure, thus promoting weight loss and protect against obesity. Recently, the microRNAs (miRNAs) that regulate thermogenesis and browning are acquiring great interest. In addition, several studies have reported that miR-21 regulate adipogenesis and could be associated with obesity. Recently, our group have demonstrated that miR-21 mimic decreases body weight by inducing thermogenesis and browning of WAT in animal model. Thus, the aim of the present study was to associate miR-21 with gold nanoparticle; which could be a good tool to deliver this miRNA to WAT; to evaluate the nanosystem citotoxicity, and to analyze its effect on body weight gain, browning and thermogenesis.
Materials and methods
The cytotoxicity evaluation of nanosystem was carried out by microscopic study and by analyzing the short and long-term effect of miR-21 mimic/Au@ treatment on blood composition of C57BL/6J mice. In addition, the effect of this nanosystem on body weight gain and on thermogenic and browning markers expression was evaluated.
Results
We observed that hematological and biochemical parameters values did not shown any significant differences between control and treated mice groups. Moreover, no tissue damage nor accumulation of nanoparticles in the organs from miR-21-mimic/An@ treated mice. In parallel, this nanosystem significantly decreased body weight gain of obese mice and increased the expression levels of browning and thermogenic markers *Ucp1, Tmem26, Pgc1-a, Prdm16 y Vegf-A* in WAT.
Conclusion
Our results suggest the potential role of mimic-miR-21/Au@ nanosystem as a possible and efficient treatment against obesity and type 2 diabetes.This work was supported by grants from: Instituto de Salud Carlos III (ISCIII)/FEDER-UE (PI18/00785) and Consejería de Transformación Económica, Industria, Conocimiento y Universidades Dirección General de Investigación y Transferencia del Conocimiento (PY20-01274) co-funded by Fondo Europeo de Desarrollo Regional–FEDER.S.L. is a recipient of a post-doctoral grant Plan Andaluz de Investigación, Desarrollo e Innovación (**DOC-01138**) from Consejería de Economía, Conocimiento, Empresas y Universidades.R.E.B. is under a contract from the 'Nicolas Monarde' (C-0030-2016) program from the Servicio Andaluz de Salud, Regional Ministry of Health of the Andalusian Government, Andalusia

DOI: 10.1530/endoabs.81.EP258

EP259

The intestinal microbiome and the adipomyokine profile of different phenotypes of obesity

Natalya Volkova[1], Lilia Ganenko[1], Yulia Naboka[1], Alexander Shestopalov[2], Ilya Davidenko[1] & Yuliya Degtyareva[1]
[1]Rostov State Medical University, Department of Internal Diseases No3, Rostov-on-Don, Russian Federation; [2]Pirogov Russian National Research Medical University, Moscow, Russian Federation

Currently, it has been established that obesity is a heterogeneous disease. There are metabolically healthy (MHO) and metabolically unhealthy obesity (MNHO) depending on the presence of cardiometabolic disorders. Potential factors that differentiate obesity into phenotypes include the gut microbiome and endocrine activity of adipose and muscle tissue. Purpose of the study was to compare intestinal microbiome and adipomyokine profile in patients with different obesity phenotypes and in healthy people. A cohort cross-sectional study was performed. The study involved 265 participants (men-44 (16.6%), women-221 (83.4%), average age - 47.1 ± 4.8 years). Formed clinical groups: group 1 ($n = 129$) - healthy people with normal body weight, group 2 - obese patients ($n = 136$). In order to isolate different obesity phenotypes, patients of group 2 were divided into 2 subgroups based on the NCEP-ATP III criteria: subgroup 2a ($n = 40$) - MHO, subgroup 2b ($n = 55$) - MNHO. Quantitative and qualitative assessment of the state of the gut microbiome was performed by metagenomic analysis. Measurement of adipokines and myokines was performed by multiplex ELISA on a Magpix analyzer. Statistical analysis was conducted in the R version of the RStudio program. As a result, in patients with MHO the presence of Lentisphaerae was less often observed and the number of Bacteroidetes was lower, but the amount of Firmicutes was higher compared to MNHO subgroup (P0.05). In obese group, the number of Bacteroidetes, Proteobacteria was increased and the amount of Actinobacteria, Firmicutes, TM7, Fusobacteria was decreased, and the phylotypes of Tenericutes, Planctomycetes and Lentisphaerae were more often verified compared with similar indicators in healthy people (P0.05). When comparing the studied adipokines and myokines in patients with different obesity phenotypes, significant differences were found for adiponectin and leptin ($P < 0,05$). In patients with MHO, the level of adiponectin and leptin was significantly higher compared with the MNHO. In patients with MHO and MNHO, the level of adiponectin was significantly lower, and leptin and asprasin - higher compared with the control group (P0.05). No significant differences in the content of myokines in different obesity phenotypes were found in our study. The obtained results indicate changes in the composition of the intestinal microbiome and adipokine profile in different obesity phenotypes. Further research is required, both to confirm the obtained results and to identify correlations between metabolic parameters with individual phylotypes of the gut microbiome and the profile of adipomyokines.

DOI: 10.1530/endoabs.81.EP259

EP260

Maternal weight gain during pregnancy and neonatal birth weight among women with gestational diabetes mellitus

Olfa Lajili, Aroua Temessek, Rim Rachdi, Yosra Htira & Feika Ben Mami
National Institute of Nutrition of Tunis, The Research Unit of GDM (Department C), Tunis, Tunisia

Introduction
Body mass index (BMI) and gestational weight gain are increasing globally. However, the association between gestational weight gain consistent with the Institute of Medicine (IOM) guidelines and neonatal birth weight among women with gestationnel diabetes (GDM) remain unclear.
Objective
The aim of our study was to assess gestational weight gain among tunisian women with GDM and his effect on neonatal birth weight.
Methods
A prospective and longitudinal study including 220 women with GDM followed at the gestational diabetes research unit of department C at the National Institute of nutrition of Tunis. The study was carried out from july 2019 to december 2020 and during the entire period of pregnancy. Height and starting weight and weight at the end of pregnancy were measured. Statistics were performed using SPSS 20.
Results
The mean pre-gestational BMI was 28.8 ± 5.2 kg/m^2. The mean term of discovery of GDM was (24 gestational week + 2day) ± (7 gestational week + 2day). The average weight gain in late pregnancy was 12.2 ± 4.6 kg. More than half of the patients (56.1%) had inadequate weight gain and 44.5% had excessive weight gain in late pregnancy. The mean birth weight was 3368.2 ± 551.2 g [1022g -5000 g]. The main neonatal outcomes were macrosomia (13.5%) and transient respiratory distress (11.4%). Patients with macrosm newborns tended to have higher pre-gestational BMI but with no significant difference between the two groups (29.3 ± 4.8 kg vs 28.5 ± 5.2 kg; $P = 0.4$). Furthermore, there was no correlation between the weight gain in late pregnancy and the birth weight ($P = 0.679$). Similarly, we did not observe an association between the incidence of macrosomia and the weight gain in late pregnancy ($P = 0.559$).
Conclusion
The half of women (65,1%) had inadequate weight gain in late pregnancy. These data point out the interest to follow the recommendations of weight gain during pregnancy in patients with GDM to prevent pregnacy outcomes including macrosomia.

DOI: 10.1530/endoabs.81.EP260

EP261

Correlation between pulse wave velocity and microangiopathy in type 2 diabetes

Chayma Besrour[1], Rojbi Imen[1], Ben Ahmed Habib[2], Mekni Sabrine[1], Mchirgui Nadia[1], Ben Nacef Ibtissem[1] & Khiari Karima[1]
[1]Hospital Charles Nicolle, Endocrinology, Tunis, Tunisia; [2]Hospital Charles Nicolle, Cardiology, Tunis, Tunisia

Introduction
Microangiopathy is defined as damage to small blood vessels, and more particularly arterioles and arteriolar capillaries that supply organs. It can occur under different conditions and it represents a complication of diabetes. The aim of this study was to examine the relationship between microangiopathic complications and arterial stiffness in type 2 diabetes.
Methods
We conducted a prospective study including 249 diabetic patients without macroangipathic complications, between July 2020 and May 2021. Using a SphygmoCor®XCEL device, we measured arterial stiffness directly by the carotid to femoral pulse wave velocity (cfPWV).
Results
The mean age of the study population was 57.53 ± 9.34 years (139 women and 110 men). The mean duration of the disease was 10.2 years.Microangiopathic complications were found in 58.2% of the patients.In this group, cfPWV was at 14.41 ± 2.84 m/s VS 12.56 ± 2.42 m/s in patients without microangiopathic complications ($P < 0.001$).Moreover, the presence of arterial stiffness multiples by 4 the risk of microangiopathic complications (Odds Ratio = 4).The ROC curve that we established to find a threshold value of the cfPWV from which this correlation appears, had an area under the curve equal to 0.694. The discriminate threshold value having the best sensitivity/specificity pair was 13.45 m/s.
Conclusion
Arterial stiffness is often increased in type 2 diabetes. Its presence contributes to the development of microangiopathic complications. Which leads us to believe that the early prevention of arterial stiffness may delay microangiopathy.

DOI: 10.1530/endoabs.81.EP261

EP262

Evolution of combined impaired fasting glucose and impaired glucose tolerance in 58 β-thalassemia major (β-TM) patients during a mean 7.7 year follow-up

Vincenzo De Sanctis[1], Shahina Daar[2], Ashraf Soliman[3], Ploutarchos Tzoulis[4], Mohamed Yassin[3] & Christos Kattamis[6]
[1]Quisisana Hospital, Ferrara, Italy; [2]College of Medicine, Sultan Qaboos University, Muscat, Oman; [3]Hamad Medical Center, Pediatrics, Doha, Qatar; [4]Department of Diabetes and Endocrinology, Whittington Hospital, London, United Kingdom; [5]Hamad Medical Center, Hematology, Doha, Qatar; [6]National Kapodistrian University of Athens, First Department of Paediatrics, Athens, Greece

Background
In patients with β- thalassemia major (β-TM) glucose dysregulation (GD) develops insidiously, aggravating prognosis and quality of life.
Objectives
The objectives of this study were to retrospectively review the extent to which β-TM patients, having combined impaired fasting glucose (IFG) and impaired

Table Clinical and laboratory parameters reported at the diagnosis of β-TM-RD and at the last visit in the 3 groups of β-TM patients.

Patient's groups	Age (yrs) at diagnosis of IFG + IGT	SF (ng/ml) at diagnosis of IFG + IGT	ALT (U/l) at diagnosis of IFG + IGT	SF peak (ng/ml)	Duration of follow-up (yrs)	SF at last observation (ng/ml)	BMI at last observation
Group A: **From IFG + IGT to β-TM-RD (13 patients)**	**21.0 ± 7.5**	**3467.7 ± 2089.2**	**104.1 ± 82.0**	**4676.5 ± 1758.8**	**4.8 ± 4.1**	**2519.1 ± 1641.6**	**23.9 ± 5.4**
Group B: **From IFG + IGT to NGT (13 patients)**	**21.3 ± 6.4**	**1319.6 ± 608.8**	**59.3 ± 31.7**	**2858.6 ± 1163.8**	**8.6 ± 4.0**	**1219.3 ± 802.7**	**23.1 ± 2.7**
Group C: **From IFG/IGT to PP (32 patients)**	**19.8 ± 5.8**	**2071.8 ± 1646.2**	**54.7 ± 36.6**	**4071.4 ± 1451.2**	**8.8 ± 5.0**	**1251.7 ± 835.5**	**22.5 ± 2.6**
Group A vs. B: **P value**	**NS**	**0.001**	**NS**	**0.004**	**0.02**	**0.017**	**NS**
Group A vs. C: **P value**	**NS**	**0.021**	**0.01**	**NS**	**0.01**	**0.001**	**NS**
Group B vs. C: **P value**	**NS**	**NS**	**NS**	**0.01**	**NS**	**NS**	**NS**

Abbreviations = **SF:** Serum ferritin; **ALT:** Alanine aminotransferase; **BMI:** Body Mass Index**: PP:** persistent prediabetes (IFG, IGT, combined IFG/IGT).

glucose tolerance test (IGT) on oral glucose tolerance test (OGTT), progressed to diabetes (DM) and to analyze the progression to DM or regression to normal glucose tolerance test (NGT).
Method
58 β-TM patients were followed for a mean duration of 7.7 years with annual or biennial OGTT. Glucose and insulin data were analysed.
Results
During the follow-up, FPG and 2-h PG levels after OGTT reverted to NGT in 13 (22.4%), deteriorated to DM in 13 (22.4%) and did not change in 32 (55.2%). A significant correlation was observed between FPG and ALT level (r: 0.3158; P:0.01) and between chronological age and serum ferritin (SF) level (r: -0.321; P:0.014). Both SF and ALT at the baseline and at the time of last observation, were independent predictors of evolution to diabetes mellitus.
Conclusion
The combination IFG/IGT in β-TM patients with severe iron overload constitutes a high-risk state for developing diabetes.

DOI: 10.1530/endoabs.81.EP262

EP263

Hormonal-metabolic and functional predictors of unfavorable cardiovascular prognosis in young patients with type 1 diabetes mellitus.

Vengrzhinovskay Oksana[1], Irina Bondarenko[2], Olga Shatskaya[1], Marina Shestakova[2], Victor Kalashnikov[2] & Natalia Mokrysheva[1]
[1]National Medical Research Center for Endocrinology of the Ministry of Health of the Russian Federation, Department of Health, Moscow, Russian Federation; [2]National Medical Research Center for Endocrinology of the Ministry of Health of the Russian Federation, Departament of Health, Moscow, Russian Federation

Background
Patients with type 1 diabetes have a significantly higher risk of coronary events, as well as diseases of the cardiovascular system.Purpose of the study – to show the relationship between metabolic, structural, and functional parameters of the cardiovascular system in young patients with DM1.
Methods
The study included 60 patients without CVD: 40 patients with DM1 and 20 patients without DM1, the groups were comparable in age, sex, AMT, heart rate, blood pressure.. All patients underwent a laboratory examination, which also included an assessment of the levels of adiponectin, resistin, electrocardiography, bioimpedancemetry, ergospirometry.
Results
In the group of patients with DM1, an increased content of adipose tissue ($P=0.036$) was revealed in the absence of a statistical difference with the group without DM in terms of BMI and correlations between the level of maximum power of exercise performance (METs) with the content of muscle tissue $P=0.09$ and with adipose tissue $P=-0.049$. In the control group, correlations were revealed - METs to % of muscle tissue $P=0.004$. The decrease in the functional parameters of the cardiorespiratory system in young patients with DM is noteworthy: the time to reach the anaerobic threshold (AP) ($P=0.008$) and the maximum oxygen consumption (VO2 max) ($P=0.034$), compared with the group of patients without DM1. Correlations were revealed in the group of patients with DM1: METs to VO2 max $P=0.001$ and to AP $P=0.004$. In the control group: METs to VO2max $P=0.001$, to AP $P=0.008$ and VO2max to AP $P=0.003$.It should also be noted an increase in the level of resistin in the group of DM1 patients compared with the group without DM1 ($P=0.044$). When conducting a correlation analysis In the group of patients with DM1, a correlation was found between VO2max and the level of adiponectin $P=0.021$.
Conclusions
Young patients with DM1 have lower functional indicators of the cardiorespiratory system, compared with patients without DM, while maintaining a high tolerance to physical activity. Also, in young patients with DM1 who do not have cardiovascular diseases, there is a significant increase in the level of resistin, which has pro-inflammatory activity and, according to many studies, is associated with an increase in cardiovascular risk.

DOI: 10.1530/endoabs.81.EP263

EP264

Association of adherence to the mediterranean diet and body composition in type 1 diabetes mellitus

Enrique Redondo, María Del Carmen Andreo-Lopez, Javier García, Teresa Zarco, Victoria Contreras Bolivar & María Luisa Fernández Soto
Hospital Universitario San Cecilio, Endocrinology and Nutrition, Granada, Spain

Introduction
Body composition is gaining great interest in some pathologies such as Type 1 Diabetes Mellitus (DM1). Adherence to the Mediterranean diet has been shown to be effective in improving the prognosis of cardiovascular disease, which is the main cause of mortality in these patients.
Objectives
To assess whether adherence to the Mediterranean diet in DM1 is associated with improvement in disease control parameters, body composition, anthropometry, dynamometry, and other cardiovascular risk factors.
Patients and methods
Cross-sectional study in 32 patients with DM1. Sociodemographic parameters, variables related to the disease, anthropometrics, dynamometry and body composition were collected using vectorial electrical impedance analysis. In addition, adherence to the Mediterranean Diet was evaluated using the validated 14-point test of the PREDIMED trial. Statistical analysis was performed using the SPSS program (SPSS, inc, v 25.0)

Results
32 DM1 patients under follow-up in the Endocrinology consultation of the HUSC of Granada were selected. Mean age was 41.5±15.2 years, 20 women (62.5%) and 12 men (37.5%). Mean BMI was 26.0±5.1 kg/m2, mean HbA1C was 7.4±1.1%, mean phase angle was 5.9±0.7°. Patients were divided according to their adherence to the Med Diet into high adherence (≧9 points) or low adherence (<9 points) according to the results of the PREDIMED trial test. 19 patients (59%) obtained 9 or more points. There were significant differences between the groups in terms of total insulin dose (37.4±14.1 vs 49.9±15.5, $P=0.024$), insulin/kg (0.53±0.2 vs 0.67±0.15, $P=0.034$) and insulin sensitivity factor (50.6±20.2 vs 37±15.56, $P=0.05$), standardized phase angle (1.2±1.5 vs 0.02±0.84, $P=0.019$) and C-reactive protein (1±0.5 vs 2.4±1.3, $P=0.047$). A tendency to the difference between the groups in terms of HbA1c and lipid profile was found, without finding statistical significance. A statistically significant difference was found between the groups, with those who were less adherent presenting higher levels of the Tg/HDL ratio.
Conclusions
In our sample, type 1 DM patients who presented greater adherence to the Med Diet showed lower insulin needs and greater sensitivity to it with improvement in the inflammatory pattern and better preservation of cell membranes measured indirectly by the angle of phase. Based on these preliminary results, we should reinforce diabetes education programs to increase adherence to the Mediterranean diet in our DM1 patients.

DOI: 10.1530/endoabs.81.EP264

EP265

Glycemic variability in pregnant women with gestational diabetes mellitus

Fatima Ushanova, Tatyana Demidova & Mariyam Izmailova
Pirogov Russian National Research Medical University, Moscow, Russian Federation

Introduction
Glycemic variability (GV) is a more accurate parameter for assessing the risk of developing diabetic complications than traditional parameters for assessing compensation. In most cases, diet therapy is used to treat GDM, while the glycemia in a pregnant woman should correspond to the glucose level in healthy pregnant women. The aim of our work is to compare two-week glycemic profiles and GV in pregnant women with GDM on diet therapy and in healthy pregnant women using the FreeStyle Libre flash monitor system.
Materials and methods
Analysis of the glycemic profile of 62 pregnant women aged 33.2±6.1 years. The average gestational age of the women included in the study was 12.6±6.4 weeks of gestation. The pregnant women were divided into 2 groups: 50 pregnant women with GDM and 12 healthy pregnant women. According to the self-monitoring diary using a glucometer, all pregnant women with GDM had target glycemic values. Each group underwent a two-week glucose profile monitoring using the FreeStyle Libre continuous monitoring system. To assess GV, the following parameters were used, reflecting various characteristics of the glycemic curve: SD characterizes the degree of scatter in glycemic values; MAGE is the average amplitude of glycemic fluctuations; MAG - reflects the rate of change in glucose levels; CONGA - duration of glycemic increase; HBGI – hyperglycemia risk index; LBGI – hypoglycemia risk index; ADDR is the average value of risks.
Results
Taking into account the peculiarities of control in GDM, the threshold values of the normal range were changed in accordance with the target values for pregnant women with GDM. Indicators of glycemia and glycemic variability were significantly higher in the group of pregnant women with GDM compared with pregnant women without carbohydrate metabolism disorders, but within the target range. The average level of glycemia in the groups was 4.724±0.37 mmol/l vs 4.24±0.34 mmol/l, respectively ($P<0.0001$). Comparative analysis of GV parameters in groups: SD - 0.8 vs 0.7213 ($P<0.05$); LI- 1.4 vs 0.8 ($P<0.05$); LBGI 5.56 vs 4.6 ($P<0.05$); HBGI- 0.43 vs 0.42 ($P=0.06$); J-index- 9.98 vs 7.9870 ($P<0.001$); MOOD- 0.96 vs 0.79 ($P=0.07$); MAGE- 2.3 vs 1.8 ($P<0.05$); ADDR- 1.02 vs 0.4210 ($P<0.05$); MAG- 3.8 vs 2.6 ($P<0.001$), CONGA index 3.9 vs 3.7 ($P=0.09$), respectively.
Conclusions
Flash glycemic monitoring can be used to obtain more detailed information about the glycemic profile, especially when it is difficult to assess the degree of GDM compensation.

DOI: 10.1530/endoabs.81.EP265

EP266

The common genetic polymorphism of KCNJ11 is associated with features of continuous glycemic profile in individuals with type 2 diabetes mellitus receiving vildagliptin monotherapy

Polina Shorokhova, Vitaly Baranov & Natalya Vorokhobina
North-Western State Medical University named after I.I Mechnikov, Department of Endocrinology named after acad. V.G. Baranov, Saint-Petersburg, Russian Federation

Background and aims
The rs5219 variant in the KCNJ11 have been consistently associated with type 2 diabetes (T2D) and therapeutic response to sulfonylureas in type 2 diabetic patients. However, the impact of KCNJ11 genetic polymorphism on the antidiabetic efficacy of vildagliptin has not yet been evaluated. This study was aimed to investigate the association of KCNJ11 rs5219 with vildagliptin glucose lowering ability by monitoring continuous blood glucose profile.
Materials and methods
We included 48 (18 men) drag-naïve patients (mean age 58.5±5.6 years; mean body mass index 31.1±4.5 kg/m^2) with newly diagnosed T2D, who had clinical indications to start vildagliptin therapy. The patients in this data set had mean HbA1c of 7.73%±1.1%. All participants received vildagliptin at an initial dose of 50 mg once a day. KCNJ11 rs5219 (C>T) genetic polymorphism genotyping was performed by real-time polymerase chain reaction. Several parameters, including mean 24-hour blood glucose level, minimum 24-hour blood glucose level, time of relatively low blood glucose, and indices of glucose variability (24-hour standard deviation), were extracted from continuous glucose monitoring (CGM) data obtained using a CGM system iPro2 for a 72-hour period.
Results
The frequencies of the CC, CT and TT genotypes were 41.7%, 37.5% and 20.8% respectively. Minor allele T frequency was 0.39. Genotype distribution followed Hardy-Weinberg equilibrium. All patients receiving 50 mg of vildagliptin per day, were divided into two groups based on rs5219 genotype: CC-genotype carriers ($n=20$) and CT/TT-genotype carriers ($n=28$). The minimum 24-hour blood glucose level was significantly lower in CT/TT- genotype carriers than in CC-genotype carriers: 4.0 [3.5; 5.4] vs 6.0 [5.9; 6.3] mmol/l ($P=0.042$) respectively. Additionally, the mean 24-hour blood glucose level tended to be lower in CT/TT-genotype carriers than in CC-genotype carriers: 6.3 [5.4; 6.8] vs 7.6 [5.9; 6.4] mmol/l and time of relatively low blood glucose tended to be prolonged in patients with rs5219 polymorphism compared to those with wild genotype: 20.0 [0.0; 75.0] vs 0.0 [0.0; 0.0] min; $P=0.075$ and 0.20 respectively. No differences in measures of glycemic variability between the genotype groups were observed: 24-hour standard deviation of CC-genotype carriers was 1.2 [0.9;1.3] mmol/l vs 0.9 [0.8;1.1] mmol/l of CT/TT-genotype carriers ($P>0,05$).
Conclusions
Despite limited sample size, we can conclude that the KCNJ11 rs5219 polymorphism is associated with better response to vildagliptin treatment in medication-naïve patients with newly diagnosed T2D, although patients with the CT/TT- genotypes are more likely to develop mild hypoglycemia than patients with CC-genotype.

DOI: 10.1530/endoabs.81.EP266

EP267

GLUCUBE: Usability validation of a non-invasive device for blood glucose measurement.

Mariola Méndez Muros[1], David Naranjo Hernández[2], Javier Reina Tosina[2], Laura María Roa Romero[2], Gerardo Barbarov Rostán[2] & María Asunción Martínez Brocca[1]
[1]Virgen Macarena University Hospital, Endocrinology and Nutrition Department, Seville, Spain; [2]University of Seville, Department of Signal Theory and Communications, Biomedical Engineering Group, Seville, Spain

Introduction
The Biomedical Engineering Group of the University of Seville, the Endocrinology and Nutrition Unit of the Virgen Macarena Hospital (ENU-VMH) and the company Igluco Tech are developing the GLUCUBE device, a new non-invasive sensor for blood glucose measurement.
Objective
First validation of usability and accessibility of the device by patients in a controlled clinical environment.
Material and Methods
General user-centered methodology. Design of questionnaires and semi-structured interviews to collect opinions, requirements and improvements

suggested by users. Selection of subjects for validation based on the heterogeneity of the sample, age, gender, socioeconomic characteristics and digital culture. From a preliminary prototype, iterative development carried out in parallel to the validation incorporating the identified improvements to the user-sensor interfaces.
Results
Study characteristics: 96 people with type I diabetes, 142 type II, 1 LADA, 19 without diabetes; 123 women; 84±19 kg weight (mean ± standard deviation); 54±16 years; 166±13 cm height, 30±7 BMI, assisted in follow-up consultations of ENU-VMH.Age group of people under 50 years old: 72 people with type I diabetes, 12 type II, 6 without diabetes; 43 women, 47 men; 80±21 kg weight; 35±10 years; 169±14 cm height, 27±7 BMI.Age group of people over 50 years old: 24 people with type I diabetes, 130 type II, 1 LADA, 14 without diabetes; 80 women, 89 men; 86±18 kg weight; 65±8 years; 165±12 cm height, 31±6 BMI.The usability and accessibility tests showed that 81% of the volunteers under the age of 50 expressed interest in having the results preferably displayed on the screen of a mobile phone, while 19% indicated the device screen as a preference. On the other hand, in the age group of people over 50 years old, only 13% of the volunteers preferred the screen of a mobile phone compared to 87% who preferred a visual interface on the device. 100% of the users positively valued the non-invasive nature of the proposed prototype and the ease of use. Regarding general aspects of the prototype, 97% of the patients indicated that the device did not need improvements and 2% suggested that voice prompts be included. 20% of users indicated a long battery life as a desirable feature for the device.
Conclusions
The introduction of user usability and accessibility validation in the design, from its early stages, guarantees the ease of use and adherence of the patient to the use of the final device.

DOI: 10.1530/endoabs.81.EP267

EP268

Psychological impact of obesity in adult women

Dhoha Ben Salah[1], Hana Charfi[1], Yossra Mejdoub[2], Hanen Maamri[2], mouna elleuch[1], Sourour Yaich[2], Jihen Jdidi[2], Faten Haj Kacem Akid[1] & Mohamed Abid[1]
[1]Hedi Cheker University Hospital, Endocrinology, Sfax, Tunisia; [2]Hedi Cheker University Hospital, Community Medicine, Tunisia

Introduction
Obesity is a global epidemic with a growing prevalence in recent decades. In Tunisia, obesity is a major problem as it is increasing in adults as well as in children and adolescents. It therefore appears important to deepen the knowledge on this pathology and especially on the psychological profile, since studies concerning the mental health of obese subjects remain rare.
Purpose
Study the psychological impact of obesity in adult women
Patients and Methods
Descriptive observational study using the quantitative approach, including 115 obese female adults who consulted the clinics of Sfax. A validated questionnaire was proposed to these patients concerning 6 dimensions: depression and anxiety (HAD scale), social phobia (LSAS score), self-esteem (RSE score), body image (BSQ-8c short version) and eating disorders (BITE scale).
Results
The average age of our population was 47.14 years. Seventy-eight percent of our patients were married. The median body weight was 93,15 +/- 17,6 kg and 54,7% of our population had stage 1 obesity. Stage 2 and 3 were present in 20,7% and 24,7% respertively. Abdominal obesity was present in 94,7% of cases. Fifty-one patients were on a diet that was prescribed mainly by family and friends (41%) and only 8% seaked medical care.Depression was present in 17,4% of our population and anxiety in 76,5%. All our patients had low self-esteem and social phobia, of which 90,4% had very low self-esteem and 40,9% had intense social phobia. Preoccupation with body image was described in 90% of our female patients and 32% had severe body image concerns. Sixty percent of our population suffered from eating disorders, of which 12,2% had bulimia.
Conclusion
Obesity is a growing concern, not only in terms of physical and social health, but also in terms of psychological health, throughout the world.

DOI: 10.1530/endoabs.81.EP268

EP269

Should we systematically detect hypothyroidism in obese subjects ?

Dhoha Ben Salah, Alaa Eddine Ben Issa, Mouna Elleuch, El Asmar Khouloud, Fatma Mnif, Nadia Charfi, Mouna Mnif, Nabila Rekik Majdoub, Faten Haj Kacem Akid & Mohamed Abid
Hedi Chaker University Hospital, Endocrinology, Tunisia

Introduction
Hypothyroidism has always been considered one of the most common endocrine etiologies of obesity. That said, would screening for hypothyroidism be justified in the face of obesity? The purpose of our study was to study the thyroid profile of obese people.
Patients and methods
We conducted a retrospective study which patients with obesity hospitalized in the diabetology endocrinology department, CHU Hédi Chaker of Sfax, between 01/10/2022 and 31/12/2022. for all patients who had consulted for obesity in which a thyroid assessment was requested as part of an etiological survey.
Results
the total number of patients was 70 obese, (12 men and 58 women), aged on average 44.57 years (±15 years). The average BMI of our patients was 38,38±6,09 k/m^2. In our study population, 30% of patients were moderately obese; 34.3% were severely obese and 35.7% were morbidly obese. No subject was known to have a history of dysthyroidism. Among patients, 6.7% ($n=5$) had subclinical hypothyroidism with TSH higher than 4 µmol/l and a normal FT4. In the latter, a thyroid check-up was done after one month returning normal. The rest of the patients ($n=65$) had no abnormalities in their thyroid function. The analytical study did not find a correlation between TSH blood level and the BMI of patients ($P=0.134$).
Conclusion
Our study shows that hypothyroidism remains a secondary cause to look for in the face of obesity with signs of appeal in favor of diagnosis instead of a systematic screening that proves to be unjustified.

DOI: 10.1530/endoabs.81.EP269

EP270

Un unexpected cause of mild hypoglycaemia in an adult

Felicia Baleanu[1], Taujan Georgiana[1], Mihaela Rosu[1], Olga Kosmopoulou[1], Blerta Papadopoulou[1], Emese Boros[2] & Iconaru Laura[1]
[1]Department of Endocrinology, CHU Brugmann, Université Libre de Bruxelles, Brussels, Belgium; [2]Paediatric Endocrinology Unit, Hôpital Universitaire des Enfants Reine Fabiola, Université Libre de Bruxelles, Brussels, Belgium

A 36-year-old Caucasian male was referred in November 2021 to our clinic, for investigations regarding his recent genetic diagnosis of congenital hyperinsulinism, revealed by genetic testing, performed after the birth of couple's second child presenting with recurrent hypoglycemia.The female newborn diagnosed with fetal macrosomia (birth at 38 weeks, 4.3 kg), required follow-up and further examinations.A massive parallel sequencing on panel of 4867 genes using Roche platform, performed on the entire family, revealed the presence in the heterozygous state of the variant c.4432G>A, p.Gly1478Arg in the ABCC8 gene in the newborn, her father and the couple's first child, born in 2018 (3.6 kg at 36 weeks), which inherited the variant, but had no suspicious event of hypoglycemia.In our patient, the condition is transmitted in the autosomal dominant mode.Each child of a carrier individual has a 50% risk of inheriting the anomaly. However, the expressivity is variable and the penetrance incomplete, therefore the severity of the phenotype cannot be predicted.Venous blood sample showed non-fasting sugar level at 62 mg/dl(3.4 mmol/l) with inappropriate normal value of C-Peptide(0.954 nmol/l) and insulin(92.9 pmol/l).7-day continuous glucose monitoring (CGM) with Dexcom G5® Mobile CGM System, highlighted several hypoglycemic events, confirmed by fingerstick measurement, going as low as 45 mg/dl (2.5 mmol/l) linked mostly to meals, occasional alcohol consumption or after a 5-hour fasting period. Going backward in time, in the light of this new medical information, the patient could relate with his condition several unexplained symptoms that he presented over time, since childhood, as mild headaches and extreme hunger.Regarding the treatment, the simplest strategy is to eat several small low-carbohydrate meals daily. If not sufficient, further treatment is based on Diazoxide, a potassium channel agonist which inhibits insulin secretion in some forms of congenital hyperinsulinism by stimulating the opening of KATP channels leading to hyperpolarization of the β-cell membrane and inhibiting insulin secretion or Octreotide, a somatostatin analog that acts to suppress insulin release downstream of the KATP channel.The patient was placed on a low-carb meal regimen with successful prevention of

hypoglycemic events.The understanding of the genetic basis of familial hyperinsulinism should borne in mind that certain patients with hypoglycemia might present genetic forms with late-onset (or late diagnosis), such as congenital hyperinsulinism.Mild hypoglycemia in an adult can be easily missed, but the underlying cause can be rare with important further implications for the patient and his offspring.

DOI: 10.1530/endoabs.81.EP270

EP271

Impact of emotional eating in the weight of woman

Victor Viana[1], Miguel Pereira[1], José Paulo Almeida[1] & Davide Carvalho[2]
[1]Department of Psychology, São João University Hospital Center, Porto, Portugal; [2]Department of Endocrinology, Diabetes and Metabolism, São João University Hospital Center, Porto, Portugal

Introduction
Obesity is nowadays one of the most important challenges in public health and, therefore, the investigation of their causes is most relevant. Among the various behavioral roots of obesity, the emotional over ingestion determined by emotional factors, i.e. emotional eating (EE), is one of them.
Objectives
To study how emotions contribute to obesity in woman.
Methods
We gathered a convenience sample 220 woman in the hospital and community settings, of which, 43 had normal weight, 37 overweight, 19 grade 1 obesity, 35 grade 2 obesity and 86 grade 3 obesity. The mean age was 39.3 ± 10.4 years and BMI was 35.3 ± 9.5 kg/m2. We applied the Emotional Appetite Questionnaire (EMAQ) that evaluates the EE determined by positive and negative emotions and by positive and negative situations. Statistical analysis was performed with the One-way ANOVA with Bonferoni correction test and Pearson's correlation test for variable association. P values $\leq$ 0.05 were considered as statistically significant.
Results
We found a positive correlation among age and BMI ($P<0.001$) and the mean of negative situations ($P<0.001$). We observed a negative correlation among BMI and education ($P<0.005$), the mean positive emotions ($P<0.001$) and positive situations ($P<0.005$). We noticed a significant age difference among normal weight vs grade 2 obesity and grade 3 obesity ($P<0.001$) participants. Normal weight and grade 3 obesity groups had different education levels ($P<0.02$). In terms of EE we observed significant differences between normal weight and grade 3 obesity ($P<0.005$) and between overweight and grade 3 obesity ($P<0.03$). Normal weight and grade 3 obesity participants had significant differences in the positive situations ($P<0.03$).
Conclusions
In this sample older and lower education participants showed a higher BMI. Woman with higher BMI appear to have more EE determined by negative emotional situations. Ingestion originated by positive emotions and situations results in lower BMI. Attending to all groups of weight classes concerning the EE, only the positive emotions distinguish the normal weight of the grade 3 obesity and the overweight. The positive situations distinguish the normal weight and the grade 3 obesity. According with some the literature, this study, corroborates the importance of the positive EE as a differential factor in the woman's weight. Thought, did not confirm the influence of the negative emotions and situations.

DOI: 10.1530/endoabs.81.EP271

EP272

Impact of bariatric surgery on cognitive function

Maria-José Barahona[1], Andreu Simó[1], Montse Ibarra[1], Mireia Libran[1], Montse Ramos[1], Veronica Perea[1], Aida Orois[1], Carmen Quirós[1] & Laura Casas[2]
[1]Hospital Universitari Mútua Terrassa, Endocrinology Department, Terrassa, Spain; [2]Hospital Universitari Mútua Terrassa, Neurology Department, Terrassa, Spain

Aim
Obesity was shown to be related to global cognitive decline, being especially altered the executive function and the information processing speed. Bariatric surgery (BS) is an effective means of weight reduction in severely obese patients and correlates with improvements in neurocognition. The mechanisms underlying these improvements are not fully elucidated.
Material and Methods
Prospective, observational study, including consecutive patients that underwent Y-de- Roux gastric bypass at our center. Fat mass (FM %) and appendicular skeletal mass index (ASMI) (kg/m^2) by dual-energy X-ray absorptiometry (DXA) and Neurocognitive Test Battery (NTB) were assesed in all patients 1 month prior BS and 12 months after BS.
Results
From a cohort of 75 patients, 15 were selected as they completed 12 months of follow-up data. Almost all patients were female (87%), mean age (56 ± 8 years), pre-BS BMI 43 ± 5 kg/m^2, % total weight loss 28 ± 5. Eleven patients had diabetes (2 T1D, 9 T2D), 4 of them were treated with insulin and excluded for the calculation of HOMA. FM% (55 ± 5 vs 44 ± 7), ASMI (7.4 ± 1.6 vs 6.7 ± 1.2) and HOMA-IR (9.23 ± 6 vs 2.28 ± 1.4) significantly decreased 12 months after BS ($P<0.005$). Furthermore, patients had better performance (raw score and scaled score) in Free and Cued Selective Reminding Test (25.4 ± 5.4 vs 29.4 ± 5.5; 9.2 ± 2 vs 11.2 ± 2), visual immediate memory (16.6 ± 10.6 vs 21.8 ± 8.4; 9.5 ± 4.5 vs 12 ± 3.4), visual delayed memory (17.6 ± 10 vs 20 ± 8; 10.3 ± 4 vs 11.5 ± 3) and Boston Naming Test (52.9 ± 4.5 vs 54.4 ± 3.7; 11.8 ± 2.3 vs 13 ± 2.2) ($P<0.005$). After regression analysis, the only independent predictor for each post-BS performance test was the performance of those tests in pre-BS, not related to changes in body composition or HOMA-IR.
Conclusions
Our preliminary results suggest improvements on verbal and visual memory and language function after BS. Both memory and language depend on temporal lobe structures. These improvements seem not to be related to body composition or insulin resistance. Larger series are needed in order to confirm these preliminary results.

DOI: 10.1530/endoabs.81.EP272

EP273

Serum xanthinoxidase activity (sxo)-glucose homeostasis association in patients with type 2 diabetes mellitus (t2dm)

Oksana Khyzhnyak[1,2], Anna Cherniaieva[1,2,3], Myroslava Mykytyuk[1,2,3] & Iurii Karachentsev[†,3]
[1]V. Danilevsky' Institute of Endocrine Pathology Problems, Clinical Endocrinology, Kharkiv, Ukraine; [2]Kharkiv Medical Academy of Post-graduate Education, Department of Endocrinology, Kharkiv, Ukraine; [3]Institute for Endocrine Pathology Problems, National Academy of Medical Sciences of Ukraine, Ukraine

Introduction
Hyperuricemia is increasingly being considered a potential pathogenic factor for T2DM, metabolic syndrome, and several adverse consequences of vascular disease. It has been suggested that xanthine oxidase may underlie the urine acid-T2DM association. The study aimed to determine the associations between clinical parameters, glucose homeostasis, and SXO activity in patients with T2DM.
Methods
125 patients with T2DM, age (58.9 ± 9.4) years. Determined WC, HC, ratio WC/HC, BMI, FBG, PBG, fasting insulin, serum urine acid (SUA), HOMA_IR, QUICKI, Caro, HOMA_β%, HOMA_S%, and SXO activity.
Results
It was found that in the total group patients with T2DM SUA depends on SXO activity ($r=0.34$; $P=0.007$). The total group established the presence of association SXO activity with fasting insulin ($r=0.45$; $P=0.001$), HOMA_β% ($r=-0.34$; $P=0.021$), HOMA_S% ($r=-0.52$; $P=0.00001$), QUICKI ($r=-0.35$; $P=0.016$), Caro ($r=-0.40$; $P=0.007$). No sexually significant differences have been established according to SUA and SXO activity in groups with different control of glycemia.
Conclusions
The patients with T2DM SUA are linearly associated with SXO activity regardless of the state of the control of glycemia serum for activity and nonlinearly associated with other parameters of glucose homeostasis. The patients with high SXO activity are by character significant higher fasting insulin, faster secretory activity of β-cells, low faster oral insulin sensitivity, and more pronounced manifestations of insulin resistance compared to patients with normal SXO activity. The level of SXO activity in patients with T2DM, regardless of the state of the control of glycemia, is determined by the SUA ($t=2.52$; $P=0.02$) and WC/HC ($t=2.87$; $P=0.007$). In patients with optimal control of glycemia, SXO activity determines fasting insulin ($t=2.68$; $P=0.015$), with suboptimal control and high risk – age ($t=-2.74$; $P=0.015$) and HOMA_IR ($t=2.62$; $P=0.02$).

DOI: 10.1530/endoabs.81.EP273

EP274

Liraglutide improves binge-eating and increases ghrelin levels in obese diabetic 2 patients

Fedir Laniush & Alina Urbanovych
Danylo Halytsky Lviv National Medical University, Endocrinology, L'viv, Ukraine

Background and aims
liraglutide belongs to glucagon-like peptide-1 receptor agonists (GLP-1 RA) and is widely used for diabetes type 2 (DT2) management as well as for obesity treatment. GLP-1 RA reduce body weight and suppress eating behavior by delaying gastric emptying and affecting arcuate nucleus in hypothalamus. Binge eating disorder (BED) is the most common eating disorder (ED) in individuals with obesity and DT2. BED is characterized by consuming large amounts of food with an associated sense of loss of control. A well-known appetite-stimulating hormone is ghrelin, secreted within the gastric mucosa. Some studies report about decreased ghrelin levels in obese, diabetic 2 patients as well as in individuals with BED. Our aim was to evaluate the effect of liraglutide on BED and ghrelin level after 3 months of administration in obese diabetic 2 patients.
Materials and methods
75 individuals (mean age – 60.1 ± 6.4 years; BMI - 33.4 ± 3.6 kg/m^2; history of diabetes < 5 years) with DT2 were recruited into the study. After completing Binge eating scale (BES) 18 patients were screened positive for BED. 8 binge-eaters (1st study group) started therapy with metformin and liraglutide 1.8 mg daily. Other 10 participants (2nd study group) used metformin and SGLT-2 inhibitors as glucose-lowering therapy. Ghrelin level was assessed at the 1st and 12th week of the study.
Results
the 1st study group which used dual therapy with liraglutide demonstrated greater weight loss compared to the 2nd group (4.3 ± 1.3 kg vs. 1.7 ± 0.8 kg, $p < 0.05$). BES-scoring improved in the 1st study group and 3 participants (37,5%) were categorized into non-binge-eaters. Baseline ghrelin level in the liraglutide group (18.8 ± 10.3 ng/ml) increased (24.9 ± 10.8 ng/ml) significantly ($P < 0.05$) but not in the 2nd group.
Conclusion
liraglutide is effective and safe for the use in obese diabetic 2 individuals with BED. It reduces body weight and stabilizes eating behavior which makes them potential candidates for the application in diabetic 2 patients with BED. Changes in ghrelin level reflect the recovery of energy homeostasis due to weight loss.

DOI: 10.1530/endoabs.81.EP274

EP275

A potential complication of diabetes: ischemic colitis

Shielah Mauntana[1] & Mahesh Gajendran[2]
[1]Paul L. Foster School of Medicine, El Paso, United States; [2]Long School of Medicine, University of Texas Health Center at San Antonio, Division of Gastroenterology, San Antonio, United States

Background
Ischemic colitis (IC) is a disorder characterized by a decrease in blood flow of the large intestine. Many factors can contribute to decreased blood flow in the arteries supplying the large intestine, such as nonocclusive causes like hypertension and atherosclerosis and occlusive causes like embolism from myocardial infarction. With Ischemic colitis's high mortality rate and its association with many cardiovascular diseases, it's important to understand the comorbidities that might lead to these events. Diabetes is known to cause atherosclerosis and other cardiovascular events. Thus, Diabetes might play a role in the development of ischemic colitis. This study aims to find and assess comorbidities like diabetes associated with admission for ischemic colitis.
Methods
We conducted a cross-sectional study of adults with IC listed as the primary ED diagnosis from 2005 to 2014 using the Nationwide Readmission Database (NRD). The characteristics of the IC-related ED visits were analyzed.
Results
The estimated number of ED visits with a primary diagnosis of IC from 2005-2014 was 541,267 people. Our results showed that the mean age of the cohort was 62 +/- 14 years, suggesting that most patients affected with ischemic colitis are elderly. 101,758 out of 541,267 ischemic colitis patients were found to have uncomplicated diabetes, amounting to 18.8% of the ischemic colitis population.
Conclusions
A notable comorbidity associated with ischemic colitis was uncomplicated Diabetes. Diabetes is marked by hyperglycemia, which can result in atherosclerosis. Atherosclerosis may lead to hypoperfusion of organs and ultimately ischemic colitis. Constipation is not only the most common gastrointestinal symptom of diabetes, but most common precipitating factor of ischemic colitis in the elderly. Most of the patients affected with ischemic colitis are elderly, based on the results. Thus, uncomplicated diabetes may be regarded as a comorbidity associated with ischemic colitis, constipation being the resulting precipitating factor.

DOI: 10.1530/endoabs.81.EP275

EP276

Lipoatrophy in type 1 diabetes treated by human insulin: a case report

Manale Azriouil, Loubna Guissi, Farah Kamel, Nawal Moussaid, Kaoutar Rifai, Hinde Iraqi & Mohamed Elhassan Gharbi
Hôpital Universitaire Ibn Sina, Endocrinology, Rabat, Morocco

Introduction
Lipoatrophy is a rare cutaneous complication in diabetes that presents with localized subcutaneous fat atrophy at the insulin injection site. We report a case of a 62-year-old man type 1 diabetic with lipoatrophy lesions on the thighs.
Case report
A 62-year-old male, with clinical history of basedow's disease, He was diagnosed type 1 diabetes (T1D) when he was 19 years old, treated with premixed human insulin for the last 4 years.His weight was 68 kg and his body mass index was 21 kg/m2, he developed subcutaneous lipoatrophy around the insulin injection site at the thighs. The rest of the physical examination was normal.The results of blood testing were: K^+4.1 mEq/l, Na^+139 mEq/l, Hb1Ac 8.9%, cholesterol 157 mg/dl, triglycerides 108 mg/dl, liver and kidney functions were normal.The type of insulin was changed to insulin analogs (aspart and glargine insulin) and the injection site was changed to the abdomen.
Discussion
Lipoatrophy, is clinically characterized by visible cutaneous depression at the injection site. With the arrival of more purified forms of insulin it has become an extremely rare complication of insulin therapy. It is more than a cosmetic problem, because of the variability of insulin absorption of insulin and therefore the glycemic controlLipoatrophy is due to mechanical trauma from repeat injections. Immune etiologies have also been suggested, furthermore, the authors stated that lipoatrophy is found more frequently in patients with other autoimmune diseases, our patient has Basedow's diseaseAvoiding injections in the lipoatrophy sites and changing the insulin needle daily help to resolve lipoatrophy. Local treatment with sodium cromolyn, low- dose oral, or subcutaneous coadministration of corticosteroid are some therapeutic options used in some studies.
Conclusion
Lipoatrophy although rare can still occur even with the use of technologically advanced newer insulin preparations. This complication of insulin therapy may be limited by regularly inspecting and changing the injection sites.

DOI: 10.1530/endoabs.81.EP276

EP277

Detection of visceral obesity in children and adolescents based on body composition analysis

Iuliia Samoilova, Mariia Matveeva, Oxana Oleynik, Daria Podchinenova, Venera Mutalimi, Ekaterina Trifonowa & Poina Zaharchuck
Siberian State Medical University, Children Diseases, Tomsk, Russian Federation

Introduction
Visceral obesity is a primary risk factor for metabolic syndrome and is associated with short- and long-term effects on physical and psychosocial health. It is now known that body mass index (BMI), which is used as the main method of diagnosing obesity, does not allow the assessment of body composition and differentiation of visceral adipose tissue.The aim of the study. To investigate the features of body composition that influence metabolic risks in primary school children.
Materials and methods.
Prior to any procedures of the study protocol informed consent was signed by the child's legal representative or self at the age of 15. We examined 519 children aged 8 to 12 years, including anthropometry (height, weight, BMI, SDS BMI). SDS BMI was calculated using Anthroplus WHO software developed by the

World Health Organization for children aged 6 to 19 years. Body composition was assessed in all participants using an Inbody 770 analyser (Inbody Co. Ltd, Korea). Statistical processing of the results was performed using SPSS Statistics 25.0.
Results
Fat mass parameters in girls and boys from the obese and overweight groups were comparable to the SDS BMI values. The 11% of normal weight girls ($n=146$) had increased body fat mass, 32.2% had increased body fat percentage, and 7.5% had visceral obesity (VO). Among all female examinees, 45.9% had decreased muscle mass. Boys with normal body weight ($n=147$) had increased fat mass in 17.7% cases, 34.7% of those examined had increased percentage of fat mass and 2.1% had visceral obesity. Among all boys surveyed, 17.5% had decreased muscle mass. Weight deficient children, irrespective of gender, had no excess fat mass but all had deficit muscle mass.
Conclusions
The results obtained in the survey are probably related to lifestyle aspects of modern children, such as low physical activity and an unbalanced diet. The revealed changes in body composition in children with normal SDS BMI indicate the need for more active diagnostic tactics and the use of additional tools to diagnose these deviations and their correction. The use of bioimpedance measurement will allow early detection of signs of visceral obesity in children, irrespective of BMI.

DOI: 10.1530/endoabs.81.EP277

EP278

Evolution of glucose-insulin homeostasis in children with β -thalassemia major (β -TM): A twenty-year retrospective ICET- A observational analysis from early childhood to young adulthood

Vincenzo De Sanctis[1], Shahina Daar[2], Ashraf Soliman[3], Ploutarchos Tzoulis[4], Mehran Karimi[5] & Christos Kattamis[6]
[1]Quisisana Hospital, Ferrara, Italy; [2]College of Medicine, Sultan Qaboos University, Muscat, Oman; [3]Hamad Medical Center, Doha, Qatar; [4]Department of Diabetes and Endocrinology, Whittington Hospital, London, United Kingdom; [5]Hematology Research Center, Shiraz University of Medical Sciences, Shiraz, Iran; [6]National Kapodistrian University of Athens, Athens, Greece

We studied retrospectively the changes of glucose-insulin homeostasis from early childhood to young adulthood in β-thalassemia major (β -TM) patients with impaired fasting glucose (IFG) vs those with normal OGTT.
Methods
All data entered in the database of β -TM patients' records from September 1983 to September 2021 were included in the study.
Results
The occurrence of dysglycemia (GD) (IFG, IGT and IFG + IGT) after 20 years of follow up was markedly higher in the group with IFG at the beginning of the study compared to the group with normal OGTT. There was no case of diabetes mellitus. In patients who had normal OGTT at baseline, a small proportion developed GD (2/9 at 15 years and only 1/8 at 20 years). On the other hand, 3 out of 9 patients with baseline IFG, had persistent IFG at 5 years. One had persistent isolated IFG and 3 developed IGT 10 years later. 5/9 had IFG after 15 years, and finally 6/8 had GD after 20 years. (table)Indices of insulin secretion and sensitivity (MI, HOMA-IR, oDI) were statistically different ($P=<0.001$) between the two groups. HOMA-IR was higher in patients who had IFG vs (6/9 patients had HOMA-IR > 2.24) vs the group with normal OGTT (2/6 patients had HOMA-IR > 2.24). This suggested a degree of insulin resistance in the etiology of GD.In both groups of patients, no correlation was observed between serum ferritin (SF), ALT and indexes of insulin sensitivity or insulin resistance.
Conclusion
Our data advocates that baseline IFG predicts future development of GD because almost half of patients with IFG at the outset had abnormal glucose handling 15 years later. Understanding the sequence of abnormalities in the progression from normal glucose homeostasis to GD and identifying the risk factors for the glycol-metabolic defects in thalassemia patients might help in the formulation of interventions.

Table Proportions of progressive dysglycemia in BTM patients with normal OGT vs those with IFG.

	BTM -Normal OGTT	BTM- Impaired Fating Glucose
	***n*=9**	***n*=9**
Age yr.	**5.4+/- 0.7**	**5.6+/- 1.7**
After 5 yr.	**1/9 IFG**	**2/9 IFG**
Total Dysglycemia	**1/9**	**2/9**
After 10 yr.	**2/9 IFG and 1 IFG+ IGT**	**3/9 IGT**
Total Dysglycemia	**3/9**	**3/9**
After 15 yr.	**2/9 IGT**	**5/9 IFG**
Total Dysglycemia	**2/9**	**5/9**
After 20 yr.	**1/9 IFG**	**2/9 IFG, 2/9 IGT, 2 IFG+IGT**
Total Dysglycemia	**1/9**	**6/8**

DOI: 10.1530/endoabs.81.EP278

EP279

Malnutrition risk using morphofunctional evaluation in hematopoietic stem cell transplantation

Concepcion Muñoz Jimenez, Carlos Alzas Teodomiro, Mireia García-Ramírez, Laura Romero, Estefania Garcia, Alfonso Jesús Calañas Continente, Maria José Molina & Aura D. Herrera-Martínez
Hospital Universitario Reina Sofía, Córdoba, Spain

Background
Malnutrition affects 30-50% of patients with hematological malignancies; it is due to the disease itself, the treatment-related catabolic process and chemo-or radio-therapy side effects (nausea, vomiting, diarrhea and mucositis). Patients with poor nutritional status have increased morbidity (treatment complications, infections, mucositis) and mortality.
Aim
To evaluate the nutritional status of all patients that underwent hematopoietic stem cell transplantation (HPSCT) in our center during April-November 2021
Methods
A novel morphofunctionalnutritional evaluation (included electrical bioimpedance, handgrip dynamometry, biochemistry, abdominal adipose ultrasoundand rectus femoris muscle ultrasound) was performed baseline and 24±9 days after HPSCT.
Results
Forty-eight patients were included; mean age 50.2±14.6;62.5% males. Lymphomas was the most common cause of HPSCT (35%), and most patients underwent an autologous transplant (56.3%). At baseline severe and moderate malnutrition (using the GLIM criteria) were observed in 21%and 37.5% of patients respectively, despite only 21% presented with BMI <20 kg/m^2. Patients lost weight during the study period (5.6±3.1%; $p<0.05$), especially fat free mass (16.7±2.3 vs 18.4±6.5; $p<0.05$), serum albumin levels, superficial and deep abdominal adipose tissue, as well as thecircumference of rectus femoris significantly decreased in most patients during follow-up ($P<0.05$).
Conclusions
Malnutrition is observed in more than 50% of patients before theHPSCT despite normal or increased BMI. Significant weight loss during the first days after HPSCT worsens the nutritional status of these patients. The novel morphofunctional nutritional evaluation provides early and additional information that could have prognostic value. Routine nutritional evaluation should be performed in all patients before HPSCT.

DOI: 10.1530/endoabs.81.EP279

EP280

C-peptide response to standardized test meal in patients with newly diagnosed type 2 diabetes mellitus

Jelena Stojanovic[1], Marina Andjelic Jelic[1,2], Miljanka Vuksanovic[1,3], Milica Marjanovic Petkovic[1,3], Biljana Jojic[1], Ana Cvetkov Grujanac[1] & Teodora Beljic Zivkovic[1,3]
[1]Zvezdara University Medical Center, Division of Endocrinology, Diabetes and Metabolic Disorders, Belgrade, Serbia; [2]University of Belgrade, Faculty of Dental Medicine, Belgrade, Serbia; [3]University of Belgrade, Medical Faculty, Belgrade, Serbia

Background
Optimal testing of beta-cell dysfunction is still elusive. Oral based solid-food tests could superiorly approximate real-life stimulation by incorporating incretin activation. Increased body fat was recently associated with better preserved beta-cell secretory response, due to gluco-lipotoxicity induced adaptation.

Objective
To assess C-peptide response to standardised test meal (STM) and its dependency on subject characteristics in newly diagnosed type 2 diabetes mellitus (DM2) patients.
Patients and Methods
STM consisted of one 60g white flour bread-roll (24g carbohydrates) and 200 ml 2.8% milk-fat yoghurt (12g carbohydrates), totalling 300 kCal, consumed over 5 minutes after overnight fasting. C-peptide was analysed at baseline and 2h post STM in newly diagnosed DM2 patients ($n=80$; 30-65 years old; 47 males) with initial HbA1c ≧ 9% and BMI 25-40 kg/m^2.
Results
Baseline C-peptide of 2.29±0.14 ng/ml, increased after STM by 1.40±0.20 ng/ml (63.6%±7.7%). In women vs. men, there was non-significantly higher baseline C-peptide (2.48±0.26 ng/ml vs. 2.16±0.15 ng/ml, $P>$ 0,05) with a significantly greater C-peptide increase (ΔCP) in STM: 1.92±0.33 ng/ml vs. 1.04±0.14 ng/ml (P 0,05). Average baseline C-peptide (2.29±0.14 ng/ml) correlated significantly with average BMI (29.7±0.5 kg/m2) ($P<0.01$; Pearson's $r=0.32$). Baseline C-peptide was significantly lower in the normally nourished (1.58±0.22ng/ml) compared to overweight (2.41±0.23ng/ml; $p<0.05$) and obese (2.46±0.22 ng/ml; $p<0.05$). STM-stimulated ΔCP was significantly lower in the normally nourished (0.68±0.21 ng/ml) compared to twice greater in the overweight (1.40±0.20ng/ml; $p<0.05$) and obese (1.71±0.44 ng/ml; $p<0.05$). Average ΔCP in STM (1.40±0.20 ng/ml) correlated significantly with BMI (29.7±0.5 kg/m2) (P 0.05; Pearson's $r=0.23$). ΔCP correlation to age was not significant.
Conclusions
Standardised test meal is a promising simple and naturalistic alternative to asses beta-cell function in-vivo through C-peptide response in patients with newly diagnosed DM2, but interpretation should respect its dependency on gender and BMI. Significant positive correlation of baseline C-peptide and its stimulated response to STM with BMI supports the hypothesis of more preserved or better adapted beta-cell reserve in the obese patients.

DOI: 10.1530/endoabs.81.EP280

EP281

Flash glucose monitoring system in a regional hospital in the south area of granada

Sara León Utrero, Victoria Contreras Bolívar, Enrique Redondo Torres, Javier García Sánchez & Pablo José López-Ibarra Lozano
Hospital Universitario San Cecilio, Servicio de Endocrinología y Nutrición, Granada, Spain

Introduction and Objectives
Poor metabolic control in Type 1 Diabetes Mellitus (DM 1) is associated with micro and macrovascular complications. The implementation of interstitial glucose monitoring systems has contributed to improving glycemic control in recent years. Our objective was to know the metabolic control in people with type 1 DM and the Flash system and to establish if there is an association between its use and glycemic control variables.
Material and Methods
Cross-sectional observational study in people with DM 1, carriers of Flash glucose monitoring system, with follow-up in a Regional Hospital (Hospital Santa Ana, Motril-Granada). Downloads were performed for the previous three months and glycemic control variables were analyzed: average glucose (mg/dl), % of time in range (TIR, 70-180 mg/dl), % above target (>180 mg/dl), % below target (< 70 mg/dl), % coefficient of variation, estimated glycosylated hemoglobin (GMI, %) and low glucose events (in no.). Statistical analysis was performed using the SPSS 15.0 program.
Results
179 patients were included, 51.9% women, with a mean age of 42.04±15.3 years. All patients were receiving basal-bolus insulin therapy. The average glucose of the last three months was 176.65±44.54 mg/dl and the estimated GMI was 7.4± 0.84%. The mean number of readings per day was 9.25±6.4. The coefficient of variation was 37.7±8.8%. The mean time within target was 53.28±19.08%, over range was 41.8±20.8% and under range was 4.9±5.4%. Taking 10 or more readings per day was statistically significantly associated with lower mean glucose levels (164.0 vs 184.6, $p<0.01$), lower estimated GMI (7.23 vs 7.55, $p<0.01$), increased time in range (59.10 vs 49.60, $p<0.01$) and decreased time above target (35.06 vs 45.72, $p<0.01$).
Conclusions
Insufficient metabolic control was observed in people with DM 1 under follow-up in a Regional Hospital. 10 or more daily readings was associated with better results in terms of glucometry. Therefore, we could recommend the active and frequent use of the FLASH sensor in people with DM 1 to achieve better metabolic control.

DOI: 10.1530/endoabs.81.EP281

EP282

Nurses knowledge in diabetes self-management education in Sfax Tunisia

Mouna Elleuch, Hana Charfi, Dhoha Ben Salah, Ameni Salah, Fatma Mnif, Nadia Charfi, Mouna Mnif, Nabila Rekik Majdoub, Faten Haj Kacem Akid & Mohamed Abid
Hedi Cheker University Hospital, Endocrinology, Tunisia

Introduction
Diabetes mellitus is a major public health problem affecting all ages worldwide. In Tunisia, 18% of the population has diabetes mellitus. In fact, it is one of the first ten causes of death in our country.Therefore, self-management education for diabetic patients play an important role in reducing diabetes complications and mortality rate. The education is conducted not only by doctors, but also by nurses.
Purpose
The aim of this study is to determine the nurses' knowledge in diabetes self-management education (DSME)
Methods
We are presenting a descriptive study including 32 nurses, 17 nurses from the endocrinology department of Hédi Chaker hospital, Sfax, Tunisia, and 15 nurses from the healthcare dispensary Mohamed Ali Sfax Tunisia.
Results
The majority of nurses: 62,50% were young, aged between 25 and 40 years old, 78% of them were female and 78,5% were married. We discovered that only 63% of the nurses were involved in nurse-led DSME and did actually have specific training in DSME. The nurses believed that the purpose of DSME is essentially to prevent complications (36%), to lead as normal a life as possible (30%), to obtain a balanced blood sugar (18%) and to improve the patient's life (16%).Only 6,25%of the nurses had real good knowledge in DSME vs 75% and 18,75% having average and poor knowledge respectively.The majority of the female nurses (56,25%) had average knowledge in DSME vs 18,75% in the male group, and only 6,25% of the female nurses knew how to properly educate the diabetes patients vs 0% in the male nurses.Total absence of DSME knowledge was mostly described in the youngest group of nurses (25-40 years old) with an average of 18,75% vs 0% in older nurses (> 40 years old).We noted that nurses having more than 10 years work experience were more efficient in educating the patients than those with less work experience.Finally, we asked the nurses to provide solutions on how to get more information about DSME, 50% of them proposed attending seminars, 44% proposed organizing ongoing training sessions and 6% didn't comment.
Conclusion
In recent years, great emphasis has been placed on the role of non-pharmacological self-management in the care of patients with diabetes. Studies have reported that nurses, compared to other healthcare professionals, are more likely to promote preventive healthcare seeking behaviors.

DOI: 10.1530/endoabs.81.EP282

EP283

Pharmacogenomics and efficacy outcome of therapy with glucagon-like peptide-1 receptor agonists in type 2 diabetes

Camille Beniga & Hassan Heshmati
Endocrinology Metabolism Consulting, LLC, Anthem, Arizona, United States

Introduction
Individual variability in drug efficacy and safety due to genetic diversity is a major challenge for clinicians. Pharmacogenetics deals with inherited differences in the efficacy and safety responses to drugs. The incidence of type 2 diabetes (T2D) is increasing worldwide and the disease is reaching pandemic proportions. T2D is treated by oral and/or injectable drugs. The interindividual variability of T2D drug actions may be caused, at least in part, by genetic factors. This review outlines the contribution of pharmacogenomics to the efficacy outcome of glucagon-like peptide-1 receptor agonists (GLP1RAs) therapy in T2D.

Methods
A systematic search of literature was conducted using the search terms pharmacogenomics, type 2 diabetes, glucagon-like peptide-1 receptor agonists, and efficacy.
Results
Pharmacogenomics has identified the relevance of approximately 56 genes in the response to 7 pharmacological classes of antidiabetic drugs. More than 460 million people worldwide have T2D. According to the American Diabetes Association and the European Association for the Study of Diabetes, GLP1RAs are recommended as a second-line treatment in the management of T2D when there is a need for combination therapy. The identified genes influencing the efficacy outcome of GLP1RAs treatment [increased or decreased efficacy based on single nucleotide polymorphisms (SNPs)] include *GLP1R* (increased or decreased efficacy with rs6923761, rs3765467, rs10305420, and rs761386 SNPs), *TCF7L2* (increased efficacy with rs7903146 SNP), *CNR1* (increased efficacy with rs1049353 SNP), *SORCS1* (increased efficacy with rs1416406 SNP), and *WFS1* (decreased efficacy with rs10010131 SNP).
Conclusion
Pharmacogenomics is becoming an important tool in medicine. Education of clinicians is essential for the implementation of genetic testing into clinical practice. The use of genotype-guided dosing can help obtaining better efficacy and safety outcomes with drugs. Potential genomic markers for targeted GLP1RAs therapy have been identified. However, the number of studies is relatively limited and more comprehensive research including larger populations is needed to determine the therapeutic implication of incorporating precision medicine with the utilization of GLP1RAs in T2D.

DOI: 10.1530/endoabs.81.EP283

EP284

Factors affecting glycemic outcomes using closed-loop systems in real-world

Lara Albert Fàbregas, David Subias Andujar, Ana Romero Gregori, Maria Florencia Luchtenberg, Albert Cano Palomares, Isabel Mazarico & Mercedes Rigla
Parc Taulí Hospital Universitari. Institut d'Investigació i Innovació Parc Taulí I3PT, Universitat Autònoma de Barcelona, Endocrinology and Nutrition, Sabadell, Spain

Aims
To evaluate real-world efficacy of closed-loop systems (CLS) (Minimed™ 780G, DBLG1 -Diabeloop- and Control-IQ™ Tandem) as well as to assess those predictive factors related with the achievement of near-normal glycemic control.
Methods
A prospective, longitudinal, and observational study was performed. It included T1D adults who initiated CLS between April and December 2021 in our hospital and provided data for ≧3 months (ninety of 130 CLS users were included). We evaluated the initial and three-months data regarding glycemic outcomes and their baseline characteristics.
Results
Ninety T1D were included (54 female, 45.1 ± 11.5 years, 76.2 ± 16.0 kg weigh, 27.4 ± 4.9 kg/m^2 BMI, baseline HbA1c 7.5 ± 0.9%). 41% were previously under multiple daily injections (MDI), 91% used continuous glucose monitoring (CGM) and 56% used an insulin bolus advisor. Different commercial CLS were used: 54 DBLG1, 18 Control-IQ™ and 18 Minimed™780G.After three months, HbA1c significantly decreased to 6.9% ± 0.7% (-0.6% ± 0.1%, p < 0.001). 58% achieved HbA1c < 7%, 25% HbA1c 7-7.5% and 17% HbA1c > 7.5%. Mean glucose management indicator (GMI) was 7.0% ± 0.4% (45% GMI < 7%, 13% GMI = 7% and 100% GMI ≤ 7.9%). Mean time-in-range (TIR) was 73% ± 10% (67% TIR > 70%) and mean time below range 54-69 mg/dl (TBR) was 1.4% ± 1.0%.Optimal glycemic control was observed among people with higher education level (GMI 6.8% ± 0.3% vs 7.1% ± 0.4%, p < 0,04) and among people under 45 years old (HbA1c 6.7% ± 0.1% vs. 7.1% ± 0.1%, p < 0.04).We observed a positive trend towards better glycemic control in women (TIR > 70% 71% vs. 61%) and in those people who exercise regularly (HbA1c ≤ 7% 75% vs. 54%; TBR < 4% 0% vs. 8%)). Overweight didn't affect glycemic control.Regarding prior treatment, a higher percentage of patients with insulin pump obtained optimal glycemic control compared with MDI (HbA1c ≤ 6.5% 34% vs. 22%). Similarly, the previous use of insulin bolus advisor related to a higher proportion of optimal HbA1c (HbA1c ≤ 6.5% 34% vs 21%).We observed a better glycemic control with the Minimed™780G system (GMI = 6.7% vs. 7.0% DBLG1 and 7.0% Control-IQ™; TIR > 70% 81% vs. 65% DBLG1 and 59% Control-IQ™ (n.s.); better TAR and TBR, but no differences in HbA1c).
Conclusions
In almost all cases the use of a CLS improved glycemic control substantially. Factors that lead to an optimal glycemic control are higher education level, younger age and the CSL system used. Other factors that could influence glycemic outcomes are female sex, previous use of insulin pump and/or insulin bolus advisor and regular exercise.Partially funded by ISCIII (PI18/01118).

DOI: 10.1530/endoabs.81.EP284

EP285

Predicting the effectiveness of metformin in patients with type 2 diabetes mellitus from molecular genetic positions

Yulia Sorokina[1], Sergey Sukhanov[2], Olga Zanozina[3,4,4] & Anna Mosina[5]
[1]Privolzhsky Research Medical University, General and Clinical Pharmacology, Nizhny Novgorod, Russian Federation; [2]Privolzhsky Research Medical University, Hospinal Therapy, Nizhny Novgorod, Russian Federation; [3]Privolzhsky Research Medical University, Regional Hospital named after N.A, Semashko, endocrinology, Nizhny Novgorod, Russian Federation; [4]Privolzhsky Research Medical University, Regional Clinical Hospital named after N. A. Semashko, Endcrinology, Nizhny Novgorod, Russian Federation; [5]Privolzhsky Research Medical University, Nizhny Novgorod, Russian Federation

Purpose
to assess the possibility of predicting the effectiveness of pharmacotherapy with metformin in patients with type 2 diabetes mellitus (DM2) depending on the single nucleotide polymorphism of the nitric oxide synthase gene.
Materials and methods
186 patients were examined, referred for planned hospitalization, the duration of DM2 was 6-8 years, the target level of glycated hemoglobin was 7.5%, the actual level was 8.3%. All patients were prescribed metformin. Single nucleotide polymorphism of the gene (SNP) eNOS3 C786T (rs 2070744) was determined by real-time PSR, the level of Klotho protein was determined by ELISA, and the level of glycated hemoglobin was determined by BioRad. According to the results of the genetic study, the patients were divided into three groups: with the CC, TC and TT genotypes (SNP) eNOS3 C786T (rs 2070744).
Results
Patients with genotype CC achieved and maintained glycated hemoglobin levels below the target in 86% of cases when metformin was used at a dose of 1700 mg per day. In the same group, the Klotho protein level was significantly higher than in the other groups ($P < 0,05$).
Conclusions
The use of metformin as monotherapy at a dose of 1700 mg/day may sometimes be sufficient in the presence of the CC genotype. The patients with TC and TT genotypes need to the combined hypoglycemic pharmacotherapy at the start.

DOI: 10.1530/endoabs.81.EP285

EP286

Age-related changes in proinsulin processing in non-diabetic individuals

Markéta Vaňková, Daniela Vejražková, Petra Lukášová, Josef Včelák & Běla Bendlová
Institute of Endocrinology, Molecular Endocrinology, Praha, Czech Republic

Introduction
To understand the pathological changes associated with glucose homeostasis in old age, it is necessary to know the natural changes in the processing of proinsulin into mature insulin. Surprisingly, while there is abundant information about insulin function in diabetics, the situation in healthy adults and old humans was rarely examined.
The study aimed
To determine how the proinsulin secretion in individuals with normal glucose tolerance changes during the process of natural aging.
Methods
A total of 761 individuals (539 women, 222 men) with normal glucose tolerance were divided into groups according to age: 1) 18-30 years 355 persons, 2) 30-45 years 234 persons, 3) 45-60 years 103 persons, 4) 60-75 years 58 people, 5) 75-90 years 11 people.Basal blood glucose, proinsulin, insulin, C-peptide levels, HOMA-R, BMI and proinsulin/insulin, proinsulin/C-peptide,

proinsulin/glycemia ratios were monitored.Parameters were compared between age groups, separately for women and men. Statgraphics software (Kruskal-Wallis, Dunn's test, *P*0.05).
Results
Blood glucose levels increased with age. The age categories up to 30 and up to 45 years had the lowest levels and differed from the older groups. The older categories no longer differed. HOMA-R increased with age and matched the development of BMI in the categories. HOMA-R was highest in women in the 60-75 category and men in the 45-60 category.Basal insulin and C-peptide levels depended on gender. For women, the highest levels were in the category of 60-75 years, for men already in the category of 45-60 years. Proinsulin levels were highest in the youngest women under the age of 30, then decreased with age and the differences were no longer significant. In men, proinsulin levels did not differ with age.The proinsulin/insulin ratio was highest in both sexes under 30 years of age. The proinsulin/glycemia ratio was also highest at age 30, but only in women. The insulin/C-peptide ratio did not change with age.
Conclusion
A cross-sectional analysis of basal proinsulin secretion in normoglycemic individuals showed that its levels were surprisingly highest in the 18-30 age group, especially in young women. The proinsulin/insulin ratio was also highest in the youngest, both sexes. All people, including normoglycemic, develop insulin resistance with age. We showed a slight age-dependent increase in insulin and C-peptide secretion, the peak of which was different in men and women. However, in normoglycemic subjects, proinsulin secretion did not increase with age.AZV-NV18-01-00399, MH-CZ-DRO-(EU00023761)

DOI: 10.1530/endoabs.81.EP286

EP287

New challenge for endocrinologists–heterozygote familial hypercholesterinemia (part 1)

Ingvars Rasa[1], Ksenija Jenbajeva[2] & Alīna Anufrijeva[2]
[1]Rīga East Clinical University Hospital, Outpatient Clinic, Rīga, Latvia; [2]Rīga Stradiņš University, Faculty of Medicine, Rīga, Latvia

Background
Heterozygote familial hypercholesterolemia (HeFH) is a common genetic disorder resulting in high low–density lipoprotein–cholesterol (LDL–C) levels. It has been established that only 3% of patients (pts) among the Latvian population were diagnosed in 2019. The early HeFH diagnosis and treatment can prevent premature cardiovascular complications and save lives. Aim. The study aimed to determine the incidence of HeFH in a single-centre endocrinologist's clinical practice in Riga East Clinical University Hospital Outpatient Clinic. Methods. We collected three years of data from medical records with HeFH (ICD-10 code E78.01) from January 2019 to December 2021. Based on LDL–C, Apo B, Apolipoprotein index (Apo Index), Lipoprotein (a) (Lp (a)), and using the Dutch Lipid Clinic Network criteria; all pts were divided into two groups: group Nr.1 – definitive FH; group Nr.2 – probable FH. Statistical analysis was conducted using IBM SPSS. Results. Altogether, there were 3720 pts in an endocrinologist's practice, from which 129 (3.47%) pts were included, 39 (30.2%) males and 90 (69.8%) females. The mean age was 49.8±12.3SD years. 58 pts (45.0%) were included in the first group, and 71 pts (55.0%) were included in the second group. Only 18 pts (14%) received lipid-lowering therapy initially. The laboratory findings in the first group before the treatment were: LDL–C 4.49 mmol/l (±1.29SD); Apo B 117.52 mg/dl (±25.11SD); Apo Index 0.79 (±0.20SD); Lp (a) 82.76 mg/dl (±62.06SD). The laboratory findings in the second group before the treatment were: LDL–C 4.12 mmol/l (±0.90SD); Apo B 98.22 mg/dl (±16.51SD); Apo Index 0.64 (±0.12SD); Lp (a) 17.47 (±23.90SD). In the first group, 36 (62.1%) pts received statin therapy, 10 (17.2%) – combination therapy with statins and ezetimibe, 6 (10.3%) pts – fibrates, 1 (1.7%) pt – combination therapy with statins and fibrate, 3 (5.2%) pts refused treatment. However, in the second group, 50 (70.4%) pts received statin therapy, 10 (14.1%) pts – fibrates, 3 (4.2%) pts – combination therapy with statins and fibrates. In both groups, we found out that LDL–C, Apo B, Apo Index decreased at the end of the study ($P=0.272$ and $P=0.499$). Conclusion. Study data suggest that HeFH is much more common than generally thought. The lipid-lowering therapy decreased LDL–C, Apo B, Apo Index. Medication use reflects the extent of underdiagnosis and undertreatment of HeFH in the community and primary and secondary care.

DOI: 10.1530/endoabs.81.EP287

EP288

Surrogate measures of insulin secretion and sensitivity (IS) in young children with beta thalassemia major on repeated blood transfusion and iron chelation therapy.

Vincenzo De Sanctis[1], Shahina Daar[2], Ashraf Soliman[3], Ploutarchos Tzoulis[4], Mehran Karimi[5] & Christos Kattamis[6]
[1]Quisisana Hospital, Pediatrics, Italy; [2]College of Medicine, Sultan Qaboos University, Pediatrics, Muscat, Oman; [3]Hamad Medical Center, Pediatrics, Doha, Qatar; [4]Department of Diabetes and Endocrinology, Whittington Hospital, University College London, London, United Kingdom; [5]Hematology Research Center, Shiraz University of Medical Sciences, Hematology, Shiraz, Iran; [6]National Kapodistrian University of Athens, Greece, First Department of Paediatrics, Athens, Greece

Table 6

Baseline variables	Children with β-TM and NGT (n: 9) Group A	Children with β-TM and isolated IFG (n:9) Group B	Controls (n.9) Group C	P-value A vs. B	P-value A vs. C	P-value B vs. C
Chronological age (yrs)	5.41±0.72	5.59±1.73	5.14±0.4	NS	NS	NS
Gender (Males/Females)	4/5	6/3	5/4	-	-	-
BMI (kg/m^2)	17.5±2.9	18.1±2.7	18.1±3.1	NS	NS	NS
Serum ferritin (ng/ml)	1,867±654.9	1,848±307.0	-	NS	-	-
ALT (U/l)	117.3±92.9	74.11±46.67	-	NS	-	-
Fasting plasma glucose (mg/dl)	84.7±7.3	108.4±5.0	76.3±7.4	< **0.001**	NS	< **0.001**
Plasma glucose 2-h after OGTT (mg/dl)	105.6±13.6	107.1±18.6	86.0±12.0	NS	< **0.05**	< **0.05**
Fasting insulin (μU/ml)	8.88±1.96	10.5±2.7	3.7±2.7	NS	< **0.001**	< **0.001**
MATSUDA INDEX (MI 0-120)	6.70±2.24	6.38±2.28	17.11±6.7	NS	< **0.001**	< **0.001**
HOMA-IR	1.92±0.53	2.85±0.77	0.72±0.52	< **0.05**	< **0.001**	< **0.001**
Insulinogenic Index (IGI)	0.53±0.29	0.74±0.68	0.75±0.16	NS	NS	NS
Oral disposition Index (oDI)	3.45±2.11	4.01±3.82	12.92±5.11	NS	< **0.001**	< **0.001**

We assessed glycemia and insulin markers in 18 young children with beta thalassemia major (BTM). Insulin markers measured included: the Homeostatic Model Assessment index of insulin resistance (HOMA-IR), Matsuda index (MI), the insulinogenic index (IGI), and the oral disposition index (oDI). 9 had normal fasting glucose (FG) and 9 had impaired fasting glucose (IFG)
Results
HOMA-IR, a marker of IR was significantly higher in children with BTM compared to normal controls. Fasting insulin was significantly higher in children with BTM patients vs normal children. Despite higher fasting insulin compared to controls thalassaemic children (group A) had higher fasting glucose levels. Both findings support an insulin resistance state early in these patients. oDI was significantly lower in children with BTM (with and without IFG) compared to normal controls.
Conclusion
These findings supported the presence of significant insulin resistance in children with BTM on repeated blood transfusion and iron chelation

DOI: 10.1530/endoabs.81.EP288

EP289

Obesity in adults with type 1 diabetes mellitus and its relation to their eating habits and physical activity

Dimitra Pappa[1], Eleftheria Barmpa[1], Maria Christou[2], Ioannis Katsaras[1], Stylianos Tigas[2] & Alexandra Bargiota[1]
[1]University Hospital of Larissa, Department of Endocrinology and Metabolic Diseases, Larissa, Greece; [2]University Hospital of Ioannina, Department of Endocrinology and Metabolic Diseases, Ioannina, Greece

Introduction
Obesity is rising worldwide and the number overweight or obese patients with type 1 diabetes mellitus (T1DM) is increased and eating habits (EH) and physical activity (PA) play an important role on glycemic control and weight gain. The aim of the present study was to examine the EH and the exercise level in patients with T1DM and their relation to body weight.
Methods
126 patients with T1DM (55/126 males, 71/126 females) attending our outpatient clinics were studied. Their mean age was 34,53 ± 11,9 years and the mean diabetes duration was 18,09 ± 10,67 years. In all patients at baseline weight, height, BMI, waist circumference (WC) and glycosylated hemoglobin (HbA1c) were measured. Food consumption and EH were assessed by a standardized semi-quantitative food-frequency questionnaire. PA was assessed by the International Physical Activity Questionnaire (IPAQ). Patients were divided in two groups according to their BMI; GroupA = BMI <25 kg/m^2 and GroupB = BMI $\geqq 25$ kg/m^2
Results
The mean BMI was 25,98 ± 5,44 kg/m^2, WC 91,8 ± 12 cm and HbA1c 7,63 ± 1,63%. In GroupA 68/126 patients (53,95%) were included with a mean BMI 22,33 ± 1,90 kg/m^{2,} WC 85,41 ± 7,82 cm, age 32,5 ± 11,72 years and diabetes duration 16,92 ± 10,38 years and in GroupB 58/126 patients (46,03%) with a mean BMI 30,25 ± 5,14 kg/m^2, WC 98,30 ± 12,00 cm, age 36,91 ± 11,76 years and diabetes duration 19,46 ± 10,93 years. GroupA had a significantly lower HbA1c compared to GroupB (7,58 ± 1,77% vs 7,69 ± 1,45%, $P = 0{,}000$).Patients in GroupB had more meals per day compared to GroupA, all patients in both groups had lunch, more patients in Group B skipped breakfast compared to GroupA (17,24% and 13,23% respectively). In GroupB patients were eating out or take away more frequently than those in GroupA. Eating out or take away was related with higher consumption of 'junk type of food'. Food and meal choices in both groups were made by the patients.In GroupA 1,47% had no PA last week, 7,35% had median and 10,29% intense PA three days last week. In GroupB 12,06% had no PA last week, 8,6% had median and 5,17% intense PA three days last week.
Conclusion
Overweight and obesity is increased among patients with T1DM with almost half of them to be overweight or obese. Overweight and obese patients have more meals per day, skip breakfast, eat out or take away more frequently, exercise less and have worse glycemic control than the non-obese ones. Education and early intervention is needed to improve these outcomes.

DOI: 10.1530/endoabs.81.EP289

EP290

Glycemic changes in relation to hepatic iron status in patients with non-transfusion dependent (NTD-SCD) and transfusion dependent sickle cell disease (TD- SCD).

Ashraf Soliman[1], Mohamed Yassin[2] & Vincenzo De Sanctis[3]
[1]Hamad Medical Center, Pediatrics, Doha, Qatar; [2]Hamad Medical Center, Hematology, Doha, Qatar; [3]Quisisana Hospital, Ferrara, Italy

Introduction
We evaluated glycemia and the iron status in patients with NT-SCD and 6 patients with TD- SCD by measuring serum ferritin level (SF), liver iron content (LIC), alanine transferase (ALT) and fasting blood glucose (FBG) over 5 years of follow up.
Results
At the initial assessment, 16 adults with (age: 33 ± 14 years), and six of TD-SCD ($n = 6$, age = 25 ± 10 years) were studied. 6/16 of NT-SCD had SF $>$ 500 µg/l, and 5/16 had high LIC ($>$ 36 µmol Fe/kg dry weight). 6/16 had elevated ALT concentrations. 2/16 had impaired fasting glucose (IFG), but none had IGT or diabetes (DM). In the TD-SCD who were receiving top-up RBC transfusion to keep Hb $>$ 10 g/dl, and oral iron chelation (Exjade), all had high LIC and 14/16 had high. ALT was high in 2/6. 1/6 had IFG.Five years later, 3/16 of NTSCD had DM and 2 had IFG. Those who developed DM had had LIC = 13, 75, and 22 mmol/kg 5 years before the development of DM. The 2/16 who developed IFG had had LIC = 27 and 39 mmol/kg DW. In TDSCD, 2/6 developed DM and 1/6 had IFG. Those who developed DM had had LIC = 127 and 20 mmol/kg and normal FBG 5 years before the development of DM. The one with IFG had previously LIC = 22 mmol/kg and normal FBG 5 years back. Echocardiography revealed abnormalities of the left ventricle, dilated left atrium and dyskinesis in 5/22.FBG was correlated significantly with the age of patients ($r = 0.68$, P0.01) but did not correlate with ferritin, LIC or BMI. LIC was correlated significantly with SF ($r = 0.89$, P 0.001)

Table

(A)	Age yr	Hb g/dl	SF ng/ml	FPG mmol/l	LIC mmol/kg d.w.
NTD-SCD	33.0 ± 14*	10.1 ± 1.9	772 ± 1300	4.7 ± 0.7	1.9 ± 1.7
TD-SCD	24.8 ± 10	8.5 ± 0.8	3310 ± 3078*	4.6 ± 0.7	11.1 ± 13.3*
(B)					
NTD-SCD	38.3 ± 14*	9.5 ± 1.2	550 ± 467	6.4 ± 2.0	2.9 ± 0.4
TD-SCD	30.6 ± 10	8.9 ± 0.9	2767 ± 2925*	5.9 ± 1.1	16.1 ± 8.9*

*P: $<$0.05 NTD-SCD vs. TD-SCD

Conclusions
A significant number of our patients with ND-SCD and TDSCD develop dysglycemia (IFG, and DM) that is correlated with age but not correlated with BMI. Glycemic data and iron status in patients with NTD-SCD vs TD SCD at the beginning of the study (A) and after 5 years of follow-up (B) (mean +/- SD)

DOI: 10.1530/endoabs.81.EP290

EP291

Description of patients with diabetic foot of neuropathic and vascular cause cared for in a multidisciplinary Diabetic Foot Unit

Ana Piñar Gutiérrez, Noelia Gros-Herguido, Fernando Losada-Viñau, Fatima Farfan-Diaz, Monica Enriquez-Pérez, Carmen Ruiz-Trillo, Felipe Pareja Ciuro, Lucas Mengibar Fuentes & Alfonso Soto-Moreno
Virgen del Rocío University Hospital, Sevilla, Spain

Objective
6% of people with diabetes present with diabetic foot as a complication, which means greater morbidity and mortality compared to those who do not. Its diagnosis and management by multidisciplinary teams including surgeons can improve these patients' care. The objective was to analyze the main characteristics of patients and health results obtained, as well as to evaluate the impact of PAD (peripheral artery disease) existence in patients cared for in our multidisciplinary Diabetic Foot Unit.

Research Design and Methods
Observational prospective study. 273 patients from two different populations (with and without PAD - classified according to the presence of distal pulses-) attended in a 14-month period in the multidisciplinary Diabetic Foot Unit were included. Data on patient's characteristics and outcomes were analyzed in order to compare them. For inference study, a comparison of medians with the non-parametric test for independent samples for the quantitative variables and an X2 test for the comparison of proportions in qualitative variables were performed.
Results
$n=273$

Table

	With pulse	Without pulse
N	135	138
Male	108(80%)	95(69%)
Age*	**60(54-67)**	**64(75-81)**
HbA1c(%)	7,6(6,7-9,5)	6.9(5,6-8,05)
Type 2 Diabetes	118(87%)	128(93%)
Previous ulcers*	**71(52%)**	**37(27%)**
Hypertension*	**88(65%)**	**114(82%)**
Dyslipemia*	**78(60%)**	**107(77%)**
Smoking history	83(61%)	63(46%)
Nephropathy	47(35%)	48(35%)
Retinopathy*	**45(50%)**	**28(32%)**
Coronary disease*	**11(8%)**	**40(29%)**
Cerebrovascular disease*	**9(7%)**	**25(18%)**
Number of consultations* Hospitalization	**3(1-6)** 38(28%)	**1(1-2)** 49(35,5%)
Amputation **Major amputation***	31(23%) **2(1,4%)**	43(31%) **17(12,3%)**
Antibiotherapy* Intravenous antibiotherapy	**87(64,4%)** 38(28%)	**71(51,4%)** 44(32%)
Revascularization		28(20%)

*$p<0.05$

Conclusions
Patients with PAD are older, and presented with a greater macrovascular burden and a history of previous ulcers. However, patients with neuropathic foot presented with more microvascular complications, with similar metabolic control in both groups

DOI: 10.1530/endoabs.81.EP291

EP292

Number of gestational diabetes risk factors associates with adverse pregnancy outcomes

Catarina Chaves[1], Catarina Cidade-Rodrigues[1], Anabela Melo[1], Odete Figueiredo[1], Ana Morgado[1], M. Céu Almeida[2], Mariana Martinho[1], Margarida Almeida[1] & Filipe M Cunha[1]
[1]Centro Hospitalar do Tâmega e Sousa, Portugal; [2]Centro Hospitalar e Universitário de Coimbra - Maternidade Dr. Bissaya Barreto, Coimbra, Portugal

Introduction
There are several known risk factors for gestational diabetes mellitus (GDM), a condition associated with worse pregnancy outcomes. Once GDM is established, the association between the presence of GDM risk factors and pregnancy outcomes is less well-known. We studied the association between the number of GDM risk factors and pregnancy outcomes in a population of women with GDM.
Methods
Retrospective study of the Portuguese multicentre GDM registry from 2012 to 2017. We analysed only singleton liveborn pregnancies and excluded women with missing data on variables of interest. GDM risk factors were: first degree family history of type 2 diabetes mellitus (FHT2D), maternal age >40 years, body mass index (BMI) $\geqq 30$ kg/m^2, previous history of GDM, and previous history of a macrosomic infant. Primary endpoints were pregnancy hypertensive disease (PHD) (pregnancy-induced hypertension or preeclampsia), preterm delivery, caesarean section, birth trauma, neonatal hypoglycaemia, and neonatal macrosomia. Women were grouped by number of GDM risk factors (none, 1, 2, 3 or more) and compared. A multivariate logistic regression analysis was built. Variables included were those with different distribution between groups and those known to be associated to the outcome under analysis.
Results and Conclusions
We studied 10 677 women with a mean age of 33 ± 5 years, 529(5.0%) had >40 years, 2924(27.4%) had a BMI$\geqq 30$ kg/m^2, 4795(44.9%) had FHT2M, 1396(13.1%) had previous history of GDM, and 529(5.0%) had history of macrosomic infant. There was 3663 (34.3%) women with 0 GDM risk factors, 4309 (40.4%) with 1, 2106 (19.7%) with 2, and 599 (5.6%) with $\geqq 3$. Women with more risk factors more often gained excessive weight during pregnancy, were diagnosed in the first trimester, had higher HbA1c, and needed insulin more frequently. They more frequently had chronic hypertension, history of abortion, and were more often multiparous. The prevalence of PHD, caesarean section, and neonatal macrosomia increased with increased number of GDM risk factors. There were no differences between groups in preterm delivery, birth trauma or neonatal hypoglycaemia. After multivariate adjustment, women with 1, 2, and $\geqq 3$ risk factors had an OR (95%CI) of PHD compared to those without risk factors of 1.35(1.058-1.68), 1.76(1.37-2.26), and 1.74 (1.20-2.52), respectively. The OR for the association with caesarean section, were 1.19(1.08-1.31), 1.59(1.41-1.79), and 2.05(1.69-2.50), respectively, and for macrosomia 1.42(1.07-1.90), 2.12(1.56-2.90) and 4.58(3.18-6.60), respectively.Women with GDM with increasing number of GDM risk factors have higher risk of PHD, caesarean section, and neonatal macrosomia.

DOI: 10.1530/endoabs.81.EP292

EP293

HbA1c response after initiation of flash glucose monitoring in adults with diabetes

Antonio Moreno Tirado, Cristina Montalban Mendez, Maria Zhao Montero Benítez, Pedro Jimenez Torrecilla, Paloma González Lázaro, Florentino Del Val Zaballos, Amparo Lomas Meneses, Francisco Javier Gómez Alfonso, Maria Lopez Iglesias & Inés Gómez García
Hospital General La Mancha Centro, Alcázar de San Juan, Spain

Introduction and Objective
Flash glucose monitoring is a form of interstitial glucose monitoring and it is indicated in patients with diabetes mellitus.The objetive of the study was to assess the effect of introducing flash glucose monitoring in adults with diabetes with respect to change in hemoglobin A1c (HbA1c).
Material and methods
Prospective observational study of adults with diabetes in our center, in whom a prescription for a flash glucose monitoring sensor was collected, started between June and November 2020. Primary outcome was change in HbA1c 12 months after initiation of flash glucose monitoring. Changes in fasting blood glucose 12 months after the start of monitoring were also studied.
Results
77 subjects (55,8% men) were analysed with an average age of 47.3 ± 13 years old with diagnosis of diabetes (71,4% DM1, 26% LADA, 2,6% DM2). The average of month with diagnosis of diabetes of our subjects were 169.8 ± 10.3 months. Only 26% of subjets were well trained in the correct calculation of carbohydrate portions. We observed how the average HbA1c baseline $7.87\pm1.2\%$, and 12 after initiation of flash glucose monitoring was $7.33\pm1.2\%$, this results was statistically significant finding ($P<0,001$). Likewise, statistically significant changes in fasting blood glucose were found, baseline 168.9 ± 74.8 mg/dl and 12 months after initiation of flash glucose monitoring 140.3 ± 48.9 mg/dl. No changes were observed in either weight or insulin dose.
Conclusions
Flash monitoring is associated with significant reduction in HbA1c and fasting blood glucose in people with diabetes. Multiple causes can justify said improvement, and more studies are necessary to demonstrate the reason for these changes.

DOI: 10.1530/endoabs.81.EP293

EP294

The melatonin receptor gene polymorphism rs10830963 is not associated with significant differences in sleep patterns and biorhythms.

Daniela Vejrazkova[1], Denisa Chocholova[2], Marketa Vankova[1], Petra Lukasova[1], Josef Vcelak[1], Martin Sladek[3], Alena Sumova[3] & Bela Bendlova[1]
[1]Institute of Endocrinology, Department of Molecular Genetics, Prague, Czech Republic; [2]Faculty of Science, Charles University, Molecular Biology and Biochemistry, Prague, Czech Republic; [3]Institute of Physiology, The Czech Academy of Sciences, Biological Rhythms, Prague, Czech Republic

Introduction
Melatonin is a crucial hormone for controlling sleep rhythms and disruption of its natural secretory rhythmicity is considered to be one of the causes of type 2 diabetes mellitus. The MTNR1B gene encodes the melatonin receptor. Polymorphism rs10830963 in this gene shows an association with fasting blood glucose and impaired glucose tolerance. Current studies suggest that carriers of the minor allele G have a slightly shifted cycle of melatonin secretion toward a later rise in the evening and a slower decline in the morning, which may interact with social pressure on early morning activity and thus adversely affect glucoregulation. The aim of this study was to determine whether the polymorphism is projected into sleep patterns, biorhythms and chronotype evaluated through a questionnaire.
Methods
A total of 268 volunteers completed the MCTQ (Munich chronotype questionnaire) to determine sleep habits and chronotype. The average age did not differ significantly between the compared genotype groups. The ratio of women/men in the groups was also similar. Genotyping was performed on a TaqMan instrument (LC480, Roche), data were evaluated by NCSS/PASS 2020.
Results
Minor variant G was present in a heterozygous constellation in 124 participants (46%) and in a homozygous constellation in 26 (10%) with an allelic frequency of 33%. The remaining 118 individuals (44%) were homozygous in the common variant C. The average length of sleep on weekdays and days off did not differ between the groups, nor did the mid-sleep phase on weekdays and days off. The chronotype calculated from the mid-sleep phase values corrected for sleep debt accumulated during working days was also comparable. The time of subjective maximum daily activity was similar in all three genotype groups, with a median at 11 a.m. The social jat lag resulting from the discrepancy between the natural biorhythm and work/social duties averaged 0.85 ± 0.698 h regardless of genotype. Interestingly, while in the groups with CG and CC genotype there were about 9% of people with very low caffeine consumption, in the group of homozygous GG carriers, individuals with low caffeine requirement were completely absent.
Conclusion
In the sample of the Czech population, we did not observe significant differences in sleep patterns and chronotype between the groups formed depending on the rs10830963 SNP genotype of the MTNR1B gene.Grant support: NU20-01-00308 and MZ CZ RVO EÚ00023761

DOI: 10.1530/endoabs.81.EP294

EP295

“ Features of the angiography of the eye bottom in patients with diabetic retinopathy” “

Firuza Urmanova, Fazilyat Bakhritdinova & Guzal Kengilbaeva
Tashkent Medical Academy, Tashkent, Uzbekistan

The purpose of the study is to study the F = features of the angiography of the eye bottom in patients with diabetic retinopathy in patients with type 2 diabetes mellitus (DM2), with different stages of diabetic retinopathy (DR).
Material and research methods
252 people were examined ($n = 504$), of which 168 patients with type 2 type and 84 practically healthy persons. The main group (I; $n = 174$) with DM2, divided into subgroups, depending on the stage of DR: Easy non-proliferative DR (NDR), moderate NDR, severe NDR and PDR. As a comparison group (II; $n = 162$), patients are included without clinical manifestations of others (III; $n = 168$) - the control group was almost healthy faces without significant ophthalm and somatic pathology.All patients conducted a standard and specialized ophthalmological examination. Optical coherent tomography in the angio mode is made using an Optical Cherent Tomograph RevOFC with an angiography module with a 3×3 mm scan area. The level of VEGF in serum was evaluated by solid-phase immunoassy analysis using Quantikine ELISA sets.
Results
Analysis of the blood flow density indicates a significant decrease (P0.05) of this indicator in a subgroup of patients with a type of type 2 without DR and an average NDR on average by 3-5% compared with the control group. While with a moderate NDR - this figure is reduced by 12%, with a severe NDR - by 17%, at DA, by 19%. The area of the phases at DM 2 of the type without OB was higher than the norm by 21%, with a light NDRT 24%, with a moderate NDR - by 28%, with a heavy NDR - by 56%, with a PDR - to 62%.
Conclusions
Detected depletion of the peripheolar vascular drawing among patients without clinical signs of others.

DOI: 10.1530/endoabs.81.EP295

EP296

Impact of glucoregulation and duration of diabetes on the incidence of diabetes chronic complications in Republic of Srpska/Bosnia and Herzegovina

Snjezana Popovic Pejicic[1,2], Nina Pejicic[2] & Ljiljana Stanivuk[3]
[1]Medical Faculty, University of Banja Luka, Banja Luka, Bosnia and Herzegovina; [2]University Clinical Center of the Republic of Srpska, Banja Luka, Bosnia and Herzegovina; [3]Institute of Public Health of the Republic of Srpska, Banja Luka, Bosnia and Herzegovina

Background/Aim.
Importance of glucoreglation qality in diabetes complication prevention was proven in numerous clinical studies. Aim of this study is to determine impact of glucoregulation and duration of diabetes on the incidence of chronic complications of diabetes in Republic of Srpska (RS).
Method
Study model included subjects with T1D and T2D who participated in the two-year project in the RS. It was a cross-sectional study with 1088 participants. Specially designed questionnaire included data obtained by objective trial, clinical examination, data on antihyperglycemic treatment, and patient’s record data regarding diabetes and diabetes complications. The quality of glycoregulation was assessed based on glycosylated hemoglobin (HbA1c) values.
Results
Finally, study included 1037 subjects, 4.6% with T1D and 95.4% with T2D, 576 women (55.5%) and 461 (44.5%) men. Poor glycemic control (Hba1c $\geqq$6.5%) was found in 61.1% of subjects ($\chi^2 = 4.874$, df = 1, $P = 0.027$) and percentage of this patients increased with longer diabetes duration. Among patients with diabetes, more than 10 years’ duration, poor glucoregulation (HbA1c $\geqq$ 6.5%) was recorded in 84.6% with T1D and 76.1% with T2D; with less than 5 years’ duration was recorded in 58.30% of patients with T1D and 48.0% with T2D. The most common complication was neuroischemic foot (55.8%), statistically significantly more frequently observed in patients with HbA1c $\geqq$ 6.5% ($\chi^2 = 5.220$, df = 1); microalbuminuria (49.2%) was reported most frequently in diabetes of 5-10 years’ duration. Polyneuropathy (42,5%) and microalbuminuria were more common in T2D ($\chi^2 = 10.217$, df = 1, $P = 0.001$), while retinopathy (25,0%) was more common in T1D. Microvascular complications were statistically significantly more common in patients with unsatisfactory glycoregulation as well as longer duration of diabetes, especially in patients with T2D and disease duration over 10 years.Cardiovascular disease was recorded in 82.0% of T2D patients with HbA1c $\geqq$ 6.5% and in 82.1% of those with HbA1c $\leq$ 6.5%, with no statistically significant difference with regard to glucoregulation quality.
Conclusion
It can be concluded that 3/5 of diabetes patients in RS (61.1%) have poor glucoregulation. Microvascular complications, have higher incidence in patients with poor glucoregulation Longer T2D duration significantly increases incidence of microvascular complications, especially disease duration of 10 years or more. Cardiovascular complications are present in high percentage regardless of quality of glycemic control. These results are similar to results from developing countries and indicate the need for implementation of additional, interventional measures for improving glucoregulation and reducing chronic complications in patients with diabetes in RS.

DOI: 10.1530/endoabs.81.EP296

EP297

Cochleo-vestibular disorders in diabetic patients

Mnif Fatma[1], Asma Zargni[1], Hanene Ben Jemaa[2], Boutheina Hammami[2], Kawthar El Arbi[1], Dhoha Ben Salah[1], Mouna Elleuch[1], Nadia Charfi[1], Faten Haj Kacem Akid[1], Ilhem Charfeddine[2] & Mohamed Abid[1]
[1]Hedi Chaker Hospital, Diabetology and Endocrinology, Sfax, Tunisia; [2]Habib Bourguiba Hospital, Department of Oto-Rhino-Laryngology, Sfax, Tunisia

Introduction
Cochleovestibular disorders in patients with diabetes is not well known as compared to other complications. The aim of this study was to evaluate the epidemiological, clinical and paraclinical characteristics of cochleovestibular dysfunction in diabetes.
Materials and Methods
This is a retrospective study of 100 diabetic patients. The patients had a clinical otological and vestibular examination as well as a tonal audiometry and a video nystagmography.
Results
The mean age of our patients was 50.97 years with extremes ranging from 17 to 82 years. A female predominance was noted with a sex ratio of 0.66. The mean

duration of diabetes was 10 years with extremes ranging from 5 to 27 years. The diabetes was type 1 in 22 cases and type 2 in 78 cases. Degenerative complications were noted in 20% of cases. These included diabetic retinopathy alone in 7% of cases, diabetic neuropathy in 6% of cases and both complications in 7% of cases. Deafness was noted in 32 cases (32%). It was a sensorineural hearing loss in all cases, more important in the medium to high frequencies. The hearing impairment was more severe in type 1 diabetes. Vestibular involvement (peripheral and/or central) was present in 24 cases (31.5%). An analytical study analyzing epidemiological characteristics, metabolic control, and the presence of degenerative complications did not find statistically predictive factors for cochleovestibular involvement.
Conclusion
In our study, we did not find any predictive factor for vestibular impairment in diabetics. However, this is only preliminary data, because our study did not include non-diabetic controls.

DOI: 10.1530/endoabs.81.EP297

EP298

Precipitating factors of diabetic ketoacidosis

Nino Matas[1,1], Anja Barač Nekić[1], Antonela Čović[2], Fran Vrandečić[3], Tatjana Bačun[4], Ivan Feldi[5], Darko Kaštelan[3], Tina Dušek[3], Karin Zibar Tomšić[3] & Anela Novak[2]
[1]Ulica Doktor Roka Mišetića, Internal Medicine, Dubrovnik, Croatia; [2]Spinčićeva Ulica, Split, Croatia; [3]Kišpatićeva Ulica, Zagreb, Croatia; [4]Ul. Bana Jelačića 10, Našice, Croatia; [5]Ulica Josipa Huttlera, Osijek, Croatia

Introduction
Diabetic ketoacidosis (DKA) is one of the most serious acute complications of diabetes mellitus (DM). In some studies, infections have been shown to be a precipitating factor in half of the subjects. On the other hand, several recent studies emphasise that poor treatment adherence is also a common cause of DKA.
Objective
To identify the most common precipitating factors for DKA in the Republic of Croatia.
Patients and Methods
This retrospective, multicentre study included DM type 1 or DM type 2 patients diagnosed with DKA between January 1, 2014, and December 31, 2018, and treated in 5 different DM treatment centres: Dubrovnik, Našice, Split, Zagreb, and Osijek. Only the first episode of DKA was included in the analysis. Patients suffering from steroid DM and DM due to endocrine disorders such as acromegaly and Cushing's syndrome were excluded.
Results
The study included 160 patients (55% men), 68% of whom had DM type 1. The median age of the respondents was 42 years (18-89). The most common cause of DKA was infection (57%), followed by poorly controlled DM (37%) and first presentation of DM (10%), while in 6% of patients DKA was due to other causes such as insulin pump failure, stroke or myocardial infarction. In the group of patients with infections, urinary tract infections (30%), gastrointestinal infections (30%), and respiratory tract infections (19%) were the most common, while 21% of patients had other sources of infection. In 39% of these patients, previously poorly controlled diabetes was present along with the infection, and in 12% of them, DKA caused by the infection was the first manifestation of the disease. In patients with DM type 2, infections were more frequently the cause of DKA than in patients with DM type 1 (P 0.05). In patients with DM type 1, poorly regulated glycemia is obviously more often the cause of DKA (31.2%) than in patients with DM type 2 (17.7%).
Conclusion
The most common precipitating factors for the development of DKA are infections and poor diabetes management, likely due to lack of patient cooperation with insulin treatment and inadequate education about the use of insulin therapy in acute illness.

DOI: 10.1530/endoabs.81.EP298

EP299

Is the 2009 CKD-EPI more accurate with or without the race coefficient for black adults from outside the United States?

Carolina Zingano[1], Gustavo Monteiro Escott[1], Bruna Martins Rocha[1], Indianara Franciele Porgere[1], Candice Cristine Moro[1], Pierre Delanaye[2,3] & Sandra Pinho Silveiro[1,4]
[1]Federal University of Rio Grande do Sul, Graduate Program in Medical Sciences: Endocrinology, Porto Alegre, Brazil; [2]ULiège, Department of Nephrology-Dialysis-Transplantation, Liège, Belgium; [3]University Hospital of Nimes, Department of Nephrology-Dialysis-Apheresis, Nîmes, France; [4]Hospital de Clínicas de Porto Alegre, Endocrine Unit, Porto Alegre, Brazil

Introduction
Diabetes is the leading worldwide cause of chronic kidney disease, which is diagnosed by measuring albuminuria and estimating glomerular filtration rate (GFR) with creatinine-based formulas, such as the 2009 CKD-EPI developed in the United States of America (USA). Nonetheless, the race coefficient (RC), present in the 2009 CKD-EPI, may overestimate GFR in other countries.
Aim
The goal of this systematic review and meta-analysis was to assess the accuracy, measured by P30 (percentage of estimated results within 30% of measured GFR), of the 2009 CKD-EPI in estimating GFR with and without the RC in black adults outside the USA.
Methods
A bibliographical search of PubMed and Embase was performed and last updated on December 5th, 2021. Eligible studies included 2009 CKD-EPI P30 accuracy values with or without the RC for black adults outside the USA. Studies which used inadequate measuring methods of GFR were excluded. Our study is registered in PROSPERO (CRD42021236613) and reported according to the PRISMA-DTA guideline. The data was extracted by independent pairs of reviewers and was pooled using a random-effects model.
Results
Our systematic review included 11 studies, with a total of 1834 black adults from Africa, South America and Europe. Eliminating the RC in the 2009 CKD-EPI formula significantly increased P30 accuracy results in these populations (from 61.9% [95% CI, 53% to 70%] to 72.9% [95% CI, 66.7% to 78.3%]; $P = 0.03$).
Conclusion
Outside the USA, the 2009 CKD-EPI should not be used with the RC, even though it is not sufficiently accurate (P30 below 75%). Thus, we endorse KDIGO guidelines to use exogenous filtration markers in black patients outside the USA when a more accurate estimation of GFR may impact clinical conduct.

DOI: 10.1530/endoabs.81.EP299

EP300

A patient with aniridia and Type 1 diabetes mellitus

Dimitra Pappa, Eleftheria Barmpa, Maistros Linaras, Panagiotis Tsakos, Nikolaos Zikos & Alexandra Bargiota
University Hospital of Larissa, Department of Endocrinology and Metabolic Diseases, Larissa, Greece

Introduction
Aniridia is a rare congenital condition which is characterized by a complete or partial absence of the iris and fovea and malformations of the lens and anterior chamber. It is usually related to mutations in PAX6, a member of a multigene family of transcription factors, which is important for the development of the nervous system, the eyes and also the endocrine pancreas and it is found to be associated with mild glucose intolerance. Complete loss of insulin secretion is rarely described and here we present such a case.
Presentation
A seventeen years old male, with congenital bilateral aniridia, and no other past medical history, referred to our department due to polydipsia, polyuria, fatigue and weight loss (10 kilograms the last five months) gradually worsening. On clinical examination his BMI was 27,73 kg/m^2, blood pressure 120/70 mmHg, pulses 82/min and he was dehydrated. From his laboratory exams his blood glucose was 391 mg/dl, glycosylated hemoglobin (HbA1c) 9,5%, C-peptide 0,6 ng/ml, Glutamic acid decarboxylase antibodies (Anti-GAD) and Pancreatic Islets antibodies (Anti-ICA) were both positive. On these findings the diagnosis of type 1 diabetes mellitus (T1DM) was made and the patient was started on insulin (basal – bolus regime). His father was fifty two years old and had also congenital aniridia and type 2 diabetes mellitus treated with oral hypoglycemic agents. A genetic test for the PAX6 gene was sent and results are expected.
Conclusion
Aniridia is a rare inherited condition and is mostly related to glucose intolerance and mild diabetes, but complete loss of insulin secretion and T1DM can also be found. Patients with aniridia need a close follow up, so that any disorder of glucose metabolism be detected on time.

DOI: 10.1530/endoabs.81.EP300

EP301

Endogenous hyperinsulinism and diabetes remission : A report of 2 cases

Senda Ben Rebai, Ibtissem Ben Nacef, Sabrine Mekni, Chayma Besrour, Youssef Lakhoua, Nadia Mchirgui, Imen Rojbi & Karima Khiari
Hospital of Charles Nicole, Endocrinology Department, Tunis, Tunisia

Introduction
Diabetes is a chronic, progressive disease characterized by elevated levels of blood glucose. In type 1 diabetes, some patients experience a "honeymoon period" shortly after diagnosis, wherein insulin needs decrease significantly and a few studies have demonstrated that drug-free glycemic control can be achieved in type 2 diabetes. We describe 2 unusual cases of endogenous hyperinsulinism and diabetes remission.
Case presentation 1
A 24 year-old female who was admitted to the hospital for hypoglycemia. She was diagnosed with type 1 diabetes at the age of 17 after an episode of Diabetic Ketoacidosis. She was treated with insulin for 6 years. During the last year, she experienced recurrent episodes of hypoglycemia that have persisted regardless of the progressive withdrawal of insulin therapy with no episodes of hyperglycemia. In the first 48 hours of glycemic control in hospital care, a symptomatic hypoglycemia was documented and a blood sample showed that her plasma glucose was 62 mg/dl, insulin level was 3,3 µUI/ml and C-peptid was 1,04 ng/ml. These levels confirmed endogenous hyperinsulinism.
Case presentation 2
A 43 year-old female who was referred to our hospital for evaluation of recurrent episodes of hypoglycemia. She was discovered having diabetes mellitus at the age of 33 and treated with insulin for the last 10 years. During the last year, she continued to have frequent hypoglycemic episodes, despite repeated dose reductions and finally she stopped the insulin therapy. Two months later, her fasting plasma glucose was 2.4 mmol/l. On admission, A blood sample showed that her plasma insulin level was 24.1 µIU/ml, C-peptide was 0.43 ng/ml and cortisol was 49 nmol/l, while glucose level was 33 mg/dl. These levels were consistent with endogenous hyperinsulinism.
Conclusion
These cases highlight the possibility of diabetes remission induced by endogenous hyperinsulinism. Diabetes remission after years of insulin therapy is uncommon and it should be investigated thoroughly.

DOI: 10.1530/endoabs.81.EP301

EP302

Effects of glucagon-like peptide 1 analogue on eating behavior in patients with obesity

Oksana Logvinova & Ekaterina Troshina
Endocrinology Research Centre, Moscow, Russian Federation

Introduction
One of the objectives of weight loss in obesity is to prevent metabolic disorders. An important component in the maintenance of the achieved results is a change of eating behavior.
Goal
To study the effect of liraglutide 3.0 mg on the dynamics of metabolic parameters and eating behavior in patients with obesity.
Materials and methods
The study enrolled 42 obese patients in whom anthropometric parameters, metabolic parameters, and eating behavior were assessed with Dutch Eating Behavior Questionnaire (DEBQ). Patients were divided into 2 groups, one of which received liraglutide 3.0 mg with lifestyle modification for 3 months. The other group was recommended to receive only lifestyle modification. The participants were re-examined after 3 months.
Results of the study
In the liraglutide group in addition to a significant decrease in body weight, BMI and waist circumference, there was a statistical trend toward lower glucose, insulin and HOMA-IR levels. When comparing the dynamics of parameters between the groups, Δ body weight, BMI and glucose in the liraglutide group were significantly superior. In reassessment of eating behavior after 3 months of treatment, no statistically significant differences were found with the initial severity of restrictive, emotional, and/or external types in both groups and, despite a more pronounced decrease in body weight in the liraglutide group, between them.
Conclusions
Three months of isolated lifestyle modification and/or its combination with liraglutide 3.0 mg is not sufficient to make a lasting change in eating behavior. However, considering that obesity is a chronic and relapsing disease, the need for eating behavior correction remains relevant to prevent disease recurrence. This substantiates the need for more long-term intervention in obesity, including drug therapy.

DOI: 10.1530/endoabs.81.EP302

EP303

Prevalence of sarcopenia with different DXA indices in a population with high-risk obesity

Elena González Arnáiz, Lucía González Roza, Beatriz Ramos Bachiller, Begoña Pintor de la Maza, David Barajas-Galindo, Isidoro Cano Rodríguez & María Ballesteros-Pomar
Complejo Asistencial Universitario de León, Endocrinology and Nutrition, León, Spain

Background
Sarcopenic obesity(SO) is an entity characterized by excess fat mass(FM) and low muscle mass (LMM) and function. Excess FM itself can lead to loss of muscle

Diagnosis	Variables	Cut-off point	Female ($n = 89$)	Male ($n = 35$)	Total ($n = 124$)
Low muscle function	HGS	Female <16 kg.Male <27 kg	13.5% ($n = 12$)	17.1% ($n = 6$)	14.5% ($n = 18$)
	ASM	Female <15 kg.Male <20 kg	6.7% ($n = 6$)	2.9%($n = 1$)	5.6% ($n = 7$)
	ASMI	Female <5.5 kg/m^2.Male <7 kg/m^2	0%	5.7% ($n = 2$)	1.6% ($n = 2$)
	TSMI	Female <6 kg/m^2.Male <9 kg/m^2	0%	2.9% ($n = 1$)	0.8%($n = 1$)
LLM	LESMI	Female <3.7 kg/m^2, Male <5.1 kg/m^2	0%	5.7% ($n = 2$)	1.6% ($n = 2$)
	ALMI	Female <5.45 kg/m^2.Male <7.26 kg/m^2	0%	2.9% ($n = 1$)	0.8% ($n = 1$)
	SMI	Female $<23.5\%$. Male $<29.9\%$	100%($n = 89$)	100%($n = 35$)	100%($n = 124$)
	ALM/W	Female $<19.4\%$. Male $<25.7\%$	83.1($n = 74$)	97.1%($n = 34$)	87.1%($n = 108$)
Low physical performance	TUG >10 seconds $\rightarrow$ Falling risk 31.4%($n = 11$) 24.2%($n = 30$)	21.4%($n = 19$)			
Severity	Low hand grip strength + Low physical performance	4.5%($n = 4$)	11.4%($n = 4$)	6.5%($n = 8$)	

mass and function at any age. The combination of obesity and sarcopenia is a proven risk factor for frailty, comorbidities and mortality. New diagnostic criteria have been developed for this entity.
Aims
To assess the prevalence and severity of SO with different indices by DXA, in a group of individuals with high-risk obesity(HRO).
Methods
Prospective observational study of individuals with HRO(BMI > 35 kg/m^2) under follow-up by the obesity unit of the Complejo Asistencial Universitario de León. We collected demographic and anthropometric variables, body composition by dual energy X-ray absorptiometry(DXA, A Lunar Idxa; GE Healthcare, USA), hand grip strength(HGS) (Dynex®,DynExgrip) and physical performance with the timed up and go test(TUG). For the diagnosis of LMM with DXA, the equations appendicular skeletal muscle mass (ASM;lean mass arms and legs–bone mass arms and legs), appendicular skeletal muscle mass index (ASMI;ASM/height^2), total skeletal mass index (TSMI; TSM/height^2, TSM:ASMx1.33), lower extremity skeletal muscle mass index (LESMI;LESM/-height^2,LESM: lean mass legs–bone mass legs), appendicular lean mass index (ALMI;ALM/height^2,ALM: lean mass arms + lean mass legs), skeletal muscle mass index (SMI;(ASM/weight) × 100) and appendicular lean mass/weight (ALM/W;(ALM/weight) × 100) were used.
Results
124 subjects were included, 71.8% women, mean age 42.6 (SD 9.0) years, mean BMI 46(SD 5.2 kg/m^2). The cut-off points and percentage of patients diagnosed with low strength, muscle mass and low physical performance are shown in the table below.
Conclusions
The prevalence of low muscle mass with DXA varies according to the parameter and setting used. The adjustment of DXA-derived parameters for muscle mass, should be made according to the investigated cohort in terms of ethnicity, BMI, sex and age range. In this population, if we take into account the two criteria; muscle mass (with SMI) and muscle function (HGS), 13% of women and 17% of men will have sarcopenia, 4.5% and 11.4% severe sarcopenia respectively.

DOI: 10.1530/endoabs.81.EP303

EP304

Empagliflozin and arterial stiffness in type 2 diabetic patients: a real clinical practice case-control study

Francesco Tassone[1], Cinzia Ferreri[2], Arianna Rossi[2], Claudia Baffoni[1], Giorgio Borretta[1] & Mauro Feola[2]
[1]A.S.O. Santa Croce & Carle di Cuneo, Division of Endocrinology, Diabetes & Metabolism, Cuneo, Italy; [2]Ospedale Regina Montis Regalis Mondovì, Division of Cardiology, Mondovì, Italy

Background
Sodium-glucose cotransporter-2 (SGLT2) inhibitors demonstrated beneficial effects on cardiovascular and renal events in patients with type 2 diabetes mellitus. The mechanisms underlying these effects are not fully elucidated. Aim of this study was to investigate whether empagliflozin is able to affect arterial stiffness/pulse wave velocity in type 2 diabetic patients.
Methods
Pulse wave velocity and other parameters of arterial stiffness were assessed before and after a 3-month treatment with empagliflozin in 16 consecutive T2DM outpatients; data were compared with 16 T2DM outpatients not treated with SGLT2 inhibitors.
Results
The sex of the patients and the duration of diabetes mellitus did not differ between groups. However age was significantly higher in the empagliflozin group at baseline compared to controls (64.1 ± 8.68 vs 74.45 ± 8.13, $P < 0.05$). Empagliflozin treatment significantly decreased HbA1c after 12 weeks of treatment (7.9 ± 0.78 vs 7.04 ± 1.09% , $P < 0.008$.). After 12 weeks' treatment, empagliflozin significantly improved PWV compared to controls not treated with SGLT2-i (ΔPWVV -0.68 ± 1.1 vs 0.89 ± 1,6 p < 0.004, $P = 0.0065$ with age and HbA1c as covariates). Moreover body weight significantly decreased in the empagliflozin group (86.75 ± 16.16 vs 81.71 ± 16.5 kg, p = 0.001) compared to controls (in whom remained unchanged) as long as BMI (30.48 ± 5.4 versus 28.75 ± 5.66 kg/m^2, $P < 0.002$) compared to controls (in whom remained unchanged). Estimated glomerular filtration rate (eGFR) remained unchanged in the two groups during the study whereas urine Albumin to Creatinine ratio significantly improved with empagliflozin (17.8 ± 46.8 vs 12.2 ± 35.7 mg/mmol, $P = 0.049$).
Discussion
In this 'real clinical practice' study the potential effect of empagliflozin treatment on arterial function in T2DM patients was extensively investigated. Arterial stiffness was significantly decreased in the group treated with the empagliflozin and the difference was significant compared to the control group. Significantly improvement in urine Albumin to Creatinine ratio suggest an improvement of endothelial function in these patients that could be involved in reducing arterial stiffness.

DOI: 10.1530/endoabs.81.EP304

EP305

Association of single nucleotide polymorphisms (SNPs) of the intestinal fatty acid-binding protein (FABP2) gene with peripheral atherosclerosis in patients with type 2 diabetes mellitus.

Sergey Sukhanov, Yulia Sorokina, Olga Zanozina & Veronika Lagonskaya
Privolzhsky Research Medical University, Hospital Therapy, Nizhny Novgorod, Russian Federation

Relevance
There is a search for candidate genes that contribute to the progression of atherosclerosis in patients with diabetes mellitus. It has been suggested that the FABP2 Ala54Thr polymorphism may be associated with the risk of atherosclerosis.
Objective
To evaluate the relationship between polymorphism of the intestinal fatty acid-binding protein (FABP2) gene Ala54Thr with peripheral atherosclerosis in patients with type 2 diabetes mellitus.
Materials and methods
We examined 40 patients with type 2 diabetes, who were in the endocrinology department of the Regional Clinical Hospital. N. A. Semashko in September-November 2021 The duration of diabetes mellitus is from 2 to 18 years, glycated hemoglobin is 8.1 ± 0.93%. The patients' age ranged from 43 to 76 years old.. All patients had grade 1-2 obesity, dyslipidemia, 36 patients were diagnosed with arterial hypertension. Patients had micro and macrovascular complications of diabetes mellitus of varying severity. Glycemic indicators (HbA1c, glycemic fluctuations using FreeStyle monitoring), lipid profile, body mass index (BMI), systolic and diastolic blood pressure (SBP and DBP) were determined, ultrasound examination of the vessels of the lower extremities and the brain was performed. Molecular genetic study was carried out on the basis of the Regional Clinical Hospital named after N. A. Semashko. We saw FABP2 (rs1799883) Ala54Thr. DNA samples isolated from whole blood leukocytes using the DNA-Express-Blood-Plus reagent kit were used for analysis, followed by analysis of the isolated DNA by polymerase chain reaction (PCR) on a CFX-96 amplifier (Bio-Rad, USA). Used reagent kits (Litekh, Moscow) in accordance with the instructions
Results
A positive association of Ala54Thr with body mass index, blood pressure level was revealed. In 50% of cases, patients were diagnosed with GG SNP (Ala/Ala), in 28% of cases - GA SNP (Ala/Thr), in 22% - AA SNP (Thr/Thr). Indicators of glycemic control, levels of triglycerides and low density lipoproteins were significantly higher in patients with the AA (Thr/Thr) group. In the same group, a lower ankle-brachial index was noted ($P = 0.04$).
Conclusions
AA SNP genotype (Thr/Thr) is associated with an increased incidence of peripheral atherosclerosis in patients with type 2 diabetes.

DOI: 10.1530/endoabs.81.EP305

EP306

Retrospective analysis of association between coronary artery disease and Glycemic Control in South Indian T2DM population

Mahadevan V
Stanley Medical College & Jayam Diabetes & Heart Specialty Clinic, Department of Endocrinology, Chennai, India

Background
Type 2 diabetes mellitus (T2DM) is independently associated with an increased risk for cardiovascular disease caused mainly by early development of vascular changes leading to atherosclerosis. Coronary artery disease (CAD) is one of the common complications However, the exact correlation between glycemic control and the risk of developing CAD remains unclear. This study sought to assess the correlation of glycemic control and risk of developing CAD in South Indian population.
Methods
This retrospective analysis was conducted amongst 1888 patients with type 2 diabetes who visited a diabetes and cardiology care center in Tamil Nadu, India between January 2017 and December 2021. This study assessed glycemic and cardiometabolic parameters including HbA1c, blood pressure, lipid levels, electrocardiogram, and ECHO reports. The statistical analysis was conducted using SPSS software and Chi-square test was used.

Results
The average age in the patient data analyzed was 62 years with an average duration of diabetes of 8.6 years. About 69% of the patients were male, while 31% were female. Among the analyzed patient cohort, 26% went on to be diagnosed with CAD within 24 months of their first visit. The average HbA1C at the time of diagnosis of T2DM was 8.3%, while that at the time of diagnosis of CAD was 9.2%. A positive correlation was found between poor glycemic control and the diagnosis of CAD within 24 months of the visit ($P < 0.01$). The mean blood pressure at the time of diagnosis of T2DM was 130/82 mm of Hg, while that at the time of diagnosis was 152/91 mm of Hg. Echo-cardiography revealed 38.9% had mild LV dysfunction, 16.29% had moderate LV dysfunction and 4% had severe LV dysfunction. Upon analyzing, it was found that 48% of the 491 diagnosed with CAD had triple vessel disease, while 31% had double vessel disease and 5% had total occlusion of coronary artery. The overall mortality in patients diagnosed with CAD was 2% at the time of reporting.
Conclusions
This analysis demonstrated a positive correlation between poor glycemic control and diagnosis of CAD. Tight glycemic control has the potential to prevent progression of cardiovascular disease among people with T2DM.

DOI: 10.1530/endoabs.81.EP306

EP307

Predictive factors for distal and symmetric polyneuropathy in diabetic patients

Mouna Elleuch, Maalej Souhir, Hsine Houda, Dhoha Ben Salah, Hamdi Frikha , Faten Haj Kacem Akid & Mohamed Abid
CHU Hedi Chaker, Endocrinology, Sfax, Tunisia

Introduction
Diabetic neuropathy is the most common cause of neuropathy worldwide and is known to affect approximately half of all diabetic patients. It significantly impairs the quality of life of patients.
Aim of the study
To establish the predictive factors of distal symmetric polyneuropathy (DSPN) in diabetic patients.
Methods
This is a descriptive cross-sectional study including 116 patients. The diagnosis of PNDS was established according to the MNSI (Michigan Neuropathy Screening Instrument) and DN4 (Neuropathic Pain Diagnostic Questionnaire) scores. We divided the patients into two groups: group one (G1) patients with DSPN (N = 67) and group two (G2) without DSPN (N = 49). Then, using SPSS software, we were able to perform a multivariate study on independent predictive factors of DSPN as well as a univariate study of factors associated with this complication.
Results
Among the sociodemographic factors, only age was predictive of DPN with $P = 0.005$ (mean age: G1 = 64.85 +/- 12.56 years versus 58.27 +/- 11.88 years for G2). The analysis of the history showed that: nephropathy ($P = 0.002$), retinopathy ($P < 0.001$), myocardial infarction ($P = 0.037$), stroke ($P = 0.020$), hypertension ($P < 0.001$) and dyslipidemia ($P = 0.006$) were associated with DSPN. Symmetrical and peripheral polyneuropathy was found in 64 subjects with a diabetes duration of more than 5 years ($P = 0.015$), in 57 with unbalanced diabetes ($P = 0.024$) and in 34 with a history of hospitalization ($P < 0.001$). Regarding treatments, biguanides ($P = 0.001$), sulfonamides ($P = 0.01$) and insulin ($P < 0.001$) were associated with symmetric and peripheral polyneuropathy. Comparison between the two groups according to biological data showed a significant difference in creatinemia ($P = 0.011$), blood glucose ($P = 0.030$) and a significant increase in HbA1c in the neuropathy group with $P = 0.001$. On multivariate analysis, the independent predictors of DSPN were retinopathy and hypertension.
Conclusion
Age, nephropathy, retinopathy, history of myocardial infarction and stroke, and the presence of other cardiovascular risk factors such as dyslipidemia and hypertension, as well as the length of time the patient has had diabetes, are the main predictive factors for distal and symmetrical polyneuropathy in patients living with diabetes.

DOI: 10.1530/endoabs.81.EP307

EP308

Depression associated factors among Tunisian diabetic patients

Malak Belkhiri[1], Boubaker Fadia[1], Ashraf Khemiri[1], Walid Bouali[2], Houcem Mrabet[1], Alaya Wafa[1], Zantour Baha[1], Sfar Mohamed Habib[1] & Lazhar Zarrouk[2]
[1]Taher Sfar University Hospital, Internal Medicine and Endocrinology Department, Tunisia; [2]Taher Sfar University Hospital, Psychiatry, Tunisia

Introduction
Diabetes mellitus and depression are two major public health problems which can coexist and influence each other. Identification of the predictive and associated factors with depression among diabetics can facilitate the task of clinicians.
Objective
Evaluate the socio-demographic and clinical factors associated with depression among patients having diabetes mellitus (DM).
Materials and methods
A cross sectional study was conducted among 260 diabetic patients followed in the Endocrinology Department at "Taher Sfar University Hospital" in Mahdia, Tunisia. Patients with a psychiatric history were excluded at the outset. Depression was diagnosed according to DSM-V criteria and the severity determined via the Hamilton score scale.
Results
Our patients were aged between 20 and 91 years old, 62.7% of the participants in the study were women. The mean duration of the diabetic disease was of 9 years (from 1 to 50 years). Type 2 diabetes was found among 92.3% of patients. According to DSM-V diagnosis criteria, we found that 15% of our patients suffered from Major Depressive disorder (MDD). Among this group having MDD, 71.8% were female, 31% belonged to the age group 35-45 years and 53.84% were married. Matrimonial status wasn't significantly linked to MDD but correlated with the severity of depression ($P = 0.048$).We also found that the majority of patients with MDD (84.6%), had at least one chronic disease in addition to diabetes and that a good proportion of them (69%) was treated with insulin. Both MDD and severity of depression were significatally linked to chronic complications of DM ($p \leq 0.001$ for both). Distal neuropathy was present among 39% of patients and this complication had a significant relationship with depression ($P = 0.025$).
Conclusion
Our study showed that diabetic patients suffering from MDD are mostly women but since proportion of women was most important in our study, these results should be evaluated. The relationship between depressive symptoms and insulin therapy can be explained by the arduousness of the injections and the increased risk of hypoglycemia causing depressive symptoms in one hand, and in the other by the failure to reach glycemic targets via other medications among depressive patients having poor treatment compliance.The risk of depression seems to be increased in diabetic patients suffering from chronic diabetic complications and screening for depression would be necessary in this case. Other studies should be conducted to determine if early screening of depression could delay insulin therapy or help prevent diabetes complications.

DOI: 10.1530/endoabs.81.EP308

EP309

Prevalence and risk factors of diabetic painful distal symmetrical polyneuropathy

Dhoha Ben Salah[1], Mariem Abdelmoula[2], Yosra Mejdoub[3], Nouha Ketata[2], Mouna Elleuch[1], Fatma Mnif[1], Nadia Charfi[1], Mouna Mnif[1], Nabila Rekik Majdoub[1], Faten Haj Kacem Akid[1] & Mohamed Abid[1]
[1]Hedi Chaker Hospital, Department of Endocrinology, Sfax, Tunisia; [2]Hedi Chaker Hospital, Department of Family Medicine, Sfax, Tunisia; [3]Hedi Chaker Hospital, Department of Epidemiology, Sfax, Tunisia

Introduction
Distal and symmetrical peripheral polyneuropathy is the most frequent type of diabetic neuropathy. Its painful form (PDN) is the most common cause of non-traumatic neuropathic pain and can place a heavy burden on patients' lives. Despite the major impact that it can have on the quality of life, PDN is generally underdiagnosed because of a large interindividual variability of symptoms and in the absence of well-established diagnostic criteria.
Aim
To determine the prevalence of PDN and to identify the different risk factors of its occurrence within Tunisian diabetic patients.
Methods
This was a cross-sectional study conducted in the endocrinology-diabetology department of Hedi Chaker hospital Sfax Tunisia, in which we collected adults with diabetes. The DN4 Questionnaire was used to diagnose PDN.
Results
A total of 185 patients were recruited. The mean age of patients was 54.9 years with a slight female predominance (54.1% Vs 45.9%). Patients with type 2 diabetes represented 82.7% against 17.3% with type 1 diabetes. The mean duration of diabetes' evolution was 12.31 years. The average of HbA1c level was 10.27%. Among diabetes' complications, PDN was the most frequent in our study (48.1%). The mean DN4 score was 3.57. Significant predictors of PDN included advanced age ($P = 0.004$), high waist circumference ($P = 0.01$), long history of diabetes ($P = 0.000017$), insulin therapy in patients with type 2 diabetes ($P =$

0.03), in addition to some comorbidities such as dyslipidemia, sedentary life style, diabetic retinopathy, erectile dysfunction and history of leg ulcer. Some features of foot examination were also found to be risk factors of PDN namely trophic disorders ($P = 0.02$), dry skin ($P = 0.00016$), hyperkeratosis ($P < 0.001$), foot deformity ($P = 0.004$), abolition of patellar and Achilles reflexes ($P < 0.001$) and positive monofilament test ($P < 0.001$)

Conclusion

In conclusion, the present study demonstrated that the prevalence of painful diabetic neuropathy is very high among our population. This emphasizes the need to screen periodically diabetic patients using a simple instrument such as the DN4 questionnaire and to educate regularly at risk patients about predictors of PDN.

DOI: 10.1530/endoabs.81.EP309

EP310

Obesity and abdominal adiposity are associated with lower urinary tract symptoms in Tunisian patients with type 2 diabetes : a cross-sectional study

Faten Haj Kacem Akid[1], Abdelmouhaymen Missaoui[1], Mariem Belhoul[2], Wafa Belabed[1], Dhoha Ben Salah[1], Mnif Fatma[1], Nabila Rekik Majdoub[1], Mouna Elleuch[1] & Mohamed Abid[1]

[1]Hedi Chaker University Hospital, Endocrinology Departement, Sfax, Tunisia; [2]Faculty of Medicine of Sfax, Departement of Family Medicine, Sfax, Tunisia

Background and Aims

Lower urinary tract (LUT) dysfunctions are highly prevalent, especially in women. Diabetes is a well-established risk factor for developing LUT symptoms. Several studies suggest that a high body mass index (BMI) may worsen the urinary discomfort in patients with type 2 diabetes (T2DM). The current survey aims to investigate the relationship between obesity and LUT dysfunctions in patients with T2DM.

Patients and Method

We conducted a descriptive and analytical cross-sectional study that included 200 patients with T2DM consulting at the Endocrinology Department of Hedi Chaker University Hospital, Sfax, Tunisia, from April 2019 to December 2019. We administrated the Urinary Symptom Profile (USP) questionnaire to all patients to assess LUT symptoms.

Results

The mean age was 59.3 $\pm$ 10.6 years, with a female predominance (55.5%). Dyslipidemia (57%) and hypertension (49.7%) were the most common comorbidities. The duration of the evolution of diabetes was 11.0 $\pm$ 7.9 years. Oral antidiabetic agents (OAD) and insulin therapy were prescribed in 40% and 13.6%, respectively. Most of the patients were receiving a mixed insulin-OAD treatment (44.2%). A glycemic imbalance was noted in 79.7%. As high as 79.5% of patients with T2DM reported symptoms related to LUT dysfunctions.We compared the body composition in two subgroups

- G1 : patients with LUT dysfunction ($n = 159$).
- G2: patients without LUT dysfunction ($n = 41$).

The mean weight in G1 was significantly more elevated than in G2 (77.5 $\pm$ 13.8 versus 70.3 $\pm$ 11.1 kg; $P = 0.003$). Similarly, G1 displayed a substantially higher BMI than G2 (29.2 $\pm$ 5.8 versus 26.4 $\pm$ 4.2 kg/m^2; $P = 0.03$). The prevalence of obesity (BMI$>$30) was significantly higher in G1 (34.0%) compared to G2 (14.6%) ($P = 0.016$). Abdominal adiposity with significantly associated with LUT symptoms, since the average waist circumference was higher in G1 in comparison with G2 (103.5 versus 95.7 cm; $P = 0.01$).

Conclusion

Diabetes and the female gender are largely linked to the onset of LUT dysfunctions in the general population. Our work highlights an additional risk of urinary dysfunction due to weight gain, high BMI, and visceral adiposity in patients with T2DM. Increasing weight is associated with urinary incontinence and other LUT symptoms, most likely because of elevated pressure on the bladder and straining the muscles that support the urethra. These mechanisms, along with hyperglycemia-related osmotic polyuria and diabetic neuropathy are responsible for a greater prevalence and worsened quality of life in this population.

DOI: 10.1530/endoabs.81.EP310

EP311

Difference of serum glucose, sodium and potassium levels in diabetic ketoacidosis

Tatjana Bačun[1,2], Željka Dragila[1], Klara Čosić[1], Dora Rudić[1], Ivan Lekić[1], Krešimir Solić[1,3] & Sran Čaloševič[4]

[1]Faculty of Medicine, Osijek, Croatia;[2]University Hospital Centre Osijek, Division of Endocrinology, Department of Internal Medicine, Osijek, Croatia; [3]Faculty of Electrical Engineering, Computer Science and Information Technology Osijek, Osijek, Croatia; [4]Emergency Medical Center of the Osijek - Baranja County, Osijek, Croatia

Background and aims

Diabetic ketoacidosis is acute complication of diabetes mellitus. Hyperglycemia is one of the diagnostic features of diabetic ketoacidosis. Electrolyte disturbances are common as well. Aim of this study is to examine whether there is a difference in serum glucose, sodium and potassium concentrations with respect to age, gender and severity of diabetic ketoacidosis.

Materials and Methods

Medical records from 1 January 2017 to 31 December 2019 were reviewed and patients with the diagnosis of diabetic ketoacidosis were selected.

Results

The study included 52 patients. Most patients belonged to the younger age group (18-24 years, 37.3%), there were more women (54.9%) and moderate diabetic ketoacidosis dominated (66.7%). The average glucose concentration was 27.10 mmol/l (median). Glucose concentration was significantly higher in the age group of 25 to 44 years and $>$ 65 years compared to the group of 18 to 24 years ($P = 0.02$). No difference in glucose concentration was found with respect to gender. The average sodium concentration was 130.00 mmol/l (median). Sodium concentration was significantly higher in the age group 18 to 24 years and $>$ 65 years compared to groups 25 to 44 and 45 to 65 years ($P = 0.002$). The average potassium concentration was 4.80 mmol/l (median). Women had significantly higher sodium concentrations ($P = 0,002$). Potassium concentration was significantly higher in the age group 25 to 44 years compared to other groups ($P = 0.01$). Men had significantly higher potassium concentrations ($P = 0.01$). The mean pH concentration was 7.19 (median). There was no association of pH levels with regards to age and gender. No significant relationship was found between glucose, sodium and potassium concentrations with regard to severity of diabetic ketoacidosis.

Conclusion

Diabetic ketoacidosis was most common in the age group 18 to 24 years and in women and was most often of moderate severity. The highest average concentrations of glucose and sodium were found in those older than 65 years, whereas potassium was high in the group 25 to 44 years. Women had significantly higher sodium concentration, while men had significantly higher potassium concentration. The severity of diabetic ketoacidosis was not related to glucose, sodium and potassium concentration.

Key words

diabetic ketoacidosis, glucose, sodium, potassium, diabetes mellitus

DOI: 10.1530/endoabs.81.EP311

EP312

Clinical characteristics and glycemic control in Tunisian patients with type 2 diabetes suffering from lower urinary tract dysfunctions: a comparative population-based survey

Faten Haj Kacem Akid[1], Abdelmouhaymen Missaoui[1], Mariem Behoul[2], Mohamed Abdellahi Mohamed Ahmed[1], Wafa Belabed[1], Dhoha Ben Salah[1], Mnif Fatma[1], Nabila Rekik Majdoub[1], Mouna Elleuch[1] & Mohamed Abid[1]

[1]Hedi Chaker University Hospital, Endocrinology Departement, Sfax, Tunisia; [2]Faculty of Medicine of Sfax, Departement of Family Medicine, Sfax, Tunisia

Background and Aims

Several studies have pointed a significant relationship between diabetic complications, glycemic imbalance, and the onset of lower urinary tract dysfunction (LUTD) in this population. The current survey aims to assess the clinical and biochemical characteristics related to glycemic control in patients with type 2 diabetes presenting with symptoms of LUTD.

Patients and Method

We conducted a comparative cross-sectional study that included 200 patients with T2DM consulting at the Endocrinology Department of Hedi Chaker University Hospital, Sfax, Tunisia, from April 2019 to December 2019. We administrated the Urinary Symptom Profile (USP) questionnaire to all patients to assess LUT symptoms. We compared the clinical and biological factors related to diabetes in two subgroups.

- G1 : patients with LUTD ($n = 159$).
- G2: patients without LUTD ($n = 41$)

Results

The mean age was similar between the two subgroups (G1:59.7$\pm$ 10.3 versus G2:58.0 $\pm$ 11.8 years old; $P = 0.36$). A slight female predominance was noted in

G2 (G1:52.0% versus G2:63.4%; $P = 0.16$). The mean duration of T2DM was significantly longer in G1 (G1:11.9 versus G2: 7.7 years; $P = 0.03$). Insulin-requiring diabetes was substantially more associated with LUTD as insulin therapy was more prescribed for G1 (G1:62.0% versus G2: 42.5%; $P = 0.025$). Unlike diabetic retinopathy ($P = 0.07$), diabetic nephropathy ($P = 0.021$) and nephropathy ($P = 0.000$) were strongly associated with the onset of LUTD. Diabetic macroangiopathy did not seem to be linked to this urinary disorder. A significant glycemic imbalance was noted in G1 with more elevated fasting plasma glucose (G1:10.7$\pm$ 4.4 versus G2:7.5 $\pm$ 1.2 mmol/l; $P = 0.000$) and higher A1C (G1:9.5$\pm$ 2.3% versus G2:8.1 $\pm$ 2.4%; $P = 0.000$). Multivariable regression analysis identified duration of evolution of diabetes (OR=1.1 ; 95%CI [1.0-1.2] ; $P = 0.033$), diabetic neuropathy (OR=6.4 ; 95%CI [2.4-17.3] ; $P = 0.000$), and A1C>7% (OR=0.4 ; 95%CI [0.2-0.6] ; $P = 0.045$) as significant risk factors implicated in the onset of LUTD.

Conclusion

Glycemic imbalance, diabetic microangiopathy, and diabetic neuropathy were found to be significant baseline characteristics associated with the onset of LUTD in the diabetic population. Glycemic control and therapeutic patient education are the most efficient preventive measures to reduce the incidence of LUTD in patients with T2DM. A multidisciplinary approach including a team of diabetologists, urologists, and physiatrists may ensure well-coordinated management of patients presenting with LUTD.

DOI: 10.1530/endoabs.81.EP312

EP313

Comparison of admissions for diabetic ketoacidosis in patients older and younger than 25 years of age at San Cecilio Clinical University Hospital in Granada

Javier García, Enrique Redondo , María Del Carmen Andreo-Lopez , Sara León Utrero & Pablo J López-Ibarra Lozano
San Cecilio Clinical University Hospital, Endocrinology and Nutrition, Granada, Spain

Introduction and objectives

Diabetic ketoacidosis (DKA) is a severe acute complication of Diabetes Mellitus (DM) and as such, on a large number of occasions will require hospital admission. As we know, it happens when there is an absolute or relative insulin deficit, although it is true that the characteristics described in the literature of these episodes are very different. Our aim was to compare the characteristics of DKA occurring in patients under 25 years of age with those of patients over 25 years of age in our setting.

Material and Methods

Retrospective observational study comparing patients older than 25 years with DM admitted for DKA at San Cecilio Clinical University Hospital in Granada, Spain with those aged 16-24 years from January 1, 2019 to December 31, 2021. Variables related to the disease (type of DM, time of evolution, associated complications...) and to the episode of DKA (precipitating factor, hospital admission time, ICU stay...) were analyzed. Analyses were carried out with SPSS 15.0.

Results

We included 39 patients older than 25 years and 22 younger than 25 years (49% women in both groups). The time of evolution of DM was significantly shorter in patients younger than 25 years (10.86 vs 19.69 years, $P < 0.05$). As comorbidities, 40.5% of those older than 25 years had alterations in the psychiatric sphere (vs 14.3% of the other group, $P < 0.05$). Regarding previous treatment, those older than 25 years had significantly lower total slow insulin doses (22.48 vs 30.71 IU, $P < 0.05$). There were no significant differences in terms of need for ICU stay (59% in both groups). The most important precipitating factors in both groups were: treatment omission, dietary transgressions and concomitant infections. Metabolic control in terms of HbA1c was worse in the group under 25 years of age (11.74 vs 10.54%, $P < 0.05$). No significant differences were observed in analytical parameters (blood glucose, pH, HCO3 and lactic acid) at admission.

Conclusions

In our work, it was observed that admissions for DKA in our center were more frequent in patients older than 25 years, as well as that these present worse metabolic control in terms of HbA1c and higher insulin needs. On the other hand, there is a tendency for the majority of DKA episodes in patients over 25 years of age to be associated with infections, while the main risk factor in younger patients is the omission of treatment.

DOI: 10.1530/endoabs.81.EP313

EP314

Gestational diabetes mellitus : Association between maternal insulin resistance with pregnacy outcomes and maternal characteristics

Olfa Lajili, Aroua Temessek, Rim Rachdi, Yosra Htira & Feika Ben Mami
National Institute of Nutrition of Tunis, The Research Unit of GDM (Department C), Tunisia

Introduction

Gestational diabetes mellitus (GDM) is the most common metabolic disturbance during pregnancy. The prevalence of GDM is rising and correlates with the increase in maternal obesity over recent decades. The aim of our study was to assess the association between maternal insulin resistance with pregnacy outcomes and maternal characteristics among tunisians women with GDM.

Methods

A prospective longitudinal study carried out during the year 2020 at the research unit of GDM of Department C at the National Institute of nutrition of Tunis. The study was conducted among 135 women diagnosed with GDM with 75 g oral glucose tolerance test (OGTT 75) between 24–28 weeks. Insulin resistance was evaluated using the homeostasis model assessment of insulin resistance (HOMA-IR). Patients are followed during pregnancy and until post partum. Statistical analyses were performed using SPSS 20.

Results

The mean age was 32.3 $\pm$ 5.3 years. The mean pre-gestational BMI was 28.31 $\pm$ 4.9 kg/m^2. Two thirds of the patients (72.4%) were overweight and 29.9% were obese. The means of fasting blood glucose and the number of abnormal glycemia values at time of OGTT 75 were respectively 0.96 $\pm$ 0.11 g/l and 1.45 $\pm$ 0.63. The means of fasting blood glucose, HbA1c and total cholesterol were 4.85 $\pm$ 0.69 mmol/l, 5.32 $\pm$0.43% and 5.87 1.25 mmol/l. One third of patients (36.3%) were diagnosed before 24 gestational weeks. The mean HOMA-IR was 3.18 $\pm$ 1.7 and 55.3% of women had insulin resistance. Macrosomia and pregnancy induced-hypertension were noted in 15.8% and 3.8% of cases. The univariable analysis showed an association between the HOMA-IR and the pre-gestational BMI, fasting blood glucose and the number of abnormal glycemia values at the time of OGTT 75, levels of HbA1c, fasting glucose value, C-peptide and total cholesterol and also with an earlier diagnosis of GDM before 24 gestational weeks (respectively $P < 0.01$, $P < 0.01$, $P = 0.004$, $P < 0.01$, $P < 0.01$, $P < 0.01$, $P = 0.049$ and $P = 0.019$). however, there was no association between the HOMA-IR and pregnacy outcomes.

Conclusion

Our study showed that The HOMA-IR was associated with advanced maternal age, higher pre-gestational BMI, higher fasting blood glucose, HbA1c, and C-peptide levels. Women followed for GDM with higher HOMA-IR remain a high risk population and more researchs are necessary to improve outcomes in this group.

DOI: 10.1530/endoabs.81.EP314

EP315

Analysis of glycemic control in type 1 diabetes patients using flash glucose monitoring

Miguel Damas-Fuentes[1,2], José Ignacio Martínez Montoro[1], Victor Simón Frapolli[1], Andrea Fernadez Valero[1] & Francisco José Tinahones Madueño[1,2]
[1]Hospital Universitario Virgen de la Victoria, Malaga, Spain; 2Instituto Investigación Biomédica de Málaga (IBIMA), Malaga, Spain

Introduction

Flash glucose monitoring expansion to an increasing number of patients with type 1 diabetes, coupled with its increased accuracy and ease of use, has increased available data on glycemic control in this population and allows detection of improvement areas in diabetes education and treatment.

Objective

To analyze main parameters standardized by ATTD consensus (2019) in our population of patients with type 1 diabetes using flash glucose monitoring.

Material and methods

Cross-sectional study carried out on May 7, 2021. Glucose profile of patients with medical follow-up in Endocrinology service in Virgen de la Victoria Hospital in Malaga were analyzed on Libreview platform. Those patients without download available in previous two weeks were excluded.

Results

1,562 patients were analyzed. 51.2% were male. Average number of readings was 10.98$\pm$8.13 daily readings with 84.11$\pm$20.74% active time. Mean glucose was 165.34$\pm$39.04 mg/dl with a standard deviation (SD) 61.81$\pm$18.80 mg/dl and a coefficient of variation 37.31$\pm$7.52%. time in range (TIR) was 58.96$\pm$18.86%, time above range (TAR) was 35.66$\pm$19.92%, and time below range (TBR) was

5.38 ± 6.25%. 28.83% patients achieved an TIR greater than 70%, 63.5% a TBR less than 5% and 33.74% a TAR less than 25%. Average interquartile range was 88.09 ± 31.14. Mean hypoglycemia number is 0.65 ± 0.54 daily events, with a mean duration of 90.53 ± 54.51 minutes.
Conclusions
Glycemic control in our cohort of patients, although similar to populations with same characteristics, is still far from parameters recommended in ATTD consensus. We must exploit flash glucose monitoring to detect possible areas for improvement both individual and populationally.

DOI: 10.1530/endoabs.81.EP315

EP316

Did the COVID-19 pandemic affect the management of gestational diabetes?

Ioannis Ilias, Stefanos Togias, Vassiliki Papadopoulou, Ekaterini Kougioumtzi, Vassiliki Mastrodimou, Ekaterini Michou, Charalampos Milionis, Evangelia Venaki & Eftychia Koukkou
Elena Venizelou Hospital, Athens, Greece

Introduction
Researchers argue that increased morbidity is noted in pregnant women during the current COVID-19 pandemic. Reports indicate that the pandemic has led to disruptions in care of persons with diabetes. Glycated hemoglobin A1c (A1c) is not sufficient in screening for gestational diabetes mellitus (GDM) but may be of use in monitoring glycemia in GDM. To the best of our knowledge no studies honed on late pregnancy glycemia (via A1c), as a surrogate of the access/quality of care for women with GDM, have been put forth.
Aim
To assess whether care for women with GDM during the COVID-19 era (via measurement of A1c in late pregnancy) was compromised, compared to the pre-COVID-19 period.
Subjects & Methods
We accessed the medical records of 90 pregnant women (49 before and 41 during the COVID-19 era; mean age + SD: 34.01 + 5.50 years) with GDM, in whom A1c was measured after the 34th week of pregnancy. We noted the following parameters: age, body weight change (diffBW) during pregnancy, presence of thyroid disease and treatment (nutrition therapy only [NT] or combined with insulin [INS]). Statistical evaluation was done with two way analysis of variance (ANOVA), analysis of covariance (ANCOVA) and with the chi square test.
Results
Fifteen of 49 and 15/49 women in the preCOVID-19 era had thyroid disease and were on INS, respectively, whereas 10/41 and 20/41 in the COVID-19 era had thyroid disease and were on INS, respectively ($P > 0.1$, Chi square). Mean + SD A1c was 5.26% + 0.42% before and 5.37% + 0.58% during the COVID-19 era ($P > 0.10$, ANCOVA), with no significant effect or differences in age, diffBW or presence of thyroid disease ($P > 0.1$ ANCOVA). The only factor that had an effect on A1c was the mode of treatment (NT or INS) both in the pre-COVID-19 era and in the COVID-19 era; women on INS had higher A1c in both time periods ($P = 0.001$, ANOVA).
Discussion
As far as late pregnancy glycemia, via A1c, is concerned, no effect of the COVID-19 era on care for women with GDM was noted. Although we have to acknowledge the non-inclusion of other parameters in our study such as perinatal outcomes, our results are in accordance with studies that show no effect of COVID-19 on adverse outcomes in pregnancy during the COVID-19 era in high-income countries (in contrast to mid/lower income ones).

DOI: 10.1530/endoabs.81.EP316

EP317

Effect of metformin on weight loss and blood pressure in obese hypertensive patients

Oksana Obertynska
National Pirogov Memorial Medical University, Vinnytsya, Ukraine

Obesity is independently associated with poor control of blood pressure (BP) and weight reduction is generally recommended as the first line of treatment. However, the challenge remains to find the appropriate approach for weight reduction to influence BP status. The aim was to investigate the effect of non-pharmacologically and pharmacologically (metformin) induced weight loss on BP in obese hypertensive patients (HP).

Methods
100 HP (mean body mass index (BMI) 32.2 kg/m^2) were included in the study (antihypertensive treatment with a mean of 1,9 ± 1.4 drugs). All followed hypocaloric diet (D) for 3 months, after that 50 patients started on metformin (M) at a mean daily dose of 2.1 ± 0.45 g with D and 50 patients followed on D for 6 months. Anthropometry, metabolic profile, including lipids and oral glucose tolerance test with insulin, uric acid, plasma aldosterone (AS) were performed at baseline and after 3, 9 months. Homeostatic model assessment HOMA-R was calculated for insulin resistance. At baseline and after 6 months HP underwent 24-hour BP measurements.
Results
At baseline was an excellent correlation between BMI and HOMA-R ($r = 0.45$, $P < .01$), AS and HOMA-R ($r = 0.31$, $P < .05$). Also, asymptomatic hyperuricemia was observed in 24.9%, dyslipidemia in 43.1%, impaired glucose tolerance in 21%. 29% of the HP had > 3 metabolic syndrome components. There was a modest no significant reduction in BMI and BP after 3 months of D in whole group. Patients on M experienced greater weight loss (-3.4 ± 2.3 versus -2.3 ± 1.2 kg, $P < .05$) and reduction in BMI (-1.9 ± 1.1 versus -1.0 ± 0.9 kg/m^2, $P < .05$). A 6-month M therapy significantly changed the levels of glucose, insulin, lipids, uric acid, HOMA-R and resulted in significantly reduced AS ($P < .01$). BP decreased more in M-treated patients than in the D group (SBP -6.7 ± 5.1 versus -2.2 ± 4.2 mmHg; DBP. -6.4 ± 3.1 versus -1,9 ± 4.2 mmHg, $P < .05$ for both). By linear regression analysis changes in BP on M was associated with HOMA-R and AS changes (0.362, $P < .05$; 0,423, $P < .05$ respectively).
Conclusions
The diet alone wasn't enough for a reduction in weight and BP in obese hypertensive patients. Weight-loss program with metformin is more effective and shows an additional antihypertensive effect in those individuals. The reduction of BP on metformin is mediated by improvement insulin/glucose homeostasis, it is accompanied by lowering of aldosterone, uric acid and lipid-lowering effects, what results in cardiovascular risk reduction.

DOI: 10.1530/endoabs.81.EP317

EP318

Role of incretins, gut microbiota and permeability in the remission of type 2 diabetes mellitus after bariatric surgery

Laura Hernández-Montoliu[1], Rocio Puig[2], Silvia Pellitero[3], Joan Vendrell[4], Sonia Fernández-Veledo[4], Fernando Guerrero[1], Anna Vidal[5] , M. Mar Rodríguez[4], Rosa Montseny[1] & Núria Vilarrasa[1,5]
[1]Bellvitge University Hospital, L'Hospitalet de Llobregat, Spain; [2]Hospital de la Santa Creu i Sant Pau, Barcelona, Spain; [3]Germans Trias i Pujol Hospital, Badalona, Spain; [4]Hospital Universitari de Tarragona Joan XXIII, Tarragona, Spain; 5IDIBELL Institut d'Investigació Biomèdica de Bellvitge, L'Hospitalet de Llobregat, Spain

Introduction
Bariatric surgery is an effective therapy for patients with type 2 diabetes mellitus (T2D). Many mechanisms have been proposed for its metabolic benefits, such as caloric restriction, weight loss, increased secretion of gut hormones like glucagon-like peptide 1 (GLP-1) and 2 (GLP-2), bile acid diversion, decrease of pancreatic and hepatic fat deposits and changes in gut microbiome.
Aims
Evaluate changes after surgery in gut microbiome profile, incretin secretion, intestinal permeability, systemic inflammation and succinate levels. Assess the associations between former variables and determine predictors of metabolic outcomes.
Material and Methods
Prospective single-center, non-blinded randomized controlled trial study, including patients with grades II and III obesity and T2D undergoing metabolic RYGB (mRYGB). At baseline and at one year after surgery we performed anthropometric, body composition, biochemical analysis including fasting IL-6 and zonulin, a standard meal test (SMT) and lipid test (LT) with plasma insulin, C-peptide, plasma GLP-1, GLP-2, succinate, and the study of gut microbiota was performed.
Results
13 patients were evaluated, 9 females and 4 males, mean age 52.6 ± 6.5 years, mean BMI 39.3 ± 1.4 kg/m^2, initial HbA1c of 7.62 ± 1.5% with 69.2% under insulin treatment. Twelve months after surgery a reduction of 33% of total weight loss at the expense of fat mass was observed. Diabetes remission was achieved in 69% of patients. Fasting plasma succinate and zonulin significantly decreased after surgery. After SMT and LT a significant increase in AUC for GLP-1 and GLP-2 and C- peptide was observed after surgery whereas AUC for glucose significantly decreased. Patients achieving T2D remission had higher initial C-peptide but similar proportion of insulin treatment and incretin response. In the

multiple regression analysis only higher initial C-peptide levels predicted better metabolic outcomes. The microbiota analysis showed a significant increase in beta diversity after surgery. Compared to pre-surgical faeces samples, certain families increased after mRYGB including Veillonellaceae, Enterobacteriaceae, Streptococaceae and Prevotellaceae, and were negatively correlated with HbA1c and BMI. On the contrary, some families significantly decreased: Eubacteriaceae, Ruminococcaceae, Clostridiaceae and Erysipelotrichaceae, and showed an inverse correlation with former parameters. Therefore, those families increasing after surgery were associated with a better metabolic profile. No association was found between microbiota families and incretin profile or gut permeability markers.
Conclusions
We showed beneficial changes in multiple aspects following mRYGB, spanning from an enhanced incretin secretion, decreased intestinal permeability and succinate levels to a shift towards a specific healthier metabolic microbiome.

DOI: 10.1530/endoabs.81.EP318

EP319

What is the impact of being overweight on the progressive genius of Crohn's disease?

Imen Akkari, Hassine Ameni, Mrabet Soumaya & Ben Jazia Elhem
Farhat Hached Hospital, Gastroenterology, Sousse, Tunisia

Background
Overweight is becoming increasingly more common among patients with inflammatory bowel disease and plays a role in the development and course of the disease especially in Crohn's disease (CD). However, there is currently little data on his impact on the evolutionary genius of CD. The aim of this study was to assess the impact of overweight on the epidemiological, clinical, therapeutic and progressive characteristics of CD.
Patients and Methods
It is a retrospective study of patients with CD hospitalized between 2016 and 2020. Demographic, clinical, therapeutic and evolution data were identified from medical records. Patients were divided into two groups based on the body mass index (BMI) at the time of diagnosis; group 1 (BMI$\geq$ 25), group 2 (BMI $<$25). A comparison of the two groups was performed
Results
A total of 56 patients were collected. The median baseline BMI was 21.59 kg /m^2 [16-29.4]. 85.7% of patients had a BMI $<$25 kg /m^2, 14.3% were overweight (n =8). The comparison of these groups shows no significant difference in terms of age, sex ratio, tobacco consumption, the duration of development of disease, disease phenotype, presence of anoperineal lesions, presence of upper digestive tract, the severity of the initial flare or the degree of initial intestinal damage assessed by the Lemann score. However, a significant association was demonstrated between overweight and a colonic localization of the disease at the time of diagnosis, compared to other localizations (P = 0.02). After a mean follow-up of 36.82 months [6 –52 months], there was no significant difference between the 2 groups concerning the occurrence of complications of CD (P = 0.76), the number of severe relapses (P = 0.21), course of intestinal damage (P = 0.59), use of systemic corticosteroid therapy (P = 0.75), immunosuppressants (P = 0.58), biotherapy (P = 0.34) or surgical treatment (P = 0.37). Extra-digestive manifestations were more frequent in overweight patients compared to patients with a normal BMI but without statistically significant difference (group 1: 37.5% vs group 2: 27.1%, P = 0.41). The possibility of achieving deep remission was similar in the two groups (group 1: 12.5% vs group 2: 8.3%, P = 0.55).
Conclusion
According to these results, being overweight in CD does not significantly alter the long-term course of the disease. Studies on larger scales are therefore necessary.

DOI: 10.1530/endoabs.81.EP319

EP320

Incidence of hypoglycemia among patients with type 2 diabetes who fasted during Ramadan

Bayar Qasim[1], Mazyar Ahmed[2] & Ayad Mohammed[3]
[1]College of Medicine, University of Dohuk, Medicine, Duhok, Iraq; 2Kurdistan Board for Medical Specialties, Erbil, Iraq; 3College of Medicine, University of Dohuk, Duhok, Iraq

Background and Objectives
Fasting causes a major change in the dietary habits including the frequency, the timing, and the patterns which will result in a major change in the metabolic response of the body. Physicians should advise the patients about the complications of diabetes mellitus during fasting especially hypoglycemia, the aim of this study is to determine the relation between type 2 diabetes mellitus and hypoglycemia and to evaluate whether this correlation is significant or not.
Patients and Methods
This is a cross-sectional prospective study, which included 304 Muslim patients with type 2 diabetes mellitus who decided to fast Ramadan during 2019 in two cities, 122 patients were from Duhok city and 183 patients from Erbil city, Kurdistan region of Iraq.
Results
Majority of patients fasted the Ramadan and the mean days of fasting were 26.96. Most patients had no attacks of hypoglycemia (85%), 4.6% have a single attack, and 8% had 4 attacks. There was no significant correlation between the hypoglycemic attacks and the variables studied in this article, such as the duration of diabetes, oral hypoglycemic agents, days of fasting, and fasting before Ramadan.
Conclusion
Physicians must warn patients about the possible risk of hypoglycemia during fating and it's the patient's own decision to continue fasting or not, however the high risk group should be advised against fasting. Lastly, the other role of physician is to adjust the dose of anti-diabetic drugs during fasting in order to minimize the risk of hypoglycemia.
References
1. Fatim, J., et al., Attitudinal determinants of fasting in type 2 diabetes mellitus patients during Ramadan. J Assoc Physicians India, 2011. 59: p. 630-4.2. Ahmed Qasim, B., Ahmad Mohammed, A., Jabbar Ahmed, M., & Khezer Ahmed, S. (2021). Pre-ramadan counseling among type two diabetic patients who decided to fast ramadan. Duhok Medical Journal, 15(1), 96-105. Retrieved from https://dmj.uod.ac/index.php/dmj/article/view/150.

DOI: 10.1530/endoabs.81.EP320

EP321

The effect of insulin resistance syndrome in obese children on the development of hypertension

Zhanar Nurgaliyeva, Dana Akhatay & Shakhniza Abdrimova
NJSC "Kazakh National Medical University named after S.D.Asfendiyarov", Department of Pediatric Diseases with a Course of Neonatology, Almaty, Kazakhstan

Objective
To investigate the state of blood pressure in children with obesity and insulin resistance.
Materials and Methods
127 obese children, age from 6 to 15 years, average age 11.5 years. Anthropometry, calculation of body mass index (BMI), waist/hip volume ratio, measurement of blood pressure (SBP, DBP), study of the level of immunoreactive insulin, glucose were carried out. Insulin resistance was determined with hyperinsulinemia above 22.0 microns/ml, a high NOMA index.
Results
obesity in the observed children was of varying degrees, the average BMI was 26.9$\pm$2.2, while the predominantly abdominal type of distribution of the subcutaneous fat layer was revealed. Impaired glucose tolerance and fasting glycemia were detected in 14 (11.0%) obese children, type 2 diabetes mellitus in 1 (0.8%) child, hyperinsulinemia was detected in 45 (35.4%) children, while the average insulin level was 56.5$\pm$8.6 μm/ml. An increase in the HOMA index was detected in 64 (50.4%) patients, the average indicator was 12.0$\pm$1.9, which made it possible to verify their insulin resistance syndrome. An increase in blood pressure was detected in 46.5 $\pm$ 4.4% of obese children, in 55.2$\pm$8.1 children with obesity and insulin resistance. The frequency of elevated SBP values in obese children was registered in 39.1%, DBP - in 24.6%. In children with obesity and the presence of insulin resistance, high rates of SBP were recorded in 53.4%, DBP - 39.7%. Also, among children with insulin resistance, there were high values of SBP and pulse pressure, which indicates the indirect influence of insulin resistance syndrome in the formation of increased peripheral vascular resistance and the development of arterial hypertension.
Conclusions
arterial hypertension is a fairly common concomitant pathology in obese children. When burdened with insulin resistance syndrome in obese children, the frequency of arterial hypertension increases and is recorded in every second sick child, which indicates a direct and / or indirect effect of insulin resistance on an increase in blood pressure.

DOI: 10.1530/endoabs.81.EP321

EP322

Lipid abnormalities in hospitalized patients with diabetes

Chaima Sdiri, Yosra Htira, Skander Msolly, Maryam Cheikhrouhou , Zohra Hadj Ali, Hedfi Imene, Chaima Jemai & Feika Ben Mami
Institut De Nutrition, Tunis, Tunisia

Introduction
Lipid abnormalities are frequent in type 2 diabetes. They increase the risk of cardiovascular events, morbidity and mortality in these patients. The aim of this study was to determine the lipid profile in patients with diabetes during hospitalization.
Method
We conducted a prospective study in the department of diabetology in the National Institute of Nutrition in Tunis from October 2021 to January 2022. This work was carried out on the medical records of hospitalized patients. Hypercholesterolemia was defined when the total cholesterol >5.2 mmol/l, Hypertriglyceridemia when a triglyceride level >1.7 mmol/l, and Low HDL cholesterol level by an HDL cholesterol level <1 mmol/l and <1.3 mmol/lin men and women respectively.
Results
We included 97 patients with diabetes with a sex ratio (M/F) of 0.6 and a mean age of 51.1 ± 17.5 years. The majority were type 2 diabetics (72%). The mean age of diabetes was 12.2 ± 8.8 years [0;34]. Pre-obesity, class I, class II and class III obesity were found in 28%, 30%, 3% and 3% of patients, respectively. The lipid profile showed hypercholesterolemia in 19% and hypertriglyceridemia in 29% of cases. Hypertriglyceridemia was correlated significantly with diabetes imbalance ($P = 0.005$) and with poor compliance with dietary rules ($P = 0.002$). Then, no significant correlation with obesity was found ($P =$ NS). In addition, Low HDL cholesterol concerned 55% of the patients. LDL cholesterol was ≥ 0.7 g/l in 86% of cases and it was correlated with the presence of coronary artery disease ($P = 0.03$). Statins were prescribed for 54% of diabetics: 49% of patients were on atorvastatin while 3% of diabetics were on simvastatin. Only one patient was on rosuvastatin.
Conclusion
Achieving glycemic control in patients with diabetes is compulsory to improve lipid profile. Lipid-lowering drugs, especially statins are often necessary to prevent cardiovascular diseases.

DOI: 10.1530/endoabs.81.EP322

EP323

Ketogenic diet and Glucagon-like peptide 1 (GLP1) receptor agonists for obesity: our experience

Elisa Pisocri, Manuela Cimorelli & Nadia Cerutti
Asst di Pavia, U.O.S.D Medicina Generale Ad Indirizzo Dietologico, Italy

Background & aims
it is now known that the benefits due to weight loss are therefore attenuated by the recovery of body weight. Two therapeutic options facilitate the maintenance of weight loss at a distance: very low caloric ketogenic diet (VLCKD) and medications; the recent literature also shows how much the recovery of weight loss is significantly lower in subjects treated with medications for obesity than in them who have taken a VLCKD or low calorie diet. The aim of this work is to describe the anthropometric characteristics of two samples of subjects, affected by obesity, treated with a VLCKD or GLP-1 agonists.
Material & Methods
The sample called "ketogenic diet group" (KD) is composed of 19 adult patients; the mean initial weight was 99.8 ± 20.3 kg and the mean initial BMI was 37.8 ± 6.4 kg/m^2. They received a VLCKD with natural foods (10) or with artificial meals (7) or artificial foods mixed with natural foods (2). The sample called "GLP-1 agonists group" (GLP-1) is composed of 19 adult patients; the mean initial weight was 106.1 ± 25.4 kg and the mean initial BMI was 38.7 ± 8.5 kg/m^2. They were treated with liraglutide (4) or semaglutide (12) or exenatide (3).
Results
The mean percentages of weight loss for the KD group and for the GLP-1 group at 2 months were 8.9% and 7.8%, at 3 months were 11% and 6.2% and at 6 months were 13.1% and 11.5%, respectively.
Conclusions
maintaining long-term weight loss is the big challenge for obesity experts. The results of the present work, despite the small number of subjects, have shown a similarity in percentage weight loss in both samples in the short-medium term (6 months). In order to observe the results reported in the most recent literature, the percentage weight loss must be observed after at least 1 year and in bigger samples. However, it is important to underline that a 5-10% weight loss leads to a reduction in the risk of developing diabetes and dyslipidemia, cardiovascular diseases, sleep apnoea, osteoarticular, gynecological and mood disorders.

DOI: 10.1530/endoabs.81.EP323

EP324

Features of the course and outcome of pregnancy in gestational diabetes mellitus in real clinical practice

Fatima Ushanova & Tatyana Demidova
Pirogov Russian National Research Medical University, Moscow, Russian Federation

Background and aims
Published data on the prevalence of GDM and its complications in real clinical practice in Russia are insufficient. To assess the prevalence of GDM among pregnant women in one of the districts of Moscow, the structure of risk factors, the course and outcomes of pregnancy in women with GDM.
Materials and Methods
A retrospective analysis of data from the primary documentation of 510 pregnant women who were diagnosed with GDM during 2019.
Results
GDM was diagnosed in 510 pregnant women out of 5000 observed (10.2%). The mean age of women was 31.9 ± 4.8 (95% CI 31.5-32.3). The diagnosis was made in the 1st trimester of pregnancy - 224 pregnant women (43.9%), in the 2nd trimester - 31.8% (162), in 18.6% (95) in the 3rd trimester. Mean values of venous plasma glucose - 5.43 [5.25; 5.7] mmol/l, HbA1c - 5.19 ± 0.4% (95% CI 5.15-5.24). Treatment with diet therapy - 84.3%, the rest - insulin therapy (in all cases, aspart and detemir were used). The structure of risk factors: burdened hereditary history - 206 (40.4%), GDM in previous pregnancies - 54 (10.6%), macrosomia in history - in 6.3% of cases; antenatal fetal death in history - 3 (0.59%). Obesity was found in 120 (23.5%) women: BMI 30-34.9 kg/m^2 was recorded - 14.3%, BMI 35-39.9 kg/m^2 - in 5.1%, BMI 40 kg/m^2 or more - 4.1%. Pregnancy complications were observed in 123 women (24.1%): in 64 (12.5%) cases - fetoplacental insufficiency; preeclampsia - 54 (10.6%); 1 of the pregnant women - eclampsia; the threat of abortion and the threat of premature birth - 1.56% and 1.96%. In 12 pregnant women (2.35%) - polyhydramnios, in 18 cases (3.52%) - oligohydramnios. Adverse pregnancy outcomes were registered in 153 women with GDM out of 213 analyzed (71.8%): caesarean section in 22.5% of cases; premature rupture of amniotic fluid - in 58 (27.2%); macrosomia - 16.43%; ruptures of the pelvic organs - 41.31%; clavicle fracture - 2 cases; cephalohematoma - 3 cases; distress syndrome - in 6 newborns (2.82%); congenital malformations - in 2 newborns. CNS depression syndrome (7.98%), fetal cerebral ischemia - in 8.92%.
Conclusions
Totally unfavorable pregnancy outcomes were significantly more common in the group with earlier manifestation of GDM (60.7%) compared with the 2nd group (37.7%) ($p<0.001$). A detailed comparison of pregnancy complications in these groups showed no statistically significant difference.

DOI: 10.1530/endoabs.81.EP324

EP325

Mitochondrial Diabetes: a case report

Hind Ouakrim, Sara Ijdda, Sana Rafi , Ghizlane El Mghari & Nawal El Ansari
Mohammed VI University Hospital, Department of Endocrinology, Diabetes, Metabolic Diseases and Nutrition, Marrakech, Morocco

Introduction
Mitochondrial diabetes represents about 1% of diabetes but still very often misunderstood. The most frequent mutation is 3243A $>$G of the mtDNA, which is responsible for the maternally inherited diabetes and deafness syndrome (MIDD). We report an observation of a patient with strong suspicion of mitochondrial diabetes.
Case presentation
43-year-old female patient, with diabetes for 5 years on an Insulin Therapy.Anamnesis:&hypen; Diabetes discovered at the Age of 38 years by an acid ketosis decompensation.- Strong heredity of diabetes: grand-mother, two uncles, two aunts, tree cousins, all on the mother's side.
- Hypoacusis in an uncle and two sisters on the mother's side.
- Blindness in grandmother and diabetic retinopathy in mother
- Diabetic nephropathy in aunt on the mother's side.

Clinical examination is without particularity with BMI at 37.86 kg/m^2. Diabetes typing immunological test is negative

Discussion
Various abnormalities (mutations or deletions) in mtDNA are thus responsible for multi-organ syndromes that include diabetes among other abnormalities. Maternally Inherited Diabetes and Deafness (MIDD) is the most common form of mitochondrial diabetes. The 3243A >G mutation affects the tertiary structure of tRNA. The consequence is a cellular energetic deficit that mainly manifests in very active metabolically organs such as the endocrine pancreas. Mitochondrial diabetes should be suspected in view of the young age of onset of diabetes, maternal transmission, and association with other extra-pancreatic disorders (neurosensory deafness, reticular macular dystrophy, neurological and muscular disorders, cardiomyopathy). The purpose of searching for the mutation is to confirm the clinical diagnostic, to deduce the risk of maternal transmission and to propose a genetic diagnostic to the relatives.
Conclusion
Knowing mitochondrial diabetes is essential for early diagnosis, systematic screening for multi-organ damage, specific and multidisciplinary management, and to offer genetic counseling.
Bibliography
1. Ming Li Yee, Rosemary Wong1. Mitochondrial disease: an uncommon but important cause of diabetes mellitus. 18-0091; September 2018.
2. Mengge Yang, The Mutations and Clinical Variability in Maternally Inherited Diabetes and Deafness: An Analysis of 161 Patients. November 2021 | Volume 12 | Article 728043.
3. T. Measa, Mitochondrial diabètes : Clinical features, diagnosis and management. La Revue de médecine interne 31 (2010) 216–221.
4. P.-J. Guillausseau, Diabètes mitochondriaux. 10-366-D-25 EMC.
DOI: 10.1530/endoabs.81.EP325

EP326

Association of fasting heart rate with fasting and post prandial blood glucose levels in Indians

Aniket Inamdar
Samarpan Clinic, Internal Medicine, Omerga, India

Background
Diabetes mellitus is associated with abnormal autonomic function. Diabetes and impaired fasting glucose are associated with increased mortality, particularly from cardiovascular causes. Several factors, including fast heart rate, have been identified to be associated with an increased likelihood of having diabetes. Heart rate is a crude index of the autonomic nervous system tone, reflecting a balance of sympathetic and parasympathetic inputs, and correlates with muscle sympathetic nerve activity and noradrenaline serum levels. Examining its potential role in diabetes risk could improve our understanding of the pathogenesis of diabetes.
Aim
Aim of our study was to establish correlation between fasting heart rate and fasting and post prandial blood glucose levels.
Materials and Methods
509 patients between age group 25 years to 75 years were studied at different centers in India. Resting heart rate was recorded on finger pulse oximeter before taking fasting blood sample. Fasting and post prandial blood samples were obtained by venepuncture and estimation was done by the hexokinase method. Diabetes mellitus was defined as use of insulin or a hypoglycemic agent, a fasting plasma glucose level of 126 mg/dl or more ($\geq$7.0 mmol/l), or a 2-hour postprandial plasma glucose level of 200 mg/dl or more ($\geq$11.1 mmol/l). Pearsons correlation test was used for statistical analysis.
Results
We found that resting heart rate was significantly higher in patients with higher fasting blood glucose levels compared with patients with normal glucose levels. This difference was statistically significant with $P = 0.002$ (r:0.137). It was also noted that fasting heart rate was also significantly higher in patients with higher post prandial blood glucose levels with P value of 0.002.
Conclusions
Our study strongly supports faster resting heart rate as an independent risk factor for incident diabetes and impaired fasting glucose. Meta-analysis of seven published studies confirmed the positive association between resting heart rate and diabetes risks. A resting heart rate is generally considered as a surrogate marker for autonomic activity, and increased sympathetic nerve system activity is associated with both acute and chronic insulin resistance. One of the most important mechanisms for increased diabetic risk might be that sympathetic activation causes vasoconstriction and decreases skeletal muscle blood flow, resulting in the impairment of glucose uptake into the skeletal muscle. Ultimately, the exact mechanism by which increased heart rate is induced remains to be elucidated; however, our findings suggest that this area of investigation may be relevant for future studies.
DOI: 10.1530/endoabs.81.EP326

EP327

Growth Assessment and Metabolic Syndrome (MetS) Criteria in children with steroid-sensitive Nephrotic syndrome (SSNS) and frequent relapses treated with long-term prednisone therapy (LTPT): Comparison between children who developed obesity versus those who did not develop obesity

Mostafa Elbaba[1], Ashraf Soliman[1], Noor Hamed[1], Fawzia Alyafei[1], Maya Itani[2], Fatima Al-Naimi[2], Doaa Al Yousef[2] & Mona Shaat Dalees[2]
[1]Hamad Medical Center, Pediatrics, Doha, Qatar; [2]Hamad Medical Center, Nutrition and Dietitic Department, Doha, Qatar

Introduction
Long term prednisone therapy (LTPT) can be associated with overweight, obesity, and short stature. Both LTPT and obesity are considered risk factor for the occurrence of the different components of the metabolic syndrome (MetS).
Aim
We studied steroid-associated metabolic and clinical adverse events in children with NS and frequent relapses treated with LTPT (obese vs non-obese).
Methods
Data of 30 children with SSNS was analysed retrospectively. 16/30 were obese after LTPT and 14 were not obese. The cumulative dose of steroids over 5 years was calculated for each child. Growth and different components of the metabolic syndrome (MetS) including impaired fasting glucose (IFG), high LDL and cholesterol, lower HD and high blood pressure were studied over this period and compared with the data for 66 age-matched obese non-nephrotic children.
Results
Analysis of data showed that children with NS who developed obesity during therapy were significantly taller than the normal weight group. The obese group had higher cholesterol, TG and LDL level compared to the non-obese group. Both groups had high prevalence of hypertension (40% in the obese group vs 35.7% in

	At Diagnosis	Age (yr)	WAZ	HAZ	BMI	BMISD	Albumin	TG	LDL	HDL	Cholesterol	FBG
		years					g/l	mmol/l	mmol/l	mmol/l	mmol/l	mmol/l
Group 1	mean	3.59	0.33	0.09	16.23	0.38	17.33	2.06	6.06	2.12	10.04	5.28
$n=16$	SD	1.98	0.72	0.68	1.33	0.81	4.29	0.75	3.06	1.45	2.66	0.74
Group 2	mean	4.41	0.07	-0.78	17.00	0.86	18.13	2.89	7.15	1.92	10.16	5.17
$n=14$	SD	2.31	0.76	1.19	1.18	0.89	4.69	1.74	3.67	1.05	3.05	0.96
	After 5 y											
Group 1	mean	5.06	1.32*	-0.4*	21.5*	1.97*	32.53	2.3*	5.7*	2.26	9.1*	5.66
$n=16$	SD	3.79	0.87	1.00	3.99	0.71	11.27	0.06	1.53	0.54	0.90	0.69
Group 2	mean	5.43	-0.50	-1.14	16.82	0.05	37.57*	0.93	4.90	2.29	7.61	5.58
$n=14$	SD	3.18	0.77	1.30	1.80	0.61	7.69	0.04	3.54	0.72	4.24	1.00

*$P<0.05$ group 1 vs group 2.Group 1 Children with NS who became obese on LT prednisone therapy.Group 2: Children with NS who did not become obese on LT prednisone therapy.

the non-obese group)
Conclusion
In children with SSNS on LTPT the development of obesity was associated with higher components of the MetS compared to the non-obese group advocating a higher risk to develop the cardiovascular and metabolic consequences.
DOI: 10.1530/endoabs.81.EP327

EP328

Treatment adherence in patients with type 2 diabetes and its associated factors

Mehrez Achwak, Rahma Khalaf, Imen Sebai, Fatma Boukhayatia, Haifa Abdesslam, Kamilia Ounaissa & Chiraz Amrouche
Institute of Nutrition of Tunis, Tunisia

Introduction
Treatment adherence is fundamental in diabetes control. The aim of our study is to evaluate treatment adherence in patients with type 2 diabetes and to determine its associated factors.
Methods
Cross-sectional study enrolling 80 type 2 diabetes patients followed up in the outpatient department of the national institute of nutrition. The Morisky questionnaire was used to evaluate treatment adherence. Age, gender, body mass index (BMI), diabetes duration and treatment, glycosylated hemoglobin (HbA1c), serum lipid profile, microvascular and macrovascular complications were assessed.
Results
The mean age was 60 $\pm$ 8 years. Of the study population, 60% were females. and 65% were insulin-treated. The mean diabetes duration was 14.9 $\pm$ 7.7 years, mean glycated hemoglobin was 10.4% $\pm$ 1.6 and mean BMI was 30.1 $\pm$ 6.2 Kg/m^2. High adherence was reported in 37% of cases, medium adherence in 28% of cases and low adherence in 35% of cases. Patients with good adherence had higher BMI (31.74 $\pm$ 6.7 Kg/m^2 vs 27.99 $\pm$ 5.55 Kg/m^2;$P = 0.03$) and better serum lipid profile including a lower triglycerides levels (1.94 $\pm$1.11 mmol/l vs 1.3$\pm$ 0.52 mmol/l ;$P = 0.003$). Lower HbA1c levels (10.89%$\pm$ 1.4 vs 10.42% $\pm$1.5 ; $P = 0.25$), lower total cholesterol levels (4.08 mmol/l $\pm$1.06 vs 4.47 mmol/l $\pm$ 1 ; $P = 0.17$) and higher HDL cholesterol levels (1.14 $\pm$0.32 vs 1.02 $\pm$0.2 ;$P = 0.13$) were associated to a better adherence but not significant. The presence of peripheral neuropathy, gastroparesis and genital autonomic neuropathy were significantly associated with low adherence ($P = 0.015$, $P = 0.007$ and $P = 0.02$ respectively). Patients with good adherence had lower prevalence of macrovascular complications including acute coronary syndrome (15.4% vs 35% ;$P = 0.1$), stroke (4.8% vs 7.7% ; $P = 0.6$) and peripheral arterial disease (38.5% vs 52.4% ; $P = 0.2$).
Conclusions
Our study highlights the beneficial impact of good adherence on lipid, and glycemic control. More awareness campaigns and counseling services should be provided by health professionals to improve treatment adherence and diabetes management.
DOI: 10.1530/endoabs.81.EP328

EP329

Metreleptin treatment in woman with familial partial lipodystrophy and severe hypertriglyceridemia

Eleftheria Barmpa, Dimitra Pappa & Alexandra Bargiota
University Hospital of Larissa, Department of Endocrinology and Metabolic Diseases, Larissa, Greece

Introduction
Metreleptin, a recombinant analogue of leptin, is the only drug available for the treatment of generalized or partial lipodystrophy. Familial partial lipodystrophy (FPL) is a rare genetic disorder characterized by selective loss of subcutaneous adipose tissue, ectopic fat deposition, decreased leptin levels, and varying metabolic disorders, which in some patients can be quite severe and life-threatening. We present here such a woman with FPL who is treated with metreleptin.
Presentation
A 53-year-old woman diagnosed with FPL (LMNA gene variant) 8 years ago, had the typical phenotypic features of the syndrome, type 2 diabetes mellitus (T2DM) (HbA1c = 8.7%) and severe hypertriglyceridemia (triglycerides = 1113.6 mg/dl) despite maximum treatment and good adherence to it. She also had extensive visceral fat, fatty liver with a marked increase in liver size, ectopic fat disposition with increased fat in the mediastinum and significant increase in pericardial fat, fibrosis of the heart septum and myocardiopathy. The patient commenced treatment with metreleptin 5.8mg per day subcutaneously. Three months after the initiation, she showed improvement in body weight and metabolic parameters (HbA1c = 6.1% and triglycerides = 349 mg/dl). A year on metreleptin treatment, improvement of fatty liver infiltration and a significant reduction of its size (from 25cm to 20 cm) was observed as well as a significant reduction of the fat in the mediastinum and pericardium. Body composition measured by dual energy X-ray absorption (DXA), showed a fat redistribution with an increase in the upper and lower extremities and a decrease in the trunk. At two years on the same dose of metreleptin, she was metabolically stable (HbA1c = 5.7% and triglycerides = 320 mg/dl), with a further reduction of liver size, at 18 cm.
Conclusions
FPL is a rare disease with varying phenotype and a broad spectrum of metabolic disorders which at times can be quite severe and life-threatening. The use of metreleptin in these patients can significantly improve such metabolic aberrations and their potentially fatal consequences.
DOI: 10.1530/endoabs.81.EP329

EP330

Study of the effects of long-term therapy DPP4i on the morphofunctional state of pancreatic endocrinocytes in the older age group in the clinic and experiment in conditions of type 2 diabetes.

Taisiia Tuchina & Alina Babenko
Almazov National Medical Research Centre, Saint Petersburg, Russian Federation

Introduction
DDP4i improves the function of β-cells and α-cells. However, there have been short-term follow-up and young subjects in many experimental and clinical studies. The imbalance of pancreatic endocrinocytes increases in adulthood and changes become less reversible. We decided that it would be useful to study the morphofunctional features of pancreatic endocrinocytes while taking iDPP4 in the older age group in the clinic and experimentally.
Materials and methods
Male Wistar rats with streptozotocin-nicotinamide-induced type 2 diabetes (DM type 2) ($n = 20$, age over 12 months) received group therapy for 24 weeks.
1. Control - healthy control group.
2. DM type 2 - DM type 2 without therapy.
3. DPP4i - Vildagliptin 1.5 mg per kg.Pancreatic preparations were made after the end of therapy. Immunohistochemical study was carried out with antibodies to glucagon, insulin.Patients ($n = 36$, over 50 years of age) were divided into groups depending on the therapy.
1. DPP4i for more than a year in combination with Metformin.
2. Metformin + sulfonylurea preparation(SU).

Insulin, glucagon, C-peptide levels were examined before and after a standard breakfast. The HOMA IR and HOMA β indices were calculated.
Results
Experiment. A statistically significant difference in the volume of β-cells (significantly less in the group DM type 2($P < 0.05$)), in the volume of α-cells (significantly more in the group DM type 2 ($P < 0.05$)) was revealed when comparing DM type 2 group with a healthy control group. A statistically significant difference($P < 0.05$) was obtained when comparing the DM type 2 group without therapy and the DPP4i group. The number of β-cells was significantly higher with iDPP4 therapy, and the number of α-cells was significantly lower. There was no statistically significant difference in the number of β- and α-cells ($P > 0.05$) when comparing the DDP4i group with the control group. Clinical part of the study. We obtained a significant difference in fasting glucagon and insulin levels between the Metformin + DPP4i and Metformin + SU groups ($P < 0.05$). More significant hyperglucagonemia and hyperinsulinemia were observed in the group receiving Metformin + SU.Discussion.Long-term use of drugs DPP4i contributed to the normalization of the number of β- and α-cells in the experiment. And also DPP4i reduced the secretory imbalance of insulin and glucagon in a clinical study. Our results show that DPP4i contributes to the normalization of the functional state of pancreatic endocrinocytes, including in older age groups.
DOI: 10.1530/endoabs.81.EP330

EP331

Development of complex of biomarkers for screening program for early diagnosis of familial diabetes mellitus

Talat Saatov[1], Kha Karimov[2], Zafar Ibragimov[1], Timur Alimov[2], Nasiba Alimova[3], Anvar Abduvaliev[1], Kodirjon Boboev[2], Elvira Ibragimova[1], Tokhir Ishankhodjaev[1], Zulaykho Shamansurova[1,4] & Abdunabi Tashtemirov[1]

[1]Institute of Biophysics and Biochemistry under Mirzo Ulugbek National University of Uzbekistan, Metabolomics, Tashkent, Uzbekistan; [2]Specialized Scientific-Practical Medical Center of Hematology, Uzbekistan Public Healthcare Ministry, Tashkent, Uzbekistan; [3]Ya.Kh. Turakulov Center for the Scientific and Clinical Study of Endocrinology, Uzbekistan Public Healthcare Ministry, Tashkent, Uzbekistan; [4]Tashkent Pediatric Medical Institute, Uzbekistan Ministry of Education, Tashkent, Uzbekistan

Diabetes mellitus (DM) is a most significant medical-social worldwide problem. Absence of reliable screening program for identification of persons with the higher risk of DM dictates a necessity of sensitive tests of early DM diagnosis. Following genealogical analysis, two experimental groups were formed; patients with type 1 DM with the familial burden (probands) and those at risk (siblings) were included into the 1st and 2nd groups, respectively. Apparently healthy subjects without carbohydrate metabolism disorders served as the controls. The screening program consisted of determination of immunological and genetic biomarkers, to name presence of specific autoantibodies to β- cells of Langergance islets (ICA) and to decarboxylase glutamic acid (GAD), A49/G polymorphisms of CTLA4 gene and INS gene rs689 in patients with the familial DM burden and persons at high DM risk. The familial DM burden was found in 71.2% of patients with type 1 DM. In the probands, significant increase of mean concentrations of ICA and GAD autoantibodies, as compared to the controls ($P < 0.001$) was found. Among the patients having siblings with DM as the first line relatives, concentrations of the GAD autoantibodies were found almost two times higher than in those with DM but without familial DM burden. Analysis of results of genotyping for CTLA4 gene A49/G polymorphisms and those of INS gene rs689 in patients with genetically determined DM burden demonstrated association of G allele and heterozygous AG genotype of CTL4 gene and T allele and heterozygous AT genotype of INS gene with the risk of DM onset. The findings are the evidence for importance of biomarkers under study for identification of genetically determined DM forms and prognosis for its progression at early preclinical stage.

DOI: 10.1530/endoabs.81.EP331

EP332

The impact of the interventions based on mobile apps in physical activity among people with Type 2 diabetes mellitus

Elissavet Lykoudi, Eugenia Vlachou, Eleni Evangelou, Anastasia Ntikoudi, Eleni Dokoutsidou & Nikoletta Margari

University of West Attica, Department of Nursing, Athens, Greece

Introduction

The mobile health (mHealth) technologies use mobiles and also wireless network and devices to offer services for improving health, promoting behavior changes and supporting self-management. The increasing global use of mobile application (app) is widely accepted in managing chronic diseases and especially among people with type 2 diabetes mellitus (T2DM).

Aim

The purpose of this study was to identify the impact of the interventions based on mobile apps in physical activity among people with T2DM which included in randomized controlled trials (RCTs).

Methods

The international bibliography was examined to present the impact of the intervention based on mobile app in physical activity among people with T2DM comparing with usual diabetes care. This study is a narrative review and for this purpose the electronic database of PubMed was searched using keywords such as "Type 2 diabetes", "mobile applications","physical activity" in English and Greek language for studies for the past 5 years. The inclusion criteria were all RCTs associated with a comparison of mobile app-based interventions and with usual diabetes care in adults with T2DM. The exclusion criteria were those not being RCTs or those which were study protocols and pilot studies.

Results

A total number of 26 RCTs were reviewed in this study. By using the search terms and by applying the eligibility criteria 6 RCTs were chosen and screened for developing this study and the non-relevant cases of 20 articles were excluded according to exclusion criteria. In the 6 RCTs that were included in the narrative review, 1.005 people participated with T2DM. Finally, these studies had separated the participants to intervention group based on mobile app and control group with usual diabetes care. The intervention group who received the mobile app with physical activity advices had increased their physical exercise and had decreased their hemoglobin A1c (HbA1c) compared to the control group with the usual diabetes care. Moreover, changes were observed between these two groups to their biomarkers and anthropometry measures such as weight, waist circumference and body mass index (BMI) in favour of the intervention group.

Conclusion

The usage of mobile apps bridges the gap between the people and the self-management of their diabetes. The findings of this review suggest that the mobile apps used by participants can significantly improve physical activity and help to adopt exercise habits. Furthermore, the new digital health care is possible to lead to a successful outcome in HbA1c levels and more over.

DOI: 10.1530/endoabs.81.EP332

EP333

Contraception in diabetic women: A review of 100 cases

Fadwa Atfi & Imane El Abbassi

CHU Ibn Rochd , Maternity Department, Casablanca, Morocco

Introduction

Contraception in women with diabetes is difficult. It is the subject of an individualised prescription, which takes into account the metabolic and vascular state as well as the gynaecological tolerance of the patient.

Materials and Methods

This is a prospective survey having concerned 100 diabetic women surveyed in the Maternity ward of the CHU Ibn Rochd of Casablanca, during a five-month period, between April and September 2021.

Results

The average age of the women was 35.2 years. Obesity was noted in 26%, hypertension in 51%, dyslipidaemia in 35% and in 35% and 5% of the women were smokers. Type 1 diabetes accounted for 35% and type 2 for 65%. Diabetes was unbalanced in 91% and complicated in 68%. Hormonal contraception was used in 42%, the intrauterine device in 28%, local methods in 20%, tubal ligation was performed in 9%. The maternal-foetal risks linked to unbalanced diabetes were known in 66%, the need for obstetrical and diabetic pregnancy monitoring in 63%, and the obligation to start insulin in pregnant diabetic women in 47%. Women who used hormonal contraception despite having a contraindication to the pill represented 30%.

Discussion

The problem of contraception must be systematically addressed in a diabetic woman of childbearing age, during each consultation, Oestrogen-progestin treatments should not be excluded from the contraceptive Oestrogen-progestin treatments should not be excluded from the contraceptive regimen in women with diabetes, type 1 or type 2, and under 35 years of age. Potential adverse impacts on blood glucose, lipid profile and micro angiopathy are apparently modest. The effects on macroangiopathy need to be integrated with other cardiovascular risk factors. The evaluation of knowledge concerning contraception will have to be the subject of several more in-depth studies in order to properly define the issue and to propose practical solutions to generalise the information with the aim of reducing the risk of unforeseen consequences on pregnancy in these women who most often have complicated diabetes.

Conclusion

The prescribing practitioner should be the subject of several studies in order to propose practical solutions to improve knowledge and contraceptive practices with the aim of reducing the unforeseen risks of pregnancy in these women.

DOI: 10.1530/endoabs.81.EP333

EP334

A Rare Case: Non Ketotic Hyperglycemic Chorea

Filiz Mercan Sarıdaş[1], Mehmet Akif Ötegeçeli[2], Ensar Aydemir[1], Coskun Ates[2], Erhan Hocaoğlu[1], Soner Cander[1], Ozen Oz Gul[2], Canan Ersoy[1] & Erdinc Erturk[2]

[1]Bursa Uludag University, Endocrinology and Metabolism, Bursa, Turkey; [2]Bursa Uludag University, Internal Medicine, Bursa, Turkey

Introduction

Hemichorea-hemiballismus, secondary to hyperglycemia, is a rare but easily treatable condition that is usually associated with poorly controlled type II diabetes mellitus. Diagnosis is based on clinical assessment and imaging. Etiology includes primarily cerebrovascular diseases, metabolic, degenerative,

infectious diseases, space-occupying lesions, basal ganglia damage due to drugs and toxic substances.
Case
Here we report a rare case of a 78-year-old woman presenting with involuntary movements on the left side of her body secondary to long standing and uncontrolled hyperglycemia. The T1-weighted magnetic resonance imaging revealed hyperintensity in the right basal ganglia. She received intensive insuline therapy and haloperidol. During the follow-up, the patient's blood glucose level and HbA1c improved, along with significant improvement in choreiform movements.
Conclusion
In conclusion, when patients with diabetes mellitus present with unilateral movement disorder, non-ketotic hyperglycemic chorea should be considered, and treatment should be started immediately after diagnosis.Key Words: Hemichorea, Hemiballismus, Hyperglycemia, T-1 hyperintensity.

DOI: 10.1530/endoabs.81.EP334

EP335

Poor glycemic control is associated with major depression among diabetic patients

Malak Belkhiri, Boubaker Fadia[1], Ashraf Khemiri[1], Houcem Mrabet[1], Walid Bouali[2], Lazhar Zarrouk[2] & Habib Sfar[1]
[1]Taher Sfar Hospital, Endocrinology, Tunisia; [2]Taher Sfar Hospital, Psychiatry, Mahdia, Tunisia

Introduction
Diabetes mellitus (DM) and depression are two frequent health conditions. Their coexistence may represent a medical challenge for clinicians. In addition, early detection of depression can help in better management of diabetes and preventing its complications.
Aim of the study
To assess depression and glycemic control among a group of patients having diabetes.
Methods
A cross sectional study was conducted among diabetic patients followed in the Endocrinology Department of the "Taher Sfar University Hospital" in Mahdia, Tunisia. Depression assessment was made using the DSM-V diagnosis criteria and glycemic control assessment with the last available fasting blood glycemia and HbA1c. The study took place over a one-year period (from October 2019 to October 2020). Patients with a previous psychiatric history were ruled out.
Results
By the end of the study, 260 diabetic patients were included, females represented 62.7%. The mean age of patients was calculated at 57.36 years . The majority of patients had type 2 diabetes (92.3%). The mean of the diabetes duration was of 9 years. Different complications of the diabetic disease were assessed in the time of the study : neuropathy (39%), retinopathy (37%) and nephropathy (24%. A regular physical activity was reported by 58.5% of our patients and a healthy diet pattern by 12.3%. A regular self-blood sugar monitoring was reported by 44.2% of the participants. According to DSM-V diagnosis criteria, the number of participants having Major Depressive disorder(MDD) were of 39 (15%). In this group having MDD, almost all patients (97.4%) had poor glycemic control with a mean of the fasting blood glycemia at 13.45 mmol/l and a mean HbA1c of 10.385%. There was a significant correlation between glycemic control and depression ($P = 0.002$).
Conclusion
Our study showed a worse glycemic control among diabetics having MDD. Clinicians should be attentive to look for depression in case they fail to meet glycemic targets. Depression can predict health-related behaviors problems, and unsatisfactory glycemic control at follow-up which can worsen depressive symptoms. A multidiciplinary approach appears necessary.

DOI: 10.1530/endoabs.81.EP335

EP336

Flash glucose monitoring and glycemic control in type 1 diabetes: Real world data

Antonio Ballesteros Martín-Portugués, Marta Iturregui, Lourdes García-García-Doncel, Concepción Cruzado-Begines, Silvia Ponce-Delgado & Maria Gloria Baena-Nieto
Jerez Hospital, Endocrinology Unit, Jerez, Spain

The use of Flash Glucose Monitoring system (FGM) for the management of type 1 diabetes mellitus (T1D) is rapidly increasing. FGM enables people with diabetes to regularly track their glucose levels without needing to perform capillary finger-stick measurements (SMBG). Clinical studies have shown improvement of glycemic control and hypoglycemia reduction, as well as better comfort and quality of life in people with type 1 diabetes (T1D) using this technology. Objectives: to asses the degree of achievement of glycemic targets in T1D patients using the flash sensor properly (>70% of the time) in our center.
Methods
We analysed registry data collected at a tertiary diabetes centre in Spain. People with T1D routinely using FGM to manage their diabetes were included in the analysis. Downloaded LibreView data of patients were collected: data regarding glucose management indicator (GMI), time within range 70-180 mg/dl (TIR), coefficient of variation (CV) and hypoglycemic events.
Results
A total of 712 patients were included in the study. 80 patients did not download any sensor data. The downloaded data were prior to 6 months in 20 patients and sensor use was <70% of the time in 116 patients. We analyzed data from patients who used the sensor appropriately (>70% of the time). Data from 488 patients (68.53%) were analyzed. The percentage of patients with a GMI< 7% was 48%, those with CV<36% were 49,8% and those with TIR>70% were 31,6%. All targets were met only in 22,5% of patients. In addition, 87.9% of patients had a high risk of hypoglycemia and 27,5% had experienced at least 1 daily hypoglycemic event.
Conclusions
There is a high percentage of T1D patients using FGM who do not use it properly. Only 15% of TD1 patients with adequate use of the sensor have good glycemic control. Metabolic control in T1D patients should be improved and strategies for proper use of FGM must be implemented.

DOI: 10.1530/endoabs.81.EP336

EP337

The possible biomarkers of the "postCovid-19 syndrome" in patients with type 2 diabetes

Sergey Sukhanov[1], Yulia Sorokina[2], Olga Zanozina[3] & Veronika Lagonskaya[3]
[1]Privolzhsky Research Medical University, Hospital Therapy, Nizhny Novgorod, Russian Federation;[2]Privolzhsky Research Medical University, General and Clinical Pharmacology, Nizhny Novgorod, Russian Federation; [3]Privolzhsky Research Medical University, Regional Hospital named after N.A,Stemashko, Endocrinology, Nizhny Novdorod, Russian Federation

COVID-19 has a significant effect on the patient's well-being even after the norm of laboratory parameters.The patients had cognitive blunting breathlessness, headache, fatigue, myalgia, weakness etc. The symptoms could last 3–12 months, from mild to severe, can lead to death.
Purpose
To determine the significance of some biomarkers characterizing the condition of a patient with diabetes mellitus after undergoing covid.
Materials and Methods
We examined 27 patients with type 2 diabetes who underwent Covid-19 4 months ago. This was the first group. The average age was 62.3 years, the duration of diabetes was 6.8 years. Glycated hemoglobin was 8.1%. The second group consisted of 18 patients without a new coronovirus infection and comparable to the patients of the first group by sex, age, duration of the disease, the level of glycated hemoglobin, complications of diabetes and concomitant diseases. The severity of of dysfunctions was assessed in points. We investigated: glycated hemoglobin (BioRad), haptoglobin, ceruloplasmin, c-reactive protein, D-dimers (ACL TOP 700 Instrumentation Laboratory), Klotho protein (ELISA).
Results
The Klotho protein levels in the first group were significantly lower than in the patients of the second group ($P = 0,024$), while the level of other indicators in these groups did not differ significantly. We noted a significant relationship between the severity of polyfunctional disorders in diabetic patients after a new coronovirus infection and the level of Klotto protein. The Klotto of protein level significantly negatively correlated with the level of glycated hemoglobin ($r = -0.8$, $P = 0.023$) and the level of c reactive protein ($r = -0.72$, $P = 0,039$).
Conclusion
The Klotho protein can be a biomarker of the "postCovid-19 syndrome" in patients with type 2 diabetes who have undergone a new coronavirus infection

DOI: 10.1530/endoabs.81.EP337

EP338

Features of some metabolic and instrumental indices in patients with type 2 diabetes mellitus and COVID-19 in oxygen deficiency developed for the first time depending on the initial compensation

Ina Darashkevich[1], Tatjana V Mokhort[2], Alena Kulaha[3] & Nataliya Bahamazava[3]
[1]Grodno State Medical University, Grodno, Belarus; [2]Belarusian State Medical University, Minsk, Belarus; [3]Grodno University Clinic, Grodno, Belarus

Patients with type 2 diabetes mellitus (DM) are one of the most vulnerable categories of patients in terms of adverse outcomes of COVID-19 infection.
Aim
To assess the features of laboratory and instrumental data in patients with COVID-19 and type 2 DM (unvaccinated) depending on the value of glycated hemoglobin (HbA1c) at the time of the onset of oxygen deficiency.
Materials and methods
The study involved 78 patients with type 2 DM and COVID 19. All the participants were divided into 2 groups. Group 1 ($n = 47$) included patients with HvA1c$\leq$7.0%, group 2 ($n = 31$) - $\geq$7.0%. The patients underwent computed tomography scan of the lungs (CT), assessment of blood oxygen saturation level (SpO2), HbA1c, C-reactive protein(CRP), ferritin, D-dimer, complete blood count on the 6-9th day of the disease.
Results
Analyzing the obtained results it was revealed that in patients of group 1 the duration of type 2 DM was 7.0 [6.0;7.5] years vs 8.9 [7.0;10.0] years in group 2 ($P = 0.031$). The HbA1 was significantly higher in group 2 -8.5 [8.0;9.8]% vs 7,0 [6.7;7.0]%, ($P = 0.001$). So, in group 1 at the time of hospitalization SpO2 was 91.0 [90.0;93.0]% vs 87.0 [86.0;89.0]% ($P = 0.005$). All the patients had bilateral interstitial pneumonia, the median value of the percentage of lung tissue damage in group 1 was 45.0 [40.0; 55.5]% vs 65.0 [60.0; 70.0]% in group 2 ($P = 0.002$) (CT lungs). In group 2 there is a higher value of CRP 52.5 [37.0; 78.0] mg/l vs 36.0 [27.0;43.0] mg/l ($P = 0.016$), ferritin value 545.0 [480.0; 550.0] ng/ml. vs 433.7 [420.0;580.0] ng/ml ($P = 0.011$). In groups 1 and 2, there were no significant differences in the indicators of erythrocytes and hemoglobin. There was a difference in the value of leukocytes 9.4 [9.0; 9.9]$\times 10^9$/l vs 5,7 [4,7; 8,3] $\times 10^9$/l ($P = 0.023$), stab neutrophils 4.0 [3.0;5.0]% vs 7,0 [6,0; 10,0]% ($P = 0.002$) and lymphocyte count 16.0 [11.0;17.0]% vs 11.0 [10.0; 14.0]% ($P = 0.013$). An increase in HbA1c is associated with a decrease in SpO2 (r =-0.78), an increase in the percentage of lung tissue damage by CTlungs (r =0.66), CRP (r =0.67), ferritin (r =0.79), D-dimers(r =0.60) in group 1. A positive correlation was registered between the HbA1c values and the percentage of lung tissue damage by CT (r =0.87), CRP(r =0.96), D-dimer (r =0.93), ferritin (r = 0.93); and a decrease in SpO2 is associated with an increase in HbA1c (r=-0.98), CTlungs (r =-0.98), CRP(r =-0.92), D-dimers (r =-0.89) in group 2.
Conclusions
Decompensation of diabetes mellitus in patients with COVID 19 is accompanied by an increased degree of damage to the lung tissue, prolonged oxygen therapy, increased values of CRP, D-dimers, ferritin, lymphopenia, and the lowest value of leukocytes.

DOI: 10.1530/endoabs.81.EP338

EP339

Impact of COVID-19 pandemic on diabetic patients

Salma Abadlia, Zouaoui Chadia, Bchir Najla, Sarra Raddadi, Annam Benchhida, Chaima Souibgui & Haroun Ouertani
Military Hospital , Endocrinology, Tunis, Tunisia

Introduction
The COVID-19 pandemic had a significant emotional and psychological impact on populations worldwide, especially vulnerable people with chronic diseases such as diabetics. The objective of our study was to assess the quality of life and psychological distress of diabetic patients and to study patients' attitudes towards managing their diabetes.
Methods
We conducted a cross sectional descriptive study involving 60 diabetic patients followed in Endocrinology-Nutrition department of the Military Hospital of Tunis during the period between February and March 2021. We used the short form questionnaire SF-12 to assess quality of life of participants, allowing us to calculate two scores; mental component score (MCS) and physical component score (PCS) with a total score ranging from 0 to 100. A higher score indicates a better health. We also used Kessler psychological distress scale (K10) with a total score ranging from 0 to 40. Low scores indicate low levels of psychological distress while high scores indicate high levels of psychological distress. Mean level of worry was assessed using a scale from 0 to 10.
Results
Our population was predominantly female (sex ratio=0.8). The average age was 52.4 years. Our patients were suffering from two or more chronic diseases in 78.4% of cases. The mean duration of diabetes was 11 years with an average HbA1c of 8.9%. The mean level of worry was 4.8. The mainly subjects of worries concerned "the shortage of anti-diabetic drugs and monitoring equipment" (78.3% and 71.7% respectively), the notion of "high risk population" (75%) and "the potential severity of the infection in diabetics" (73.3%). Patients were more observant for their treatment and in monitoring their glycemia in respectively 45% and 38.3% of cases. Nevertheless, physical activity was reduced in 36.7% and food intake increased in 26.7% of cases. MCS and PCS were 39 $\pm$10.4 and 37.4$\pm$9.3, respectively. The mean K10 score was 12.9$\pm$8.8. In univariate analysis, MCS, PCS and K10 were significantly associated with gender (P = 0.03; 0.009 and 0.005 respectively). PCS was associated with age ($P = 0.025$).
Conclusion
The quality of life of diabetic persons is impaired. This involves the implementation of a monitoring, follow-up and support strategy by the health system for these patients.

DOI: 10.1530/endoabs.81.EP339

EP340

COVID-19 pandemic: Impact on follow up care of insulin-requiring diabetic patients

Asma Kardi, Radhouen Gharbi , Ben Salem Maram, Manel Jemel, Hajer Kandara, Marwa Chiboub & Ines Kammoun
Institut De Nutrition, Tunis, Tunisia

Introduction
COVID-19 is a novel pandemic affecting globally. It has led to an unprecedented global health crisis assessing health system's preparedness to deal with health disasters. The aim of our study was to evaluate the impact of COVID-19 on the follow up care of diabetic patients.
Methods
We conducted a retrospective study in 100 insulin-requiring diabetic patients. Data regarding treatment availability, weigh, glycemic control and follow up care during two years before (T1: 2018-2019) and during the pandemic of COVID-19 (T2 : 2020-2021) were collected.
Results
The study population included 60 women and 40 men. The mean age was 58.6 $\pm$ 1.3 years. Among our 100 patients, 30% have type 1 diabetes mellitus and 70% have type 2 diabetes mellitus. Fifty-seven patients were using insulin alone and 43 patients were treated by insulin with metformin. Hypertension and dyslipidemia prevalence was respectively 55% and 56%. Insulin had always been available. However, metformin, anti-hypertensive drugs and anti-dyslipidemic drugs disponibility in public health facilities decreased, with respectively 57%, 36% and 75% of cases before pandemic versus 79%, 59% and 85% in T2 ($P = 0.022$, $P = 0.004$ and $P = 0.332$ respectively). Eight patients missed at least one medical consultation in T1 versus 46 patients in T2 ($P <$ 10-3). Fundoscopy and screening for microalbuminuria were performed respectively in 83% and 89% of patients in T1 and in 41% and 87% in T2 ($P <$ 10-3, $P = 0.839$ respectively). Glycosylated hemoglobin increased in 75% of patients. Its mean raised from 8.9% to 9.3% ($P <$ 10-3). The percentage of patients with well-controlled diabetes decreased from 29% in T1 to 19% in T2 ($P = 0.013$). A weight gain was documented in 57% of patients. The mean of weight increased from 76.9 Kg to 78.3 Kg ($P <$ 10-3). Out of 100 patients, cardiovascular events were documented in one patient in T1 and in five patients in T2 ($P = 0.219$).
Conclusion
A significant impairment in the follow up care of diabetic patients and their glycemic control has been revealed through our study. This can be partially explained by the impact of lockdown on treatment facilities availability, healthy lifestyle habits and by the stressful condition related to this pandemic. However, defective health systems have contributed to worsen this critical situation. Hence, effective preparedness are needed in future so that complications can be minimized.

DOI: 10.1530/endoabs.81.EP340

EP341

Diabetes distress and its clinical determinants in Type 2 diabetes patients

Najoua Lassoued, Marwa Majdoub, Mehrez Achwak, Khalil Chadly, Zantour Baha, Alaya Wafa & Sfar Mohamed Habib
Taher Sfar University Hospital, Endocrinology Department, Mahdia, Tunisia

Introduction
Diabetes distress (DD) refers to the emotional burdens and worries, often hidden, that are part of the spectrum of the patient experience when managing a chronic and demanding disease like diabetes. The objective of this work was to determine the prevalence of DD and its clinical determinants in type 2 diabetic patients.
Patients and methods
Cross-sectional study conducted on 92 type 2 diabetic patients who consulted on an outpatient basis between April and June 2021. DD was assessed using the Diabetes Distress Scale (DDS).
Results
The average duration of diabetes was 10.35 years. 69.6% of patients presented with moderate to severe distress related to diabetes. The dimension of lifestyle distress had the highest score among the DDS subscales. There was a correlation between age, level of education, social coverage, rate of follow-up, HbA1c level and DD. HbA1c levels and rate of follow-up were the main predictors of DD.
Discussion and conclusion
The results of this work underscore the importance of identifying DD in type 2 diabetics. High levels of DD have been significantly associated with poor glycemic control, poor diabetes self-management, and poor quality of life. More work is needed to better explore and manage psychological comorbidity in type 2 diabetics.

DOI: 10.1530/endoabs.81.EP341

EP342

A diabetic foot case with bilateral charcot arthropathy

Ensar Aydemir, Erhan Hocaoglu[1], Coskun Ates , Filiz Mercan Saridas, Soner Cander , Ozen Oz Gul, Canan Ersoy & Erdinc Erturk
Uludag University Medical School, Bursa, Turkey

Background
Diabetic foot infections are an important cause of morbidity and mortality associated with poor glycemic control, polyneuropathy and micro/macrovascular diseases. The clinical, laboratory, radiological, pharmacological and/or surgical evaluation is required. We report a case of diabetic foot infection with bilaterally charcot joint.
Case
A 52-year-old female patient with type 2 diabetes mellitus (DM), hypertension (HT), coronary artery disease (CAD) and peripheral artery disease (PAD) applied to our endocrine clinic with ulcerated lesion on the sole of the right foot. Eight years previously she had undergone a left first metatarsophalangeal (MTP) joint amputation due to underlying diabetic foot. On examination, she had a bilaterally neuropathic arthropathy (Charcot joint). Her plasma glucose level was 272 mg/dl, HbA1C of%7.8, erythrocyte sedimentation rate (ESR) of 46 mm/h and C-reactive protein (CRP) of 41.2 (normal range, 0-5) mg/l with normal renal and liver function tests in the first laboratory evaluation. Two-sided X-Ray and magnetic resonance imaging (MRI) of the ankle and foot revealed destructive joint disease without osteomyelitis (Figure 1). The diagnosis of diabetic foot infection was made, and treatment with intravenous piperacillin/tazobactam and teicoplanin for two weeks, then the patient improved. After clinical and biochemical improvements, the patient was discharged with oral antibiotics.
Discussion
Uncontrolled diabetes mellitus is the most common cause of non-traumatic amputations. Chronic, progressive and destructive arthropathy may develop in diabetic patients associated with sensory, autonomic and motor neuropathy. Treatment of charcot neuroarthropathy is based on multidiciplinary team management. Inappropriate and late approach of diabetic foot infection often results to amputation of any limb.

DOI: 10.1530/endoabs.81.EP342

EP343

Foot risk assessment in diabetic patients

Zeineb Zemni[1], Daii Raja[1], Olfa Lajili[2], Emna Bornaz[3], Amal Salem[4], Salma Abadlia[5], Htira Yosra[1], Hedfi Imene[1], Zohra Hadj Ali[1] & Faika Ben Mami[1]
[1]National Institute of Nutrition Of Tunis, Department C, Tunis, Tunisia; [2]Military Hospital of Instruction of Tunis, Hygiene Service, Tunis, Tunisia; [3]National Institute of Nutrition of Tunis, Department B, Tunis, Tunisia; [4]National Institute of Nutrition of Tunis, Outpatient Department and Functional Explorations, Tunis, Tunisia; [5]Military Hospital of Instruction of Tunis, Endocrinology Departement, Tunis, Tunisia

Background
The management of diabetic foot starts with prevention, mainly based on the early detection of peripheral neuropathy and peripheral arterial disease, called podiatric risk assessment. This risk must be evaluated in all type 2 diabetics since the discovery. The aim of this study was the assessment of diabetic foot ulcer risk according to International Working Group on the Diabetic Foot (IWGDF) and the identification of risk factors for developing foot lesions.
Methods
We conducted a descriptive, cross-sectional study that concerned 60 diabetic patients hospitalized in the Department C of the National Institute of Nutrition between July and September 2021.
Results
Mean age of patients was $59,1 \pm 12,23$ years with sex ratio 0.66. Half patients were hypertensive, 64,4% had a personal history of dyslipidemia and 34% were smokers. All patients had Type 2 diabetes with evolution duration $9,33 \pm 6,26$ years. The majority of patients (91,7%) had uncontrolled diabetes and 66,7% had microangiopathy (retinopathy and nephropathy). Thirteen patients (21%) had a foot at risk. On clinical examination, neuropathy was found in 21% of cases, while lower limb arteriopathy in 14,3%. Patients were classified into four risk groups according to IWGDF criteria as follows: grade 0: 78,3%; grade 1: 13,3%; grade 2: 6,7% and grade 3: 1,7%. There was statistically significant relationship between LDL cholesterol ($P = 0,035$), microangiopathy ($P = 0,003$) and foot risk grade. Patient's sex, BMI, diabetes duration, smoking, and HBA1c did not have significant association with risk of diabetic foot ulcer.
Conclusion
Diabetic foot remains a major health problem and a frequent cause of limb amputation. Podiatric risk assessment represents a key tool to avoid many dreaded complications.

DOI: 10.1530/endoabs.81.EP343

EP344

Relationship between kidney function and the level of amylinemia in patients with diabetes mellitus

Nataliia Pashkovska & Iryna Tsaryk
Bukovinian State Medical University, Department of Clinical Immunology, Allergology and Endocrinology, Chernivtsi, Ukraine

Background
Chronic kidney disease (CKD) is one of the leading causes of disability and mortality in patients with different types of diabetes mellitus (DM). However, relationships between kidney function and serum amylin levels are still controversial, especially in patients with heterogeneous types of diabetes. The objective of the study was to determine the features of the glomerular filtration rate (GFR) in patients with DM depending on the level of amylinemia.
Methods
89 patients with DM and CKD were examined, as well as 15 representatives of the control group. The patients were divided into three groups by the types of DM (25 patients with classical type 1 diabetes mellitus (T1DM), 36 patients with latent autoimmune diabetes in adults (LADA), 28 patients with type 2 diabetes (T2DM)) and by the GFR stages (G1-21, G2-49, G3a-48, G3b-17, G4-10). GFR was determined by the CKD-EPI formula. Serum amylin levels were measured using the ELISA method.
Results
The level of amylinemia in patients with GFR stages G1 and G2 probably did not differ in comparison with the control and among themselves. In the group of patients with GFR stage G3a, the level of serum amylin was 7.7 times higher than the control, 3.7 times higher than the G1 group, but did not differ from the one in group G2. In patients with GFR of stage G3b, the above indicator was 14.7 times higher relative to the control, 7.2 times higher relative to the group of individuals with GFR of stage G1, 3.5 times higher than the G2 stage and 1.9 times higher

than the G3a stage. The serum level of amylin in the group of patients with GFR stage G4 was significantly higher by 26.0 times compared to the control, 12.7 times – in the group of patients with GFR stage G1, 6.1 times – in the group of patients with GFR of stage G2, 3.4 times – in the group of patients with GFR of stage G3a and has not changed compared to the G3b group. In patients with DM positive correlations were found between the content of amylin and insulin, C-peptide, HOMA-IR index and creatinine ($P<0.05$), in the group of patients with T2DM - between serum amylin and GFR ($P<0.05$).

Conclusion

The level of amylin was increased in proportion to the stages of GFR in patients with T2DM and LADA, which indicates the role of hyperamilinemia in the development of CKD in this category of patients.

DOI: 10.1530/endoabs.81.EP344

EP345

Acute pancreatitis revealing major hypertriglyceridemia at 94 g/l!

Kaoutar Rifai, Loubna Guissi, Salma Ahallat, Hind Iraqi & Mohamed Elhassan Gharbi
Ibn Sina University Hospital, Endocrinology, Rabat, Morocco

Introduction

Hypertriglyceridemia (HTG) is a rare but well-known cause of acute pancreatitis, which can be fatal with an overall mortality rate of 36-50% in the most severe forms.

Case presentation

A 29-year-old patient was admitted to the emergency department with abdominal pain, bilious vomiting and alteration of general condition. Physical examination showed hemodynamic shock with diffuse abdominal tenderness. The Laboratory results showed a serum lipase of 546 U/l (higher than 6 times the upper limit of normal), a severe hypertriglyceridemia at 94 g/l and hypercholesterolemia at 11 g/l. Abdominal ultrasound did not show lithiasis, abdominal CT scan revealed Balthazar grade E pancreatitis and magnetic resonance cholangiopancreatography (MRCP) did not show microlithiasis of the gallbladder and biliary ducts. Pancreatic autoantibodies were negative. The diagnosis of acute pancreatitis due to major hypertriglyceridemia was made. The patient was managed with fasting, intravenous hydration, heparin and fibrate therapy. The evolution was marked by a clinico-biological improvement.

Discussion

The association between acute pancreatitis and HTG is widely recognized. It presents 12-38% of all acute pancreatitis. The symptomatology of this acute pancreatitis is unremarkable. The management of major hypertriglyceridemia is based on symptomatic treatment combining effective analgesia, parenteral nutrition, adequate hydration and lipid-free nutrition. Other therapies have been reported, such as heparin infusion and insulin. Plasma exchange may be useful, although its clinical efficacy has not been proven.

Conclusion

Hypertriglyceridemia is a rare cause of acute pancreatitis. It requires specific treatment to overcome the acute phase and prevent recurrence.

DOI: 10.1530/endoabs.81.EP345

EP346

A new case of hypoglycemia of unrelated etiology.

Daniel Medina Rivero[1], Isabel Mateo Gavira[2] & Esteban Sánchez Toscano[2]
[1]Hospital Universitario Puerta del Mar, San Fernando, Spain; [2]Hospital Universitario Puerta del Mar, Cádiz, Spain

Male, 29 years old. Go to consultations in our center for a second opinion for assessment of hypoglycemia. The patient has reported, for 3 years, symptoms consisting of episodes of dizziness and headache predominantly during the day, which subside after eating food, and which increase in frequency in relation to exercise. He provides capillary glycaemia objectified in family glucometer between 40-70 mg / dl coinciding with the episodes. The patient was initially treated at another center, which after a study (04/2012: glucose 62 mg/dl, insulin 5.89 mcIU/ml, C-peptide 4.5 ng/ml, TSH 1.93 mcIU/ml, HGH 0.09 ng/ml, IGF-1 264 ng/ml, basal cortisol 16.09 mcg/dl) is classified as reactive hypoglycemia and hygienic-dietary measures are prescribed by means of a divided diet and avoiding the intake of rapidly absorbed carbohydrates. We admitted the patient to perform a fasting test (07/2012), which was positive at 30 hours (glycemia 36 mg/dl, insulin 4.46 mcIU/ml, C-peptide 1.51 ng/ml) compatible with hyperinsulinemic hypoglycemia. Treatment with diazoxide 100 mg 1-0-1 was prescribed at discharge. A localization study consisting of an abdominal CT scan was performed, which revealed a doubtful 1.4 cm lesion in the body of the pancreas. It is completed with pancreatic MRI that does not describe the lesion mentioned in the CT. To determine the etiology, the patient was admitted on 09/2012 to perform an arterial calcium stimulation test by selective pancreatic catheterization, which was negative for insulinoma, since only a 21% increase in blood insulin was observed in the splenic artery and no it is observed in the rest (hepatic or superior mesenteric). It is decided in principle management with medical treatment and follow-up with imaging tests. It is performed during the same CT scan of the pancreas every 2 years and 2 echoendoscopies. In the last ultrasound endoscopy performed (10/2017), pancreatic lesions compatible with insulinoma were still not observed. There is talk of diffuse ultrasound changes in pancreatic tissue, to rule out nesidioblastosis. The patient remains relatively controlled with medical treatment and pancreatic surgery is not proposed.

DOI: 10.1530/endoabs.81.EP346

EP347

The efficacy of liraglutide for weight loss in a patient with relapse in obesity after bariatric surgery – case report

Anna Dabrowska[1,2] & Jaroslaw Dudka[1]
[1]Medical University of Lublin, Department of Toxicology, Lublin, Poland; [2]Endocrinology Outpatient Clinic, Lublin, Poland

Introduction

Obesity is a chronic disease which has become a global epidemic. Approximately 7% of deaths per year is associated with obesity, especially because of its complications such as cardiovascular diseases, type 2 diabetes or cancer. Lifestyle interventions are the first line of management but additional pharmacotherapy or bariatric surgery should be considered in more severe cases.

Case report

A 40-year-old woman was referred to Endocrinology Outpatient Clinic because of severe obesity. She underwent laparoscopic sleeve gastrectomy few years ago which led to weight loss. However, a return to unhealthy eating habits as well as an insufficient physical activity, have caused obesity recurrence. The patient has been treated with metformin 1 g because of insulin resistance, perindopril 5 mg due to hypertension and venlafaxine 150 mg because of depression. Despite of metformin implementation, diet and activity interventions, the reduction of weight has not been achieved. At the first endocrinology consultation, the patient had a body weight of 124 kg and a body mass index of 43.97 kg/m^2. Blood pressure was 137/85 mmHg under treatment. The laboratory tests revealed normal liver and renal function. The pituitary function (corticotropic, thyroid, gonadal, and somatotroph axes) was also confirmed as normal. US abdomen examination showed signs of hepatic steatosis and lack of gall bladder which has been removed due to cholelithiasis. Fasting laboratory test results showed: total cholesterol of 183.0 mg/dl, LDL-cholesterol of 110.2 mg/dl, triglycerides of 109.0 mg/dl, HDL-cholesterol of 51 mg/dl. Oral glucose tolerance test at time 0-60-120 min, after a 2-week break in the use of metformin, revealed glucose levels: 100-278-99 mg/dl and insulin levels 10.8-75.9-18.4 μUI/ml, with mild insulin resistance at fasting (HOMA-IR 2.67). Thus, considering severe obesity, unresponsive to diet and lifestyle interventions, complicated by hypertension, impaired fasting glucose, hepatic steatosis and depression, a GLP1-receptor agonist therapy with liraglutide has been proposed, from a starting dose at 0.6 mg up to a final dose at 3.0 mg per day. No side effects have been registered during therapy so far. At the last follow-up visit, four months after introducing liraglutide, the patients' weight was 108 kg (BMI 38.29 kg/m^2), with a total weight loss of 16 kg (-12.9%).

Conclusions

Liraglutide effectively reduces body weight and may be a safe option of treatment in patients with severe obesity. It should be also considered in subjects with obesity recurrence after bariatric surgery, as an alternative management to reoperation.

DOI: 10.1530/endoabs.81.EP347

EP348

Assessment of the Podiatric Risk on Diabetics: Cross-Sectional Study in Regard to 200 Patients

El Amri Abir[1], Nadia Ben Amor[1], Rihab Yamoun[2], Faten Mahjoub[2], Sirine Nsir[3], Amany Amorri[3], Ramla Mizouri[1], Rym Ben Othman[1], Olfa Berriche[1] & Jamoussi Henda[1]
[1]National Institute of Nutrition, Tunisia; [2]Faculty of Medicine Of Tunis, Tunisia; [3]University of Tunis El Manar, Tunisia

Introduction
The diabetic foot is a frequent, serious and costly complication of diabetes. The prevention of diabetic foot involves a systematic podiatric evaluation of diabetic patients to identify the foot at risk. The aim of our study was to determine the podiatric risk in a Tunisian diabetic population according to the classification of the International Working Group on the Diabetic Foot (IWGDF) and the factors associated with podiatric risk.
Methods
It was a prospective cross-sectional, descriptive and analytical study conducted over a three-month period including patients aged 18 years and older with a confirmed diagnosis of type 1 and type 2 diabetes, hospitalized in nutrition department A between 1 August and 31 October 2021. Subjects under 18 years of age or hospitalized for conditions other than diabetes were excluded from the study.
Results
The study enrolled 200 patients and the sex-ratio was 0.72. The average age of the cohort was 53 years. 74.2% of the patients were running type 2 diabetes. Of them, 75% had dyslipidemia and 82% were overweight or obese. High Blood Pressure was found in 51% of cases. The capillary blood glucose and glycated hemoglobin were respectively around 12.26 mmol/l and 10.8%. Prior ulceration and/or amputation were noted in 9% of cases. The gradation of the foot risk according to the International Working Group on the Diabetic Foot (IWGDF) was established as follow: grade 0 (76.3%), grade 1 (12.6%), grade 2 (6.3%), grade 3 (4.8%). Risk factors most associated with foot injury occurrence included diabetic peripheral neuropathy ($P = 0.000$), the absence of pulse perception ($P = 0.000$), chronic peripheral artery occlusive disease (PAOD) ($P = 0.000$), diabetic retinopathy ($P = 0.002$) and diabetic nephropathy ($P = 0.017$).
Conclusion
The prevention of diabetic foot in emerging countries is accessible by a systematic clinical examination of all diabetic feet and the awareness of adapted footwear. Long-term studies are needed to evaluate whether the intervention of podiatrists starting at an early phase would lead to a reduction in major foot problems.

DOI: 10.1530/endoabs.81.EP348

EP349

Cutaneous manifestations of diabetes mellitus

El Amri Abir[1], Nadia Ben Amor[1], Rihab Yamoun[2], Faten Mahjoub[2], Amany Amorri[3], Sirine Nsir[3], Rym Ben Othman[1], Ramla Mizouri[1], Olfa Berriche[1] & Jamoussi Henda[1]
[1]National Institute of Nutrition, Tunisia; [2]Faculty of Medicine Of Tunis, Tunisia; [3]University of Tunis El Manar, Tunisia

Introduction
Diabetes mellitus (DM) is the most common endocrine disorder. The skin manifestations of diabetes can vary depending on the duration of the disease and the control of blood glucose levels. Almost all patients with DM eventually develop skin changes due to the long-term effects of hyperglycemia on microcirculation and skin collagen. This study was conducted to find the hospital based prevalence of mucocutaneous manifestations in patients with diabetes mellitus, their clinical pattern and relationship with glycemic control and duration of the disease
Methods
It was a longitudinal observational study including 200 patients aged 18 years and older with a confirmed diagnosis of type 1 and type 2 diabetes, admitted in nutrition department A for any reason between 1 August and 31 December 2021.
Results
Among 200 patients with DM, 88(44%) were males and 112(565%) were females. The mean age of the patients was 51.85 $\pm$ 18.35 years and mean total duration of diabetes was 11.87 $\pm$ 8.9 years. Of them, 135 (67.5%) had one or more dermatoses. The common skin disorders for which patients sought treatment were: xerosis (55.5%), plantar hyperkeratosis (41.3%), onychomycosis (39.2%), and inter-toe intertrigo (18.2%). Risk factors most closely associated with mucocutaneous manifestations included High Blood Pressure ($P = 0.000$), diabetic peripheral neuropathy ($P = 0.018$) and obesity or overweight ($P = 0.000$) . But there is no statistically significant relationship with nephropathy ($P = 0.14$) or retinopathy ($P = 0.58$).
Conclusion
Skin problems are quite common among diabetic population. Diabetes-related skin lesions can serve as a gateway for microorganisms and possible secondary infections. The early detection of mucocutaneous manifestations in DM is important to be able to avoid and manage the complications and prevent disability.

DOI: 10.1530/endoabs.81.EP349

EP350

Dapagliflozin can Induce and Maintain Type 2 Diabetes Remission

Mahmoud Younis
Egypt Ministry of Health, Kafr Elsheikh, Egypt

Introduction
Type 2 diabetes mellitus, has gained a lot of attention in recent years as one of the most important chronic progressive diseases in the world, which slowly crawls towards longevity and which involves many chronic complications, which are dangerous to health and the economy. Sodium-glucose cotransporter-2 (SGLT2) inhibitors represent a category of newly discovered drugs that work by preventing glucose reabsorption in the proximal renal tubules. (SGLT2) Inhibitors may induce type 2 diabetes remission. Design: Randomized, -controlled trial, 6-month trial.
Materials and Methods
100 type 2 diabetes patients were randomized into 2 groups.
Results
The results show a statistically significant decrease of A1C levels after 3 and 6 months treatment with dapagliflozin and significant change in A1C levels after 3 months treatment of glimepiride but a no significant change in the next 3 months. The results also show a statistically significant decrease in BMI in the dapagliflozin group after 6 months of treatment.
Conclusion
As type 2 diabetes is one of the most disabling diseases, it is necessary to find a drug that can lead to remission. Dapagliflozin can lead to type 2 diabetes remission.KeywordsDapagliflozin, Inhibitors, Type 2 Diabetes

DOI: 10.1530/endoabs.81.EP350

EP351

Double Trouble. Metformin and empagliflozin induced lactic acidosis - A case report

Bhavna Sharma, Michele Mantega, Mahesh Deore, Ian Seetho, Shivashankar Seechurn, Elaine Hui, Mushtaqur Rahman & Asjid Qureshi
Northwick Park Hospital, United Kingdom

63 years old with sarcoidosis since 2018 and type 2 diabetes was referred by GP for hypercalcemia related to likely dehydration and sarcoidosis. She was started on a weaning dose of prednisolone and empagliflozin. She had already been on metformin for several years. She was discharged after calcium improved from 2.97 mmol/l to 2.83 mmol/l. She was advised to follow up in Ambulatory care in 1 week for repeat calcium levels. On follow up, noted to have calcium levels of 2.67 mmol/l. Lactate noted to be 6.9 with a pH of 7.3 (calculated anion gap 13.1 mmol/l). Patient noted to be completely asymptomatic with normal systemic exam. Given fluids in ambulatory care , however, lactate noted to be rising at 7.7 with negative ketones and normal sugars. Empagliflozin was stopped and insulin was initiated with normalization of lactate with minimal fluid therapy. A literature review noted a similar case by Tomigana et al[1] with lactic acidosis after initiation of empagliflozin along with metformin. Cellular dehydration with inhibition of enzymes may contribute to high lactate in the patients treated with metformin and an SGLT2 inhibitor. Lactate should be checked in unwell patients on metformin and an SGLT2 inhibitor. The effect of this complication on mortality/morbidity is unclear and further research is needed.
Reference
1. Tominaga T, Ozaki M, Kanda M, Maeda R, Otuka H, Otake K, et al. A Case of Lactic Acidosis after Resumption of Metformin and SGLT2 Inhibitors. *Ann Clin Case Rep*. 2021; 6: 1924.

DOI: 10.1530/endoabs.81.EP351

EP352

Long-term impact of digitally administered Breathe Well-being Diabetes Reversal Program (BDRP) in individuals with type 2 diabetes mellitus

Pawan Kumar Goyal[1], Surajeet Kumar Patra[2], Aditya Kaicker[2], Rohan Verma[2], Seema Goel[2], Rupali Jangid[3], Saleha Rehman[3] & Venugopal Madhusudhana[3]
[1]Fortis Hospital, Shalimar Bagh, Delhi, India; [2]Breathe Well-Being, New Delhi, India; [3]THB (India), Gurugram, India

Introduction
Breathe Well-being Diabetes Reversal Program (BDRP) delivers personalized lifestyle management (LSM) curriculum including education, lifestyle, and health-related content, based on patient's health profile and preferences. The program assists the physicians in making clinical decisions by providing comprehensive lifestyle data, which facilitates patient adherence and aids in achieving positive health outcomes.
Objective
To estimate the long-term impact of digitally administered BDRP on lifestyle measures in individuals with T2DM in India
Methodology
BDRP provides a 4-month digitally administered LSM intervention with additional stress reduction module- a "Happiness and Lifestyle Coach" combined with meditation. Individuals with T2DM were divided in 3 cohorts (1:1:1) treated with (a) BDRP with doctor-prescribed medication ($n = 60$), (b) BDRP with doctor-prescribed medication and personalized stress reduction module ($n = 61$), (c) Only doctor-prescribed medication (control group; $n = 60$). After 4-months of intervention, cohorts 1 and 2 with high (H: $>70\%$) and medium (M: $\geq 50\%$-$< 70\%$) adherence and cohort 3 were followed up to 19 months. Informed consent was obtained.
Results
Of 60 and 61 individuals in cohorts 1 and 2, 46.7% (28) and 54.1% (33) showed H and M adherence. In H and M cohort 1, BMI (kg/m^2) reduced from 32.6 and 31.2 at baseline to 29.5 and 28.7 at 19 months ($P = 0.003$; $P = 0.000$), respectively. In H and M cohort 2, BMI reduced from 32.9 and 31.9 at baseline to 29.7 and 28.7 at 19 months ($P = 0.001$; $P = 0.000$), respectively. Body weight (kg) in H and M cohort 1 reduced from 90.2 and 85.4 at baseline to 81.6 and 78.4 at 19 months ($P = 0.003$; $P = 0.000$). For H and M cohort 2, body weight reduced from 88.1 and 88.0 at baseline to 79.8 and 79.2 at 19 months ($P = 0.001$; $P = 0.000$). In control group, BMI and body weight reduced from 32.0 and 88.1 to 31.8 and 87.5 ($P = 0.029$; $P = 0.025$). At 19 months, HbA1c levels $<6.5\%$ were observed in 78.6% and 81.8% individuals in H and M cohorts 1 and 2. Penn State Worry Questionnaire (PSWQ) score average changed from 57.5 and 55.5 to 42.1 and 42.1 for cohort 1 (H and M), and 54.9 and 59.8 to 33.9 and 41.0 for cohort 2 (H and M) at 19 months, respectively.
Conclusion
Clinically meaningful reductions in BMI, body weight, HbA1c, and stress levels were observed in both cohorts. Cohort 2 showed greater improvement in stress levels than cohort 1. Study findings supported the promising role of digitally administered BDRP on lifestyle measures of individuals with T2DM.

DOI: 10.1530/endoabs.81.EP352

EP353

Sodium-glucose cotransporter-2 (SGLT-2) inhibitor-induced diabetic ketoacidosis and Fournier's gangrene

Mona Abouzaid , Chien Nee Gan & So Pye
North Tees and Hartlepool NHS Foundation Trust, Diabetes & Endocrinology Department, Stockton on Tees, United Kingdom

Introduction
The Food and Drug Administration (FDA) had issued warnings on the increased risk of diabetic ketoacidosis and Fournier's gangrene with patients using Sodium-glucose cotransporter-2 (SGLT-2) inhibitors. Herein, we report a case of simultaneous Fournier's gangrene and diabetic ketoacidosis after initiation of treatment with Empagliflozin.
Case Presentation
We report a case of a 54-year-old woman with type 2 diabetes on empagliflozin presented feeling unwell. Blood glucose level raised at 32.7 and ketones of 2.2 mmol on admission. Blood gas showed acidosis of pH 7.242 (7.35 - 7.45), bicarbonate of 21.2 mEq/l (22 - 26) and base excess of - 6.5 mmol/l (-2 to +2). She was started on diabetes ketoacidosis treatment. Empagliflozin was suspended. Blood results showed raised C-reactive protein of 353 mg/l. She reported new incontinence of both urine and faeces for 2 weeks. Examination revealed perianal fistula, extensive perineal erythema, pus with central necrotic area on left perineum, inflammation of left labia with a patch of necrosis in left groin crease. She was commenced on broad spectrum intravenous antibiotics. CT scan showed marked diffuse subcutaneous fatty infiltration and oedema on the left side of the perineum and left buttock with suspected fluid collection of the left labia measuring 29x14mm, multiple enlarged left inguinal lymph nodes. She underwent surgical drainage and debridement. Histology showed ulceration and necrotizing abscess with fat necrosis which confirmed the diagnosis of Fournier's gangrene. Humulin M3 twice daily was initiated. She then recovered well.
Conclusion
To our knowledge, only 4 cases reported in the literature worldwide presented with simultaneous Fournier's gangrene and diabetic ketoacidosis after initiation of treatment with (SGLT2) inhibitors. Health care professionals should be aware of this extremely rare but life-threatening adverse events. They should assess patients for Fournier's gangrene if suspected.

DOI: 10.1530/endoabs.81.EP353

EP354

Impact of depression in type 2 diabetics with Covid 19: 38 cases

Kolsi Boulbaba[1] , Rihab Ben Abdallah Kolsi[2], Sidina Mohamed Elmoctar[1], Mohamed Dammak[1], Khouloud Boujilbéne[1], Kawthar Elarbi[1], Asma Zargni[1], Faten Hadj Kacem[1] & Mohamed Abid[1]
[1]CHU Hedi Chaker Sfax Tunisia, Endocrinology and Diabetology, Sfax, Tunisia; [2]Faculté des sciences de Sfax Tunisia, Biology, Sfax, Tunisia

Introduction
Diabetes, like any chronic disease, generates in addition to the somatic consequences, serious psychological repercussions, depression and diabetes emerging respectively in the 4th and 9th rank of the most important causes of disturbances in number of years of life corrected for the disability factor. (DALYS).
Patients and methods
Descriptive retrospective study of 38 post-Covid diabetics collected from the endocrinology – diabetology department of CHU Hédi Chaker, Sfax, Tunisia. Screening for depression using the Beck Scale (BDI).
Results
The average age of our patients was 45.5 years with a sex ratio (M / F) of 1.5. All of our patients had type 2 diabetes. The mean duration of diabetes was 9.5 years. The majority of patients (77%) had an HbA1c$>$ 7.5%. According to the Beck scale, 63.6% of our patients had experienced a feeling of sadness after Covid, of which almost 25% were unable to cope. Feelings of discouragement, failure and guilt were found, respectively, in%, 64% and 45% of cases. A state of fatigue was noted in half of our patients and 42.4% were unable to work. Overall, all of our patients experience post-Covid depression to varying degrees: it was severe in 30.3%, moderate in 54.5% and mild in the rest of our diabetic patients. None of our patients admitted to having a suicide plan and 45% felt that death would set them free. Only 25% of nurses are interested in the psychological side of post-Covid diabetics, 40% of whom encourage them to consult a psychiatric hospital.
Conclusion
All people with diabetes should be screened for symptoms of depression or anxiety. Screening for and managing the psychological consequences of diabetes is essential. Screening for and managing the psychological consequences of diabetes in adolescents is essential for improving the quality of life of these patients and better controlling their disease.

DOI: 10.1530/endoabs.81.EP354

EP355

Distinct inflammatory signatures of upper- and lower-body adipose tissue in postmenopausal women with normal weight and obesity

Ioannis Lempesis[1,2,3], Nicole Hoebers[2], Yvonne Essers[2], Johan WE Jocken[2], Ellen E Blaak[2], Konstantinos N Manolopoulos[1,3] & Gijs H Goossens[2]
[1]Institute of Metabolism and Systems Research (IMSR), College of Medical and Dental Sciences, University of Birmingham, Birmingham, United Kingdom; [2]Department of Human Biology, NUTRIM School of Nutrition and Translational Research in Metabolism,, Maastricht University Medical Centre, Maastricht, Netherlands; [3]Centre for Endocrinology, Diabetes and Metabolism, Birmingham Health Partners, Birmingham, United Kingdom

Background
Abdominal obesity is associated with insulin resistance and increased cardiometabolic disease risk, whereas lower-body fat accumulation seems

protective against metabolic derangements. Differences in upper-body and lower-body adipose tissue (AT) function seem to underlie these opposing associations. Here, we investigated the inflammatory signature of upper- and lower-body AT in women with normal weight and obesity, as well as in human primary abdominal (ABD) and femoral (FEM) adipocytes.
Methods
Twenty-one healthy postmenopausal women (aged 50–65 years) with normal weight (BMI 18–25 kg/m^2) and obesity (BMI 30-40 kg/m^2) were recruited. The *in vivo* secretion of adipokines from ABD and FEM subcutaneous AT was determined after an overnight fast using the arterio-venous balance technique. Furthermore, adipokine expression and adipocyte size in ABD and FEM AT were examined. Finally, the expression and secretion of adipokines were investigated *in vitro* using differentiated human primary ABD and FEM subcutaneous adipocytes derived from the same individuals.
Results
Plasma leptin ($P < 0.001$) and PAI-1 ($P = 0.036$) concentrations, as well as abdominal and femoral adipocyte size were higher in women with obesity compared to normal weight. No significant differences in fat cell size and blood flow were found between ABD and FEM AT. There was significant net release of leptin and MCP-1 across ABD and FEM AT (all $P = 0.001$), and fractional release of MCP-1 was higher in ABD than FEM AT ($P = 0.023$). Gene expression of leptin ($P = 0.010$), PAI-1 ($P = 0.080$) and TNF-α ($P = 0.090$) were lower in ABD than FEM AT and increased in obesity. *In vitro*, IL-6, PAI-1 and leptin gene expression was higher, while adiponectin and DPP-4 gene expression were lower in adipocytes derived from the ABD compared to FEM region. Finally, ABD adipocytes derived from women with obesity secreted less MCP-1 compared to femoral adipocytes ($P = 0.013$).
Conclusions
The present study demonstrates for the first time that there are differences in the expression and secretion of pro-inflammatory adipokines between ABD and FEM AT and human primary adipocytes in postmenopausal women, independent of adipocyte size.

DOI: 10.1530/endoabs.81.EP355

EP356

A unique family with early-onset, severe obesity and hypopituitarism harboring different POMC pathogenic mutations.

Lauriane Le Collen[1,2,3], Brigitte Delemer[1], Christine Poitou-Bernert[4,5], Vaxillaire Martine[1,2], Jean Michel Petit[6], Saveanu Alexandru[7,8,9], Clement Karine[4,5], Froguel Philippe[2,3] & Bonnefond Amélie[2,3]
[1]University Hospital of Reims, Department of Endocrinology Diabetology, Reims, France; [2]EGID/ Pasteur Institute of Lille, Inserm/CNRS UMR 1283/8199 , Lille, France; [3]University of Lille, Lille, France; [4]Pitié-Salpêtrière Hospital, Nutrition Department, Paris, France; [5]Sorbonne Université, INSERM, NutriOmics Research Unit, Paris, France; [6]University Hospital Dijon-Bourgogne, Dijon, France; [7]Aix-Marseille Université Marseille Medical Genetics , Institut National de la Santé et de la Recherche Médicale (INSERM), U125, Marseille, France; [8]Assistance Publique-Hôpitaux de Marseille , Centre de Référence des Maladies Rares de l'hypophyse HYPO, Marseille, France; [9]Assistance-Publique des Hôpitaux de Marseille,Hôpital de la Conception, Laboratory of Molecular Biology, Marseille, France

Objective
We describe two first cousins presenting with neonatal corticotropic deficiency and severe, early-onset obesity. This study aims to identify the molecular etiology of these disorders in both cases and highlights the limits of genetic investigations.
Methods
We collected the clinical-biological data of the family and, more particularly, of the two first cousins (A and B). We performed several constitutive Next-generation Sequencing (NGS) protocols focused on genes causing monogenic forms of pituitary deficits or obesity. The pathogenicity of variants was assessed via the guidelines of the American College of Medical Genetics and Genomics.
Results
Patients A and B had very early-onset obesity (> +3DS at 1year) with neonatal corticotropic deficiency and Combined Pituitary Hormonal deficiency (CPHD). The initial sequencing of three genes causing pituitary deficiency (*TPIT*, *PROP1*, *LHX3*) was negative. Then, by another targeted sequencing protocol, we found that Patient A carried a pathogenic compound heterozygous variant in *POMC* (NM_001035256.3: p.Tyr139* and p.Cys28*). However, Patient B only carried the *POMC* p.Tyr139* variant at heterozygous state, inherited from her mother (aunt of Patient A). Whole-exome sequencing in Patient B allowed us to identify a second pathogenic heterozygous variant in the proximal promoter of *POMC* (c.-11C>A) that was inherited from her father. This non-coding variant was previously reported pathogenic in the literature, with a deleterious effect on POMC activity according to *in vitro* analyses. Patient A is currently being treated effectively with an MCR4 agonist, decreasing BMI from 41.5 kg/m^2 to 25 kg/m^2 after three years.
Conclusions
We described the segregation of three different pathogenic *POMC* mutations within the same family with a CPHD phenotype and severe, early-onset obesity. One of them was challenging to identify because of the limitations of targeted NGS.

DOI: 10.1530/endoabs.81.EP356

EP357

An evidence-based framework to evaluate melanocortin-4 receptor (MC4R) pathway relevance for obesity-associated genes

Megan E Vogel, Ida H Moeller, Alastair S Garfield & Bhavik P Shah
Rhythm Pharmaceuticals, Boston, United States

Introduction
The MC4R pathway is the principal regulator of mammalian energy balance through its modulation of energy intake and energy expenditure. Variants in genes associated with the MC4R pathway can result in rare genetic diseases of obesity. Clinical data in patients with certain genetic defects in the MC4R pathway indicate that setmelanotide, an MC4R agonist, may effectively reduce weight and hunger in scientifically rationalized obese subpopulations in which MC4R-pathway deficiency is a contributing factor to obesity. Here we introduce an evidence-based framework designed to evaluate various genes' relevance to the MC4R pathway to identify those genetic patient populations most likely to benefit from long-term setmelanotide therapy.
Methods
This framework utilizes a set of clinical (human genetics) and non-clinical experimental evidence to evaluate MC4R pathway relevance and is based on the core principles of the NIH ClinGen *Gene-disease Clinical Validation* approach which is the industry standard for assessing gene-disease relationships. Human genetic evidence helps define the contribution of the gene to human obesity, while experimental evidence assesses involvement of the gene in the function of MC4R pathway. The cumulative weight of this evidence is used to classify MC4R pathway genes into 4 strength-based tiers: very strong, strong, moderate, weak. The nature, quantity, and quality of evidence required for each tier builds upon that of the previous tier, with higher ranked genes being more likely to define patient populations potentially responsive to long-term setmelanotide treatment.
Results
Based on a comprehensive literature review, 118 MC4R pathway genes were identified and rank ordered: 8 "very strong", 29 "strong", 22 "moderate", 59 "weak". Importantly, clinically meaningful weight and hunger score reductions following treatment with setmelanotide have been previously demonstrated in patients with obesity due to variants in 6 genes, all initially classified as "very strong" or "strong", lending credence to this framework for the selection of patient populations most likely to benefit from long-term setmelanotide therapy.
Conclusions
This framework provides robust means of selecting MC4R pathway relevant genes and supports clinical investigation of setmelanotide responsiveness in an additional 31 "very strong/strong" genes including *LEP*, *SIM1*, *MRAP2*, and *KSR2*. A clinical trial is currently underway for patients with these gene variants.

DOI: 10.1530/endoabs.81.EP357

EP358

Reduction in Oxytocin levels predict body weight loss in patients with obesity after a very low carbohydrate ketogenic diet (VLCKD).

Rossella Tozzi[1], Sabrina Basciani[2], Rebecca Rossetti[2], Angela Balena[2], Davide Masi[2], Renata Risi[2], Gabriele Veroi[2], Elena Colonnello[2], Maria Chiara Massari[2], Mariaignazia Curreli[2], Elena Gangitano[2], Mikiko Watanabe[2], Stefania Mariani[2], Lucio Gnessi[2] & Carla Lubrabno[2]
[1]Sapienza University of Rome, Molecular Medicine, Roma, Italy; [2]Sapienza University of Rome, Experimental Medicine, Section of Medical Physiopathology, Food Science and Endocrinology, Roma, Italy

Background
Oxytocin (OXT) enhances glucose uptake and lipid utilization in adipose tissue and skeletal muscle.Dysfunction of the OXT system could underlie the pathogenesis of weight gain. Men and women with obesity were reported to have higher OXT blood levels compared to normal weight subjects. In contrast,

metabolic syndrome has been associated with reduced fasting serum oxytocin in larger scale mixed gender studies.
Aim
Data regarding the oxytocin system in rodent obesity models and human subjects with obesity appear divided. This study aimed to investigate the concentrations of OXT in a population affected by obesity before and after a very low carbohydrate ketogenic diet (VLCKD) induced weight loss.
Materials and methods
Subjects with obesity were enrolled at the Center of High Specialization for the treatment of Obesity (CASCO), Umberto I Polyclinic, Sapienza University of Rome. At baseline (t0) and after eight weeks of VLCKD (t1), all patients underwent clinical evaluation, biochemical routine assessment, DXA examination for body composition (Hologic Inc., Bedford, MA, USA, QDR 4500W) and venous blood sampling in EDTA plus 500 KIU/ml of aprotinin (Abcam ab146286) for plasma OXT determination (Abcam, Ab133050, ELISA kit). Achievement of ketosis was monitored by measuring urinary β-OH-butyrate.
Results
40 patients (26 females and 14 males) suffering from obesity were enrolled, (age $= 55.5 \pm 7$ years and BMI $= 35.7 \pm 4.3$ Kg/m^2). OXT level at baseline (t0) was 1166 ± 403 pg/ml, with no differences between males and females. At t0 OXT positively correlated with BMI and hip circumference. After VLCKD, a significant weight reduction was seen (mean BMI $= 32.7$ kg/m^2, mean weight loss $=$ -8.8 kg) and OXT (t1) significantly decreased (728.2 ± 201.7 pg/ml, $P < 0.001$). Baseline OXT positively correlated with t1urinary β-OH-butyrate, after adjustment for age ($r = 0.335$, $P = 0.046$). A strong inverse age adjusted correlation between weight loss and baseline OXT was also reported ($r = -0.458$, $P < 0.005$). A regression analysis showed that the reduction in OXT between t1 and t0, the grade of ketosis during VLCKD and baseline%fat mass were all predictors of weight loss (R20.422; $P = 0.025$).
Conclusion
Our study demonstrated that higher OXT levels associates with BMI and with ketosis induction. A lower OXT reduction during a VLCKD seems to be unfavorable for achieving weight loss. Differences in assay method used for measuring OXT, as well as expression patterns of oxytocin receptors, could explain the partial discrepancy of our results with the literature. Peripheral actions of oxytocin deserve further investigations

DOI: 10.1530/endoabs.81.EP358

EP359

Response of the human gastric epithelium to sleeve gastrectomy surgery

Rachel Ben-Haroush Schyr[1], Botros Moalem[2], Dana Sender[2], Amit Elad[2], Aya Bardugo[2], Ayelet Etzyoni[2], Yhara Arad[2], Yuval Ishai[3], Ki Suk Kim[4], Ariel Benson[3], Ronit Grinbaum[3], Linda Samuelson[4], Nechemi Grinstein[3], Darleen Sandoval[5] & Danny Ben-Zvi[1]
[1]Hebrew University of Jerusalem, Israel; [2]Hebrew University of Jerusalem, Israel; [3]Hadassah Medical Center, Israel; [4]University of Michigan Medical School, United States; [5]University of Colorado, United States

The gastric mucosa is a dynamic and regenerative tissue that functions in extreme conditions of low pH, mechanical insults and bacterial exposure. The mucosa is composed of pit and neck cells which secrete protective mucus, parietal and chief cells that secrete acid and digestive enzymes, enteroendocrine cells that affect motility, secretion and satiety, rare tuft cells, and at two stem-cell compartments. We studied the response of the gastric mucosa to sleeve gastrectomy surgery: a bariatric or weight-loss surgery in which most of the stomach is removed. Histological analysis and single-cell sequencing of gastric mucosa from patients with no history of surgery, and of patients that had surgery years ago revealed that the gastric mucosa adapts to the new anatomy. We observed an increase in proliferation of the stem cells in the isthmus, in the number of cells per crypt, and a change the composition of the enteroendocrine cell population. Moreover, enterochromaffin-like cells that normally secrete histamine change their transcriptional program and express hormones and neurotransmitters that were not expressed prior to surgery. Mathematical modeling pointed to the hormone Gastrin as a main driver for this adaptation. Theoretical predictions from the model were verified using gastrin knockout mice that underwent sleeve gastrectomy. Altogether, our study reveals how the stomach adapts to a new anatomy imposed by a bariatric surgery, and identifies a new set of signals secreted from the endocrine cells of the stomach following surgery.

DOI: 10.1530/endoabs.81.EP359

EP360

Long-term safety of diazoxide choline extended-release (DCCR) tablets in patients with prader-willi syndrome

Evelien Gevers[1], Jennifer Miller[2], Merlin Butler[3], Nicola Bridges[4], Tony Goldstone[5], Kathryn Obrynba[6], Parisa Salehi[7], Eric Felner[8], Lynne Bird[9] , Ashley Shoemaker[10] , Laura Konczal[11] , Melissa Lah[12] , Jack Yanovski[13] , Moris Angulo[14], Jorge Mejia-Corletto[15], David Stevenson[16] , John Wilding[17] , Jennifer Abuzzahab[18] , Guftar Shaikh[19] , David Viskochil[20] , Verghese Mathew[21] , Kristen Yen[22] , Michael Woloschak[22] & Anish Bhatnagar[22]
[1]Queen Mary University of London Barts Health NHS Trust, London, United Kingdom; [2]University of Florida Gainesville, Gainesville, United States;[3]Kansas University Medical Center, Kansas City, KS, United States; [4]Chelsea and Westminster Hospital, London, United Kingdom; [5]Hammersmith Hospital, London, United Kingdom; [6]The Research Institute at Nationwide Children's Hospital, Columbus, United States; [7]Seattle Children's, Seattle, United States; [8]Emory Children's Center, Atlanta, United States; [9]Rady Children's Hospital of San Diego, San Diego, United States;[10]Vanderbilt University, Nashville, United States; [11]UH Cleveland Medical Center, Cleveland, United States; [12]Indiana University School of Medicine, Indianapolis, United States; [13]National Institutes of Health, Bethesda, United States; [14]NYU Winthrop Hospital , Mineola, United States; [15]NYU Langone Hospital-Long Island, Pediatrics, Division of Pediatric Endocrinology, Mineola,; [16]Stanford University , Palo Alto, United States; [17]Aintree University Hospital NHS Foundation Trust, Liverpool, United Kingdom; [18]Children's Minnesota, Saint Paul, United States; [19]Royal Hospital for Children, Glasgow, Paediatric Endocrinology, Glasgow, United Kingdom;[20]The University of Utah, Salt Lake City, United States; [21]Hull and East Yorkshire Hospitals NHS Trust, Hull, United Kingdom; [22]Soleno Therapeutics, Inc., Redwood City, United States

Background
Prader-Willi syndrome (PWS), a rare genetic neurobehavioral-metabolic condition, is characterized by hyperphagia, accumulation of excess fat, hypotonia, and behavioral/psychological complications. There are no currently approved medications to treat hyperphagia in patients with PWS; DCCR is under development as a treatment for PWS.
Objectives and Methods
The objective was to evaluate long-term safety of DCCR in individuals with PWS. 125 participants with genetically-confirmed PWS ≥ 4 years old with hyperphagia were treated with oral daily DCCR in multi-center studies conducted at 29 sites in the US and the UK: a 13-week, Phase 3, double-blind, placebo-controlled study (DESTINY PWS) and its long-term, open-label extension study (to 52 weeks and beyond). The target DCCR dose was ≥ 3.3 mg/kg (optimal dose 4.2 - 5.8 mg/kg). 103 patients received DCCR for 52 weeks and 54 patients received DCCR for at least 78 weeks.
Results
Overall, DCCR was well tolerated with the majority of adverse events (AEs), (77.6%) having grade 1 or 2 severity. Treatment-emergent adverse events (TEAEs) occurred in 98.4% of participants. Drug related TEAEs occurred in 80.0% of participants. Twenty participants experienced serious adverse events (SAEs), for which only two participants were considered drug-related (one patient with peripheral/pulmonary edema and another with fluid retention). There were no SAEs leading to death. The most common TEAEs were hypertrichosis (61.6%), peripheral edema (34.4%), and hyperglycemia (22.4%). TEAEs infrequently resulted in discontinuation of study drug (7.2% of participants). These results are consistent with the observed safety profile of DCCR from prior studies. Consistent with the expected AE of hyperglycemia, fasting glucose rose through Week 26 (mean change from baseline $\pm$ SD mmol/l $= 0.35 \pm 0.81$) and returned nearly to baseline by 15 months of treatment (0.11 ± 0.61). HbA1c followed a similar pattern, increasing at 26 weeks and returning nearly to baseline by 15 months. In participants experiencing hyperglycemia, the AE resolved with continued treatment in about half of cases. About 90% of peripheral edema cases resolved while treatment continued, requiring infrequent dose adjustment (7%) or the need for diuretic treatment (3%). Most cases of hypertrichosis ($>80\%$) were mild and only in one instance led to discontinuation. About 35% of cases of hypertrichosis were resolved/resolving at Week 52.
Conclusions
DCCR was ell tolerated beyond 52 weeks of administration. The most common treatment-emergent adverse events were expected based on prior studies of DCCR. These included hypertrichosis, peripheral edema and hyperglycemia, which were typically mild and resolved without treatment in most cases.

DOI: 10.1530/endoabs.81.EP360

EP361

Menstrual cycle characteristics in women with type 1 diabetes mellitus

Maria Ilieva-Gerova[1], Presiyana Nyagolova[1], Daniela Koleva-Tiutiundjieva[1], Maria Orbetzova[1] & Ralitsa Raycheva[2]
[1]Medical University - Plovdiv, Clinic of Endocrinology and Metabolic Diseases "Sv. Georgy", University Hospital, Department of Endocrinology, Faculty of medicine, Plovdiv, Bulgaria; [2]Medical University - Plovdiv, Department of Social Medicine and Public Health, Faculty of Public Health, Plovdiv, Bulgaria

Background
Women with diabetes mellitus type 1 (DMt1) are known to have a higher prevalence of reproductive disorders, including delayed menarche, menstrual cycle abnormalities and polycystic ovary syndrome (PCOS)-like phenotype.
Objective
To evaluate the menstrual cycle characteristics of women with type 1 diabetes mellitus as well as to compare them with healthy women of reproductive age.
Methods and patients
The study included 37 women with DMt1 and 38 clinically healthy women serving as a control group. A detailed gynecological anamnesis was obtained: age at menarche, menstrual cycle interval (MC), menstruation lenght, dysmenorrhea, pregnancies, births, miscarriages. Oligomenorrhoea was defined as having a menstrual cycle longer than 35 days throughout at least the past year. Primary dysmenorrhea wad defined as painfull menstruation unrelated to a secondary pelvic disease. The metabolic control was evaluated by the glycated haemoglobin (HbA1C). Anthropometric measurements, basal levels of testosterone (T), thyroid-stimulating hormone (TSH) and serum prolactin were studied in all participants. Body mass index (BMI) was calculated.
Results
There was no statistically significant difference in terms of age ($P = 0.26$) and BMI ($P = 0.57$) in the studied population. Euthyroid function and normoprolactinaemia were reported in all participants. Women in the DMt1 group had statistically significantly higher T and HbA1C levels than healthy controls ($P = 0.000$). There was no significant difference in the age at menarche or menstruation lenght in women with DMt1 compared to the control group. The mean duration of MC in DMt1 group was (32.73 ± 5.9), comapred to the control group (30.29 ± 2.53), without reaching statistical significance ($P = 0.07$). 14 women (37.8%) with DMt1 reported oligomennorhea. A statistically significant difference between the relative proportion of diabetic women with dysmenorrhea (51.4%) compared to healthy controls with dysmenorrhea (23.7%) (z-test, $P < 0.05$) was observed. Women with DMt1 had a higher number of pregnancies ($P = 0.005$), births ($P = 0.03$) and miscarriages ($P = 0.03$) compared to healthy controls. A significant correlation was found between T and dysmenorrhea ($r = 0.508$, $P = 0.001$) and with oligomennorhea ($r = 0.664$, $P = 0.000$). There was also a positive significant relationship between dysmenorrhea and oligomennorhea ($r = 0.648$, $P = 0.000$).
Conclusion
Despite satisfactory metabolic control, women with DMt1 have higher frequency of menstrual cycle irregularities. Early and precise examination of menstrual cycle characteristics of women with DMt1 is essential for developing a better approcah towards the reproductive dissorders observed in diabetic women.
Key words
type 1 diabetes mellitus, oligomennorhea, dysmenorrhea, menstrual cycle, testosterone.
DOI: 10.1530/endoabs.81.EP361

EP362

Imidazole-osmium reduces elution of lipids from cryofixed rat hepatic tissue for ultrastructural analysis

Sabine Dürr[1], Siegfried Reipert[2], Martin Kršsák[3], Cécile Philippe[4], Viktoria Ehret[3], Matthias Luft[5,6], Arno Schintlmeister[7], Thomas Scherer[3] & Clemens Fürnsinn[3]
[1]Medical University of Vienna, Wien, Austria; [2]University of Vienna, Core Facility Cell Imaging and Ultrastructural Research, Wien, Austria; [3]Medical University of Vienna, Department of Medicine III, Wien, Austria; [4]Medical University of Vienna, Department of Biomedical Imaging and Image-Guided Therapy, Wien, Austria; [5]Medical University of Vienna, Department of Plastic, Reconstructive and Aesthetic Surgery, Wien, Austria; [6]Karl Landsteiner University of Health Sciences, Department of Plastic, Aesthetic and Reconstructive Surgery, St. Poelten, Austria; [7]University of Vienna, Wien, Austria

Introduction
Transmission electron microscopy (TEM) is the main tool for studying the ultrastructural properties of metabolically diseased tissue. For impactful micrographs as well as for interpretation of TEM specimens, the integrity of cellular components is crucial. Elution of substances is a major problem in TEM preparation with no universal solution found so far. Investigating fatty liver disease in a rat model, an important factor is the depiction of undamaged lipid droplets. Imidazole, a highly polar heterocyclic compound, is hypothesized to enhance the binding ability of osmium tetroxide. This study aimed to investigate the effect of imidazole-osmium application before cryopreparation to prevent elution from lipid droplets.
Methods
Perfusion-fixed (4.5% phosphate buffered formaldehyde, pH 7) hepatic tissue from male Sprague-Dawley rats ($n = 6$; 8 weeks old) on high fat diet (60% of calories as fat; fed for 4 weeks) was processed for TEM. Prior to the procedure of high pressure freezing and freeze substitution, samples ($n = 3$) were pre-exposed to 1% OsO<ce:inf>4</ce:inf> in 0.1M imidazole for 30 min. For comparison, a control group was not subject to such pre-exposure ($n = 3$). Specimens were embedded in Agar 100 resin, and the ultrastructure was analyzed in ultrathin sections (70 nm, Leica EM UC7; ZEISS Libra 120 TEM).
Results
Screening a multitude of ultrathin sections from steatotic rat livers from three separate animals revealed expletive electron dense material within the membrane of lipid droplets in imidazole-osmium pre-treated tissue. At variance to this, the conventional approach without imidazole pre-treatment displayed translucent areas with minimal granular content.
Conclusion
The chemical bond between osmium tetroxide and imidazole obviously reduced the elution of contrastable lipid molecules from lipid droplets prior to preparation and high pressure freezing with freeze substitution. This procedure promises a major advantage in the ultrastructural study of fat accumulation in hepatic tissue. Further investigations including NanoSIMS (Nanoscale secondary ion Mass Spectrometry) will be conducted to confirm this hypothesis.
DOI: 10.1530/endoabs.81.EP362

EP363

Homocysteine level in diabetic subjects with venous thrombosis

Sana Fendri[1], Boudaya Mariem[1], Ben Salah Raida[2], Jamoussi Kamel[1] & Bahloul Zouheir[2]
[1]Hedi Chaker Hospital, Laboratory of Biochemistry, Sfax, Tunisia; [2]Hedi Chaker Hospital, Internal Medicine, Sfax, Tunisia

Introduction
Homocysteine is an intermediate sulfur amino acid in the metabolic pathways of cysteine production from methionine, which is increasingly involved in various pathological processes (arterial thrombosis, depression, schizophrenia, dementia). We are interested in the course of our work to study the variation of homocysteine levels in diabetic subjects with venous thrombosis.
Materials and methods
This is an observational case-control study, comparing 47 healthy control subjects with 47 patients admitted to the internal medicine department for the management of deep vein thrombosis confirmed by radiological examination. These two groups were matched according to age, sex and body mass index. The homocysteine assay and fasting blood sugar were done by an enzymatic method. The assay of glycated hemoglobin was carried out by the reference method (high performance liquid chromatography)
Results
The mean age of patients and controls was 40.8 ± 10.5 years with ranges of 18 and 59 years. The two groups consisted of 27 men (57.5%) and 20 women (42.5%) with a sex ratio of 1.35. The diabetic subjects in our population were 14.8% in the patient group and 12.7% in the control group (without statically significant difference). Hyperhomocysteinemia was significantly correlated with the presence of diabetes with $P = 0.006$ with a mean level of 26.28 ± 10 µmol /l in diabetic subjects against a mean level of 12.3 ± 5.9 µmol /l in non-diabetic subjects.
Conclusion
Homocysteine is a sulfur amino acid involved in many cardiovascular pathological processes which should be systematically screened for in all diabetics.
DOI: 10.1530/endoabs.81.EP363

EP364

Development of an electrochemical immunosensor based on competition assay for the detection of biomarkers in human urine samples

Sharmaine Reintar[1,2], Christoph Haudum[1,2], Josep Lluis Acero[3], Ciara ÓSullivan[3] & Barbara Obermayer-Pietsch[1]
[1]Medical University of Graz, Department of Internal Medicine, Division of Endocrinology and Diabetology, Graz, Austria; [2]Center for Biomarker

Research in Medicine (CBmed), Graz, Austria; [3]Universitat Rovira i Virgili, Departament d'Enginyeria Química, Tarragona, Spain

Introduction
Diabetes mellitus (DM) is a disease characterized by increased glucose levels, mostly either due to insulin deficiency (type 1 DM) or a decreasing ability of insulin receptor binding (type 2 DM) or both. Biomarker measurements such as fasting glucose and haemoglobin A1c are vital to detect and monitor DM. In addition to these parameters and antibody testing, insulin determination has been used for classifying different types of DM. However, the disadvantage of insulin measurement is a rapid degradation in the blood through hepatic metabolism. Moreover, interferences may arise from exogeneous insulin injection. In contrast, C-peptide is co-secreted along with insulin in equimolar quantity, consisting of 31 amino acids and a longer half-life of 30 minutes compared to 3-5 minutes with insulin. Therefore, it can be detected in urine samples, reflecting insulin metabolism by non-invasive samples, as this is also not subjected to exogeneous insulin interference.
Objective
We aim to validate urinary C-peptide as a reliable and sensitive biomarker for determination of the beta cell function using a point-of-care approach.
Method
The proof-of-concept for electrochemical detection of C-peptide is based on competition format. We utilize a self-assembled monolayer for covalent attachment of the coating C-peptide onto the screen-printed electrodes. Various concentrations of C-peptide were measured using an antibody against C-peptide, labelled with an enzyme to generate the signal, and a laptop/mobile phone used as the output reader.
Result
We are able to show that our proof-of-concept works for C-peptide determination. The developed sensor obtained a limit of detection of 3.5 μg/ml in spiked urine samples. In addition, the assay showed a high specificity to C-peptide with no known cross-reactivity to other related structures such as insulin.
Conclusion
Further evaluation of the assay is ongoing in our laboratory to further improve the sensitivity of the assay. Overall, our proof-of-concept for the determination of urinary C-peptide is a reliable and it can be miniaturized for easy-to-use portable assay which can be used to support diagnosis and monitoring of DM to prevent the progression of the disease and further complications.

DOI: 10.1530/endoabs.81.EP364

EP365

Epidemiology, clinical and complications profile of diabetes mellitus patients hospitalized in libya: a retrospective audit

Sarah Abdulrazik[1], Ahmed Misherghi[2,3], Aida Alktounei[3] & Muhammed Elhadi[4]
[1]The Libyan Biotechnology Research Center, Genetic Engineering, Tripoli, Libya; [2]Faculty of Medicine, University of Tripoli, Medicine, Tripoli, Libya; [3]The National Diabetes and Endocrine Center, Statistics, Tripoli, Libya; [4]Faculty of Medicine, University of Tripoli, Medicine, Tripoli, Libya

Introduction
It was estimated that about one-sixth of the Libyan population have diabetes mellitus. However, there were no previous studies about the hospitalized patients and clinical presentation and outcomes. In this study.
Aim
We aimed to determine the clinical profile and complications of diabetic patients admitted to the largest diabetic center in Libya and evaluate the mortality and admission pattern.
Methods
Patients with diabetes mellitus were identified from the National Diabetes and Endocrine Center in Tripoli, Libya. A retrospective audit of diabetes mellitus cases was conducted from January 2018 to December 2019. Demographic, clinical, admission, complications, and outcome data were obtained.
Results
One thousand one hundred seventy-seven patients were included; 599 had type 1 diabetes, 575 had type 2 diabetes. The median interquartile range (IQR) of age for the patients was 40 (24 - 59) years. Of those patients, 665 (56.5%) were female and 512 (43.5%) were male. The most common causes of hospitalization were diabetic ketoacidosis (DKA) (58.6%), hyperglycemia (21.8%), uncontrolled sugar level (11%), hypoglycemia (3.4%), and several other causes. The median (IQR) of fasting blood sugar level was 231 (175 – 298) mg/dl. Approximately 18.3% have concomitant hypertension. Diabetes complications were as follows: hypertensive kidney disease (0.6%), history of cerebrovascular accident (0.8%), hypothyroidism (1.6%), and urinary tract infection (3%). All-cause mortality was 2.8%.
Conclusion
These results indicate substandard diabetic care for patients in Libya. It also outlines a high rate of diabetic ketoacidosis (DKA), a life-threatening condition for diabetic patients and requires intensive care that is lacking in Libya. Improvement in emergency care for diabetic patients in Libya is advocated to avoid future morbidity and mortality.

DOI: 10.1530/endoabs.81.EP365

EP366

Characterization of a cohort of patients with type 1 diabetes during their unstructured transition to adult care

Fernando Braca[1], Yeray Novoa[1] , Juan Carmelo Betancor Acosta[1], Paula Fernandez-Trujillo[2], Dacil Alvarado Martel[3], Josu Gonzalez Martin[4] & Ana Maria Wagner[3]
[1]Hospital Materno Infantil de Gran Canaria, Las Palmas de Gran Canaria, Spain; [2]University Hospital of Gran Canaria Dr. Negrin, Las Palmas de Gran Canaria, Spain; [3]Instituto Universitario de Investigaciones Biomédicas y Sanitarias, Las Palmas de Gran Canaria, Spain; [4]Hospital Insular, Unidad de Investigación, Las Palmas de Gran Canaria, Spain

Background and aims
Transition of patients with type 1 diabetes (DM1) from pediatric to adult care is challenging and international guidelines recommend effective transition programs. The aim of this study is to describe our baseline situation, without a structured transition program, and to identify factors associated with worse glycemic outcome.
Materials and Methods
This is an observational, retrospective study of patients with DM1, aged 14 or more on 09/03/2020. We analyzed demographic variables and variables related with metabolic outcomes and complications. A descriptive statistical analysis was performed and comparisons were made pre- and post-transition (Studenťs t, Wilcoxoňs test), using R Core Team 2020, 3.6.3. Factors associated with changes in HbA1c and admissions were assessed (Spearmaňs R, Mann-Whitneýs test, chi-squared). A p-value < 0.05 was considered significant.
Results
We have currently included 67 patients (58.21% male), 64.2% of whom had adult-care follow-up. HbA1c was 7.7% +/- 1.1 before transition and 8.5% +/- 1.8 (P 0.007) thereafter, despite an increase in their daily insulin dose (0.84 +/- 0.3 UI/kg vs 0.92 +/- 0.3 UI/kg, P 0.008). During transition, 29.8% of patients had at least one admission to the hospital for acute complication, mainly diabetic ketoacidosis (DKA) or hyperglycemia. Patients who had a continuous glucose monitor (CGM) (24.6%) had a significant improvement in HbA1c during transition (-0.54% +/- 1.3) when compared to those without (+ 0.84% +/- 1.53%, P 0.045) and had no admissions for DKA (vs 26.1% without CGM (p 0.028)). Worse glycemic control was also associated with a lower height percentile (Spearmaňs R 0.38, p 0.0031), higher levels of triglycerides (Spearmaňs R 0.33, P 0.031), LDL-cholesterol (Spearmaňs R 0.62, $P < 0.001$) and total cholesterol (Spearmaňs R 0.59, $P < 0.001$). Admissions due to acute complications were associated with loss of follow-up (P 0.043, OR 4.29, IC 1.19 - 15.41) and a longer time between last pediatric visits and first adult appointment (191 +/- 266.18 vs 449.87 +/- 420.26 days, P 0.037).
Conclusion
Despite the small size of this cohort, we observed a worsening of glycemic and metabolic outcomes during the unstructured transition. We also observed an increased risk for acute complications in patients with loss of follow-up. The association between the use of CGM and improved glycemic control and lower risk of hospital admission has to be interpreted with care, given the retrospective nature of the study, but it could be related with the "booster" education received with the device.

DOI: 10.1530/endoabs.81.EP366

EP367

Levels of IL-10 in CD4+ and CD8+ in patients with Type 2 diabetes mellitus and their correlation with mediterranean diet and anthropometric variables

Carolina Knott Torcal[1,2], Sara Jiménez Blanco[1] , Nuria Sánchez de la Blanca Carrero[1], Ana Serrano-Somavilla[1], Rebeca Martínez-Hernández[1], Jessica Jiménez Díaz[1], Alicia Justel Enriquez[1], Miguel Sampedro-Nuñez[1], Mónica Marazuela[1] & Alba Garcimartin[1,2]

[1]University Hospital La Princesa, Endocrinology and Nutrition Department, Madrid, Spain; [2]Complutense University of Madrid , Faculty Of Pharmacy, Madrid, Spain

Introduction
Type 2 Diabetes Mellitus (T2DM) is a multifactorial and complex chronic disease characterized by insulin resistance and a dysfunctional adipose tissue. T2DM patients usually present a state of low-grade inflammation due to a dysregulation of the cytokine production. Consequently, this seems to contribute to insulin resistance and beta cell failure associated with the progression of this disease.
Objective
To examine expression of Interleukine-10 (IL-10) in CD4+ and CD8+ lymphocytes in patients with T2DM compared to healthy individuals and its correlations with anthropometric parameters and Mediterranean diet.
Materials and methods
Blood samples were drawn from patients with T2DM ($n = 36$) and healthy controls ($n = 12$) from University Hospital La Princesa. Peripheral blood mononuclear cells (PBMCs) samples were obtained and incubated with monoclonal antibodies (anti-CD4, anti CD8, anti-IL10). Data were acquired in FACSCanto flow cytometer. Adherence to Mediterranean diet and electrical bioimpedance were performed. Continuous variables were examined with Spearman's rho analysis, whereas categorical variables were analysed using Student's *t*-test/Wilcoxon test o one-way ANOVA/Kruskal-Wallis. Statistical analysis was conducted with R version 4.0.3.
Results
From our cohort, 47.22% and 50% were women in patients and controls, respectively. Mean age was 34.58 ± 10.39 years in controls and 61.52 ± 8.66 years in patients. IL-10 levels were increased in patients compared to controls in both CD4+ and CD8+ populations. CD4+IL10+, normalized by absolute lymphocyte count, were three times higher ($P = 0.004$) in patients than in controls (0.499 ± 0.404 and 0.158 ± 0.187, respectively). Regarding CD8+, results showed even more differences, revealing almost four times higher levels of CD8+IL-10+ ($P = 0.002$) in T2DM than in healthy controls (1.304 ± 1.102 and 0.336 ± 0.436, respectively). Within the patient cohort, significant differences were also found regarding sex, specifically in CD4+IL-10+ ($P = 0.032$), with women showing almost double the expression compared to men (mean 0.602 vs 0.377). Interestingly, a significant inverse correlation was observed between adherence to a Mediterranean diet and both CD4+IL-10+ ($r = -0.447$, $P = 0.010$) and CD8+IL-10+ ($r = -0.536$, $P = 0.002$). Regarding body composition, a significant inverse correlation was shown between fat free mass and CD4+IL-10+ ($r = -0.434$, $P = 0.013$) and CD8+IL-10+ ($r = -0.347$, $P = 0.052$), as well as a significant direct correlation between fat mass and CD4+IL-10+ ($r = 0.434$, $P = 0.013$) and CD8+IL-10+ ($r = 0.347$, $P = 0.050$).
Conclusions
IL-10 expression was increased in CD4+ and CD8+ populations in T2DM, and significant correlations were found between Mediterranean diet and body composition.

DOI: 10.1530/endoabs.81.EP367

EP368

Is MGP an inflammatory marker?

Natascha Schweighofer[1,2], Caterina Colantonio[3], Christoph W Haudum[1,2], Barbara Hutz[1], Ewald Kolesnik[3], Albrecht Schmidt[3], Andreas Zirlik[3], Thomas R Pieber[1,2], Nicolas Verheyen[3] & Barbara Obermayer-Pietsch[1]
[1]Department of Internal Medicine, Division of Endocrinology and Diabetology, Medical University of Graz, Graz, Austria; [2]CBmed GmbH, Center for Biomarker Research in Medicine, Graz, Austria; [3]Department of Internal Medicine and University Heart Center Graz, Division of Cardiology, Medical University of Graz, Graz, Austria

Matrix-GLA-protein (MGP) was repeatedly associated with inflammation markers during the last decade. It is expressed in leucocytes and is a regulator of immune response. Due to posttranslational modification, there are 4 forms. The form responsible for immunomodulation is still unknown. Since the predicted active form - carboxylated, phosphorylated MGP - is not directly associated with immunomodulation, we aimed to investigate the association of dp-ucMGP (dephosphorylated, uncarboxylated) with systemic inflammation parameters and diseases with a known inflammatory component. We analysed data from the BioPersMed cohort ($n = 792$, 55.8% females, mean age 58 +/- 9 years), a prospective cohort of asymptomatic subjects at cardiovascular risk. Dp-ucMGP was measured with IDS-iSYS InaKtif MGP Kit (Immunodiagnostic Systems Holdings PLC, UK). The tertiles ranged from 0 to 410 (1st), 411 to 515 (2nd) and 516 pmol/l to highest value (3rd). C-reactive protein (CRP), cystatin C and ferritin were measured via immunotubidimetry at a Roche Cobas c system (Roche Diagnostics, Vienna, Austria). CRP: values >5 mg/ml, cystatin C: values >0.95 mg/ml and Ferritin: values >140 ng/ml (females) or >360 ng/ml (males) were defined as increased. Sarcopenia was defined by appendicular skeletal muscle mass index. Appendicular skeletal muscle mass was determined by Lunar iDXA (GE Healthcare GmbH, Austria). We defined diabetes mellitus (DM) according to ADA criteria. The presence of non-alcoholic fatty liver disease (NAFLD) was determined based on medical records. Dp-ucMGP correlates significantly with CRP and cystatin C (Rho: 0.204, 0.348, respectively; $P < 0.001$ both) but not with ferritin. CRP, cystatin C and ferritin increase significantly ($P < 0.001$, $P < 0.001$, $P = 0.028$, respectively) per dp-ucMGP tertile. Furthermore, persons with increased CRP, cystatin C or ferritin show significantly increased dp-ucMGP levels ($P = 0.002$, $P < 0.001$, $P = 0.048$, respectively). Dp-ucMGP levels are significantly higher in DM patients ($P < 0.001$) (as CRP, cystatin C, ferritin, all $P < 0.001$) and in persons with NAFLD ($P = 0.006$) (as CRP and ferritin, both $P < 0.001$) and lower in sarcopenic individuals ($P = 0.012$) as CRP ($P = 0.011$) and ferritin ($P = 0.049$). MGP might not only be an interesting biomarker for the development of diseases via regulation of calcium homeostasis but also for the modulation of immune responses. Out of the MGP subforms dp-ucMGP could be a good candidate and needs further investigation.

DOI: 10.1530/endoabs.81.EP368

EP369

Development of THE allele-specific PCR method for studying insulin gene rs689 polymorphism

Talat Saatov[1], Zafar Ibragimov[1], Timur Alimov[2], Elvira Ibragimoya[1], Tokhir Ishankhodjaev[1], Zulaykho Shamansurova[1,3], Kha Karimov[2], Shakhnoza Azimova[4], Kodirjon Boboev[2] & Anton Makhnyov[4]
[1]Institute of Biophysics and Biochemistry under Mirzo Ulugbek National University of Uzbekistan, Tashkent, Uzbekistan; [2]Specialized Scientific-Practical Medical Center of Hematology, Uzbekistan Public Healthcare Ministry, Tashkent, Uzbekistan; [3]Tashkent Pediatric Medical Institute, Uzbekistan Ministry of Education, Tashkent, Uzbekistan; [4]Academician S.U. Yunusov Institute of Chemistry of Plant Substances, Uzbekistan Academy of Sciences, Tashkent, Uzbekistan

Background
Insulin gene (INS) is known to be responsible for production of insulin by the pancreatic β-cells. It includes variable number of tandem repeats (VNTR) of oligonucleotide consequence (ACAGGGGT (G/C) (T/C) GGGG) in the promoter region (Bell et al, 1981,1982); being the gene involved in the susceptibility to various pathologies. The allele-specific PCR allows direct diagnosis of some genetically determined disorders is rather simple and precise. However, by today, there have been no data on the use of the allele-specific PCR for the INS gene rs689 polymorphism.
Aim
The work was initiated to develop a protocol for simple, quick and precise PCR method to determine INS gene rs689 polymorphism.
Materials and methods
To study INS gene rs689 polymorphism, we used a modified method of allele-specific PCR. Original design of primers was performed by means of bioinformation analysis of NCBL database, Genome Browser with BioEdit app. The genotyping was performed using Applied Systems-2720 programmed thermocycler.
Results
To pick up the INS gene nucleotide sequence from the NCBL database is the first step of the procedure. Oligoprimers was synthetized at the Academician S.U. Yunusov Institute of Chemistry of Plant Substances, Uzbekistan Academy of Sciences. The INS gene polymorphic region (rs689) was amplified by means of allele-specific PRC. The primers synthetized as the result of the step were the basis for development of novel test-system intended for determination of INS gene rs689 polymorphism by allele-specific PCR. The efficacy of the method was assessed in the studies in the frames of research grant for patients with diabetes mellitus.
Conclusion
The modified protocol based on the allele-specific PCR intended for study on the INS gene rs689 polymorphism was developed. The protocol can be used in study on various pathologies in diabetes mellitus, insulin resistance, polycystic ovarian syndrome, adenocarcinoma esophagogastric junction, neurodegenerative disorders, etc.

DOI: 10.1530/endoabs.81.EP369

EP370

Compliance and quality of life in people with type 2 diabetes

Elona Shehu[1], Anastasia Ntikoudi[1], Eleni Dokoutsidou[1], Georgia Fasoi[1], Polyxeni Mangoulia[2], Eleni Evangelou[1], Athanasios Tsartsalis[3], Andromachi Vryonidou- Bompota[4], John Komninos[3] & Eugenia Vlachou[1]

[1]University of West Attica, Nursing, Athens, Greece; [2]Evangelismos General Hospital, Athens, Greece; [3]Athens Naval Hospital, Endocrinology Department, Athens, Greece; [4]Korgialenio- Benakio General Hospital, Endocrinology Department, Athens, Greece

Introduction
Type 2 diabetes mellitus (DM2) is the most common disease in the spectrum of metabolic disorders, with its prevalence increasing significantly in recent years. It is estimated that by 2035, 592 million people will have type 2 diabetes. People with type DM2 have high rates of depression and a quality of life that is poorer than that of the general population. Another important factor in the quality of life of people with DM2 is the compliance of patients with the treatment which affects the outcome in the management of diabetes.
Purpose
The purpose of this study was to investigate the quality of life in people with DM2, the compliance with medication and other guidelines of health care professionals, and finally correlate these variables.
Material and Method
This cross-sectional study included two questionnaires, regarding the compliance and quality of life in a Greek population with DM2. The procedure was performed in two phases by distributing the questionnaires twice, three to five months apart. The convenience sample consisted of 73 adult patients with DM2.
Results
The results of the present study showed greater impact in the quality of life regarding sex life, freedom to eat and freedom to drink while less impact was observed on dependence from others. In terms of compliance with the medical instructions and medication, it was found to be statistically increased after a 15-minute nursing intervention. Regarding the glycosylated hemoglobin levels, the mean value was lower in the second measurement in a statistically significant degree after the intervention. Age, gender, lower level of education and low financial status did not seem to be associated with low quality of life scores in the present research study.
Conclusions
Health care professionals should consider not only the clinical parameters but also the lifestyle of each person with DM2 considering the physical, spiritual, cultural, social background and gender differences. Individualized care plans should be developed with a focus on patients, aiming on diet, exercise, and individual counseling to achieve optimal quality of life and compliance with the treatment.

DOI: 10.1530/endoabs.81.EP370

EP371

Virulence of SARS-COV-2 in diabetic patients

Oumeyma Trimeche, Imen Zemni , Amine Hadj Mabrouk, Gara Amel, Jdira Salem, Wassim Frigui, Iyed Barbana, Anas Bouazizi, Rahma Mansour, Yosra Bouzid, Cyrine Bennasrallah, Maryem Kacem, Hela Abroug , Manel Ben Fredj, Ines Bouanene & Asma Belguith
Fattouma Bourguiba Hospital, Monastir, Tunisia

Introduction
Diabetes is a serious disease that can lead to a depression of the immune system and thereby it is incriminated in serious complications of many infectious diseases among which is Covid 19. The aim of our study is to determine the virulence of SARS-COV-2 in diabetic patients.
Methods
This is a transversal study conducted in the department of epidemiology at Fattouma Bourguiba Hospital in Monastir, in October 2020. The data was collected from calling the positive patients by phone 30 days after the initial infection.
Results
We collected the data of 1118 patients who had covid 19 in October 2020. The predominant variant in that period was the alpha variant. Forty-nine of our population were diabetic. Therefore, the prevalence of diabetes was 4,1%. Their sex ratio was 0,75. Most of our diabetic patients were aged above 65 years (13,9%). While 0,5% and 4,5% were aged between 19 to 39 years and 40 to 64 years, respectively. Diabetes was significantly associated with an increase in the rates of hospitalization in covid 19 patients ($P < 0,01$). In fact, the rates of hospitalization in this population corresponded to 22,9% versus 5,2% in non-diabetic patients. Moreover, diabetes increased the risk of oxygen therapy ($P < 0,01$). Of our 49 patients 12 (24,5%) needed oxygen therapy. As for non-diabetic patients, 68 out of 1134 (6%) needed oxygen. Two out of 48 diabetic patients died (4, 2%). However, out of 1018 non diabetic patients, only 6 were dead (0,6%). Thus, it seemed that diabetes increased the death rate ($P = 0,047$). Twenty out of 45 diabetic patients had post covid syndrome which corresponds to a prevalence of 45,5%. As for non-diabetic patients 572 out of 1124 reported symptoms related to post covid syndrome (50,9%). The association between diabetes and post covid syndrome was not significant ($P = 0,479$). The most reported Covid-19 symptoms among our diabetic patients were dyspnea (14,3%), cough (8,1%), fatigue (8%) and headaches (6%).
Conclusion
Our study demonstrates the significant impact of diabetes in hospitalization, the need for oxygen therapy and death in covid 19 patients while it dismisses the association between diabetes and post Covid-19 syndrome.

DOI: 10.1530/endoabs.81.EP371

EP372

Follow-up gestational diabetes in a telemedicine system in pandemic COVID19

Esther Delgado Garcia , Paloma Perez Lopez , Marta Sanchez Ibañez, Maria Nieto , Lourdes De Marcos White , Amelia Santader Cartagena & Daniel de Luis Roman
Hospital Clinico Universitario de Valladolid, Endocrine, Valladolid, Spain

Background
Gestational diabetes mellitus (GDM) is common complication in pregnancy. During pandemic COVID-19, endocrine service iniciate telemedicine in medical care and monitoring blood glucose.
Purpose
The purpose of this study was to asses metabolic control and pregnancy outcome during pregnancy in telematic consult.
Materials and Methods
Descriptive study of 20 patients were assesed in telematic review in the first wave of the COVID-19. GDM was defined according to NDDG 1979. Glucose targets were defined by a capillary fasting glucose target <95 mg/dl and a 2-hour postprandial capillary glucose <120 mg/dl. Good control was defined as: $< 5\%$ of the glycemic values were not within the target range,
Results
20 patients (age 36,6 $\pm$ 3.0 years; HbA1c levels 5.3% $\pm$0.2).19 patient had a risk factors for predisposition to GDM include obesity (85%), history of gestational diabetes (50%) and family history of type 2 diabetes mellitus (45%). The week of the first consultation was on average at week 34 +/- 9.5. The median goal achievement was at week 37 [37-37,5] 19 had a good control and the mean dose of insulin for glycemic control was 13.05+-16.02 units. Non differences were found with respect to prolonged labor and preeclampsia with our prepandemic registration.
Conclusion
The first wave of the COVID-19 pandemic did not seem to have a negative impact on pregnancy outcomes in GDM women, despite patients with gestational diabetes were later referred to our clinics.

DOI: 10.1530/endoabs.81.EP372

EP373

The benefits of breastfeeding on weight loss and glycemic control

Amal Elkhomri, Bensbaa Salma , Nassim Essabah Haraj , Siham El Aziz & Asma Chadli
CHU Ibn Rochd, Endocrinology-Diabetology and Metabolic Diseases Department, Casablanca, Morocco

Introduction
Breastfeeding has benefits for infant health, but also for maternal health, lactation has a positive impact on glucose homeostasis and weight loss. This can be explained by the needs of milk production. The mammary gland needs glucose to make lactose. The objective of this study is to evaluate the impact of breastfeeding on glycemic control and weight loss
Materials and Methods
Prospective study conducted in the department of endocrinology and diabetology including 90 patients followed for diabetic pregnancy. The analysis was carried out by SPSS version 25 software.
Results
The results had objectified a mean age of 35 years, predominantly type 2 diabetes (89%), a mean weight at conception was 80kg, Only 13% of the patients had planned their pregnancy, 57% of the patients were on insulin, 83% of the patients were breastfeeding, 36% of them were exclusively breastfeeding, the predominant duration of breastfeeding was more than 12 months (37%), postpartum weight loss was observed in 74.4%, glycemic control was observed in 60% and significantly associated with exclusive breastfeeding ($P = 0.000$), as

well as with the duration of breastfeeding of more than 12 months ($P = 0.000$), the latter was correlated with postpartum weight loss ($P = 0.02$)
Conclusion
Our results underline the positive impact of breastfeeding on weight loss and glycemic control, hence the need to systematically insist on breastfeeding in women with diabetes.

DOI: 10.1530/endoabs.81.EP373

EP374

Modulation of antimony mediated therapy for an optimal insulin secretion during visceral leishmaniasis

Sukrat Sinha
Nehru Gram Bharati University, Department of Zoology, Prayagraj, India

Objective
Visceral Leishmaniasis is a macrophage associated disorder for the treatment of which antimony based drug like Sodium Antimony Gluconate has been the first choice in the recent past. About 5 percent of the patients may develop insulin dependent diabetes mellitus. It appears to have a direct action on pancreatic beta cells, resulting in initial insulin release followed by impaired insulin secretion. Within this context we looked into alternate therapies of treatment along with SAG on triggering the CD2 epitope.
Methods
We have evaluated the effect of combining CD2 with conventional antimonial (sb) therapy in protection in BALB/c mice infected with either drug sensitive or resistant strain of Leishmania donovani with 3 million parasites via-intra-cardiac route. Mice were treated with anti CD2 adjunct SAG sub-cutaneously twice a week for 4 weeks. Assessment for measurement of weight, spleen size, anti-Leishmania antibody titer, T cell and anti-leishmanial macrophage function was carried out day 0, 10, 22 and 34 post treatments. Insulin levels were also determined on the same intervals.
Results
The combination therapy was shown boosting significant proportion of T cells to express CD25 compared to SAG monotherapy. Although, the level of IFN-γ was not statistically different between combination vs monotherapy ($P = 0.298$) but CD2 treatment even alone significantly influenced IFN- γ production than either SAG treatment ($P = 0.045$) or with CD2 adjunct SAG treatment ($P = 0.005$) in Ld-S strain as well as in Ld-R strain. The influence of CD2 adjunct treatment was also documented in anti-leishmanial functions in macrophages. Interestingly insulin levels were observed to be optimal on supplementing SAG along with CD2.
Conclusion
SAG along with CD2 could be used as a potential therapy to overcome incidences of Diabetes mellitus during Visceral Leishmaniasis.

DOI: 10.1530/endoabs.81.EP374

EP375

Phenotypical variability in hepatocyte nuclear transcription factor 1 beta (HNF1β) gene mutation – A five case report

Guilherme V de Assunção[1], Liliana Fonseca[2], Catarina Mendes[3], Sofia Teixeira[2], Maria João Oliveira[3], Jorge Dores[2], Teresa Borges[3] & Helena Cardoso[2]
[1]Centro Hospitalar e Universitário do Porto, Porto, Portugal; [2]Centro Hospitalar e Universitário do Porto, Endocrinology, Diabetes and Metabolism, Porto, Portugal; [3]Centro Hospitalar e Universitário do Porto, Pediatric Endocrinology Unit, Porto, Portugal

Introduction
MODY 5 is a rare form of autosomal dominant monogenic diabetes with a broad phenotypical spectrum that occurs with pancreatic and extra-pancreatic clinical manifestations, such as: malformation and dysfunction of the pancreas, nephrourologic anomalies, impaired renal function, hepatopathy and neurocognitive defects. It is caused by a mutation of the gene encoding hepatocyte nuclear transcription factor 1 beta (*HNF1β*).
Case 1
Male, 8 years-old with a history of developmental delay, facial dysmorphia, macrocephaly and pielic dilatation. At the age of three a genetic test revealed 17q12 microdeletion associated with *HNF1β* mutation. Blood analysis revealed a HbA1c: 5,4% and C-peptide (C.pep): 1.09ng/ml (RR: 1.1-4.4). To date, at the age of eight, he remains euglycemic, with a HbA1c 5,5% and a C.pep 0,94 ng/ml, without any treatment.
Case 2
Male, 15 years-old, diagnosed with renal cysts and motor skills disorder. At age of 14 a genetic test revealed 17q12 deletion. To this date the patient remains euglycemic, with a HbA1c: 5,2%, without any treatment.
Case 3
Female, died at 49 years of age with sepsis, with a history of developmental delay, diabetes diagnosed at 16 years of age, kidney chronic disease and hepatopathy of unknown etiology. Started hemodialysis at the age of 43, renal transplant at 46 years-old. Genetic test revealed a 17q12 deletion associated with *HNF1β* mutation. She was on insulin therapy.
Case 4
Male, 16 years-old, diagnosed with CKD G2A2 KDIGO, multiple bilateral renal cysts and pielic dilatation. At age of six, a diagnosis of diabetes was made (insulin deficiency symptoms and no acute complications) and started insulin. Abdominal CT scan revealed pancreatic agenesis. C.pep <0.02 ng/ml. Genetic test revealed: *HNF1β* - c.301G>T(p.E101*). Currently the patient is on functional insulin therapy. HbA1c: 7.2%.
Case 5
Male, 23 years-old with progressive renal dysfunction due to bilateral renal cysts, underwent kidney transplant at the age of 19. After a few weeks diabetes was diagnosed (HbA1c 8% and C.pep. 3.89 ng/ml) and started on insulin. Genetic test revealed: *HNF1β* – variant c.443C>T (p.S148L). Last visit: HbA1c 8,3%, C.pep. 4.06 ng/ml, Cr: 2.5 mg/dl and GFR: 36 ml/min/1.73 m^2.
Conclusion
HNF1β gene mutation phenotype is variable and there are no pathognomonic manifestations, nevertheless, it should be suspected in patients with unusual diabetes and multisystem involvement unrelated to diabetes, especially, renal disease. Diabetes in these mutations can develop at any age. Neurodevelopmental disorders, diabetes, nephrourologic anomalies and hepatic abnormalities may raise suspicion of a 17q12 deletion syndrome.

DOI: 10.1530/endoabs.81.EP375

EP376

The growth effects of long-term (five years) prednisone therapy in frequently relapsing nephrotic syndrome of childhood: impact on statural growth and weight gain

Ashraf Soliman[1], Noor Hamed[1], Mostafa Elbaba[1], Fawzia Alyafei[1], Maya Itani[2], Fatima Al-Naimi[2], Doaa Al Yousef[2] & Mona Shaat Dalees[2]
[1]Hamad Medical Center, Pediatrics, Doha, Qatar; [2]Hamad Medical Center, Nutrition and Dietitic Department, Doha, Qatar

Nephrotic syndrome (NS) in children usually has an onset between 2-8 years of age and steroids form the mainstay of management. Therapy may affect growth in children with relapsing NS.

Table 1 Longitudinal growth data of NS patients on LTPT

	Age years	WT kg	WTSD	HT cm	HTSD	BMI kg/m^2	BMISD
Mean	3.99	17.66	0.19	102.17	-0.38	16.67	0.65
SD	2.19	6.40	0.77	16.35	1.09	1.34	0.90
Mean	6.72	26.97	0.70	118.98	-0.35	18.29	0.97
SD	2.50	11.77	1.37	15.16	1.02	4.22	1.51
Mean	8.93	34.88	0.42	126.91	-0.79	19.98	1.10
SD	3.85	21.30	1.28	21.44	1.21	5.68	1.28

Table 2 Percent abnormalities after 3 and 5 years of LTPT

	Beginning	After 3 yr.	After 5 yr.
BMISDS > 2	2/32	7/32	8/32
% Obesity (OB)	6.25%	21.88%	25.00%
BMISDS >1<2 (OW)	6/32	7/32	10/32
% OB	18.75%	21.88%	31.25%
Total OB and OW	8/32	14/32	18/32
	25.00%	43.75%	56.25%

Aim
This study was carried out to investigate linear growth and weigh gain in children with NS and multiple relapses who receiving long-term prednisone therapy (LTPT) for 5 years.
Methods
Data of 30 children with SSNS was analysed retrospectively. They received prednisolone only in the standard dose for the initial episode at 2 mg/kg/day for six weeks followed by 1.5 mg/kg on alternate days for six weeks and relapses were treated with 2 mg/kg/day till remission followed by 1.5 mg/kg/day for four weeks. (height, HtSDS, weight, BMI and BMISDS) were recorded each clinic visit along the treatment period. Growth data were correlated with the cumulative dose of steroid.
Results
The mean cumulative prednisone = 125+/- 28 mg /kg/yr given over an average duration of 5 years. The HtSDS was not affected after 3 years (from -0.38 to -0.35 respectively) but decreased to -0.79 after 5 years (-0.4 SD loss). The BMISDS increased from 0.65 to 0.97 and 1.1 after 3 and 5 years respectively. Obesity (OB) and overweight (OW) increased from 25% pre-treatment to 59.2% after 5 years of treatment. Hypertension was detected in 12.5% and 23% of patients after 3 and 5 years of treatment.
Conclusion
Long term prednisone therapy (for 5 years) with a mean cumulative dose of prednisone = 125 +/- 28 mg/kg/yr. was associated with a small decrease in the HtSDS but significant increase in the BMISDS, OW, obesity and hypertension.

DOI: 10.1530/endoabs.81.EP376

EP377

Degenerative complications after insulin therapy: are there benefits to prescribing analogue insulin compared to human insulin?

Rim Rachdi, Olfa Lajili, Hajer Moalla, Nessrine Souissi, Kamilia Ounaissa, Haifa Abdesselem & Chiraz Amrouche
The National Institute of Nutrition in Tunis, Diabetology Outpatient Department, Tunis, Tunisia

Introduction
Over the past two decades, the development of genetic engineering techniques has led to the emergence of insulin analogue that have the advantage of improving diabetics quality of life compared to human insulin. The aim of our study was to compare the frequency of occurrence of degenerative complications in two groups of patients with type 2 diabetes (T2D) on human insulin (NPH) and analogue insulin, and thus determine whether or not there are benefits to prescribing analogue insulin.
Materials and methods
Prospective comparative study involving 88 T2D patients, carried within the National Institute of Nutrition in Tunis and hospitalized for insulin therapy. Patients were divided into two groups: (G1) including 44 patients on human insulin and (G2) including 44 patients on analogue insulin. The presence or absence of degenerative complications was noted in both groups 18 months after insulin.
Results
Median age was 55,6 years in G1 versus 52,8 years in G2 (P = NS). Median diabetes duration was 7,1 years in G1 compared to 8,92 years in G2 (P = NS). Peripheral neuropathy was the most common complication in both groups (59,1% in G1 versus 68,2% in G2; P = NS). Diabetic retinopathy was present in 36,6% in G1 versus 40,4% in G2 (P = NS). Diabetic nephropathy was more present in G1 than in G2 (28,9% versus 20%; P = NS). Impaired renal function was more present in G1 than in G2 (41% versus 39%; P = NS). Coronary heart failure was the most common macrovascular complication in both groups (29,6% in G1 and 25,3% in G2). There was no statistically significant difference (P = NS) between the two groups for each of the macrovascular complications.
Conclusion
The two groups were comparable for the frequency of occurrence of different micro and macro vascular complications. In addition, patients on insulin analogue were less likely to develop diabetic nephropathy, renal failure and coronary heart failure.

DOI: 10.1530/endoabs.81.EP377

EP378

Diabetes in the elderly: adherence and particularities of treatment

Ramla Mizouri, Faten Mahjoub , Rym Ben Othman , Nadia Ben Amor, Berriche Olfa & Jamoussi Henda
Institut National de Nutrition de Tunis, Service A, Tunis, Tunisia

Introduction
Elderly diabetics are often fragile patients at high cardiovascular risk. The medical, human and socio-economic impact of diabetes is heavy in the elderly. Symptoms in this particular population are often insidious and atypical, which can delay diagnosis and the establishment of effective treatment. Indeed, management is not always easy because it must take into account multiple parameters. The objective of our study was to study the observance and particularities of treatment in elderly diabetics.
Methods
We conducted a retrospective observational study at the National Institute of Nutrition and Food Technology in Tunis, over a period from January 2018 to September 2021. Data were collected from patients' medical observation records. We prepared an information sheet which was used for the statistical analysis of the data.
Results
We collected 35 elderly diabetic patients. The age of the patients varied from 70 to 89 years with an average age of 76.2 ± 4.5 years. Our population was characterized by a female predominance (66%). The average duration of diabetes in our population was 5.89 ± 3.91 years with extremes ranging from 1 to 14 years. The average age of discovery was 70.29 ± 4.44 years with extremes ranging from 65 to 79 years. All of our patients were type 2 diabetics. Glycated hemoglobin varied between 6.5% and 13.9% with an average of 8.9 ± 1.9%. More than half of the population had an HbA1c greater than 8.5%. About half of the study population were on oral antidiabetics alone. Insulin therapy was prescribed in 54% of the population, of which only two patients were on insulin analogues. For patients on insulin therapy, the most prescribed therapeutic regimen in our population was the basal regimen (56%) with an average daily dose of basal insulin in the order of 0.47 ± 0.25 U/Kg/d. Therapeutic non-compliance was mentioned in 54% of patients. The main reasons for stopping treatment were the unavailability of drugs at local dispensaries (26%) and adverse effects (21%) dominated by digestive disorders due to metformin.
Conclusions
Diabetes in the elderly remains an area to be discovered. Few studies have been carried out to date. The field therefore remains open to many studies, especially in terms of therapy.

DOI: 10.1530/endoabs.81.EP378

EP379

Effect of iSGLT-2 on renal function and lipid spectrum in patients with type 2 diabetes mellitus

Sitora Muminova
Tashkent Pediatric Medical Institute, Endocrinology, Tashkent, Uzbekistan

Diabetes mellitus (DM) is a global medical and social problem of our time, which is faced by medical science and healthcare in almost all countries of the world. The situation in Uzbekistan follows the global trend. According to 2019 data, 230 610 patients with diabetes are registered in the country: 18 349 patients with type 1 diabetes and 212 261 - with type 2 diabetes. According to screening studies, the prevalence of type 2 diabetes in Uzbekistan over the past 14 years has increased 1.6 times and, according to the latest data (2015).
Aim
To study the functional state of the kidneys and lipid metabolism while using iSGLT-2 in patients with type 2 diabetes mellitus with diabetic nephropathy.
Materials and Methods
We studied 40 patients with T2DM with DN (CKD C2, A2). The average age was 52.7 ± 3.78 years; diabetes experience - 8 years; BMI-30 ± 0.17; Hb1C-9.2 ± 0.4%; fasting glycemia –10.2 mmol/; eGFR-78 ml/min; TG-2.7 ± 0.44; total cholesterol-3.4 ± 0.72; MAU 32 ± 0.125.
Results
6 months after the start of ingestion of iSGLT-2, the patients showed an improvement in renal function and lipid metabolism. According to laboratory data, there is a significant ($P < 0.001$) decrease in creatinine levels by 7.4 μmol/l (93.8 ± 0.05) and an increase in eGFR by 5.3 ml/min /1.73 m^2. Despite the fact that the doses of statins did not change, we observed a significant ($P < 0,05$) decrease in total cholesterol levels by 1.04 mmol/l and triglycerides by 1.17 mmol/l.
Conclusion
In our study, we observed a significant decrease in the level of atherogenic fractions of the lipid spectrum. Also, the dynamics of creatinine and eGFR levels confirms the safety of the drug and some nephroprotective effect, which manifests itself with a sufficiently short observation period.

DOI: 10.1530/endoabs.81.EP379

EP380

Patient experience and outcome of teleconsultation in management of T2DM during COVID-19 Pandemic in Semi urban and village population in Kerala

Jayakrishnan B
Senior Consultant Diabetology, SafeCare Clinics, Tirur, Kerala, India

Background
Coronavirus pandemic had pushed both doctors and patients to adapt to teleconsultation for routine consultations in management of type 2 diabetes (T2DM). Telemedicine is believed to be an effective resource in health access but its experience to the patient and its outcome of management are not well understood in semi urban and village population of India. Thus, this study aims to assess the experiences and outcomes of T2DM management by tele-consultation in these population.
Methods
This Cross-sectional observational study was conducted involving 250 patients with type 2 diabetes who availed teleconsultation services in two diabetes care centers in Tirur, Kerala between March 2021 to August 2021. Patient experience was obtained through an online survey questionnaire and the glycemic outcomes are gathered from base line and end of 3 months.
Results
About 135 (54%) of the patients were male, while 115 (46%) were female. Majority of the teleconsultation occurred in the 45–65-year age group. The mean duration of diabetes was 9.1 $\pm$ 4.2. Majority of T2DM patients were on $\geq$ 2 OADs (61.2%). Around 32.8% patients were using Insulins along with oral therapy. Patient experience survey response was received from 210 patients. 190 (90.47%) of patients were happy with the quality of conversations with their physician in terms of advice and instructions. Further 175 (83.33%) were satisfied with the duration of consultation. Around 195 (92.85%) would be happy to use teleconsultation again, while 200 (95.23%) would recommend teleconsultation to their friends and family. The reduction of HbA1c was 0.7% [TCV1-9.2 $\pm$ 13 vs TCV2 -8.5 $\pm$ 2.2]. There was minimal change in BMI 0.73 kg/M2 [TCV1 -29.87 $\pm$ 4.2 vs TCV2 29.14 $\pm$ 2.5] was observed. The self-reported hypoglycemia events were less 15 (6%) patients, no documented severe hypoglycemia.
Conclusions
The patient experience and outcomes result of the study indicate that telemedicine may confer better diabetes management during and beyond COVID-19 pandemic in sub-urban and village population in Kerala

DOI: 10.1530/endoabs.81.EP380

EP381

Mistakes revealed during continuous glucose monitoring in patients with poorly controlled Type 1 diabetes

Volha Shyshko[1,2], Tatjana V Mokhort[2], Parsa Paryavi[2], Vahid Rasekhjahromi[2] & Alena Yurenia[1]
[1]Minsk City Clinical Endocrinology Center, Endocrinology, Minsk, Belarus; [2]Belarusian State Medical University, Endocrinology, Minsk, Belarus

Introduction
There is no doubt that continuous monitoring systems can improve diabetes control. The aim of the study was to determine typical deviations of glucose and mistakes in insulin treatment, self-control, predisposing to the poor blood control.
Materials and methods
30 patients with type 1 diabetes were included, mean age 21$\pm$7.8, mean age of diabetes manifestation 19.2$\pm$13.9 years, mean duration oa diabetes – 15.3$\pm$7.5. Including criteria: type 1 diabetes, basal-bolus regimen of insulin injection, HbA1c above individual target level for more than 1 year. Excluding criteria: acute diseases, failure of chronic diseases. We conducted constant glucose monitoring (CGM) using blinded system (patients didn't see results during monitoring). CGM lasted 7 days in all patients and 1988 readings were measured by the device. According to the protocol patients should have recorded in provided for them diary carbohydrates (CH) amount, doses of insulin and measure glucose levels with glucometer at least 4 times a day.
Results
We revealed statistically significant difference between HbA1c (8.9$\pm$2.1%) measured in laboratory during CGM and calculated HbA1c (7.0$\pm$1.2%) measured during monitoring (according to the results of standardized protocol) ($P < 0.05$). As far as patients were instructed to record CH, insulin doses and blood glucose levels measured at least 4 times a day it's possible to assume that one or all parts of this daily routine are lost in patients with diabetes who didn't achieve target HbA1c. Increased blood glucose levels during night (47.0$\pm$29.0%) were associated with higher HbA1c during CGM ($r = 0.5$, $P < 0.05$). The higher dose of basal insulin (21.3$\pm$9.1U) was associated with higher HbA1c measured in laboratory ($r = 0.5$, $P < 0.05$) and increased glucose during night ($r = 0.5$, $P < 0.05$).
Conclusion
1. Calculated HbA1c and laboratory HbA1c differ for approximately 2% in patients with poorly controlled diabetes. 2. Nocturnal hyperglycemia is associated with higher HbA1c level and higher doses of basal insulin.

DOI: 10.1530/endoabs.81.EP381

EP382

Medication Adherence in Patients with Type 2 Diabetes

Ajili Rihab, Salah Amani, Lassoued Najoua, Boubaker Fadia, Zantour Baha, Alaya Wafa & Sfar Habib
University Hospital Tahar Sfar, Endocrinology, Mahdia, Tunisia

Introduction
Medication Adherence (MA) is the extent to which patients follow medical instructions. Poor MA is frequently encountered in the majority of chronic diseases, including diabetes. The aim of our study was to evaluate MA in patients with poorly controlled type 2 diabetes mellitus (T2DM).
Patients and methods
We conducted a cross-sectional study over a period of 2 months, including patients with poorly controlled T2DM, followed at the endocrinology department of university hospital Taher Sfar Mahdia. MA was assessed using the Morisky compliance questionnaire.
Results
A total of 59 patients were included with a mean age of 64.1$\pm$9.6 years (56.8% were females). The mean duration of diabetes was 15.7$\pm$7.6 years. Diabetes was complicated in 81.4% of cases. The average hemoglobin A1c was 10.63%. Polymedication was observed in 76.5% of patients with an average of 9.6 medications per day. Therapeutic education was performed in only 38.6% of patients. According to the Morisky score, 26.4% of patients had a good MA, 41.7% had medium MA and 31.9% had low MA. Forgetting is the first cause of this bad MA. Patients on insulin had a better MA compared to those on oral antidiabetic medications ($P = 0.001$).
Discussion and conclusion
MA is a challenge in the management of diabetes to achieve therapeutic goals and to prevent long-term degenerative complications. Hence the interest of therapeutic education, a process that must be continuous in the course of care in order to optimize this MA.

DOI: 10.1530/endoabs.81.EP382

EP383

Does the insulin pump improve glycaemic control in patients with type 1 diabetes?

Messaoudi Najoua[1], Imane Assarrar[1], Nisrine Bouichrat[1], Tahri Abir[1], Siham Rouf[2] & Hanane Latrech[2]
[1]Mohammed VI University Hospital Center, Faculty of Medicine and Pharmacy, University of Mohammed 1st, Department of Endocrinology-Diabetology and Nutrition, Oujda, Morocco; [2]Faculty of Medicine and Pharmacy of Oujda, Mohamed the First University, Department of Endocrinology-Diabetology-Nutrition,Laboratory of Epidemiology, Clinical Research and Public Health, Oujda, Morocco

Introduction
Insulin pump therapy is recommended more and more in type 1 diabetic patients in order to achieve and maintain optimal glycaemic control. The objective of our study was to determine the effectiveness of insulin pump therapy in improving metabolic control in type 1 diabetic patients.
Patients-Methods
This is a retrospective, descriptive and analytical study including 20 patients with type 1 diabetes treated by insulin pump, between 2017 and 2021. All patients received a clinical evaluation, analysis of the glycaemic cycle and a dosage of HbA1c at the time of the start of insulin pump and during the evolution. Statistical analysis was performed by SPSS version-21.
Results
The mean age of the patients was 16,8 $\pm$ 8,1 years with a sex ratio (M/F) of 0,42. Thirty per-cent were children. The mean duration of diabetes was 5,8 $\pm$ 4,8 years. Seventy-five per-cent of patients practiced functional insulin therapy. The indications for insulin pump treatment were mainly hypoglycaemia and instable diabetes. During follow-up, we found a statistically significant decrease in insulin requirements, improvement in mean HbA1c and maintenance of control during

follow-up, with a marked reduction in the number of hypoglycaemia events per week.
Conclusion
Insulin pump therapy appears to be reliable and effective when used appropriately, combined with appropriate therapeutic education and glycaemic monitoring to maintain long-term glycaemic control.
Key words: Type 1 diabetes – insulin-pump – glycaemic-control
DOI: 10.1530/endoabs.81.EP383

EP384

Regulation of glycemia in patients with type 2 diabetes with oral antidiabetics, insulin and combination therapy

Tatjana Bačun[1,2], Ana Damjanović[1], Ivan Lekić[1], Dunja Šojat[3] & Marko Pirić[3]
[1]Faculty of Medicine Osijek, Osijek, Croatia; [2]Clinical Medical Center Osijek, Division of Endocrinology, Department of Internal Medicine, Osijek, Croatia; [3]Osijek Health Center, Osijek, Croatia

Aim of the study
The objectives of this study were to determine the regulation of glycemia (measured by fasting glucose levels and HbA1c) in patients with type 2 diabetes and to examine whether there is a difference in therapy (oral antidiabetics, insulin, combination), age, sex and BMI.
Study design
Cross-sectional research with historical data.
Patients
The study included 102 patients of both sexes (56% women and 44% men) with a diagnosis of type 2 diabetes who were examined in the Health Center Osijek, Croatia.
Materials and Methods
The following data were collected in family medicine clinics: age, sex, body weight and height, as well as data from laboratory findings (fasting glucose levels, HbA1c, AST, ALT, urea, creatinine, total cholesterol, HDL-cholesterol, LDL-cholesterol, triglycerides).
Results
HbA1c and median glucose levels were lowest in subjects on oral antidiabetic therapy (6.9% and 7.9 mmol/l), in subjects on insulin (7,4% and 8,2 mmol/l), while in subjects on combination therapy, the values were highest (9% and 9.8 mmol/l); the difference in HbA1c was also statistically significant (Kruskal-Wallis test, $P = 0.02$). An association between HbA1c and glucose values with age, sex, and body mass index has not been established.
Conclusion
A statistically significant difference was observed between HbA1c values and the type of therapy, i.e., the difference was observed between subjects on oral antidiabetics and those on combination therapy, which indicates the importance of additional education of patients on self-control and achieving fasting and postprandial glycemic targets. No statistically significant difference was observed in the parameters of glycemic regulation (fasting glucose, HbA1c) with respect to age, sex and body mass index of the subjects.Key words: type 2 diabetes; glycemia; HbA1c; insulin; oral antidiabetics
DOI: 10.1530/endoabs.81.EP384

EP385

Adult-onset loss of the hepatocyte growth hormone receptor (GHR) is associated with increased autophagy in livers of male mice in the context of natural daytime fasting

Andre Sarmento-Cabral[1, 2,3,4,5,6,], Elena Gutierrez-Casado[5,6], Mercedes del Rio-Moreno[5,6], Mari C Vazquez-Borrego[5,,6,7] & Rhonda D Kineman[5,6]
[1]Maimonides Institute for Biomedical Research of Córdoba (IMIBIC), GC27 OncObesity and Metabolism, Córdoba, Spain; [2]University of Córdoba, Department of Cell Biology, Physiology, and Immunology, Córdoba, Spain; [3]Hospital Universitario Reina Sofía (HURS), Córdoba, Spain; [4]Centro de Investigación Biomédica en Red de Fisiopatología de la Obesidad y Nutrición, (CIBERobn), Madrid, Spain; [5]University of Illinois at Chicago, Department of Medicine, Section of Endocrinology, Diabetes, and Metabolism, Chicago, IL, United States; [6]Jesse Brown Veterans Affairs Medical Center, Research and Development Division, Chicago, IL, United States; [7]Maimonides Institute for Biomedical Research of Córdoba (IMIBIC), GE09 Research in Peritoneal and Retroperitoneal Oncological Surgery, Córdoba , Spain

Liver autophagy, as assessed by accumulation of LC3-II and p62 proteins, is positively correlated with the severity of nonalcoholic steatohepatitis (NASH) in humans. Since growth hormone (GH) is negatively associated with liver steatosis and NASH development, and our laboratory has reported that steatosis and NASH develops in a mouse model of adult-onset, hepatocyte-specific GH-Receptor knockdown (aHepGHRkd), we sought to determine if GH directly regulates the hepatocyte autophagy program, and whether this regulation is mediated via STAT5B activation. To this end, adult GHRfl/fl male mice were treated with adeno-associated viral vectors to generate GHR-intact control (AAV8-TBGp-Null), aHepGHRkd (AAV8-TBGp-Cre) or aHepGHRkd mice with constitutive activation of STAT5B (AAV8-TBGp-Cre + AAV8-TBGp-Stat5bCA). Livers were analyzed 7 days post AAV injection, a time when steatosis is observed in aHepGHRkd mice. We first evaluated the level of p62 and LC3-II proteins in liver lysosomal fractions by western blot, from mice euthanized at 1800h (end of the normal sleep cycle, natural fasting), a time of enhanced autophagy. In this condition, we did not observe any differences in p62 or LC3-II protein levels between control, aHepGHRkd or aHepGHRkd + Stat5bCA. Since p62 and LC3-II are involved in the initiation of autophagy, but are rapidly cleared in the autolysosome, we repeated the study after treating the mice with leupeptin, that blocks Cathepsin B, H and L and impairs amphysome-lysosome fusion, leading to a build-up of p62 and LC3-II. In this scenario, we observed that aHepGHRkd resulted in an increase in accumulation of p62 and LC3-II, compared with GHR-intact controls, and Stat5bCA partially reversed this effect. Current literature suggests that autophagy increases in the steatotic liver to protect against NASH progression. Therefore it is possible that the increase in autophagy observed in aHepGHRkd mice is not directly due to loss of GHR signaling but secondary to the development of steatosis, since Stat5bCA also reduces steatosis in aHepGHRkd mice. Therefore, although additional studies are required to determine if GHR/STAT5 plays a direct role in regulating the autophagy process in the liver, our data suggest this remodeling process could be altered in the context of GH signaling alteration during NAFLD development.
Funding
This work was funded by NIH R01DK114326 and VA Merit BX001114 (to RDK)
DOI: 10.1530/endoabs.81.EP385

EP386

Predictive factors of postoperative septic complications after flexible ureteroscopy for urinary stones

Maatougui Jasser[1], Raboudi Mehdi[1], Chayma Besrour[2], Ouertani Haroun[2] & Ghozzi Samir[1]
[1]The Military Hospital of Tunis, Urology, Tunis, Tunisia; [2]The Military Hospital of Tunis, Endocrinology, Tunis, Tunisia

Introduction
The recent advent of flexible ureteroscopy made endoscopic approach to kidney and proximal ureteral calculi evolve to a real effective procedure. However, this technique is not free of postoperative complications. The aim this study was to assess the predictive factors of septic postoperative complications following flexible ureteroscopy for upper urinary tract stones.
Methods
This is a descriptive retrospective study concerning 92 patients who underwent flexible ureteroscopy for renal and proximal ureteral stones in the urology department of the military hospital of instruction of Tunis between January 2015 and December 2021. Septic complication we defined as the occurrence of postoperative fever, urosepsis, septic shock or death. We used multivariate logistic regression to assess predictive factors of septic postoperative complications.
Results
The mean age was 50 years [20 - 82]. Regarding the medical history of our patients: Diabetes was found in 29 cases (32%), occupying the first place, followed by high blood pressure in 24 cases (26%) and chronic renal failure (20%). We identified postoperative complications following 26 interventions (28%) of which 13% were septic. Predictive factors of postoperative Sepsis after flexible ureteroscopy were: Diabetes ($P = 0.032$). a history of urolithiasis ($P = 0.023$). a history of extracorporeal shock wave lithotripsy ($P = 0.009$). In our study, a quarter of diabetic patients had developed postoperative sepsis. This complication was found in only 7.9% of non-diabetic patients. Statistically, the difference was significant ($P = 0.032$).
Conclusion
In light of our studies, diabetic patients have a significantly higher risk of occurrence of postoperative infectious complications. This population may require specific perioperative preparatory measures to reduce operative morbidity.
DOI: 10.1530/endoabs.81.EP386

EP387

Screening for distal and symmetric polyneuropathy in the diabetic patient: 116 cases

Mouna Elleuch, Maalej Souhir, Hsine Houda , Dhoha Ben Salah , Mohamed Abdellahi Mohamed Ahmed , Faten Haj Kacem Akid & Mohamed Abid
CHU Hedi Chaker, Endocrinology, Sfax, Tunisia

Introduction
The prevalence of diabetes in the world population is increasing day by day so that its frequency reaches epidemic proportions. As a result, the complications of diabetes are becoming more and more frequent. Diabetic neuropathy, the most common complication which affect up to half of the patients.
Purpose of the study
To establish the prevalence of distal symmetrical polyneuropathy (DSPN) in diabetic patients and demonstrate the importance of screening for this complication.
Methods
This is a descriptive cross-sectional study conducted among 116 patients during their usual appointment at the consultation. Data collection was done over a period of 2 months from August 1 to September 30, 2021. All patients had a complete neurological examination. We used the Michigan Neuropathy Screening Instrument (MNSI) and the DN4 Neuropathic Pain Diagnostic Questionnaire to establish the prevalence of the disease in our population.
Results
We included 116 participants divided into 47 men and 69 women. The mean age was 62.07 [24 - 89 years]. Type 2 diabetes was noted in 79% of the popultion. The average duration of diabetes was 12,35 years. The average blood sugar was 7,9 mmol/l. HbA1c $\leq$7% was noted in 27% of cases. The mean MNSI History score was 3.76 and 23% of patients had a score $\geq$7 indicating the presence of diabetic neuropathy in them.The mean MNSI physical score was 3.82 and 51% of patients with a score $\geq$ 2.5 had diabetic neuropathy. The mean DN4 score was 3.25. Our results showed that 42 patients (36%) had neuropathic pain with a score $\geq$ 4. Thus, PNDS was diagnosed in 57.8% of our patients. This prevalence was established on the basis of DN4 and or MNSI scores. The podiatric risk was grade 2 in 29% and grade 3 in 12%.
Conclusion
Distal and symmetrical polyneuropathy is very frequent in diabetic patients and causes a consequent morbidity. It is therefore imperative to detect it early enough for a better management.

DOI: 10.1530/endoabs.81.EP387

EP388

Diabetic muscle infarction : a case study

Ons Maaoui, Sabrine Mekni, Imen Rojbi, Youssef Lakhoua, Nadia Mchirgui , Ibtissem Ben Nacef & Karima Khiari
Hospital of Charles Nicolle, Endocinology, Tunis, Tunisia

Introduction
Diabetic muscle infarction (DMI) is a rare complication of long-standing, poorly controlled diabetes, and it's more common in patients with micro-vascular complications. Herein, we present a case of DMI occurring in patient on hemodialysis.
Case presentation
A 44-year-old man on maintenance hemodialysis presented with an acutely painful and swelling in his left calf. He had a 21-year history of poorly controlled type one diabetes, with micro-vascular complications (nephropathy and retinopathy). On physical examination: his skin was pale, his temperature was 37°c , his heart rate was 80 beats per minute and his blood pressure was 150/80 mmHg. His left calf was swollen and tender with no edema or inflammatory signs. Biochemical findings showed: C-reactive protein (CRP) 42 mg/l, CPK 179 U/l (39-308) and LDH 382 U/l (140-280). A Doppler ultrasound showed no sign of deep vein thrombosis, but demonstrated edema of the superficial tissues which prompted the practice of an MRI showing thickening of the lateral gastrocnemius muscle with edema. It is the seat of a lack of enhancement extending over 3 cm with the interposition of a few fibers of marked enhancement. The thickening and muscle edema was more important in the posterior compartment of the leg. It also showed edematous infiltration of fascia and subcutaneous cellulitis without significant enhancement and minimal fatty degeneration of the different muscle compartments of the leg. The patient was put on analgesics and activity restriction in the acute phase followed by gradual mobilization.
Conclusion
Diabetic muscle infarction is a rare and under-reported condition that should be suspected in any diabetic dialysis patient who develops a painful, swollen muscle.

DOI: 10.1530/endoabs.81.EP388

EP389

Gestational diabetes: a review of 64 cases

Fadwa Atfi & Imane El Abbassi
CHU Ibn Rochd, Maternity Department, Morocco

Introduction
Gestational diabetes (GD) is the consequence of an exaggerated insulin resistance associated with a defect insulin secretion. It is a high-risk pregnancy due to its maternal and foetal complications, the pathogenesis of which involves maternal hyperglycaemia.
Materials and methods
This is a retrospective study of 64 parturients, carried out from January 1, 2019 to January 1, 2020 in the gynaecology obstetrics of the Lalla Meryem maternity hospital of CHU Ibn Rochd of Casablanca.
Results
The average age of our parturients was 31 years, and they were multiparous in 81.24% of cases. Obstetrical complications were dominated by HTAG (14.06%), urinary tract infections (12.50%); while macrosomia (51%) and foetal death in utero (14.06%) are the two major foetal complications. The caesarean section rate was 75%.
Discussion
These high rates of maternal-foetal complications lead us to insist on early diagnosis of gestational diabetes in order to ensure a normal course of the pregnancy and to reduce the risk of complications, without forgetting the interest of follow-up and monitoring of complications in the far postpartum period for both the mother and the child. The improvement of obstetrical and perinatal prognosis depends above all on and multidisciplinary care involving the cooperation of different professionals, in particular diabetologists, gynaecologists, obstetricians, attending physicians dieticians, etc. The pharmacist also has a role of listening and advising, which can be useful to the patient. In addition, his involvement could be one of the solutions in the future in the screening of gestational diabetes. Through this study, we were able to identify the epidemiological and therapeutic characteristics, the risk factors involved, screening modalities and maternal-foetal morbidity, which allowed us to deduce the difficulties encountered during screening, diagnosis, and treatment
Conclusion
Gestational diabetes is a public health problem whose prevalence is increasing in our societies. Its short and long-term impact on children and mothers requires appropriate diagnosis and management.

DOI: 10.1530/endoabs.81.EP389

EP390

Uricemia in hypertensive type 2 diabetics: the forgotten metabolic parameter

Faten Haj Kacem Akid, Hamdi Frikha, Cyrine Chehaider, Ameni Salah, Dhoha Ben Salah, Mouna Mnif, Nadia Charfi, Fatma Mnif, Nabila Rekik Majdoub, Mouna Elleuch & Mohamed Abid
Hedi Chaker University Hospital, Department of Endocrinology, Sfax, Tunisia

Introduction
Hyperuricemia is a common metabolic feature in patients with metabolic syndrome.
Aim
The aim of our work is to study the correlation between uric acid level and the metabolic profile in hypertensive type 2 diabetic patients.
Methods
This is a retrospective descriptive study of hypertensive type 2 diabetic patients followed in the endocrinology department of Hedi Chaker University Hospital of Sfax, Tunisia between 2019 and 2021. Hyperuricemia was defined as uric acid level $\geq$ 360 µmol/L
Results
100 patients were included. Mean age was 62.14 $\pm$ 12.7 years with a sex ratio (M/F) of 0.65. Diabetes has been diagnosed since 13.73 $\pm$ 9.6 years on average with a mean HbA1c of 11.06 $\pm$ 2.5%. Hyperuricemia was found in 23.75% of cases overall and in 29.41% of patients with diabetic nephropathy (DN). Uricemia was inversely correlated with HDL cholesterol levels (r =-0.31, P = 0.009) and creatinine clearance (r =-0.35, P = 0.05). On the other hand, uricemia was positively correlated with triglyceride levels (r = +0.7, P = 0.009), duration of diabetes (r = +0.3, P = 0.05), and albuminuria level (r = +0.45, P = 0.02). There was no significant association between uric acid and LDL cholesterol, HbA1c, BMI, total cholesterol, and blood pressure (systolic and diastolic). Uric acid was correlated primarily with renal function in type 2 diabetics. Our results also showed a significant association between uric acid levels and triglyceride and HDL levels, which could be attributed to a fructose-enriched diet.

Conclusion
Hyperuricemia has been found to correlate with major metabolic parameters in patients with diabetes notably those with DN. Its importance contrasts with the paucity of studies about its cardiovascular effects and the lack of clear guidelines regarding its management.

DOI: 10.1530/endoabs.81.EP390

EP391

Cardiovascular risk in diabetic patients with chronic kidney disease: One more turn of the screw

Abdelmouhaymen Missaoui, Mnif Fatma, Asma Zargni , Kawthar El Arbi , Dhoha Ben Salah, Mouna Elleuch , Faten Haj Kacem Akid, Nadia Charfi, Mouna Mnif , Nabila Rekik Majdoub & Mohamed Abid
Hedi Chaker University Hospital, Endocrinology Department, Sfax, Tunisia

Background
Poor glycemic control in patients with diabetes mellitus(DM) is a well-documented responsible factor for microvascular complications, especially eye and kidney damage. The onset of chronic kidney disease(CKD) marks a serious turning point in the clinical history of DM in terms of cardiovascular prognosis. Our study aims to assess the cardiovascular risk(CVR) in diabetic patients with CKD.
Method
We conducted a retrospective descriptive study on 88 type 2 diabetic patients with CKD, admitted during 2019-2020 to the Endocrinology-Diabetology Department of Hedi Chaker University Hospital, Sfax, Tunisia.
Results
The mean age was 68.7±10.9 years with a male predominance(52.3%). Active smokers represented 12.5%. We noted a family history of CKD and early cardiovascular events in 12.5% and 5.7% of cases, respectively. The mean duration of the evolution of diabetes was 13±9 years. We highlighted a glycemic imbalance in 80.2% of patients with a mean fasting plasma glucose of 2.78±1.5g/l and an average HbA1C level of 9.68±2.5%. Dyslipidemia and hypertension were encountered in 94% and 86.4% of cases, respectively. Obesity affected 35.7% of the patients with a mean BMI of 28,53 ± 5.11 kg/m^2. Macroangiopathy was documented in 29.5%, mainly ischemic heart disease (19.3%) and stroke (9.1%). Diabetic retinopathy was diagnosed in 53.5%. The mean glomerular filtration rate(GFR) was 32.2±13.81 mL/min/1.73 m^2. Most patients were Stage 3 CKD (56.8%) whereas 30.5% were stage 4 and 12.5% stage 5. Hemodialysis was undergone for 7.9%. Albuminuria was positive in 52.2% with mean proteinuria of 1.46±2.4 g/24 h. According to the European Society of Cardiology 2021 CVR assessment, all patients are among the very high CVR range.
Discussion
Diabetic nephropathy (DN) is the first leading cause of CKD in the world. Chronic hyperglycemia is responsible for the vascular damage and progression of CKD to terminal-stage and recourse to hemodialysis. In addition to traditional CVR factors, GFR impairment and albuminuria are independent markers of CVR and overall morbidity in diabetic patients. This risk is proportional to the severity of CKD and would be maximal in hemodialysis patients. We recommend screening annually for DN using a urine dipstick test and serum creatinine measurement. Achieving the best glycemic control (A1c<7%), treating high blood pressure (<130/80 mmHg or < 125/75 mmHg if proteinuria >1.0 g/24 h and increased serum creatinine), using nephroprotective renin-angiotensin-aldosterone system blockers, and treating dyslipidemia (LDL-cholesterol<0.55 g/l) are effective measures for preventing the development of microalbuminuria, delaying the progression to more advanced stages of CKD and reducing the overall cardiovascular mortality in diabetic patients.

DOI: 10.1530/endoabs.81.EP391

EP392

Diabetic foot: a tunisian experience

Mouna Elleuch, Hamdi Frikha , Dhoha Ben Salah, Fatma Mnif, Mouna Mnif, Nadia Charfi , Nabila Rekik Majdoub , Faten Haj Kacem Akid & Mohamed Abid
Hedi Chaker University Hospital, Department of Endocrinology, Sfax, Tunisia

Introduction and aim
Diabetic foot (DF) is associated with increased morbimortality and cost of diabetes management. The aim of this study is to describe the epidemiological, clinical and paraclinical characteristics and follow-up outcomes of patients with diabetic foot in a Tunisian center.
Methods
It is a monocentric retrospective study of 210 patients with diabetic foot followed at the endocrinology department of the Hedi Chaker Sfax University Hospital between 1997 and 2020.
Results
Patients were predominantly men (79.6%), aged 59.14±12.24 years on average. Over 85% of patients were type2 diabetics, 90.4% of whom had a chronically imbalanced condition. In our population, diabetes has been diagnosed since 13.21±8.2 years while DF was the revealing factor of diabetes in 7 patients (3.4%). Approximately one third of the patients lived in poor socioeconomic conditions and 24% were illiterate. Half of the patients were obese and 25.2% were smokers. The mean time to consultation was 45.83 days (median = 15 days). The most common reason for admission was major hyperglycemia associated with DF (75.1%) while ketoacidosis was found in 29 patients (14.1%). Half of patients had lower limb arterial disease (LLAD) upon admission while peripheral neuropathy was present in 81.6% of patients. The most frequent triggers of DF were unfelt trauma (26.7%) and foot-shoe conflict (12.1%). The involvement was bilateral in 51 patients. Clinical findings showed DF infection, ulceration and plantar perforation were present in 72, 62 and 59 cases respectively. Eighteen percent patients were at gangrene stage upon admission. Lab investigation showed a mean blood glucose level at 15 ± 6.81 mmol/l. The most frequently isolated germ was *Staphylococcus aureus* (29 cases). Antibiotic therapy was prescribed in 62.1% of cases for a mean duration of 19.9 ±18.6 days. Amputation was the outcome for 44 patients and the mortality rate was 1.9%. In monovariate analysis, the predictive factors for amputation were the presence of LLAD (OR=4; $P = 0.02$), osteitis (OR=34; $P < 0.001$) and gangrene (OR=18; $P < 0.001$).
Conclusion
Despite major advances in therapeutic options, DF remains a major public health issue. Therapeutic education and primary prevention are essential to reduce the frequency and severity of DF complications and ensure early management.

DOI: 10.1530/endoabs.81.EP392

EP393

Diabetic nephropathy and hypertension

Meriam Dalhoum , Zohra Hadj Ali, Ines Bani, Yosra Htira & Faika Ben Mami
National Institute of Nutrition, Department C, Tunis, Tunisia

Introduction
Diabetic nephropathy is a a dreadfull complication of diabetes and it is the leading cause of chronic kidney disease worldwide. Hypertension is a major cause of progression of this complication.
Objective
To determine the prevalence of diabetic nephropathy, to search a correlation between the presence and duration of arterial hypertension and the occurrence of diabetic nephropathy.
Patients and methods
This is a retrospective study carried out about 184 type 2 diabetic patients, followed at the department C of the National Institute of Nutrition in Tunis.
Results
The mean age was 61±10 years, with a sex ratio M/F of 0.56. The mean duration of diabetes was 14±8 years, the mean glycated hemoglobin (HbA1c) was 10.6%. Nephropathy was present in 37% of cases. In the subpopulation of patients with nephropathy, it was noted that 67% of patients were at the stage of micro albuminuria, 44.2% were in renal failure, mean clearance of creatinine was 57 ml/min and 79% were hypertensive. The presence of nephropathy was correlated with the duration of evolution of hypertension (74% had a duration of evolution of more than 05 years) and 62% of patients were in blood pressure imbalance.
Conclusion
Blood pressure control is crucial in diabetic patients, it allows nephroprotection and an improvement of the cardiovascular prognosis.

DOI: 10.1530/endoabs.81.EP393

EP394

The association of hypertension and type 2 diabetes

Meriam Dalhoum , Zohra Hadj Ali, Ines Bani, Yosra Htira & Faika Ben Mami
National Institute of Nutrition, Department C, Tunis, Tunisia

Introduction
The association of hypertension and type 2 diabetes is frequent. These two pathologies constitute each a cardiovascular risk factor with a cumulative effect which increases the cardiovascular morbi-mortality of hypertensive diabetics.

Objective
To measure and compare the frequency of degenerative complications of diabetes in hypertensive and non-hypertensive diabetics.
Patients and method
The study was descriptive, retrospective and included 184 type 2 diabetic patients followed at the service C of the National Institute of Nutrition of Tunis.
Results
The mean age was 61 ± 10 years, with a sex ratio M/F of 0.56. The mean duration of diabetes was 14 ± 8 years, the mean glycated hemoglobin (HbA1c) was 10.6%. It was noted that 69.5% of patients had hypertension. The prevalence of microangiopathy was globally higher in hypertensive diabetics than in non-hypertensive patients (retinopathy: 33.6% vs 8.9%; neuropathy: 26.6% vs 17.8%; nephropathy: 43% vs 3.6%). Similarly, the prevalence of macroangiopathies was higher in hypertensive diabetics (stroke: 3.9% versus 0.54%; coronary artery disease: 18.8% versus 1.6%; and cerebral artery disease: 6.3% versus 1.8%).
Conclusion
Hypertension is often associated with type 2 diabetes. It worsens the cardiovascular prognosis and accelerates the onset of degenerative complications. Adequate management of arterial hypertension is therefore necessary to reduce the cardiovascular risk of diabetic patients.

DOI: 10.1530/endoabs.81.EP394

EP395

The blood lead level is the meaningful indicator to metabolic syndrome in healthy populations

Kyu Rae Lee , In Cheol Hwang , Kyung Kon Kim , Heuy Sun Suh & Ki Dong Ko
Gachon University, Family Medicine, Incheon, Rep. of South Korea

Background
Lead is known as an environmental toxic pollutant and hormonal regulatory confounder associated with obesity. Recent China scientific report shows that blood lead level (BLL) is closely related with body mass index. Therefore, we investigated the association between the prevalence of metabolic syndrome and blood lead levels in healthy general population without hypertension, dyslipidemia, and diabetes.
Methods
We assessed the socio-demographic (height, weight, alcohol and smoking, income, education and living area, waist circumferences), cardio-metabolic variables (blood pressures, fasting plasma glucose, glycated hemoglobin and HDL cholesterol, triglyceride, high sensitivity C-reactive protein), BLL after fasting over eight hours from 1,381 healthy subjects without hypertension, dyslipidemia, and diabetes, among 8,238 subjects in 2017 KHANES (Korea Health Analysis and Nutrition Examination Survey) dataset. Chi-square tests for categorical variables, Pearson's correlation analysis, student *t*-test for continuous variables were performed. *P*-value <0.05 was considered as significant at both sided using by SPSS packages for windows (version 18, USA).
Results
As a total of 1,381 subject (43.22 +/- 0.39 years, female 55.3%), mean BMI and WC were 23.52 +/- 0.099 kg/m^2, 79.98 +/- 0.285 cm. The BLL was correlated with BMI, WC, age, sex, income, education, living location, alcohol, smoking, occupation, systolic pressures, diastolic pressures, fasting plasma glucose, total cholesterol, HDL-cholesterol. ($P < 0.05$) The BLL was very significantly correlated with BMI, WC after controlled for age, income, education, marriage, smoking, alcohol, occupation, energy intake. ($P < 0.05$, $P < 0.001$) In addition, we found hypertension, hyperglycemia, hypercholesterolemia, and hypertriglyceridemia, high sensitivity-CRP, high glycated hemoglobin, and low HDL-cholesterolemia in higher group than lower group in BLL. ($P < 0.05$) Furthermore, it was more evident for the significant difference between two groups in women than men. ($P < 0.01$)
Discussion and Conclusion
As the endocrine regulator related with metabolism, the blood lead level might be associated with body weight. However, the clear mechanism between them would not be determined. BLL was closely related with metabolic syndrome in healthy general population without diabetes, hypertension, and dyslipidemia. Further controlled longer clinical trial would be considered in the future.

DOI: 10.1530/endoabs.81.EP395

EP396

Impact of bariatric surgery on body composition and cognition: a pilot study

Andreu Simó-Servat[1,2], Montserrat Ibarra[1], Mireia Libran[1], Nuria Alonso[1], Silvia Rodriguez[1], Montse Ramos[1], Veronica Perea[1], Luis García-Pascual[1], Aida Orois[1], Carmen Quirós[1] & Maria Jose Barahona Constanzo[1]
[1]Hospital Universitari Mutua de Terrassa, Endocrinology, Terrassa, Spain; [2]Terrassa, Endocrinology, Terrassa, Spain

Aim
Bariatric surgery (BS) modifies body composition. The aim of the study was to establish the first step toward the introduction of the ultrasound (US) and bioelectrical impedance analysis (BIA) in the evaluation of body composition before and after BS. In addition, as obesity was shown to be related to global cognitive decline, we aim to determine possible changes in cognitive test before and after BS.
Material and Methods
a prospective pilot study of patients with obesity who underwent BS in our hospital. Fat mass (FM) and lean mass (LM) were calculated by BIA, and skeletal muscle index (SMI) was used for estimating muscle mass. We measured thigh muscle thickness (TMT) and subcutaneous fat (SF) of quadriceps by US. In the same visit, Montreal Cognitive Assessment (MOCA) test was done. All subjects were assessed 1 month before surgery and 12 months after it.
Results
32 patients were included (75% female, mean age: 40.15 years, mean BMI: 43.79 kg/m^2). BS reduced BMI 6,63 ± 1,25 kg/m^2 on average ($P = 0.001$). About body composition, significant reductions in FM (7.26 ± 0.99 kg, CI 95% 5.23 to 9.29, $P = 0.001$) and SF (0.24 ± 0.08 cm, CI 95% 0.07 to 0.41, $P = 0.007$) were found. Conversely, although a significant increase in LM (3.76 ± 0.72 kg, CI 95% 2.29 to 5.23, $P = 0.001$) was observed, TMT (0.05 ± 0.12 cm, CI 95% -0.3 to 0.19, $P = 0.634$) and SMI (0.33 ± 0.17 kg/height^2, CI 95% -0.01 to 0.68, $P = 0.057$) did not change. When BIA and US were compared, we found a significantly correlation between the FM and SF (pre-surgical: $r = 0.42$, $P = 0.01$; post-surgical: $r = 0.52$, $P = 0.003$) and between SMI and TMT (pre-surgical: $r = 0.35$, $P = 0.04$; post-surgical: $r = 0.38$, $P = 0.03$). Lastly, MOCA score significantly increased after BS (1.13 ± 0.52, CI 95% 0.06 to 2.19, $P = 0.04$).
Conclusions
Our results suggest that US evaluation of TMT and SF may be complementary to BIA-derived SMI assessment for estimating muscle mass. Likewise, we also detected a possible improvement in the cognitive function of patients after BS.

DOI: 10.1530/endoabs.81.EP396

EP397

Correlation of obesity with diminished neutralizing antibody count

Teona Nutsubidze, Lasha Uchava & Elen Giorgadze
National Institute of Endocrinology, Endocrinology, Tbilisi, Georgia

The obesity epidemic, which has persisted for more than 45 years, is now being faced concurrently with the coronavirus pandemic, with deadly effects. The complex changes caused by obesity, such as chronic inflammation, are known to be detrimental in patients with COVID-19. 33.2% of the Georgian population is obese (1). Therefore, we aimed to explore the synergistic effects between obesity and SARS-CoV-2. The objective of our study is to compare the presence of neutralizing antibodies among obese and non-obese individuals 22 weeks after COVID-19 vaccination. The findings should have important implications for fine-tuning revaccination protocols for people with obesity.
Materials and Methods
In-vitro chemiluminescence immunoassays were used to quantify the serum neutralizing antibodies to SARS-CoV-2 in 30 individuals in an outpatient setting. Only patients who had received the second COVID-19 vaccine dose at least 22 weeks earlier were included in the study. Patients were divided into two subgroups according to BMI, with 15 patients with BMI >30 kg/m^2 in the obese group and 15 patients with BMI <30 kg/m^2 in the control group. In both subgroups,40% of patients had recovered from COVID-19. The exclusion criteria for the study were the presence of autoimmune diseases, current use of immunosuppressants, or a history of COVID-19 in the prior 8 weeks. Limitations

Table 1. Values are presented as mean. BMI: body mass index.

Parameter	Control Group BMI < 30	Obese Group BMI >= 30
Gender (M/F)	3/12	6/9
Age	37	47
Duration since Second Dose (weeks)	22	22
Previous Infections		
Yes	40%	40%
No	60%	60%
nABs (μg/ml)	19,3846	1,8362

of this study include the small study population size and the lack of baseline data verifying the presence of antibodies 3 weeks post-vaccination.
Results
The serum samples of immunized patients with obesity showed lower antibody counts than those in the non-obese group. The mean amount of neutralizing antibodies in the obese group was 1,8362 µg/ml, compared with 19,3846 in the control group.
Conclusion
Our study showed a strong correlation between BMI and a sustained immune response, because most immunized patients with obesity had diminished amounts of neutralizing anti-SARS-CoV-2 antibodies after 22 week.

DOI: 10.1530/endoabs.81.EP397

EP398

Berberis vulgaris: perspectives in the treatment of non alcoholic fatty liver disease

Mnif Fatma[1], Asma Zargni[1], Kawthar El Arbi[1], Dhoha Ben Salah[1], Salma Bousetta[2], Mouna Elleuch[1], Nadia Charfi[1], Mouna Mnif[1], Nabila Rekik Majdoub[1], Faten Haj Kacem Akid[1] & Mohamed Abid[1]
[1]Hedi Chaker Hospital, Diabetology and Endocrinology, Sfax, Tunisia; [2]Institute of Biotechnology, Sfax, Tunisia

Introduction
Berberis vulgaris is a plant, of the family Berberidaceae. Berberine is the main active compound of the barberry. It is an iso quinoline alkaloid of intense yellow color. Berberis vulgaris is used in several medical purposes, including liver protection, anti-oxidant, antimicrobial agent. It also seems to reduce the level of cholesterol in the blood and triglycerides. Our study aims to investigate the effect of the dietary supplement "Berberis Vulgaris" made from the extract of the dried root bark, on the metabolic parameters in patients with hepatic steatosis (NAFLD) .
Patients and Methods
This is a double-blind randomized clinical trial conducted on 60 patients with NAFLD, divided into two equal groups: (G1) treated with berberine and (G2) treated with placebo. All patients received 3 capsules each day before meals. Weight, body mass index (BMI), Waist circumference (WC), liver transaminase levels and lipid profile were recorded in both groups before and after treatment.
Results
Our population included 17 men (28.33%) and 43 women (71.67%). The average age of patients included in G1 is 47.71 years for men and 58.48 years for women while in G 2 it is 58.9 years and 76 years respectively. The majority of patients in both groups have a family history of metabolic diseases. The majority of NAFLD patients had metabolic diseases such as diabetes in 40% of G2 patients and dyslipidemia in 40% of G2 patients and hypertension in 46.67% of G1 patients. The average weight in G1 was 80.47 kg comparable to that of G2 which was 79.55 kg. The BMI was 33.12 in G1 patients and higher in G2 patients which was 29.12 kg/m^2. On the other hand, the WC was higher in G1 than in G2 (108 cm versus 104 cm). In G1: a decrease in weight, BMI and WC was noted. Liver enzymes: ASAT and ALAT levels decreased from 18.15 to 16.5 IU/l and from 20.88 to 18 IU/l respectively. But they remained increased in G2. Cholesterol, blood glucose and especially triglycerides levels were largely decreased under treatment and remained unchanged under placebo. Abdominal ultra sound examination didn't show a significant change in steatosis.
Conclusion
Considering the decrease in liver enzymes, Triglycerides and cholesterol observed in G1 patients after the use of the dietary supplement Berberis Vulgaris, it can be said that berberine has a positive effect on hepatic and metabolic parameters and may soon be a cornerstone in the treatment of hepatic steatosis.

DOI: 10.1530/endoabs.81.EP398

EP399

Impact of obesity severity on the metabolic profile of obese patients

Rim Rachdi, Berriche Olfa , Ben Ali Khaoula, Eya Safi , Nadia Ben Amor , Rym Ben Othman, Ramla Mizouri, Faten Mahjoub & Jamoussi Henda
The National Institute of Nutrition in Tunis, Diabetology Department A, Tunis, Tunisia

Introduction
Obesity is one of the major public health issues worldwide and is known to be associated with an increased risk of severe metabolic and cardiovascular complication. The aim of our study was to assess the impact of obesity severity on the metabolic profile of obese patients.
Materials and methods
Cross-sectional descriptive study involving 68 obese patients carried within the National Institute of Nutrition in Tunis. The patients were divided into two groups: 34 patients with a BMI between 30 and 34,99 kg/m^2 (G1) and 34 patients with a BMI $\geq$40 kg/m^2 (G2). Each patient underwent clinical examination, fasting blood sampling for metabolic profile and an abdominal ultrasound for fatty liver disease.
Results
Median age was 47,67 years in G1 versus 46,85 years in G2 (P = NS). A clear female predominance was noted in both groups with an F/H sex ratio of 4,66 in G1 and 16 in G2. The average BMI was 32,67 kg/m^2 in G1 compared to 44,55 kg/m^2 in G2. The average waist circumference was significantly higher in G2 than in G1 (130 cm vs 112,94 cm, $P <$ 10-3). The prevalence of diabetes was 35,29% in G1 and 23,53% in G2 (P = NS). Mean fasting blood glucose levels were comparable in both groups (7,79 mmol/l in G1 and 7,4 mmol/l in G2, P = NS). The prevalence of dyslipidemia was higher in G2 (23,53%) than in G1 (17,65%), P = NS. The mean total cholesterol level in mmol/l was comparable between the two groups (4,80 in G1 vs 4,87 in G2, P = NS). The mean triglycerides level in mmol/l was significantly higher in G2 than in G1 (1,33 in G1 vs 1,71 in G2, P = 0,0024). The average HDL cholesterol level in mmol/l was higher in G1 than in G2 (1,28 in G1 vs 1,20 in G2, P = NS). The mean uric acid level in micromol/L was significantly higher in G2 than in G1 (350,61 in G2 versus 284,64 in G1, $P <$ 10-3). Fatty liver disease prevalence was higher in G2 than in G1 (11,76% vs 5,88%) with no statistically significant difference (P = NS).
Conclusion
Our study showed that the severity of obesity is associated with a higher prevalence of metabolic disorders justifying early management of obesity in order to delay the onset of these abnormalities.

DOI: 10.1530/endoabs.81.EP399

EP400

Association of chemerin and serum advanced glycation end products in patients with autoimmune thyroiditis

Sára Bak-Csiha[1], Sándor Halmi[1], David Hutkai[1], István Molnár[1], Mónika Katkó[1], Hajnalka Lőrincz[2], Mariann Harangi[2], György Paragh[2], Endre Nagy[1], Miklos Bodor[1] & Berta Eszter[1]
[1]University of Debrecen, Endocrinology, Debrecen, Hungary; [2]University of Debrecen, Metabolism, Debrecen, Hungary

Background
Hypothyroidism due to autoimmune thyroiditis leads to atherogenic lipid profile and metabolic changes. The formation of advanced glycation end products (AGEs) increases with hyperglycemia, hyperlipidemia and oxidative stress. Degradation of AGEs after AGEs-receptor 1-mediated intracellular uptake and renal clearance of soluble AGEs generated by certain cells like macrophages play a crucial role in the decrement of circulating AGEs level. Chemerin is an adipokine produced by adipose tissue and liver and acts as a chemoattractant for immune cells and promotes adipocyte differentiation. Chemerin also appears to induce insulin resistance in skeletal muscle. To date, the association of AGEs and chemerin has not been investigated in thyroid disorders.
Subjects and Methods
In our study we investigated the association between thyroid hormone levels, thyroid antibodies, the components of lipid metabolism, renal and liver function, anthropometrical parameters and AGEs. We enrolled one hundred and ten patients (9 men, 101 women, mean age 49.3 $\pm$ 16.7 years, mean BMI 27.5 $\pm$ 5.8 kg/m^2) from the outpatient clinic of Endocrine Department of University of Debrecen, Faculty of Medicine. All patients had autoimmune thyroiditis with various thyroid hormone status from hypo- to hyperthyroidism. Serum AGEs concentrations were determined by autofluorescence. Thyroid hormone levels, anti-thyroperoxidase (aTPO) concentration and lipid parameters were measured by routine laboratory methods. Chemerin levels were measured by ELISA method.
Results
Median serum AGEs level was 10.4 (9.4 – 11.8) AU/µg protein, median chemerin level was 91.2 (79.8 – 104.8) ng/ml, while mean total cholesterol level was 5.3 $\pm$ 1.1 mmol/l. Mean fT3 and fT4 were 4.56 $\pm$ 0.76 and 17.8 $\pm$ 3.7 pmol/l, respectively. Significant negative correlation was found between fT3 and log AGEs/total protein levels. There was a significant correlation between log chemerin, total cholesterol, log creatinine, log ApoB100 and log AGEs/total protein levels. However, we could not find correlation between log AGEs/total protein levels and aTPO levels.
Conclusions
The significant negative correlation between log AGEs/total protein levels and fT3 levels might be the consequence of T3 regulatory effect on metabolism. However, further clinical investigations are needed to clarify this relationship.

DOI: 10.1530/endoabs.81.EP400

EP401

Efficacy of a groupal lifestyle intervention programme for weight loss in obesity

Manuel Cayón-Blanco , Dolores Cepero , M José López-Pérez , Lourdes García-García-Doncel & Maria Gloria Baena-Nieto
Jerez Hospital, Endocrinology Unit, Jerez, Spain

Introduction
Obesity is one of the most important problems worldwide in recent times. Groupal lifestyle intervention programmes are efficacious in the management of obesity. While exercise and healthy dietary habits have consistently been shown to improve various metabolic markers, adherence to these behaviors is low and methods that increase adherence to health behaviors are needed.
Objective
The primary objective of this study is to evaluate the effectiveness of a groupal weight loss programme for weight loss in obesity and its efficacy in improving health parameters related to obesity.
Materials and Methods
All participants received a groupal lifestyle intervention focused on diet, physical activity, and behavior change strategies. The duration of program was 6 months. Clinical and biochemical parameters were evaluated before and after the intervention.
Results
A total of 112 patients were included. At baseline, the mean body-mass index (BMI) for all participants was 46.1 $\pm$ 14.2 kg/m^2, and the mean weight was 125.8 $\pm$ 22.1 kg. The mean age was 46.9 $\pm$ 14.3 years and 72.5% were women. 60.4% had hypertension and 23.1% were diabetic. Of the 112 patients, 82 patients completed the follow-up (78.57%). 21.43% of the patients did not attend the appointments and left the program. The percentage of participants who lost 5% or more of their initial weight was 47.6%; In 18.8%of them the weight loss was $<$ 5% and 19.6% of patients did not lose weight. Of the 39 patients who achieved the weight loss goal, a significant decrease in BP, basal glycemia, Hba1c, uric acid, T-cholesterol, and triglycerides was observed. The patients who completed the follow-up and had the best results were the oldest and those with the most comorbidities.
Conclusions
The establishment of a groupal weight loss programmes achieves objective weight loss in most patients with a benefit in analytical parameters. Less adherence to our protocolized programme was shown in younger patients, which could be due to less interest and lack of awareness of the disease. Future studies with a longer follow-up period would be interesting.

DOI: 10.1530/endoabs.81.EP401

EP402

Bariatric Surgery in Type 1 Diabetes patients: a single centre study

Tanya Chopra, Alice Wills & Foteini Kavvoura
Royal Berkshire NHS Foundation Trust, Centre for Diabetes and Endocrinology, Reading, United Kingdom

Background
Bariatric surgery significantly aids weight loss, improves glycaemic control and/or induces remission in Type 2 Diabetes patients. However, the impact of bariatric surgery in Type 1 diabetes (T1D) patients is less well-understood. With an increasing prevalence of obesity within the T1D population, it is important to identify whether bariatric surgery improves glycaemic control and prevents future complications.
Aim
To evaluate the effect on BMI, excess weight loss, HbA1c and insulin requirements over the course of a year following bariatric surgery, in patients with T1D in a large bariatric centre.
Methods
Between 2016-2020, 647 patients underwent bariatric surgery at Royal Berkshire Hospital, UK; 6 (0.9%, 83% female, mean age 49 years) had T1D and were retrospectively identified. The bariatric surgery type, BMI, HbA1c, basal insulin (BI) requirements and excess weight loss at time of referral, 6 and 12 months post-operatively were recorded. Information on short-acting insulin doses was not collected due to data inconsistencies.
Results
The majority of patients underwent a Roux-en-Y gastric bypass ($n = 5$) compared to gastric sleeve gastrectomy ($n = 1$). A sustained improvement in BMI was noted post-operatively, (-10 kg/m^2 at 6 months and -14 kg/m^2 at 12 months). A mean excess weight loss of 53.4% and 74.8% was achieved at 6 and 12 months, respectively. There was a reduction in mean daily BI requirement overall, with a 60% reduction in insulin noted at 6 months and 50% reduction at 12 months (38.8 units at referral vs 16.2 units at 6 months vs 19.2 units at 12 months post-operatively). HbA1c decreased at 6 months (mean -6 mmol/mol [-11 to +2 mmol/mol]) (pre-op mean 62mmol/mol) but this was not sustained at 12 months post-op compared to time of referral (mean -1 mmol/mol [-13 to +2 mmol/mol]).
Conclusion
Bariatric surgery resulted in a sustained improvement in excess weight loss and BMI in patients with T1D. Improvement in daily insulin requirements were noted, particularly in the short-term. However, the reduction in insulin requirements did not correspond with a reduction in HbA1c, with only short-term benefits seen. The majority of our patients had well-controlled diabetes at referral and improvement in glycaemic control was not the primary reason for surgery. The small number of patients and short follow-up may preclude definitive conclusions on the benefit of bariatric surgery in glycaemic control and complications in T1D patients in the long-term.

DOI: 10.1530/endoabs.81.EP402

EP403

Covid-19 infection in an individual with Down Syndrome, obesity, and hypothyroidism: a case from the UAE

Esphie Grace Fojas[1], Shamma Al Shamsi[2], Mohamed Salah Noshi[3], Tomader Ali[1] & Nader Lessan[1]
[1]Imperial College London Diabetes Centre, Abu Dhabi, United Arab Emirates; [2]Tawam Hospital, Al Ain, United Arab Emirates; [3]Sheikh Khalifa Medical City, Abu Dhabi, United Arab Emirates

Covid-19 infection severity has been associated with pre-existing conditions including obesity. Individuals with Down Syndrome (DS) are potentially at high risk. Reports on the outcomes of Covid-19 infection in individuals with DS are scant. Here we present such a case. MA is a 27-year old Emirati male with DS, obesity and hypothyroidism. He was brought to the ER with a history of hemoptysis (2 days), fever and cough (1 week). He tested positive for Covid-19. Initial investigations showed high CRP (44 mg/l), and mildly elevated ferritin (541 mcg/l) and D-dimer (0.93 mcg/ml). A chest CT scan showed classic Covid-19 pneumonia features with moderate severity score of 10/25. On Day 7 post-admission, his condition deteriorated; septic shock secondary to gram negative septicaemia with multi-organ failure developed. He required ventilator support and was intubated in ICU. Oliguric/anuric acute kidney injury (creatinine 882 mmol/l) followed, requiring hemodialysis; thrombocytopenia and deranged liver function tests were reported. He was prescribed full course COVID-19 regimen with multiple courses of broad-spectrum antibiotics and antifungal medication. After 10 days, MA was extubated but remained on oxygen supplementation, until finally weaned off oxygen completely. His renal function gradually recovered; his transaminitis and thyrombocytopenia resolved. His severe hypernatremia (sodium 170 mmol/l) improved on hypotonic fluid. MA was discharged after 5 weeks with a 10-day ICU stay. Post-Covid, swollen legs, uncontrolled headache, hair loss, and weight loss (9 kg) were noted. Hypothyroidism was inadequately controlled (TSH 11.72 mIU/l) 3 months post-discharge requiring thyroxine dose increase (150 to 175 mcg OD). This report highlights management challenges of COVID 19 infection in individuals with DS who often have other co-morbid conditions including obesity. Hospital admission can be prolonged and the course complicated by multi-organ failure. Specific preventative strategies including social distancing measures and vaccination schedules are needed for people with DS.

DOI: 10.1530/endoabs.81.EP403

EP404

Diagnosis of sarcopenia using biomipedance analysis

Iulia Samoilova, Mariia Matveeva, Daria Podchinenova, Oxana Oleynik, Venera Mutalimi[1] & Ekaterina Choroshunova
Siberian State Medical University, Tomsk, Russian Federation

Objective
To study the peculiarities of the composition in patients over 50 years old.Materials and Methods: The study involved 136 adults aged 50 to 82 years. All subjects underwent complex examination, which included anthropometry (height, weight, body mass index (BMI)) and body composition analysis using Inbody 770 (Inbody Co.Ltd., Korea). Statistical processing of the results was performed using MedCalc Statistic software.
Results
women's age was 60[55.0;64.0] years, weight 74.5 [66.3;85.2] kg, height 159[156.0;164.0] cm, BMI 29.4 [25.0;33.8] kg/m^2. Body fat mass was

31.4[21.8;39.9] kg, body fat percentage 42.4 [37.2;48.0]%, visceral fat area 164.2 [127.7;201.5] cm^2, skeletal muscle mass 23.6[21.3;26.0] kg, appendicular muscle mass 6.48 [5.9;7.3] kg according to bioimpedanceometry. Appendicular muscle mass deficiency was found in 15.0% of the women's group. In the group of women with a normal BMI, 78.8% had changes in body composition according to bioimpedance measurements (increased body fat mass, percent body fat mass); 42.1% had visceral obesity; appendicular muscle mass deficiency was found in 52.6%. Male age was 58.5 [50.0;65.0] years, weight 92.4 [77.2;106.9] kg, height 173.5 [168.0;180.0] cm, BMI 30.9 [25.8;34.7] kg/m^2. Body fat mass was 26.5 [16.3;40.3] kg, body fat percentage 31.8 [21.8;39.5]%, visceral fat area 128.8 [83.6;189.0] cm^2, skeletal muscle mass 34.6 [29.9;40.5] kg, appendicular muscle mass 8.8 [7.9;9.2] kg according to bioimpedance measurement. The prevalence of reduced appendicular muscle mass in men was 12.5%. In the group of men with a normal BMI, 71.4% had changes in body composition by bioimpedance analysis (increased body fat mass, percent body fat mass); 42.1% had visceral obesity.
Conclusions
in some cases BMI did not reflect the actual degree of fat deposition and did not allow for differentiation between fat and muscle mass. The observed changes in body composition among those examined with a normal BMI indicate the need for more active diagnostic tactics and the use of additional tools for early detection and correction of these abnormalities, due to their association with reduced life expectancy and quality of life, as well as the risk of developing a number of metabolic disorders.

DOI: 10.1530/endoabs.81.EP404

EP405

Impact of obesity on the development of respiratory abnormalities

Ramla Mizouri, Rym Ben Othman, Nadia Ben Amor, Faten Mahjoub, Rihab Yamoun, Salma Abadlia, Berriche Olfa & Jamoussi Henda
Institut National de Nutrition de Tunis, Service A, Tunis, Tunisia

Introduction
Obesity exposes to multiple complications, including cardiovascular and metabolic ones. It can also cause respiratory problems, which are still insufficiently researched. The objective of this study was to detect respiratory abnormalities in a group of obese people followed in an obesity unit.
Methods
This was a descriptive and analytical cross-sectional study of 100 obese patients consulting at the human obesity research unit of the National Institute of Nutrition in Tunis. Each patient underwent a clinical examination (history, anthropometric parameters, eating habits, symptoms of obstructive sleep apnea syndrome) and a biological assessment.
Results
The average age of our patients was 45.08 $\pm$ 13.93 years, with a clear female predominance (88%). The average weight was 103.76 $\pm$ 17.9 kg. The average BMI was 38.95 $\pm$ 5.72 kg/m^2. The average waist circumference was 123.88 $\pm$ 13.13 cm and the average fat mass was 45.98 $\pm$ 12.22 kg. Sedentary lifestyle was noted in 60% of the study population. 44% of the subjects were overweight, 33% had class I obesity, 20% had class II obesity and 3% had class III obesity. The majority of our population (72%) had central obesity. Within this population, 53.5% had dyspnoea, 65% had nocturnal snoring, 50% described daytime sleepiness and 31.3% experienced apnea during sleep. The analytical study showed a positive association between BMI and the onset of possible nocturnal snoring. On the other hand, no positive association was found between BMI and the following factors: dyspnea, daytime sleepiness and the onset of apnea during sleep.
Conclusions
The diagnosis of obstructive sleep apnea requires a systematic and early approach to clinical screening for respiratory disorders. Better accessibility to respiratory explorations would improve the quality of care in this population.

DOI: 10.1530/endoabs.81.EP405

EP406

Pregnancy in women with diabetes: A review of 100 cases

Imane El Abbassi & Fadwa Atfi
CHU Ibn Rochd , Maternity Department, Casablanca, Morocco

Introduction
Pregnancy in diabetics is one of the most frequent forms of high-risk pregnancy. It requires diabetic-obstetric-neonatalogical collaboration. Its risks affect the fetomaternal prognosis in the short and long term. Materials and methods: The aim of our work is to establish the main difficulties in the management of diabetic pregnancy. This is a retrospective study of 100 pregnant diabetic patients followed at the maternity hospital of CHU IBN ROCHD of CASABLANCA, for a period of 2 years. Results: The average age of the patients was 32 years. In 40% of the cases, it was a type I diabetes and 49% a type II diabetes. Gestational diabetes, on the other hand, represented only 11%. Gestational age at the time of the first consultation is on average 2 months, the monitoring rhythm is one consultation per month. Self-monitoring of blood glucose is performed in only 19% of cases. Diabetic pregnancy was complicated by foetal death in 14% of cases, macrosomia in 15% of cases, urinary or genital infection in 17% of cases, spontaneous abortion in 6% of cases and pregnancy toxemia in 1% of cases.
Discussion
The prognosis of pregnancy in diabetic women has improved considerably over the last few years in developed countries, thanks to better management, based on the planning of the pregnancy, justifying the use of reliable contraception, perfect glycaemic control even before conception, rigorous obstetrical, diabetic and neonatal monitoring, and the active participation of the patient. In the light of our study and its comparison with some data in the literature, we feel it is appropriate to emphasise a number of points: The importance of preconception management, in order to optimise glycaemic control before pregnancy, based on education and the implementation of insulin therapy techniques. Good management also requires the motivation of the diabetic woman who must collaborate with a multidisciplinary team. Facilitating access to material means for control and treatment is essential.
Conclusion
Diabetic pregnancy is a high-risk pregnancy for the mother and the foetus. Good medical surveillance by a multidisciplinary team from the preconceptional period until delivery allows a significant reduction in fetomaternal complications. Patient education and information are an integral part of the management of diabetic pregnancy.

DOI: 10.1530/endoabs.81.EP406

EP407

Diabetes and pancreatic cancer: what link?

Faten Haj Kacem Akid, Asma Zargni, Kawthar El Arbi, Dhoha Ben Salah, Mnif Fatma, Nadia Charfi, Mouna Mnif, Nabila Rekik Majdoub, Mouna Elleuch & Mohamed Abid
Hedi Chaker Hospital, Diabetology and Endocrinology, Sfax, Tunisia

Introduction
Pancreatic cancer is one of the digestive system cancers whose prognosis has not been improved, both in terms of early diagnosis and prognosis, despite the progress in clinical, radiological and biological investigation. A significant number of patients present at the time of diagnosis of this cancer, or just before, a relatively recent onset diabetes. The link between diabetes and pancreatic cancer is established, but it is sometimes difficult to distinguish whether its occurrence is the cause or the consequence of diabetes. Hereby we report 4 observations.
Observation
The 1st case was a 64-year-old woman. The diagnosis of a metastatic biliopancreatic adenocarcinoma was discovered fortuitously on abdominal ultrasound. Palliative chemotherapy was indicated. Diabetes was discovered during the pre-chemotherapy workup with a blood glucose level of 5 g/l. She was on insulin therapy. The 2nd and 3rd cases: Male patients aged 57 and 71 years respectively, diabetic for 1 year and 3 months on Metformin. A pancreatic adenocarcinoma was discovered in front of weight loss and jaundice. Both of them were treated surgically and put on insulin therapy. The 4th case was a man of 84 years old hospitalized for inaugural diabetic ketosis with an altered general condition. During his hospitalization, he developed jaundice associated with abdominal pain. Abdominal ultrasound revealed an extensive process at the head of the pancreas.
Discussion-Conclusion
The relationship between pancreatic carcinoma and diabetes has been shown in different studies, but whether it is a cause or a consequence of diabetes is not clear. Pancreatic tumors are three times higher in the diabetic population than in the general population. Pancreatic cancer presents problems that we do not know how to solve, especially the circumstances in which cancer should be sought in a patient with diabetes. In two of our observations diabetes preceded pancreatic cancer. The pathophysiological mechanisms of diabetes mellitus in these cases are multiple. At present, there is no systematic screening strategy for pancreatic cancer in diabetics. Particular attention should be paid to any diabetic patient with disturbances of the liver function.

DOI: 10.1530/endoabs.81.EP407

EP408

Hypothroidism and cardiovascular risk in type 2 diabetic's patients

Ines Bani, Zohra Hadj Ali, Meriam Dalhoum, Yosra Htira & Feika Ben Mami
National Institute of Nutrition of Tunis, Department C, Tunis, Tunisia

Introduction
Hypothyroidism is a frequent endocrinopathy in type 2 diabetes (T2D) which can influence the cardiovascular profile in these patients. Our aim was to study the relationship between hypothyroidism and the occurrence of cardiovascular events in patients with T2D.
Method
It is a retrospective study, including 184 T2D patients, conducted in the department C of the National Institute of Nutrition of Tunis during the year 2021.
Results
The average age of our patients was 61 ± 10 years, predominantly female 64.1%, with an average duration of diabetes of 14 +/- 8 years. The prevalence of hypothyroidism was 14%. Patients with diabetes and hypothyroidism were mostly female (72%), and more than half of the patients were older than 65 years. These patients had dyslipidemia in 84% of cases. Obesity and metabolic syndrome were present in 64% and 72% of patients respectively. The average body mass index was 31 ± 6 Kg/m^2. Hypothyroidism was significantly associated with macro-angiopathy complications ($P = 0.038$) mainly coronary artery disease ($P = 0.027$). A significant association was also notified with renal failure ($P = 0.046$).
Conclusion
The coexistence of T2D and hypothyroidism predisposes to an increased cardiovascular and renal risk in type 2 diabetic's patient. This highlights the importance of early detection of this pathology.

DOI: 10.1530/endoabs.81.EP408

EP409

Abstract withdrawn

DOI: 10.1530/endoabs.81.EP409

EP410

To study the Diabetic Foot at risk using an A 60 second Foot Screening Tool and Risk classification based on the comprehensive foot examination in patients of diabetes - At a Tertiary care Center East India

Kishore Behera[1], Uttam Soren[1] & Binod Kumar Behera[2]
[1]AIIMS Bhubaneswar, Endocrinology & Metabolism, Khordha, India; [2]AIIMS Bhubaneswar, Community Medicine & Family Medicine, Khordha, India

Introduction
The aetiology of a diabetic foot ulcer is multifactorial. The three principal components that ascertain the likelihood of ulceration in a diabetic foot are peripheral neuropathy, repeated minor trauma and deformity. Aims:To find the prevalence of diabetes patients having the foot at risk using the Simplified 60-Second Diabetic Foot Screen tool (SSDFST).
Objectives
To find out the diabetic foot at risk.
1. To ascertain the dispersal of various categories of the foot at risk in patients with diabetes and the factors that modify it
2. To find out the association of neuropathy to the various diabetes risk factors.

Materials and Methods
This was a cross-sectional study comprising of 128 patients; a detailed history and examination including neurological and vascular assessment were performed attending a Tertiary Care Hospital. Patients were screened for the risk of diabetic foot using the SSDFST. The detection of loss of protective sensation (LOPS) using a simple 10-g monofilament test (10 g M) was highly predictive of subsequent ulceration had been reported by the Seattle Diabetic Foot Study. Foot at risk was correlated with demographic and clinical features. Data were analyzed using descriptive and inferential statistics, significant at $P = 0.05$.
Results
Out of 128 patients;92(72%), 36(28%) were male and female respectively. The mean duration of diabetes was 7.42 ± 6.233 years (range 1-27). The mean age, BMI, of the study population was 53.125 ± 10.997 years; 25.93 ± 4.464 kg/m^2 respectively. sOut of 128 patients, 82(64%) were normal without any risk factor for diabetic foot, and 46 (36%) patients had at least one risk factor for the diabetic foot using SSDFST. About 36% of patients were combinedly qualified for the foot at risk into (category 1, 2 and 3); among which 06 (5%) were placed under (category 1). 18 (14%) patients were classified into risk category 2 with LOPS + PAD and 22 (17%) into category 3 with a history of ulcer and /or amputation. The duration of diabetes, previous foot ulcer, deformity, absent pedal pulses, active ulcers, neuropathy, all these factors ($P = 0.05$) were significantly associated with neuropathy measured by 10 g M.
Conclusions
Our study revealed that one-third of our patients had at least one risk factor for the diabetic foot by using an SSDFST. About one-fifth of our patients had neuropathy detected by monofilaments. One-tenth of the study population were aware of proper foot care practice.

Keywords
Diabetic foot, Simplified 60-Second Diabetic Foot Screen tool (SSDFST, 10 gm monofilaments.
DOI: 10.1530/endoabs.81.EP410

EP411

Cognitive decline and diabetes: what is the relationship?

Nour Hentati, Zohra Hadj Ali, Maryam Naifar, Yosra Htira & Feika Ben Mami
National Institute of Nutrition and Food Technology of Tunis, Tunisia

Introduction
The number of elderly with cognitive decline has been increasing. Several studies have shown that diabetes is a risk factor for cognitive impairment. Chronic hyperglycemia is implicated, probably by promoting the development of cerebral microvascular disease but physiopathology is complicated.
Methods
The study involved thirty-seven diabetic patients hospitalized in the department C of National Institute of Nutrition and Food Technology of Tunis and who responded to the mini-mental-status examination (MMSE) scale.
Results
We included in our study thirty-seven diabetics patients over 65 years old. The sex ratio (M/F) was 0.68. The mean age was 70.9 ± 3.5 years and the mean duration of diabetes was 15 ± 9.1 years. The mean HbA1C was 10.5 ± 2.3 and the mean BMI was 29 ± 6.9. We examined the frequency of cognitive impairment using the MMSE. An MMSE score of 26 or less was adopted as an indicator of cognitive impairment. The average MMSE score was 22 ± 6.5. The prevalence of cognitive impairment in our sample was 56.8%. The score declined with increasing age and long diabetes evolution. The cognitive impairment was associated with low level of education and the presence of hypertension and there were no significant association with the smoking.
Conclusion
Cognitive impairment is highly prevalent among the elderly. Subjects with disturbed glucose metabolism may be at risk of impaired cognitive function, as these disturbances can influence cognition through atherosclerosis, thrombosis and hypertension. That's why, routine screening of cognition in older subjects with diabetes is recommended.

DOI: 10.1530/endoabs.81.EP411

EP412

Retinal vein occlusion: let's stay classic and don't forget diabetes!

Selma Massanou[1], Asma Kefi[1], Khaoula Ben Abdelghani[2], Mounira El Euch[1], Syrine Sassi[1], Sami Turki[1] & Ezzedine Abderrahim[1]
[1]Service de Médecine Interne A, Hôpital Charles Nicolle, Tunis, Tunisia; [2]Service de Médecine Interne A, Hôpital Charles Nicolle, Tunis, Tunisia

Introduction
Retinal vein occlusions (RVO) are a heterogeneous group of disorders characterized by impaired venous return from retinal circulation. RVO can be classified into branch retinal vein occlusion (BRVO), hemiretinal vein occlusion (HRVO), and central retinal vein occlusion (CRVO) depending on the site of the obstruction. Major risk factors for BRVO include systemic arterial hypertension, arteriosclerosis, and diabetes, although many associations have been reported including thrombophilia and inflammatory conditions such as Behcet disease.

Herein we report a BRVO in a young man in whom Behcet's disease was suspected.
Observation
A non-smoking 36-year-old patient, type 1 diabetic for 14 years on insulin, with no other significant medical history, presented in ophtalmology department for a brutal decrease in unilateral visual acuity of the right eye. Admission examination found visual acuity 4/10 right, 10/10 left, with skin lesions on both legs. Fluorescein angiography showed BRVO in the right, with bilateral minimal diabetic retinopathy. OCT macula scan found significant macular edema in the right eye requiring intravitreal injections of anti-vascular endothelial growth factor (anti-VEGF). Given the notion of recurrent mouth ulcers and nodular skin lesions, the patient was referred to internal medicine department for suspicion of Behcet's disease. The admission examination found no erythema nodosum, no pseudofolliculitis, no oral or genital ulcer scars. There was no neurological manifestation, no uveitis. Dermatological examination found eruptive lesions on both legs made up of multiple confluent and circumferential erythematous and brownish macules. There were infiltrated erythematous purple inflammatory nodules on the posterolateral sides of leg, some varicosities and oedema. A skin biopsy showed non-specific necrotic remodeling of the hypodermis compatible with lipodermatosclerosis. Glycated haemoglobin (HbA1c) at 7.3%. Besides, blood count ionogram, lipid and thyroid analyzes were normal. An exhaustive etiological investigation. As part of the etiological assessment, looking for Behcet's disease, coagulopathy, or connectivitis, pathergy test was negative. HLA typing didn't show HLA B27 or B51 antigen. In addition, antinuclear antibodies, anti-extractable nuclear antigen, anti-cyclic citrullinated peptides, cryoglobulinemia and antiphospholipid antibodies were all negative. In addition, thrombophilia investigation didn't reveal any anomalies. Therefore, this episode was attributed to diabetes, which is already at the stage of degenerative complications (diabetic retinopathy), and the patient was referred to his ophthalmologist and endocrinologist for follow-up.
Conclusion
Among the wide spectrum of RVO, diabetes remains one of the main causes. Until today, it still one of the leading causes of vision loss. So let's stay classic and don't forget diabetes!

DOI: 10.1530/endoabs.81.EP412

EP413

The association of serum magnesium and risk of morbidity and mortality in patients admitted to the intensive care unit: A stratified analysis based on COVID-19 infection classification

Mitra Kazemijahromi[1], HamidReza Samimagham[2] & Azadeh Moradkhani[2]
[1]Endocrinology and Metabolism Research Center, Hormozgan University of Medical Sciences, Bandar Abbas, Iran; [2]Clinical Research Development Center, Shahid Mohammadi Hospital, Hormozgan University of Medical Sciences, Bandar Abbas, Iran

Background
Magnesium deficiency is a common clinical electrolyte abnormality in critically ill patients, related to the higher mortality risk, which is easily ignored. We aimed to investigate the association between magnesium levels and mortality and morbidity in patients admitted to the (ICU) based on COVID-19 infection classification.
Method
A total of 69 patients admitted to the ICU of Shahid Mohammadi Hospital were included in the study. The serum magnesium was measured in IUC patients. Data on score systems SOFA and APACHE, length of ICU stay, and duration of mechanical ventilation was determined. The mortality and morbidity were determined in patients. Also, the COVID-19 infection was detected by PCR test.
Results
The mean $\pm$ SD age of patients (34.8% male) was 52.56 $\pm$ 16.43 years. Out of 69 patients, 18 patients (26.1%) died during hospitalization, and 24 patients (34.8%) required mechanical ventilation. The prevalence of COVID-19 infection was 39.1%(27 patients). Our results showed that there is no difference in serum magnesium in patients based on mortality status. Also, no difference was found in magnesium levels in patients based on most of the morbidities status; however, the magnesium level of patients with kidney failure was significantly higher than patients without kidney failure ($P < 0.05$). Based on the COVID-19 infection classification, there was only a positive correlation between Hypomagnesemia and the length of ICU hospitalization in patients without COVID-19 ($P < 0.05$).
Conclusion
Our findings showed no difference in magnesium levels of patients based on mortality status. Based on morbidities status, patients with kidney failure had higher serum magnesium than those without kidney failure. Also, our results showed no difference in magnesium levels of critically ill patients based on COVID-19 infection status.

DOI: 10.1530/endoabs.81.EP413

EP414

Prevalence of pre-diabetes and diabetes mellitus in polycystic ovarian syndrome (PCOS)

Habib Ullah[1], Kalsoom Noor[1] & Abdul Aziz[2]
[1]Sandeman Provincial (CIVIL) Hospital, Quetta, Pakistan; [2]The Aga Khan University Hospital (AKUH), Karachi, Pakistan

Objective
To determine prevalence of pre-diabetes and diabetes mellitus in polycystic ovarian syndrome (PCOS).
Study Design
Cross sectional study. Non probability consecutive sampling was done.
Sample Size
The estimated sample size was 84 women with 95% confidence level and confidence limit of $\pm$5%.
Setting
Outpatient departments of Medicine and Gynaecology & Obstetrics at a tertiary care hospital of Quetta, Pakistan.
Period
January 2021 to October 2021.
Methodology
All women of age 18-40 years who fulfilled the Rotterdam criteria of PCOS were included. Those having fasting blood sugar (FBS) $\geq$ 126 mg/dl or 2 hour blood sugar $>$ 200 mg/dl on OGTT were said to have diabetes mellitus. Those having FBS between 100-125 mg/dl were said to have impaired fasting glucose (IFG) and those having 2 hour blood sugar between 141-199 mg/dl were said to have impaired glucose tolerance (IGT). Their age, BMI and Oral glucose tolerance test (OGTT) results were documented in the proforma. For analysis SPSS version 20 was used.
Results
The mean age in our study was 29.12 $\pm$ 6.39 years and mean BMI was 30.49 $\pm$ 4.83 kg/m^2. A screening OGTT revealed that 7.1% of PCOS individuals have type 2 diabetes mellitus and 30.9% had pre-diabetes (IFG, IGT).
Conclusion
The prevalence of pre-diabetes and diabetes is high in PCOS, the main risk factor is increased BMI. Prevention and education should be undertaken in such individuals to avoid future complications.

Key words: PCOS, Diabetes Mellitus, Developing Country
DOI: 10.1530/endoabs.81.EP414

EP415

Flash glucose monitoring in patients with type 1 diabetes

Mireia García-Ramírez, Ana María Moyano-Sánchez, Paloma Moreno-Moreno, Ángel Rebollo-Román & Maria Angeles Galvez Moreno
Hospital Universitario Reina Sofía, UGC Endocrinología y Nutrición, Córdoba, Spain

Objective
Flash glucose monitoring (FGM) allows non-invasive glucose level assessment. Our objective was to describe the characteristics of these patients and their glycemic control expressed as HbA1c and times in range.
Methods and patients
Observational longitudinal clinical study between January 2021 and December 2021 in patients with DM1 between 14 and 18 years.
Results
95 patients included. Mean age: 16.64 $\pm$ 1.25 years, with a mean DM evolution time of 6.46 $\pm$ 3.93 years. 47.4% women. Mean HbA1c 7.81 $\pm$ 1.77%. FGM metrics: 54.17 $\pm$ 21.25% time in range, 23.61 $\pm$ 9.72% time between 180-250 mg/dl, 17.05 $\pm$ 18.26% time above 250 mg/dl, 4.21 $\pm$ 4.09% time between 54-70 mg/dl, 1.06 $\pm$ 2.21% time below 54 mg/dl. Glycemic CV 38.14 $\pm$ 7.45%. Classically, patients with a HbA1c below 7% were described as well-controlled patients. 32.6% of patients in our series achieved this target. Nowadays, among users of FGM, those categorized as well-controlled patients have to achieve a TIR $>$ 70%, TAR $<$25% and a TBR $<$4% with a CV $<$33% along with an use $>$ 70% of time. 9.5% of patients in our series achieved this target.
Conclusion
- In our series, there are more patients categorized as well-controlled using HbA1c $<$ 7% (32.6%) than using the FGM metrics (9.5%).
- FMI has revealed that using HbA1c is not enough to achieve a good glucose control in our patients.

DOI: 10.1530/endoabs.81.EP415

EP416

Lipid profile and deep vein thrombosis

Boudaya Mariem[1], Sana Fendri[1], Ben Salah Raida[2], Jamoussi Kamel[1] & Bahloul Zouheir[2]
[1]Hedi Chaker Hospital, Laboratory of Biochemistry, Sfax, Tunisia; [2]Hedi Chaker Hospital, Internal Medicine, Sfax, Tunisia

Introduction
Homocysteine is an intermediate sulfur amino acid in the metabolic pathways of cysteine production from methionine, which is increasingly involved in various pathological processes (arterial thrombosis, depression, schizophrenia, dementia). We are interested in the course of our work to study its implication on the lipid balance in patients with venous thrombosis.
Materials and methods
This is an observational case-control study, comparing 47 healthy control subjects with 47 patients admitted to the internal medicine department for the management of deep vein thrombosis confirmed by radiological examination. These two groups are matched by age, sex and body mass index. The homocysteine assay was done by an enzymatic method. The determination of total cholesterol and triglycerides was carried out according to an enzymo-colorimetric method. The HDLc assay was performed using an endpoint enzymatic solubilization method.
Results
The mean age of patients and controls was 40.8 $\pm$ 10.5 years with extremes of 18 and 59 years. The two groups consisted of 27 men (57.5%) and 20 women (42.5%) with a sex ratio of 1.35. Cholesterolemia did not show a significant difference (P = 0.63) between the group of patients (mean 4.33 $\pm$ 10 mmol/l) and controls (4.73 $\pm$ 0.9 mmol/l). the triglyceremia did not show a significant difference (P = 0.78) between the group of patients (mean of 1.42 $\pm$ 0.76 mmol/l) and controls (mean of 1.26 $\pm$ 0.6 mmol/l). HDLc was significantly (P <0.001) lower in patients (mean 1 $\pm$ 0.25 mmol/l) compared to controls (mean 1.33 $\pm$ 0.3 mmol/l). Homocysteine was significantly (P <0.001) higher in diseased subjects (mean 17.42 $\pm$ 5 µmol/l) compared to control subjects (mean 9.41 $\pm$ 3.1 µmol/l). Statistical analysis showed that homocysteine correlated positively with LDLc (P = 0.002; r = 0.392) and negatively with HDLc (P = 0.002; r = -0.392).
Conclusion
Homocysteine is a sulfur amino acid involved in many disease processes; this can be partly explained by the effect on lipid metabolism with a decrease in HDLc and an increase in LDLc with their toxic cellular effects.

DOI: 10.1530/endoabs.81.EP416

EP417

Prevalence of metabolic syndrome and its correlates in young PCOS women in South India

Jayashree Gopal[1] & Madhulika Dixit Dixit[2]
[1]DiabEndoIndia, Chennai, India; [2]Indian Institute Of Technology, Biotechnology, Chennai, India

Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders in women, affecting approximately 5% to 8% of premenopausal women. Insulin resistance is believed to be a key pathophysiologic factor and increases the risk of associated metabolic syndrome (MetSyn) and diabetes. We looked at the presence of insulin resistance in young women with PCOS from South India. The data is derived from a larger study of polycystic amenorrheic women looking at endothelial progenitor cell response to a glucose challenge.
Methods
The study population included 39 women with anovulatory cycles and polycystic ovaries on USG. The control group were 20 age and BMI matched healthy volunteers, with normal menstrual cycles. Fasting and postprandial glycemic, lipid, insulin and hormonal measurements were compared between the two groups. Categorical variables and proportion estimates were evaluated for statistically significant difference (P < 0.05) using student's t-test and chi-square test as appropriate.
Results
As defined by the NCEP ATP III criteria, 41% (15 out of 36) of the young PCOS women (average age 22.5$\pm$4.7 years) had metabolic syndrome compared to none (0 out of 20) in the control group (average age 22.2$\pm$3.7 years). Both the groups were matched with respect to BMI, and waist hip ratio. Only the mean waist circumference was significantly higher ((96.6 $\pm$ 12.8 cms versus 90 $\pm$ 9.9 cms, P = 0.04840) in the PCOS women compared to control population. Both insulin resistance and insulin secretion parameters were significantly higher in the euglycemic PCOS as compared to the control group. The insulin resistance was estimated by the HOMA IR (2.94 $\pm$ 2.01 in PCOS vs 1.65 $\pm$ 0.58 in the control, P value 0.0005) and insulin secretion by the HOMA-β values (150.2 $\pm$ 56.86 in PCOS vs 110.9 $\pm$ 29.9 in control group, P value 0-001). The strongest predictor of the presence of metabolic syndrome was the waist circumference (r value 0.64), followed by the HOMA IR (r value 0.66).
Conclusions
In this study, the prevalence of MetSyn was significantly higher in young women with PCOS compared to control group. Waist circumference and HOMA IR are strong predictors of MetSyn. MetSyn is also associated with a higher HOMA-β value in the PCOS women. The high prevalence of insulin resistance and MetSyn drives home the need to screen more aggressively for the metabolic syndrome and insulin resistance in young women with PCOS.

DOI: 10.1530/endoabs.81.EP417

EP418

New-onset diabetes after transplantation (NODAT). A case report

Cristina Contreras Pascual[1], Paloma González Lázaro[1], Antonio Moreno Tirado[1], Maria Zhao Montero Benítez[1] & Susana Álvarez López[2]
[1]Hospital La Mancha Centro, Endocrinology Department, Alcázar de San Juan, Spain; [2]Alcázar de San Juan, Primary care physician, Alcázar de San Juan, Spain

New-onset diabetes after transplantation (NODAT) is a serious complication after a solid organ transplantation. It has been reported to occur in 4% to 25% of renal transplant recipients, 2.5% to 25% of liver transplant recipients, 40% to 60% of hepatitis C virus (HCV) infection and 2% to 53% of all solid organ transplantations. The diagnosis is performed using unmodified criteria for diagnosing diabetes in the general population and risk factors are the commonly recognized factors for developing diabetes: obesity, diabetes family history, dyslipidemias, etc. Recent studies suggest that hyperglycemia is associated with an increased risk of hepatitis C virus-related fibrosis development and glycemic control may reduce the risk and severity of recurrence. In addition, it is well known that liver function plays an essential role in glycemic metabolism. That's why it is important to be aware of this bidirectional relation to decrease morbidity and mortality and preserve quality of life. In this report, we describe a NODAT case after liver transplantation whose hyperglycemic state could have preceded a worsening of HCV infection. A 42 years-old woman affected by HCV infection and cirrhosis undergo liver transplantation. After the surgery, she started a posttransplant immunosuppressive treatment (prednisone). Initially her glycemic control was excellent, but five years later she asked her doctor complaining of polyuria and polidipsia. Her endocrinologist performed a blood test that shown a high glycosylated hemoglobin (HbA1c) level (11.6%) and quickly started basal insulin therapy. The study showed a normal C-peptide and negative GAD antibodies, her weight was 70 kg and she had not another diabetes risk factors. Throughout the following years, because of suboptimal control, it was necessary to add a short-acting insulin in the mayor meal (basal-plus insulin regimen) and after one year it was necessary to add insulin also in the other meals (basal-bolus regimen). HbA1c levels decreased to 7%, but some months later the patient suffered a HCV infection recurrence with stage 4 fibrosis. The Digestive System Unit quickly started Sirolimus, a direct-acting antiviral agent. Then, the patient started to lose weight and a year afterthat she had lost 12 kg. Some months later, the patient achieved sutained virological response and insulin sensitivity improved, allowing to decrease insulin therapy until it was withdrawn. In the long run, HCV infection can lead to cirrhosis, hepatocarcinoma and death in some patients. Physicians should be aware of the importance of NODAT and addressing insulin resistance to improve disease prognosis.

DOI: 10.1530/endoabs.81.EP418

EP419

Latent autoimmune diabetes in adults revealed by graves' disease

Boutheina Mohamed Ali[1], Mohamed Hamid Abdillahi[2] & Aicha Ahmed[2]
[1]CHU Ibn Sina, Endocrinologie, Rabat, Morocco; [2]CHU Ibn Sina, Rabat, Morocco

Introduction
LADA (Latent Autoimmune Diabetes in Adults), is defined by the association of diabetes after 30 years, the presence of antibodies against pancreatic beta cells and the non-use of insulin therapy within 6 months of diagnosis. Graves' disease is the first cause of hyperthyroidism associating thyrotoxicosis, goiterand exophthalmos with a prevalence 5 times higher in women.
Case report
37-year-old female patient with no notable history, labeled type 2 diabetes, put on oral antidiabetics with good clinical and biological evolution. One (1) year later faced with a glycaemic imbalance, weight loss amounting to 20 kg (Patient was overweight with BMI at 28 kg/m^2) and signs of thyrotoxicosis without

orbitopathy, a thyroid assessment was made (TSH < 0.05 FT4 = 1.92 FT3 = 7.15), TSH receptor antibodies were positive confirming the diagnosis of Graves' disease. Faced with autoimmunity, weight loss and glycemic imbalance, a dosage of antibodies anti-GAD (glutamic acid decarboxylase) was done and came back positive, confirming the diagnosis of LADA in our patient for which she was put on insulin therapy with a good clinical and biological evolution.

Discussion

Epidemiological studies show that 10% of all subjects with diabetes have the characteristics of LADA. Screening with anti-GAD auto antibodies can identify with certainty. The frequency of thyroid autoimmunity in LADA varies in the literature between 20 et 30%. In the cases of patients without goiter or orbitopathy (like our patient), the dosage of TSH receptor antibodies (TRAb) or scintigraphy are useful to confirm the diagnosis of Graves' disease. This work highlights the association of LADA and Graves' disease suggesting an autoimmune poly-endocrinopathy type 2.

Conclusion

In any patient with autoimmune disease, regular monitoring is indicated to detect the outbreak of a possible autoimmune polyendocrinopathy.

References

1. Hawa, M. and all. (2013). Adult-onset autoimmune diabetes in Europe is prevalent with a broad clinical phenotype: Action LADA 7. *Diabetes Care*, 36(4), 908–913.

2. Joubert, M. (2019). *DT1 lent*, 1–4.

DOI: 10.1530/endoabs.81.EP419

EP420

Flash glucose monitoring in DM1: Our experience in a secondary referral hospital

Mª del Carmen Serrano Laguna, Ana Barrera-Martín, Ángel Rebollo-Román, Julia Silva-Fernández & Maria Angeles Galvez Moreno
Hospital Universitario Reina Sofía, UGC Endocrinología y Nutrición, Córdoba, Spain

Objective

Flash glucose monitoring (FGM) allows non-invasive glucose level assessment. Our objective was to describe the characteristics of patients in a secondary referral hospital and their glycemic control expressed as FGM targets.

Methods and patients

Observational longitudinal clinical study between January 2021 and December 2021 in patients with DM1 referred to a secondary care center in Montilla (Córdoba).

Results

101 patients included. Mean age: 42.38 ± 15.63 years, with a mean DM evolution time of 19.46 ± 12.49 years. 44.6% women. Mean HbA1c 7.75 ± 1.13%. FGM metrics: 56.57 ± 18.58% time in range, 23.5 ± 10.74% time between 180-250 mg/dl, 15.87 ± 17.05% time above 250 mg/dl, 3.90 ± 4.50% time between 54-70 mg/dl, 0.84 ± 1.90% time below 54 mg/dl. Glycemic CV 37.31 ± 7.32%. Among users of FGM, those categorized as well-controlled patients have to fulfill the following criteria: TIR ≥ 70%, TAR ≤ 25%, TBR ≤ 4% with a CV ≤ 36% as long as ≥ 70% of glucose data is obtained. In 64.4% of our patients ≥ 70% of glucose data was registered with FGM. In this subgroup 10.8% of patients fulfilled well-controlled criteria. The reason why patients did not achieve the criteria of adequate control is shown in table 1.

	Fulfill criteria		Not fulfill criteria	
Parameter	**n**	**%**	**n**	**%**
TIR	14	21.5	51	78.5
TAR	18	27.7	47	72.3
TBR	41	63.1	24	36.9
CV	28	43.1	37	56.9

Conclusion

- In our series of patients, more than a third of them (35.6%) don't present with enough FGM data. ‐ensp;Out of patients with enough FGM data, only 10.8% patients of them achieve a good control if we use FGM criteria for adequate glycemic control.
- Among the criteria of good glycemic control, TIR is the least achieved in our patients (21.5%), whereas adequate TBR was the most achieved criterium (63.1%).

DOI: 10.1530/endoabs.81.EP420

EP421

The effects of Semaglutide on glycaemic control and weight, in type two diabetic patients, in our diabetic day center

Azhar Al-Shaibany [1], Olivia Mc Cabe[2,3] & Shah Shabaht[1]
[1]Our Lady's Hospital, Endocrinology and GIM, Navan, Ireland; [2]Our Lady's Hospital Navan, Co. Meath, Navan, Ireland; [3]Our Lady's Hospital, Diabetes Day Center, Navan, Ireland

Introduction

Type two diabetes is characterized by a chronic metabolic state (obesity, high blood pressure, and dyslipidemia) and insulin resistance. There is insufficient pancreatic insulin production and ineffective use of the produced insulin resulting in abnormally high blood glucose levels (hyperglycaemia). Metabolic syndrome and diabetes are associated with increased cardiovascular risk, reduced life expectancy and a reduction in quality of life. Glucagon-like peptide 1 (GLP-1) receptor agonists are used in type 2 patients whose HbA1c remains uncontrolled despite the use of multiple oral therapies. This audit was designed to evaluate the effect of Semaglutide initiation on HbA1c and weight change in patients from diabetic day centre of our Lady's hospital Navan.

Method

Patients with type two diabetes commenced on Semaglutide were identified from their medical notes from the diabetic day centre of OLHN. Patients were commenced on once weekly Semaglutide of 0.5 mg sub cutaneous once weekly and up titrated to a dose of 1mg as tolerated. In total 30 patients were identified and included in this audit. The mean age of participants was 52 years. All patients had in person review prior to commencement to identify them as candidates for treatment and have an objective weight and HbA1c recorded prior to commencement.

Results

85% patients commenced on Semaglutide achieved the Nice guidelines standard reduction in HbA1c. More than 75% of patients commenced on Semaglutide lost > 5% of their body weight and the remaining had modest weight reduction (< 5%).

Conclusion

From our snapshot audit we have demonstrated that patients in our hospital demonstrated significant reductions in both HbA1c and/or weight when commenced on either 0.5 or 1 mg of Semaglutide once weekly.

DOI: 10.1530/endoabs.81.EP421

EP422

Chronic diabetes imbalance in hospitalized patients: what are the causes?

Skander Msolly, Yosra Htira, Chaima Sdiri, Maryam Cheikhrouhou, Zohra Hadj Ali, Hedfi Imene, Chaima Jemai & Feika Ben Mami
Institut De Nutrition, Tunis, Tunisia

Introduction

Diabetes balance is associated with a reduction in mortality and in cardiovascular risk in patients with diabetes [1,2]. The aim of this study was to determine the causes of chronic diabetes imbalance in hospitalized patients with diabetes.

Methods

A cross-sectional study was conducted in a department of diabetology at the Institute of Nutrition of Tunis during 3 months (from September 2021 until December 2021). Patients hospitalized for an imbalanced diabetes were included.

Results

We included 65 patients. The sex ratio (M/F) was 0.66. Among patients included,84.6% were type 2 diabetics, while 15.4% were type 1 diabetics. The mean age was 55.04 ± 16.69years [16-87]. The mean Body Mass Index (BMI) was 29.09 ± 6.95 kg/m^2 [16.63- 51.14]. The mean glycated hemoglobin (HbA1c) level was 10.88% ± 1.6 [7.5 -14]. The Mean hospital stay was 5.07 ± 2.53 days [2 -15]. Almost all the patients (92.3%) were receiving insulin. Diet deviation and therapeutic errors were found respectively in 64.6% and 40% of patients with chronic diabetes imbalance. Poor compliance and skipped injections were found in 26.2% of patients. Lipodystrophies were found in 10.8% of cases. Symptoms of insulinopenia were found in 26.2% of patients. Infections were documented in 6.2% of patients among whom urinary infections were found in 77.4% of cases. Improper handling of insulin was found in 3% of patients.

Conclusion

Any diabetes service should provide highly structured diabetes education program to help people with diabetes learn basic information about diabetes and its management, adopt healthy eating habits through nutrition education, including meal-planning.

References
1. Arnold LW, Wang Z. The HbA1c and All-Cause Mortality Relationship in Patients with Type 2 Diabetesis J-Shaped: A Meta-Analysis of Observational Studies. *Rev. Diabet. Stud. RDS*. 2014;**11** (2):138-52.
2. Cavero-Redondo I, Peleteiro B, Álvarez-Bueno C, Rodriguez-Artalejo F, Martínez-Vizcaíno V. Glycatedhaemoglobin A1c as a risk factor of cardiovascularoutcomes and all-cause mortality in diabetic and non-diabeticpopulations: a systematicreview and meta-analysis. *BMJ Open*. 1 juill2017; **7** (7):e015949.

DOI: 10.1530/endoabs.81.EP422

EP423

Dietary rules in type 2 diabetic patients: degree of compliance and determining factors

Mehrez Achwak, Wafa Alaya, Selma Mohsen, Najoua Lassoued, Fadia Boubaker & Baha Zantour
Taher Sfar University Hospital, Tunisia

Introduction
Nutrition is a cornerstone of the adequate management of Type 2 diabetes mellitus (T2DM). The aims of our work are to evaluate the degree of observance of dietary rules in T2DM patients, and the factors that influence this observance.
Methods
Cross-sectional study including 84 type 2 diabetic patients followed up in the outpatient endocrinology department of Taher Sfar university hospital from September to November 2021. The data was collected in face-to-face interviews with patients.
Results
The average age was 59 $\pm$ 12 years, with a male predominance (58% of cases). The mean duration of diabetes was 9.4 $\pm$ 6.4 years. The mean HbA1c was 9.9% $\pm$ 2.4. Compliance to dietary recommendation was reported by less than half of patients (46% of respondents). Taking meals based on a dietary plan was reported in 15% of patients, having 3 meals plan per day in 88% of cases, with a regular meal time in 84% of cases, and all these factors were significantly associated to a better glycemic control ($P < 10^{-3}$). Cutting down sweets and sugary was reported in 57%, and fried food and fat intake in 71% of cases and both were significantly associated to a better glycemic control ($P < 10^{-3}$ and $P = 0.04$ respectively). Men and women were comparable in the degree of application of dietary rules. Besides, urban residents had better dietary practice than rural residents. Barriers for adherance to dietary recommendations were: cultural backround and communal network in 86% of cases, poor self-discipline and lack of motivation in 70% of cases, poor dietary knowledge and lack of education in 67% of cases, financial constraints in 51% of cases, lack of awareness in 33% of cases, lack of self-control in 21% of cases, fear of hypoglycemia in 19% of cases and eating outside home (in work) in 9% of cases.
Conclusion
Dietary compliance in T2DM patients is still far below the objectives. It is determined by several factors, in particular dietetic education which proves to be insufficient. Through the mutual efforts, health-care professionals can help their patients in achieving health goals by individualizing their nutrition interventions.

DOI: 10.1530/endoabs.81.EP423

EP424

Particularities of diabetes discovered after the age of 65

Ramla Mizouri, Faten Mahjoub, Nadia Ben Amor, Rym Ben Othman, Berriche Olfa & Jamoussi Henda
Institut National de Nutrition de Tunis, Service A, Tunis, Tunisia

Introduction
Diabetes mellitus is a disease that is progressing at an alarming rate in the world. In the elderly, the symptoms are often insidious and atypical, which can delay the diagnosis and the establishment of effective treatment. Indeed, management is not always easy because it must take into account multiple parameters. The objective of our study was to study the clinico-biological and etiological profile of diabetes discovered after the age of 65 years.
Methods
We conducted a retrospective observational study at the National Institute of Nutrition and Food Technology in Tunis, over a period from January 2018 to September 2021. Data were collected from patients' medical observation records. We prepared an information sheet which was used for the statistical analysis of the data.
Results
We collected 35 elderly diabetic patients. The age of the patients varied from 70 to 89 years with an average age of 76.2 $\pm$ 4.5 years. Our population was characterized by a female predominance (66%). Hyper-LDLemia type dyslipidemia was present in 69% of cases with an average duration of evolution of 3.35 $\pm$ 2.56 years. Hypertension was present in 40% of the study population. Diabetes was discovered incidentally in 49% of cases. The average duration of diabetes in our population was 5.89 $\pm$ 3.91 years with extremes ranging from 1 to 14 years. The average age of discovery was 70.29 $\pm$ 4.44 years with extremes ranging from 65 to 79 years. All of our patients were type 2 diabetics. Fasting blood sugar was on average 10.47 $\pm$ 4.32 mmol/l with extremes ranging from 6.1 to 29.4 mmol/l. The glycated hemoglobin varied between 6.5% and 13.9% with an average of 8.9 $\pm$ 1.9%. More than half of the population had an HbA1c greater than 8.5%. Diabetic retinopathy was present in 40% of patients. Peripheral neuropathy was present in 27% of patients with an average DN4 score of 4.3 $\pm$ 1.3. Autonomic neuropathy was mainly manifested by gastroparesis (29%) and orthostatic hypotension (11%). Macroangiopathic complications were dominated by coronary insufficiency (11%) and history of stroke (9%).
Conclusion
These results should encourage the medical community to strengthen screening for diabetes in the elderly and to systematically search for cardiovascular risk factors and, in particular, geriatric syndromes which are often overlooked.

DOI: 10.1530/endoabs.81.EP424

EP425

Correlation of body mass index with random blood sugar levels in rural indians – a hospital based study

Aniket Inamdar[1], Bharat Saboo[2] & Abhisekh Shrivastav[3]
[1]Samarpan Clinic, Internal Medicine, Omerga, India; [2]Prayas Diabetes Center, Diabetology, Indore, India; [3]R & R Hormone Clinic, Endocrinology, Jabalpur, India

Background
Obesity is the most important modifiable risk factor in the pathogenesis of type 2 diabetes. Prevalence of diabetes is increasing in India, possibly due to a rise in obesity and changing lifestyles with nutrition transition. Body mass index (BMI) is positively and independently associated with morbidity and mortality from type II diabetes mellitus, hypertension, cardiovascular disease and other chronic diseases. In Caucasian and Asian populations, a strong association has been depicted between BMI and mortality. Glucose homeostasis is usually tightly regulated and when individuals' transition from normal glucose metabolism to prediabetes and diabetes, glycemic variability increases. Studies thus suggest that random blood sugar (RBS) elevations provide an early warning sign of glycemic dysregulation.
Aim
The main objective was to determine the correlation between BMI and RBS of patients in rural India.
Materials and Methods
310 patients from age 30 to 85 years who visited our hospital in rural India from January 10.2021 to February 27.2021 were included in this study. Random blood glucose was estimated using the glucose oxidase method using venous sample. BMI was calculated using standard formula using patients weight in kilograms (kg) and height (m^2). Using this, the patients were categorized as underweight ($<$ 18.5 kg/m^2), normal or lean BMI (18.5–22.9 kg/m^2), overweight (23.0 –24.9 kg/m^2) and obese ($\geq$25 kg/m^2) based on the revised consensus guidelines for India. One way ANOVA, post hoc Tukey test and Pearson's correlation test were used to analyse the data.
Results
Statistical analysis showed positive correlation between BMI and RBS. As BMI increased, there was rise in RBS with $P = 0.001$. Comparison of RBS with BMI using one way ANOVA test showed that the mean value of RBS in Obese individuals (165.92) is highest followed by overweight (143.36), normal or lean BMI (137.07) least in underweight individuals (124.34). This difference was statistically significant with a test value of 5.636 and p value of 0.001.
Conclusions
In this present study, BMI and RBS were positively correlated among the 310 subjects who participated in the study. Individuals who are overweight tend to have a detrimental and inactive lifestyle, which might also contribute to the development of adiposity, insulin resistance, hyperglycemia and other cardiovascular risk factors. Strategically, it is crucial to prevent prediabetes and diabetes by controlling risk factors, such as weight gain or excessive weight by promotion of regular physical activity and balanced diet.

DOI: 10.1530/endoabs.81.EP425

EP426

Association of fasting plasma glucose levels with wake-up timings in diabetic patients in India

Aniket Inamdar[1] & Bharat Saboo[2]
[1]Samarpan Clinic, Omerga, India; [2]Prayas Diabetes Center, Indore, India

Background
The median sleep time per night has been declining in the world consistently over last 5 decades. The timing of sleep is distinct characteristic of sleep patterns that may impact metabolic disease risk independent of sleep duration, possibly through the effects of circadian rhythms on metabolism. The sleep and wake up timings are driven by both endogenous circadian rhythms that regulate sleep propensity, energy homeostasis and metabolism as well as by sociocultural factors that influence behaviour. As diabetes mellitus carries a high risk of cardiovascular-related mortality, the impact of sleep deprivation on glucose regulation suggests a mechanism whereby short sleep time might increase mortality.
Aim
Aim of our study was to determine the association of wake-up timings with fasting plasma glucose levels in rural Indians.
Materials and Methods
512 diabetic patients between age group 25 years to 75 years who visited our hospital in rural India from September 11, 2020 to June 15, 2021 were studied. Sleep timings and wake up timings were noted. Fasting plasma glucose levels were obtained by venepuncture after an overnight fast of at least 8 hours and blood glucose estimation done by the hexokinase method. One way ANOVA and post hoc Tuckey test were used for analysis.
Results
We found that fasting plasma glucose was significantly higher in patients who wake up after 0700 hours compared with patients who wake up early before 0600 hours. This difference was statistically significant with *P* value of less than 0.001. Furthermore, fasting plasma glucose values were significantly less (better) in the patients who wake up before 0500 hours.
Conclusions
Our study supports that waking up early (before 0600 hours) in the morning can lead to better fasting glucose levels compared to those who wake up after 0700 hours. One possible explanation for these associations is circadian disruption, which occurs when different endogenous circadian rhythms are not synchronized with one another and/or with the external world. Circadian disruption could occur when the timing of volitional behaviours, including sleeping and eating, are not aligned with the endogenous circadian rhythms of associated physiological processes, such as sleep propensity, insulin sensitivity, or glucose metabolism. Waking up early provides more time to do physical activity and also for recreational purpose which leads to better fasting blood glucose levels. Further research is necessary to determine whether sleep and wake up timings do in fact lead to alterations in glucose metabolism.

DOI: 10.1530/endoabs.81.EP426

EP427

The role of deferoxamine (DFO) in insulin resistance and diabetes

So-Yeon Ahn[1], Min Woo Song[2], Jae Yeop Jeong[2], Tae Ho Kim[3], Sung-E Choi[4], Yup Kang[4], Hae Jin Kim[2], Ja Young Jeon[2], Seung JIN Han[2], Nami Lee[2] & Kwan-Woo Lee[2]
[1]Busan Bumin Hospital, Division of Endocrinology and Metabolism, Department of Internal Medicine, Busan, Rep. of South Korea; [2]Ajou University School of Medicine, Department of Endocrinology and Metabolism, Suwon, Rep. of South Korea; [3]Seoul Medical Center, Division of Endocrinology and Metabolism, Department of Internal Medicine, Seoul, Rep. of South Korea; [4]Ajou University School of Medicine, Department of Physiology, Suwon, Rep. of South Korea

Iron also plays an important role in many physiological processes, including redox balance, inflammation, and metabolism. It is reported perturbation of iron (Fe) homeostasis has also been associated with metabolic diseases. Iron reduction, with iron chelator, has preventive effects in cardiovascular remodeling and obesity. On the other hand, deferoxamine (DFO) increases hypoxia and collagen production in the kidney. Thus, the effects of DFO on metabolic disease remains controversial. As a result, we investigated the effects of DFO on obesity, inflammation, insulin resistance, and diabetes in db/db mice models with type 2 diabetes. An in vivo study was performed on 7-week-old db/db mice. Mice were treated with DFO (100 mg/ kg) or placebo every other day for 16 weeks. After treatment, an intraperitoneal glucose tolerance test and immunohistological examinations were performed. Fasting insulin and serum lipid levels were measured at the end of the study. Also, genes involved in inflammation and lipid metabolism were analyzed by real-time PCR. The DFO treated mice showed improved obesity, insulin resistance, and decreased levels of plasma inflammatory cytokines, total cholesterol, free fatty acid, and triglycerides. Fasting glucose in mice was also reduced by DFO treatment. Immunoblot analysis shows transferrin receptor 1 (TfR1) levels were increased in skeletal muscles of db/db mice models with type 2 diabetes. But DFO treatment decreased transferrin receptor 1 (TfR1) levels in skeletal muscles. DFO treatment also attenuated inflammatory cytokines and lipid deposition in the liver. Therefore, we consider the fine tuning of iron levels through DFO treatment as highly suggestive for preventing and/or treating insulin resistance and diabetes.

DOI: 10.1530/endoabs.81.EP427

EP428

Assessment of hypoglycemic properties of extracts from some medicinal plants in the experimental diabetes model

Talat Saatov[1], Elvira Ibragimova[1], Sanobar Irgasheva[1], Mokhammad Mustafakulov[1], Malika Salakhutdinova[2], Tokhir Ishankhodjaev[1], Nigora Samarkhodjaeva[1] & Bakhodyr Zainutdinov[1]
[1]Institute of Biophysics and Biochemistry under Mirzo Ulugbek National University of Uzbekistan, Metabolomics, Tashkent, Uzbekistan; [2]A.S. Sadykov Institute of Bioorganic Chemistry, Uzbekistan Academy of Sciences, Tashkent, Uzbekistan

Phytotherapy is the integral part of the combined treatment for diabetes mellitus. A large number of plants possessing hypoglycemic activity are described in the literature, but only small part of them is in use. Hypoglycemic effect of medicinal plants is preconditioned by the wide spectrum of compounds with biological activity in their composition. Flowers of carthamus (*Carthamus tinctorius*) and leaves of celery (*Apium graveolens*) are known to possess a number of therapeutic effects. In combination, bioactive compounds are known to amplify each other's effects. In this connection, we have studied hypoglycemic activity of aqueous extracts of carthamus flowers and celery leaves, as well as the mixture of their extracts in rats with alloxan diabetes. The extracts were administered intragastrically for 2 weeks. The experimental animals were divided into 5 groups. Intact animals were included into the 1st group, the 2nd groups consisted of animals with alloxan diabetes (alloxan controls), the 3rd one included those administered with carthamus flowers, the 4th group consisted of those administered with celery leaves; animals with alloxan diabetes administered with the mixture of carthamus flowers and celery leaves (1:1) were included into the 5th one. Our findings demonstrated the reduction in the blood glucose of all animals with experimental diabetes after a course administration of the extracts, as compared to the alloxan controls. Thus, blood glucose in rats with alloxan diabetes for 2 weeks administered with the mixture of carthamus flowers and celery leaves was found to reduce from 18.4 mmol/l to 5.7 mmol/l and 8.5 mmol/l. respectively, while in rats with alloxan diabetes it declined due to regeneration of β-cells to 13.5 mmol/l. Following the course administration of the extracts, the blood glucose in animals similarly reduced reaching the normal parameters. Hypoglycemic effect of the extracts under study increased in this order: celery extract, carthamus-celery mixture and carthamus extract.

DOI: 10.1530/endoabs.81.EP428

EP429

Patient with pancreatic diabetes and insulin pump

Dimitra Pappa, Eleftheria Barmpa, Maistros Linaras, Panagiotis Tsakos, Nikolaos Zikos & Alexandra Bargiota
University Hospital of Larissa, Department of Endocrinology and Metabolic Diseases, Larissa, Greece

Introduction
Pancreatic diabetes is a special category of diabetes due to diseases of the exocrine pancreas, characterized by both insulin and glucagon deficiency and clinically could be very challenging to control. We present a case of a woman with pancreatic diabetes treated with sensor augmented pump therapy after undergoing total pancreatectomy for a nonfunctional pancreatic neuroendocrine tumor (NET).
Presentation
A sixty-one years old woman underwent two years ago total pancreatectomy for a non-functioning neuroendocrine tumor. Consequently she developed pancreatic diabetes and was treated with a basal - bolus insulin regime. Her diabetes was poorly controlled despite all efforts due to severe, frequent and sudden hypoglycaemic attacks, affecting her quality of life. Her HbA1c was 8.5% and

her Time in Range (TIR) was 28%, Time above range (TAR) 56%, Time below range (TBR) 16%, Glucose management Indicator (GMI) 8.5%, Glucose Variability (GV) 34.1% and Average Glucose (AG) 233 mg/dl. To achieve a better management of her diabetes, a sensor augmented pump (SAP) therapy was initiated and she was greatly improved (TIR 60%, TAR 40%, TBR 0%, GMI 7.5%, GV 30.6% and AG 173 mg/dl) and hypoglycemia was not a problem any more. Conclusion:Treating patients with pancreatic diabetes could be very challenging. Sensor augmented pump therapy can greatly improve their glycemic control, but most of all their quality of life.

DOI: 10.1530/endoabs.81.EP429

EP430

Low serum epidermal growth factor level is associated with lack of diabetic control in type 2 diabetes mellitus in diabetic patients in Jordan

Ahmed Al-Dwairi & Mahmoud Alfaqih
Jordan University of Science and Technology, Faculty of Medicine, Irbid, Jordan

Background
The worldwide type 2 diabetes mellitus (T2DM) prevalence is increasing dramatically. Inflammation is involved in the pathogenesis of T2DM and development of insulin resistance. Lack of diabetic control is associated with alteration in the endocrine milieu and various health sequalae's. The aim of this research was to assess if uncontrolled T2DM is associated with increased serum levels of inflammatory cytokines and growth factors when compared with controlled T2DM in diabetic patients in Jordan.
Methods
A single institution, cross sectional study design was used in this research. One hundred and ten patients with controlled DM (HbA< ce:inf>1c<ce:inf> < 7.0%), and 105 age-, gender- and body mass index–matched patient with uncontrolled (HbA< ce:inf>1c<ce:inf> ≥7.0%) DM were recruited from the internal medicine clinic in King Abdullah University Hospital in Jordan. An antibody membrane array was used to evaluate the difference in serum levels of inflammatory cytokines, followed by enzyme-linked immunosorbent assay to confirm the results.
Results
fasting blood glucose, serum insulin, triglyceride and HOMA-IR were significantly higher in the uncontrolled T2DM group ($P < 0.01$). Antibody membrane array showed that epidermal growth factor (EGF) is lower in the uncontrolled T2DM, and this was confirmed by ELISA (158.77 + 111.7 vs 95.9 + 82.7 pg/ml, $P = 0.002$. The binary logistic model was used to predict the likelihood of being uncontrolled diabetic based on EGF levels. After controlling for age, gender, and BMI, EGF was statistically associated with diabetes control; lower EGF levels predicted uncontrolled diabetes.
Conclusion
Our data identify a novel link between serum EGF levels and the status of glycated hemoglobin indicative of diabetic control.

DOI: 10.1530/endoabs.81.EP430

EP431

Body composition and insulin resistance in type 1 Diabetes Mellitus

María Del Carmen Andreo-Lopez, María Teresa Zarco-Martín, Javier García-Sánchez , Victoria Contreras-Bolívar, Pablo López-Ibarra-Lozano & María Luisa Fernández-Soto
Granada, Clinical Nutrition Unit. Endocrinology and Clinical Nutrition Service. San Cecilio University Hospital, Granada, Spain

Introduction
DM 1 is proposed as a condition of accelerated muscle aging and mitochondrial dysfunction as a common link regulating muscle deterioration in aging and DM 1. Loss of muscle mass is associated with insulin resistance, metabolic syndrome and cardiovascular complications.
Objectives
To analyze body composition and metabolic variables related to insulin resistance in overweight/obese patients with DM1.
Material and Methods
Observational, cross-sectional study in patients with DM1 followed up in the Diabetes Clinic of the Hospital Universitario San Cecilio, Granada. Weight (kg) and height (m) were determined and BMI (kg/m^2) was calculated. The recruited individuals were classified according to BMI > or < 25. Demographic variables (age in years), metabolic variables (years of disease, insulin sensitivity factor - FSI- and glycosylated hemoglobin determined by analysis (HbA1c)) and body composition (measurement with AKERN® bioimpendanciometry of fat-free mass (FFM) in%, skeletal muscle mass (SMM) in kg. Calculation of skeletal muscle mass index (SMMI) in kg/m^2).
Results
Forty persons with DM1 were included. 48% had BMI > 25, mean age 43 ± 15 years and suboptimal glycemic control in both groups (BMI < 25: 7.3 ± 1.2 vs BMI > 25: 7.8 ± 1.1, $P = 0.21$).

	IMC < 25	IMC ≥ 25	P
Edad (años)	34.9 ± 14.8	43.2 ± 15.1	0.085
Años DM1	17.4 ± 14.7	27.1 ± 12.7	0.032
FSI	51 ± 23.4	38.4 ± 13	0.042
MLG (%)	76.3 ± 6.1	64.2 ± 9.5	0.00
SMM (kg)	23.1 ± 6.2	24 ± 5.9	0.65
SMI (kg/m^2)	6.5 ± 9	7.44 ± 0.9	0.002

Conclusions
In persons with DM 1 and overweight or obesity, parameters related to less muscle mass and higher insulin requirements are detected, a context associated with insulin resistance. It could be important to establish strategies aimed at maintaining a healthy weight (muscular strength and resistance exercise tables together with a Mediterranean pattern diet avoiding excess calories and optimizing the insulin therapy dose) to reinforce muscular behavior and increase insulin sensitivity, especially in diabetics with more years of evolution with the aim of avoiding metabolic deterioration.

DOI: 10.1530/endoabs.81.EP431

EP432

Metabolic impact of flash glucose monitoring system in patients with type 1 diabetes mellitus

Jose Antonio Ariza Jimenez, Eyvee Arturo Cuellar Lloclla, Virginia Hernando Jiménez & Jose Alvaro Romero Porcel
Virgen de Valme University Hospital, Endocrinology and Nutrition, Seville, Spain

Introduction
Adequate glycemic control is essential in the diabetes prognosis. It has been described that the use of glucose monitor systems leads to an improvement in different metabolic parameters as well as facilitating decision making.
Material and methods
Retrospective observational study to evaluate the metabolic impact of flash sensor implantation in a cohort of patients with DM1 of Virgen de Valme University Hospital of Seville. All patients with implantation of the glucose monitoring system in the period 1/1/2020 to 3/31/2020 were included. Subsequently, different metabolic parameters were compared at baseline and at 3, 6 and 12 months after implantation. SPSS program was used for statistical analysis.
Results
154 patients (46.7% men and 53.3% women) have been analyzed. Mean age 40.3 ± 1.02 years. MDI treatment 87.3% vs CSII 12.7%. Previous HbA1c mean to the sensor was 8.03 ± 1.35%, with a sustained reduction observed at 12 months (8.03 ± 1.35% vs 7.68 ± 1.01%; $P = 0.036$). Number of capillary controls before sensor was 3.57 ± 0.23, with an increase in sensor scans at 12 months (3.57 ± 0.23 vs 10.62 ± 0.69; $P = 0.000$). Coefficient of variation before sensor was 47.15 ± 2.08%, with a decrease observed at 12 months (47.15 ± 2.08 vs 37.66 ± 0.63%; $P = 0.000$). Hypoglycemia percentage before sensor was 13.83 ± 1.26%, with a decrease observed at 12 months (13.83 ± 1.26% vs 5.36 ± 0.49%; $P = 0.000$). Percentage of time in range before sensor was 48.8 ± 2.38, with an increase observed at 12 months (48.8 ± 1.26 vs 59.58 ± 1.48; $P = 0.001$). Percentage of hyperglycemia before sensor was 38.08 ± 2.54, with a decrease observed at 12 months (38.08 ± 2.54 vs 35.06 ± 1.6; $P = 0.043$).
Conclusions
- The implantation of the sensor has shown, as in the literature, improvement in metabolic control in terms of HbA1c, number of controls, coefficient of variation, hypo/hyperglycemia time and time in range.
- Some parameters showed initial improvement but attenuated over time.

DOI: 10.1530/endoabs.81.EP432

EP433

Why do diabetic patients fail to break the fast in hypoglycemia? About 58 cases

Nezha Raki, Nassim Essabah Haraj, Siham El Aziz & Asma Chadli
UHC Ibn Rochd, Endocrinology and Metabolic Disorders, Casablanca, Morocco

Introduction
Ramadan fasting is associated with an increased risk of hypoglycemia in diabetics.
Purpose of the study
To assess the prevalence of diabetic patients who are unable to break the fast in the event of hypoglycemia.
Method
Descriptive prospective study, including diabetic patients followed in the Endocrinology department of the CHU Ibn Rochd in Casablanca from April to June 2021.
Results
Our study included 58 type 2 diabetic patients, all authorized to fast according to the DAR 2021 risk score. The average age was 57.4 years. Most patients were on sulfonylureas (SH) (51.7%). All our patients received pre-Ramadan education on the need to break the fast in the face of any hypoglycemia. Among the patients observing the fast, 24% presented hypoglycaemia, of which 28% did not break the fast. Hypoglycaemia occurred more frequently in patients on combination insulin and oral agents (OADs) (57%) compared to OADs alone (28%). This reluctance was explained by the occurrence of mild hypoglycaemia close to the time of breaking the fast in 57% of patients.
Conclusion
Despite the pre-Ramadan education of diabetics on the need to break the fast in the face of hypoglycemia, there is a worrying prevalence of patients who are unable to break it.

DOI: 10.1530/endoabs.81.EP433

EP434

Management of diabetic patients during the Ramadan fast: application of international recommendations in clinical practice About 91 cases

Nezha Raki, Nassim Essabah Haraj, Siham El Aziz & Asma Chadli
UHC Ibn Rochd, Endocrinology and Metabolic Disorders, Casablanca, Morocco

Introduction
Fasting during the month of Ramadan is a religious rite. Fasting is not without risks in diabetic patients. Several recommendations and consensus of experts have recently made it possible to establish proposals to optimize the management of diabetes during Ramadan, and to specify the authorized population for this sacred practice.
Purpose of the study
To assess the prevalence of type 2 diabetics authorized to fast according to the DAR 2021 recommendations and to compare it with that of the old IDF 2016 classification.
Method
Descriptive prospective study, including diabetics type 2 wishing to fast, followed in the endocrinology and metabolic diseases department of the CHU Ibn Rochd in Casablanca from April to June 2021.
Results
Our study included 91 type 2 diabetic patients with an average age of 58.7 years. The average duration of diabetes was 9.5 years. The average HbA1c was 8.1%, 42% of our patients were on insulin, 43% were on sulfonylureas (SH). In order to compare the recommendations, we classified our patients into 3 groups: group 1: Authorized to fast by the 2 classifications (25.3%), group 2: Not authorized according to the 2 classifications (35.2%) and group 3: 39.5% authorized fasting only by DAR. Among the group 3, 27.7% were on insulin therapy, 33.4% on SH. Acute complications, mainly hypoglycaemia, were observed in 44.5% of these patients.
Conclusion
The latest DAR 2021 recommendations allow a very large diabetic population to fast in Ramadan compared to the old classification. Waiting for more cautious recommendations, the fasting decision must be adapted to each patient, even when the risk score is reassuring.

DOI: 10.1530/endoabs.81.EP434

EP435

Dietary survey in diabetic patients during Ramadan

Sara Ragbi, Nassim Essabah Haraj, Siham El Aziz & Asma Chadli
Uhc Ibn Rochd, Endocrinology and Metabolic Disorders, Casablanca, Morocco

Introduction
Ramadan is considered a sacred period during which Muslims practice fasting from sunset until dawn changing the rhythm of life and eating habits. The objective of this study is to evaluate diabetics diet during and after the holy month.
Patients and methods
Descriptive cross-sectional study, including diabetic patients, seen during the month of Ramadan, conducted at the Department of Diabetology and Endocrinology of the CHU Ibn Rochd of Casablanca. Data collection was done by interrogation, followed by an assessment of dietary intake by a 24-hour dietary survey conducted during and after Ramadan.
Results
A total of 74 patients were included, of which 51.35% were female. The mean age was 55.9 years. All patients were type 2 diabetics with a mean duration of 13.7 years and a mean HbA1c of 9.7%. Insulin-treated patients represented 81.08%. Only 24.3% of our patients have fasted. During Ramadan, the total daily caloric intake was lower in the fasting group than in the non fasting group (1658.70 kcal/d versus 1860.41 kcal/d). Among the fasting group, carbohydrate consumption was higher than among the non-fasting group during Ramadan with respectively 52.35% versus 46.59% but fat consumption was higher among the non-fasting group. Fiber and water consumption was lower during Ramadan. The diet of the fasting group during Ramadan was inadequate while that of non-fasters was excessive in lipids, putting them at risk of complications.
Conclusion
The change in lifestyle during the month of Ramadan influences the dietary practices of diabetic patients which can lead to an inadequate diet hence the interest of a nutritional education program before Ramadan.

DOI: 10.1530/endoabs.81.EP435

EP436

Insulinoma with Poland Syndrome

Suhail Ahmed[1], Saba Qureshi[2], Shahzeel Raza Qureshi[2], Joshua Ajay[1], Shahid Ahmed Khan[1], George Botoros[3], Satis Kumar[1] & Umesh Kumar Dashora[1]
[1]Conquest Hospital, Endocrinology, Hastings, United Kingdom; [2]Mercy Hospital, General Internal Medicine, Hastings, United Kingdom; [3]Eastbourne District General Hospital, General Internal Medicine, United Kingdom

23-year-old scaffolder, fit and well, presented several times to A&E with episodes of fitting which comprised of an energy surge followed by typical neuroglycopenic and autonomic signs of hypoglycaemia. He was only found to be hypoglycaemic after a severe episode where paramedics were called to his home and discovered his blood sugars to be 1.8 mmol/l with a serum insulin was measurable. His symptoms were moderately relieved by eating a combination of sugary food like honey and a starchy carbohydrate. Insulinomas are the most common cause of hypoglycaemia as a result of hyperinsulinism, though only occurring in 1-4 persons per million[1] They commonly present with autonomic symptoms such as sweating, tremor and palpitations and neuroglycopenic symptoms which include disorientation, behavioural and personality changes, visual disturbances, seizure, and coma. He had multiple presentation to emergency department with shoulder dislocation, Computed Tomography (CT) imaging demonstrated absence of the right pectoralis muscle indicative of Poland syndrome. Poland Syndrome (PS), occurring only in 1 in 20000 new-borns, typically presents with missing or underdeveloped muscles on one side of the body, resulting in abnormalities that can affect the chest, breast, shoulder, arm, and hand. The extent and severity of the abnormalities vary among affected

Test	Results	Units	Reference Range
Plasma glucose (fasting)	1.8	mmol/l	4.1 – 6.1
Serum C-Peptide	612	Pmol/l	298 - 2350
Serum Insulin	4.9	mIU/l	4.4 – 26.0

Assay provided by King's Hospital.

individuals[2] Currently the aetiology of PS is unknown though likely to be genetic. Various syndromic and metabolic potential causes of hyperinsulinism hypoglycaemia have been found, one of which may be due to a sporadic mutation in the UCMA gene, causing 10p13-14 duplication in Poland Syndrome. [3,4] . This case is the first reported case of insulinoma as the cause of hyperinsulinism along with Poland syndrome both of which are rare and unique clinical presentations in themselves. Hyperinsulinism/Insulinomas can present with normal bloods and ECG once symptoms have passed. There is an association between Poland Syndrome and Hyperinsulinism, this link can help in earlier diagnosis/ruling out of one another.

DOI: 10.1530/endoabs.81.EP436

EP437

Post COVID-19 complication in patient with diabetes insipidus: what we know nowadays?

Iryna Kostitska[1], Nadiia Zherdova[2], Antonina Piddubna[3], Oksana Zhurakivska[4] & Olga Zhurakivska[4]
[1]Ivano-Frankivsk National Medical University, Endocrinology, Ivano-Frankivsk, Ukraine; [2]Centre of Innovative Medical Technologies, Kyiv, Ukraine; [3]Bukovinian State Medical University, Chernivtsi, Ukraine; [4]Ivano-Frankivsk National Medical University, Ivano-Frankivs'k, Ukraine

A major cause of morbidity is post COVID-19 complications. The symptoms of carbohydrate dysfunction can be due to has relationship with coronavirus disease. In patients with chronic disorders after SARS-CoV-2 infection, aggravation of pre-existing symptoms has also been noticed. Diabetes insipidus (DI) may be at risk of dysnatraemia when developing respiratory complications of COVID-19. Particularly, the combination of two or more concurrent disorder is a major problem in patient treatment. Especially when one of the diseases is a predictor of another. This not only complicates the diagnosis but also prolongs the duration of treatment, sometimes complicating an algorithm of management and reduces its effectiveness. Thus considering the above mentioned facts, we would like to focus your attention on such comorbidities as post COVID-19 complication: diabetes melletus (DM) in patient with DI, and give a sense of this problem on the basis of clinical case study. A 69-year-old female with a past medical history of DI diagnosed five years ago treated with nasal spray desmopressin (10 µg intranasal twice daily) after COVID-19 pneumonia who later manifested DM. She was diagnosed with COVID-19 infection with nasopharyngeal reverse transcriptase polymerase reaction (RT-PCR) at an outpatient clinic 60 days ago. IgG against SARS-CoV-2 was positive. After two month for the treatment of COVID-19 pneumonia the patient complaining of polydipsia, polyuria and nocturia during the previous month. Laboratory examinations showed abnormally increased blood sodium (serum sodium -156 mmol/l) and chloride (serum chloride – 115 mmol/l) and decreased urine osmolality and specific gravity of 1.006. Thyroid function tests were normal. The level of glycosylated hemoglobin (HbA< ce:inf>1</ce:inf>C) was 7.0%, blood sugar levels ranged from 7.6 to 19.0 mmol/l. After additional examination the patient with DI was diagnosed with DM. The patient was prescribed treatment with metformin at a daily dose of 1500 mg during the meal to correct carbohydrate metabolism and added doses of desmopressin (20 µg intranasal twice daily). After 3 months, the therapy resulted in patient's improvement of the general conditions and compensation of DM was achieved: no episodes of hypoglycemia were recorded; the HbA1C level was 6.4%; glycemia levels ranged from 5.4 to 8.0 mmol/l; and normalization of electrolytic metabolism.

Conclusions

Further studies are needed to clarify the link between COVID-19 and DM in patient with DI, to provide the optimal management.

DOI: 10.1530/endoabs.81.EP437

EP438

Protective effect of a marine plant on hepatic toxicity induced by a hyperlipidemic diet

Rihab Ben Abdallah Kolsi[1], Kolsi Boulbaba[2] & Noureddine Allouche[1]
[1]Faculty of Sciences, Sfax, Tunisia; [2]CHU Hedi Chaker, Sfax, Tunisia

Introduction

In recent decades, metabolic diseases have continued to increase. Several investigations concerning the origin of these diseases such as dyslipidemia, hypercholesterolemia, diabetes, etc., have been elucidated. These pathologies have been attributed to lifestyles and mainly to diet. Obesity is a serious metabolic and energy disorder, which has become a real major public health problem.

Materials and methods

We were interested in studying the effect of a high-fat diet on liver function, as well as the effect of the extract on rats receiving a hyperlipidemic diet. The variations in liver toxicity parameters in the different groups were highlighted by the study of biochemical parameters and confirmed by the study of liver histology.

Results

Under our experimental conditions, the obese had a significant elevation of serum levels of AST, ALT, LDH and CPK of 32%, 31%, 43% and 22%, respectively. While, administration of the extract to the obese improved all indices of liver toxicity. Histological sections of the livers of rats subjected to a hyperlipidemic diet for 42 days showed the appearance of lipid droplets which correspond to a deposit of fat in the hepatocytes. Whereas, CNSP and orlistat exerted a protective effect against the development of non-alcoholic hepatic steatosis in HFD-rats, objectified by a notable decrease in lipid vacuolations.

Conclusion

Finally, we noted that the result of these positive effects of the CNSP studied on hepatic toxicity was translated by restoring effects of the histological organizations of the liver, making them comparable with those of normal controls. This confirms the important role of this natural product in the fight against oxidative stress and the prevention of hyperlipidemia.

DOI: 10.1530/endoabs.81.EP438

EP439

Time restricted feeding 16/8 improves metabolic parameters and fatty liver in obese mice

Camila Astudillo[1], Paula Acevedo[1], Karina Ceballo[1], Marcela Julio[2], Mauricio Dorfman[3] & Gonzalo Cruz[1]
[1]Centro de Neurobiología y Fisiopatología Integrativa (CENFI), Instituto de Fisiología, Facultad de Ciencias, Universidad de Valparaíso, Valparaíso, Chile; [2]Grupo de NeuroGastroBioquímica, Instituto de Química, Facultad de Ciencias, Pontificia Universidad Católica de Valparaíso, Valparaíso, Chile; [3]Division of Metabolism, Endocrinology & Nutrition, Department of Medicine, University of Washington, Seattle, United States

Obesity is a major health problem that is crucial in the pathogenesis of diabetes mellitus, cardiovascular diseases, and some types of cancer. Intermittent fasting is an eating pattern in which periods of fasting, lasting from 12 up to 36h, are alternated with periods of eating. Time restricted feeding (TRF) 16/8 is a type of intermittent fasting that is being used to lose weight and for treating metabolic disorders. Several studies in humans have shown a slight effect of TRF on body weight but more consistent effects on metabolic parameters. However, the molecular mechanisms by which these effects occur are poorly understood. We aimed to investigate if TRF 16/8 in mice reproduced the metabolic effects observed in human and tested if TRF 16/8 reduces inflammation in obese mice. We used C57BL/6J mice under a high fat diet for 12 weeks (60%KCal in fat) to develop obesity associated with glucose intolerance and fatty liver. Then we exposed the animals to TRF 16/8 (feeding in active phase) for 6 weeks. We found that TRF decreases body weight without changes in epididymal or subcutaneous fat, it reduces fasting glycemia, improves glucose tolerance, decreases liver weight, and decreases gut epithelial permeability. In addition, TRF increases blood ketone bodies, in particular l-hydroxybutyrate (BHB). These results show that 6 weeks of TRF are enough to produce metabolic improvements in obese mice. Since obesity is characterized by a low-grade inflammatory state and BHB may have anti-inflammatory effects, we propose that BHB induced by TRF has anti-inflammatory effects in the brain and periphery that explain why TRF improves metabolic parameters in obese mice.

DOI: 10.1530/endoabs.81.EP439

EP440

Metabolic syndrome in mediterranean patients with mental illness

Salem Jdira[1], AbdelMouhaymen Missaoui[2], Oumeyma Trimeche[2], Houda Hsine[1], Wafa Abbes[1] & Ines Khochtali[2]
[1]Gabes Regional Hospital, Departement of psychiatry, Gabes, Tunisia; [2]Fattouma Bourguiba University Hospital, Endocrinology Departement, Monastir, Tunisia

Introduction

Metabolic Syndrome (MetS) represents a cluster of vascular risk factors related to insulin resistance such as abdominal obesity, hypertension, and glucose and lipid dysregulations. Multiple studies suggest an increasing metabolic risk in psychiatric patients.

Objectives
We aim to assess epidemiological and clinical features of MetS in a Mediterranean psychiatric population.
Methods
We conducted a descriptive cross-sectional study involving 126 patients attending the psychiatry department at Gabes regional hospital, Tunisia, from 2019 to 2020. MetS was diagnosed based on the 2005-IDF criteria.
Results
The mean age was 45.5 ± 12.8 years with a sex-ratio(M/F) of 1.07. The majority were married (49.2%), from urban areas(53.2%), low educational bac kgrounds (59.5%), and low-socioeconomic status households (64.3%). The rate of unemployment was 54%. Addictive behaviors were reported in 35.7% mainly tobacco (31.7%) and alcohol (3.2%). The leading mental diseases were schizophrenia and psychotic disorders (43.7%), depressive disorder (18.3%), bipolar disorder (16.7), and anxiety disorder (16.7%). Obesity was the most common metabolic comorbidity in 37.3% of patients. Dyslipidemia, diabetes, and hypertension were recorded in 17.5%, 12.7%, and 8.7%, respectively. The prevalence of MetS was 25.4%.
Conclusions
The bidirectional interplay between MetS and psychiatric disorders is due to behavioral aspects (sedentary lifestyle, smoking, unhealthy diet), somatic disturbances (chronic inflammation, hypothalamic-pituitary-adrenal axis dysregulation, and insulin resistance), in conjunction with an established metabolic-dysregulating effect of some antipsychotics. A possible shared genetic bac kground between these conditions has also been debated. Psychiatrists should screen their patients for comorbid MetS before and during treatment. Preventive and curative measures should be organized cooperatively with a multidisciplinary team (endocrinologists, diabetologists, and cardiologists) to reduce this serious cardiometabolic burden.

DOI: 10.1530/endoabs.81.EP440

EP441

Low hdl cholestero and cardiovascular risk in type 2 diabetes

Ines Bani, Zohra Hadj Ali, Meriam Dalhoum, Yosra Htira & Feika Ben Mami
National Institute of Nutrition of Tunis, Department C, Tunis, Tunisia

Introduction
Low high-density lipoprotein (HDL) is a frequent metabolic abnormality, associated with diabetes, may increase the cardiovascular risk of patients with type 2 diabetes. We aimed in this study, determine the prevelence of hypo HDL cholesterol and assess the associated cardiovascular risk.
Method
It is a retrospective study, including 184 type 2 diabetic patients, conducted in the department C of the National Institute of Nutrition of Tunis during the year 2021. HypoHDl cholesterol was considred if the patients had HDLc (<40mg/dl (men); < 50mg/dl (women)).
Results
The study included 184 patients (118 women, and 66 men), with mean of age 61 +/- 10 years. The prevalence of low HDL cholesterol was 44.6%. Patients with low HDl cholesterol had a slight female predominance (52.5%). Hypertension was present in 70% of patients. Patients were obese and overweight in 56% and 31% of cases, respectively with an average body mass index of 30.63 +/- 5. In addition, they had hepatic steatosis in 28% of cases. the majority of patients had a Glycated hemoglobin out of target (92.5%), with an average HB1AC 10.5 +/- 2%. Moreover a hyper LDL cholesterolemia and hypertriglyceridemia were noted in 39 and 63.4% respectively. coronary artery disease was present in 32.9% of patients.
Conclusion
Low HDlc is a common situation in type 2 diabetes and increases the cardiovascular risk in these patients.

DOI: 10.1530/endoabs.81.EP441

EP442

Regulation of glycemic variability in endothelial model: cross-talk between miRNAs and microfilaments in the activation of early fibrotic pathways

Lucia La Sala[1], Pamela Senesi[2], Daniele Capoitanio[2], Elena Tagliabue[1], Anna Ferrulli[2], Ileana Terruzzi[2] & Livio Luzi[1,2]
[1]Multimedica, Lab of Cardiovascular and Dysmetabolic Diseases, Milano, Italy; [2]University of Milan, Milano, Italy

Glycemic variability (GV), a complex phenomenon affecting subjects with diabetes, is one of the main contributors to the risk to develop both acute and long-term complications in type 1 (T1D) and type 2 (T2D) subjects. DNA double-strand breaks, apoptosis, overgeneration of reactive oxygen species (ROS) and the induction of some regulatory micro-RNAs, sustain the ominous mechanisms mainly attributable to GV. The characteristic cellular phenotype induced by GV is scarcely defined. Aims of this study are: 1) to describe a global pattern about the regulation of the major proteins differentially expressed in a cellular (human endothelial cells) model of GV and 2) the role of microRNAs on the pathways activated during the *in-vitro* long-term exposures to GV. We utilized human endothelial cells exposed for 21 days to high and oscillating glucose concentration (25 mM and 5-25 mM, respectively). The omic-based analysis integrating proteomic (2D-DIGE and MALDI/TOF) and miRNA discovery, identified a dataset of proteins and micro-RNAs differentially regulated by the oscillating and high glucose conditions. In particular, microarray of immunoprecipitated target bound to miR-146a-5p identified the main mRNA transcripts in this model. We found a protein identified both in proteomic and microarray experiments, vimentin, which is the principal protein involved in the activation of fibrotic pathways. Immunofluorescence analysis showed that the increased expression of vimentin is due to silencing of miR-146a-5p. Our set of data constitutes the "Proof of Principle" about the ability of the omic-approaches (proteomic analyses coupled with miRNome) to reveal potential biomarkers for the GV model. Future perspective is to draw the GV cellular signature along with associated functions and mechanisms.

DOI: 10.1530/endoabs.81.EP442

EP443

Mediterranean diet rich in olive oil and vascular diabetes complications

Ramla Mizouri[1], El Amri Abir[1], Rihab Yamoun[2], Faten Mahjoub[2], Sirine Nsir[3], Amany Amorri[3], Rym Ben Othman[1], Olfa Berriche[1], Nadia Ben Amor[1] & Jamoussi Henda[1]
[1]National Institute of Nutrition, A, Tunis, Tunisia; [2]Faculty of Medicine of Tunis, Tunisia; [3]University of Tunis El Manar, Tunisia

Introduction
Olive oil is the most representative food of the traditional Mediterranean Diet (MedDiet) that, besides having high-monounsaturated fatty acids content, contains other minor components with biological properties. Olive oil as a food, and the MedDiet as a food pattern are associated with a decreased risk of cardiovascular disease, obesity and diabetes mellitus. The aim of this study was to determine the relationship between adherence to the Mediterranean Diet and vascular complications among diabetic patients.
Methods
It was a prospective cross-sectional study conducted over a three-month period including patients aged 18 years and older with a confirmed diagnosis of type 1 and type 2 diabetes. We completed a 14-Item MedDiet adherence screener in face-to-face interview with the participant to assess dietary habits. Three categories of adherence to the MedDiet were identified (low ≤5, median 6-9, high ≥10 points of the 14-item questionnaire).
Results
The study enrolled 109 patients, 48% were males and 52% were females. The average age of the cohort was 53.7 years ± 17.8 years. 78.7% of the patients were running type 2 diabetes. Of them, 57.4% had dyslipidemia and 68% were overweight or obese. High Blood Pressure was found in 47.2% of cases. The capillary blood glucose and glycated hemoglobin were respectively around 12.41 mmol/l and 10.55%. Diabetic patients with low, median or high adherence to the MedDiet represent 11%, 64%, and 25% respectively. We found an inverse significant relationship between the adherence to MedDiet and nephropathy ($P = 0.02$, $r = -0.15$), chronic peripheral artery occlusive disease ($P = 0.034$, $r = -0.21$), coronary artery disease ($P = 0.046$, $r = -0.2$) and body mass index ($P = 0.049$, $r = -0,15$). However, there wasn't association with retinopathy ($P = 0.9$) or diabetic peripheral neuropathy ($P = 0.32$).
Conclusions
The beneficial effects of increased adherence to a Mediterranean-type diet on the prevention of type 2 diabetes complications are now well known and may in part be mediated by weight modulation. Our study concluded that MedDiet reduces the incidence of diabetic nephropathy, chronic peripheral artery occlusive disease and coronary artery disease but it had no beneficial effect on the incidence of diabetic retinopathy or peripheral neuropathy.

DOI: 10.1530/endoabs.81.EP443

EP444

Prevalence and Risk Factors for Diabetic Lower Limb Amputation

El Amri Abir[1], Rym Ben Othman[1], Rihab Yamoun[1], Ramla Mizouri[1], Amany Amorri[2], Sirine Nsir[2], Faten Mahjoub[1], Nadia Ben Amor[1], Olfa Berriche[1] & Jamoussi Henda[1]
[1]National Institute of Nutrition, Tunisia; [2]University of Tunis El Manar, Tunisia

Introduction
The progressive increase in diabetes is likely to increase the incidence of amputations. Despite a wealth of research highlighting the importance of early detection and management, prevention practices remain poor, with inconsistent patient follow-up and compliance. The aim of our study was to assess the prevalence and risk factors for lower limb amputation in a third-line hospital among diabetics.
Methods
It was a retrospective study including patients aged 18 years and older with a confirmed diagnosis of type 1 and type 2 diabetes, hospitalized in nutrition department A between 1 September and 31 December 2021. Subjects under 18 years of age and those with non-diabetic foot amputations (e.g. traumatic or neoplastic) were excluded from the study. Subjects hospitalized for conditions other than diabetes were also excluded.
Results
The study enrolled 209 patients comprising 88 males and 121 females. The average age of the cohort was 51.8 years $\pm$ 18.3 years. Lower limb amputation was twice as common in type 2 diabetics. It occurred in 4.4%, more commonly amongst men (9% versus 0.8%; $P = 0.004$). Of them, 78% had dyslipidemia, 85% were overweight or obese and 65% had high blood pressure. Risk factors most closely associated with amputation included diabetic retinopathy ($P = 0.001$), diabetic nephropathy ($P = 0.005$), diabetic peripheral neuropathy ($P = 0.002$) and chronic peripheral artery occlusive disease (PAOD) ($P = 0.01$). Although average glycosylated hemoglobin A1C (Hba1c) levels was higher amongst amputees, it was statistically insignificant.
Conclusion
Considering the correlation between amputation and other microvascular complications of diabetes, it would be justifiable to detect and manage these complications early in order to limit their aggravation and prevent the occurrence of other complications. Several factors offer potential for modification for the prevention of amputations but require further study. These include blood pressure, glycosylated hemoglobin, and smoking.

DOI: 10.1530/endoabs.81.EP444

EP445

GLIM criteria and nutritional assesment in patients with heart failure

Ana María Moyano Sánchez[1], Carlos Manuel Alzás Teomiro[1], Concepción Muñoz Jiménez[1], Mireia Isabel García Ramírez[1], José López Aguilera[2], Manuel Crespín[2], María José Molina Puerta[1], María Ángeles Gálvez Moreno[1] & Aura Herrera Martínez[1]
[1]Reina Sofía University Hospital, Endocrinology and Nutrition, Córdoba, Spain; [2]Reina Sofía University Hospital, Cardiology, Córdoba, Spain

Background
Heart failure (HF) is a chronic inflammatory syndrome, with increased morbidity, mortality, and decreased quality of life. The publication of GLIM criteria has standardized the diagnosis of malnutrition. With these criteria, the nutritional status of patients with heart failure, who usually have normal weight, overweight or obesity, has acquired a new perspective, since malnutrition may affect the clinical evolution and prognosis of these patients.
Objective
To evaluate nutritional parameters including body composition using bioimpedance, adipose and muscle ultrasound in patients with HF and to determine the incidence of malnutrition using the GLIM criteria.
Methods
Thirty-eight patients with at least one hospital admission during the previous year were included. Anthropometric, biochemical, ultrasound and functional tests were collected. Statistical analysis was performed with SSPS v.24.
Results
In our cohort 72.2% were males, 75% of the patients had overweight or obesity and 58.3% presented with malnutrition according to the GLIM criteria; among them, 41.6% with BMI>25 kg/m^2. Patients with malnutrition tended to have a higher rate of hospitalization due to HF in the previous 12 months (2.1 vs 1.7; $P = 0.420$), increased length of stay in hospital (5.25 vs 4.5 days; $P = 0.43$) and increased vitamin D defficiency (58.8% vs 41.2%). There was no relation between the presence of malnutrition, serum NT-proBNP nor ejection fraction measured by echocardiogram. Altered serum nutritional parameters were observed in 65% of patients, 21% had decreased hand dynamometry values. The mean of the Up And Go test was 20.87 seconds. Median value of adipose tissue thickness in rectus femoris (measured by ultrasound) was 0.68 cm, with a median circumference of 8.8 cm and an area of 3.5 cm^2 in the referred muscle. Patients with malnutrition presented lower longitudinal axis of the rectus femoris ($P < 0.05$). Abdominal adipose tissue ultrasound revealed a total thickness of 2.19 cm, the median values were: superficial adipose tissue 0.63 cm, deep adipose tissue 0.92 cm and preperitoneal adipose tissue 0.54 cm.
Conclusions
GLIM criteria has a key role in early detection and diagnosis of malnutrition in patients with HF. The nutritional status assesed by serum parameters, body composition and muscle evaluation techniques might be related with the clinical evolution of these patients.

DOI: 10.1530/endoabs.81.EP445

EP446

Prevalence of early postpartum glucose intolerance in Spanish women with gestational diabetes mellitus

Nerea Eguilaz Esparza, M Dolores Ollero, Yolanda Mayayo Remirez, Ana Irigaray, Ander Ernaga Lorea, Marta Toni García & Juan Pablo Martínez De Esteban[1]
García Orcoyen Hospital, Estella, Spain

Introduction
Women with gestational diabetes mellitus (GDM) have an increased risk for developing glucose intolerance in postpartum. The aim of our study was to describe the general characteristics of pregnant women with GDM and to assess the prevalence of glucose intolerance in early postpartum by postpartum oral glucose tolerance test (ppOGTT).
Methods
Retrospective study from January 2017 to December 2020 including patients with GDM followed at endocrinology department of Garcia Orcoyen Hospital in Estella (Spain). Relevant data of pregnancy and postpartum were recorded. Diagnosis of GDM was performed using the two-step strategy at 24–28th week of gestation. Early pregnancy screening was perfomed in women at increased risk of undiagnosed diabetes, defined by the American Diabetes Association (ADA). After delivery, a ppOGTT was performed, and prediabetes and type 2 diabetes were diagnosed according to the ADA criteria.
Results
A total of 84 women with GDM were included. The mean age was 33.7 $\pm$ 5.1 years (21 to 47 years), 42.2% were caucasian and family history of diabetes was found in 48.8% of them. 36.9% of women were primiparous ($n = 31$) and 23/53 women with previous pregnancies had history of GDM. Mean pregestational BMI was 28.2 kg/m^2 $\pm$ 6.2 (19 to 49). GDM was diagnosed in the 1st trimester in 20 women, in the 2nd trimester in 63 women and in the 3rd trimester in 1 woman During pregnancy, insulin therapy was required in 44% women. The average maternal weight gain was 8.2 $\pm$ 5.0 kg. 14.3% of fetus were above the 90th percentile and 4.8% newborns were macrosomes. After delivery, 58.3% of women ($n = 49$) performed the ppOGTT at 17 weeks postpartum, with the following Results: 33 women had a normal response; 14 women had prediabetes (8 had impaired fasting glycemia, 3 had impaired glucose tolerance and 3 women had a combination of both) and 2 women had type 2 diabetes criteria.
Conclusion
The proportion of women with GDM who underwent postpartum glucose testing is low due to high prevalence of loss of follow up after delivery. One-third of women who underwent ppOTTG after delivery had glucose intolerance.

DOI: 10.1530/endoabs.81.EP446

EP447

The effect of lockdown during covid 19 pandemic on HbA1c control among diabetes patients in georgia ajara

Liana Jashi[1,2], Ketevan Dundua[3], Rusudan Kvanchakhadze[3] & Tamar Peshkova[4]
[1]Clinic Solomed, Endocrinology, Batumi, Georgia; [2]David Aghmashenebeli University of Georgia, Medicine, Tbilisi, Georgia; [3]David Aghmashenebeli University of Georgia, Medicine, Tbilisi, Georgia; [4]Batumi Shota Rustaveli State University, Medicine, Batumi, Georgia

Background
The COVID-19 pandemic changed to the daily life of individuals. These included lockdown and social distancing During COVID-19 pandemic. Healthcare providers from different institutions had to adapt to the way of supporting and managing patients with different chronic conditions including diabetes. The implementation of lockdown affected diabetes care. COVID-19 pandemic enabled healthcare professionals to apply innovation including social networks/ telemedicine/telephone clinics to manage diabetes patients and other patients needing outpatient follow up.
Aim
To assess the effect of lockdown on diabetes control among diabetes patients in Georgia Ajara Single Centre experience.

Method
Retrospective cohort study identified patients who were reviewed in the diabetes clinic before and after the pandemic and the A1C levels before December 2019 and in 2021.The data was obtained clinic notes. Demographic data were obtained including type of diabetes mellitus, gender, age. Outcomes assessed were change in HbA1C (worsening or improvement), if the patients had diabetes review during the pandemic (social networks/telemedicine) and whether HbA1C blood tests were done.
Results
In total the results of HbA1C of 78 patients were identified.37 were females, 41 were males. The patients were aged between 17-to 77 years, mean age 52 years. There was improvement in HbA1c in 19 patients (24.4%) (Despite pandemic and lockdown), and there was deterioration of HbA1c in 59 (patient) 75.6% of all patients. 9 (11.7%) Patients were type 1 diabetes patients 62(79.4%) were type 2 diabetes. 7 patients (8.9%) were Late Onset Diabetes of Adults (LADA).
Discussion
In Georgia the first lockdown measure prevented spread of prevent spread of COVID-19 was introduced in March 2020.This resulted in disruption of patients care especially those with chronic condition including diabetes. The worsening of diabetes control in these patient is explained by lack of exercise, weight gain and poor diet and probably poor compliance. The patients in this study reported anxiety and stress due uncertainty of COVID-19 pandemic and probably this contributed to worsening HbA1C. HbA1C in 75.6% of patients in this study deteriorated compared to 24.4% whose diabetes control improved. COVID-19 pandemic has helped healthcare professional to be more flexible and innovative in managing patients with diabetes and other chronic conditions.

DOI: 10.1530/endoabs.81.EP447

EP448

Sudden deafness revealing type 2 diabetes: a case report

Meriam Dalhoum, Zohra Hadj Ali, Ines Bani, Yosra Htira & Faika Ben Mami
National Institute of Nutrition, Department C, Tunis, Tunisia

Introduction
Sudden idiopathic deafness is often a diagnosis of elimination. It is defined by an isolated sensorineural hearing loss (sensorineural deafness) unilateral and without obvious etiology but a vascular hypothesis is plausible. We report in this context a case of unilateral sudden hearing loss revealing type 2 diabetes (T2DM).
Observation
This is a 40-year-old man, sedentary, with no particular pathological history, a 20-pack/year smoker and occasional alcoholic, who presented with sudden deafness justifying his hospitalization in an otorhinolaryngology department. The clinical examination revealed a blood pressure of 130/80 mmHg, a body mass index of $30Kg/m^2$, and android obesity. The examination included otoscopy, tinnitus, neurological examination and audiometric examination confirming sensorineural hearing loss. The diagnosis of SBI was made in the face of a negative etiological investigation and he was treated with hyperbaric oxygen therapy. The biological workup revealed high blood glucose levels at 15.12 mmol/l, Hb1Ac at 9.3%, and hyperTriglyceridemia at 3.6 mmol/l. The diagnosis of T2DM was established and he was treated with a dual therapy (Metformin and Glimeperide) associated with hygienic-dietary rules.
Conclusion
Sudden onset deafness is a medical emergency requiring a rapid, global and adapted management of the affected patients. It is an infrequent pathology, unknown in the physiopathology is not well elucidated and which can be explained by a vascular or metabolic mechanism as we report this clinical case.

DOI: 10.1530/endoabs.81.EP448

EP449

How to position Sodium Glucose cotransporter-2 inhibitors in the management of Diabetes in acromegalic patients- Another point of view

Adnan Zaina[1], Ali Abid[2], Elena Golden[2] & Eldad Arad[2]
[1]Bar-Ilan University, Azrieli Faculty of Medicine, Division of Endocrinology and Metabolism, Zvulon Medical Center, Clalit Medical Health Care Services, Safed, Israel; [2]Clalit Health Services, Division of Endocrinology and Metabolism, Zvulon Medical Center, Israel

Context
Diabetes mellitus represents one of the most frequent metabolic comorbidities and occurs in 30% to 40% of patients with acromegaly. Patients with acromegaly develop insulin resistance due to GH excess, and in those with longstanding disease, insulin deficiency may occur. Moreover, the use of second-generation somatostatin receptor ligands (SRLs) pasireotide might contribute to the increased development in new-onset diabetes and the worsening of hyperglycemia. Management of type 2 diabetes (T2DM) has been revolutionized since the introduction of sodium-glucose cotransporter 2 inhibitors (SGLT2i) with their beneficial protective cardiovascular and renal effects in patients with and without diabetes. The current treatment recommendations for diabetes management in acromegaly are similar to the general population. However, the use of incretin-based therapy such as glucagon-like peptide-1 (GLP-1) agonists and dipeptidyl peptidase-4 (DPP-4) inhibitors are more considered as second-line treatment modalities after metformin in patients with diabetes and acromegaly while the use of SGLT2i class is a less recommended option due to increased risk of diabetic ketoacidosis (DKA) in patients with acromegaly. We present our recommendations to define the position of SGLT2i in the treatment of diabetes in patients with acromegaly.
Evidence acquisition
Our recommendations are based on our experience with the use of SGLT2i in clinical practice in this subgroup of patients and the recently available published data.
Evidence synthesis
Acromegaly disease activity should be considered one of the important criteria for the management of diabetes in this subgroup of patients when considering treatment with SGLT2i. This criterion is driven by the fact that DKA was the initial manifestation in unrecognized active acromegaly according to recently published data. Thus, we recommend considering treatment with SGLT2i according to ADA, EASD, and ESC guidelines for patients with controlled acromegaly - defined as age-sex normalized IGF-1 levels, random GH $<$ 1μg/liter, nadir GH after OGTT $<$0.4 μg/liter- that was achieved postoperatively with or without pharmacological treatment such as SSAs, GH receptor antagonist and dopamine agonists as monotherapy or in combination. For patients with active acromegaly treatment with incretin-based therapy as second-line therapy is more favorable, in such cases, the use of SGLT2i is less recommended due to increased tendency for DKA.
Conclusions
we recommend a more liberal strategy in using SGLT2i among patients with controlled acromegaly and diabetes. However, for patients with active acromegaly incretin-based therapy is more favorable.

DOI: 10.1530/endoabs.81.EP449

EP450

Case report of a patient with type 2 diabetes and severe hypomagnesemia

Martina Jambrović, Maja Mikolaj Kiric & Andreja Maric
General Hospital Čakovec, Department of Internal medicine, Čakovec, Croatia

Introduction
GLP-1 agonists and metformin are widely used antidiabetic drugs with excellent blood glucose-lowering effects, but patients very often develop side effects. The most common side effect of these two groups of drugs is gastrointestinal intolerance in the form of vomiting, diarrhoea, general weakness and dizziness.
Case Report
A 58-year-old male patient was hospitalised for the second time in one month due to a recurrence of dizziness, vomiting, ataxia and epileptic seizures. The patient had a history of type 2 diabetes mellitus treated with GLP-1 agonist dulaglutide 1.5 mg once weekly, metformin 2×1000 mg and glimepiride 2 mg. His medical history included arterial hypertension, hyperlipidaemia, coronary artery disease, OSA syndrome and nicotinism. Performed diagnostic procedures ruled out the neuroradiological cause of the problem and a metabolic cause of the problem was suspected. An electrolyte check was performed and severe hypomagnesaemia Mg $<$ 0.25 mmol/l (0.65-1.05 mmol/l) was found, the other electrolytes were normal (K 3.6 mmol/l, Na 143 mmol/l, Cl 95 mmol/l, Ca 2.38 mmol/l). Due to the weight loss, persistent diarrhoea and gastric discomfort, the patient was suspected of malabsorption due to severe hypomagnesaemia, but this was ruled out by comprehensive gastroenterological treatment (gastroscopy, colonoscopy and abdominal ultrasound revealed no cause of malabsorption, PHD result ruled out coeliac disease and anti-tTG test is ongoing). He was treated with parenteral magnesium supplementation, which resulted in clinical recovery and normalisation of blood magnesium levels. A malabsorption syndrome due to GLP-1 agonists and metformin was suspected. These drugs were excluded from therapy and intensified insulin therapy was introduced. At the next follow-up, the patient was subjectively better, taking oral magnesium supplements and insulin therapy was continued with the basal-bolus regimen for diabetes treatment.
Conclusion
GLP-1 agonists and metformin are excellent drugs in the treatment of diabetes, but it is necessary to pay attention to the rare side effects of these two groups of drugs and to change the therapy if severe side effects occur.

DOI: 10.1530/endoabs.81.EP450

EP451

Metabolic syndrome in Cushing's syndrome

Fatima Zahra El Jaafari, Charlène-Ludwine Bifoume Ndong, Sana Rafi, Ghizlane El Mghari & Nawal El Ansari
CHU Mohammed VI Marrakech, Endocrinology, Diabetes, Metabolic diseases and Nutrition, Marrakech, Morocco

Introduction
Metabolic disorders are a relevant cause of morbidity and disability in patients with Cushing's syndrome (CS) even after a successful treatment. The aim of our study was to assess the prevalence of metabolic syndrome in our CS patients, as central obesity, dyslipidemia, diabetes, and hypertension, and to discuss the main adverse effects of CS on metabolism and emphasize the importance of long-term monitoring and treatment of these complications.
Patients and Methods
It's a retrospective and descriptive review of thirty-four patients records presenting Cushing's syndrome. They were divided according to waist circumference, lipid, glucose and tension profiles, before and after treatment.
Results
45% of our patients had dysglycemia,30% had dyslipidemia, and 23% had arterial hypertension with a pathological waist circumference, a mean age of 29.3 years old, and a female predominance. A decrease of this disorders after surgery or medical treatment were also noted.
Conclusion
Glucocorticoid excess leads to increased dysglycemia, dyslipidemia, visceral adiposity, and hypertension, which together delineate the metabolic syndrome, and increase cardiovascular morbidity and mortality. Treatment modalities and rapidity of controlling hypercortisolism is of paramount importance and have varied impacts on metabolic disorders.

Keywords
Cushing's syndrome; Metabolic syndrome; Dysglycemia; Dyslipidemia; Hypertension; Obesity.

DOI: 10.1530/endoabs.81.EP451

EP452

"Characteristics of cerebral hemodynamics in patients with type 2 diabetes on program hemodialysis"

Urmanova Yulduz[1], Alisher Kholikov[2] & Mekhinbonu Khalimova[3]
[1]Tashkent Pediatric Medical Institute, Tashkent, Uzbekistan; [2]Republican Specialized Scientific Practical Medical Center of Endocrinology of Public Health Ministry named by acad. Ya.Kh. Turakulov, Department of Hemodyalisis, Tashkent, Uzbekistan; [3]Tashkent Pediatric Medical Institute, Department of Endocrinology, Tashkent, Uzbekistan

The goal is to study the changes in the parameters of cerebral hemodynamics in patients with diabetes mellitus of type 2 receiving program hemodialysis.
Material and methods of research
We have been viewed and surveyed in just a period from January 1, 2019 to June 1, 2021 g - 117 patients suffering from type 2 diabetes mellitus, with chronic kidney insufficiency V stage on program hemodialysis. Of these, women were 58, men -62. The average age of men amounted to 67 $\pm$ 4.2 years, and the average age of women is 64 $\pm$ 5.6 years. 20 patients of the relevant age amounted to a group of control. The number of hemodialysis sessions in patients varied from 2 to 162. All patients were carried out by all studies that included generally crystal biochemical, hormonal blood tests, an ultrasound of internal organs, dopplerography of the main arteries of the head, consulting narrow specialists.
Results
It was revealed that as the degree of the degree of brain ischemia decreased and the Linear blood flow rate in all the main arteries of the head were decreased: carotid artery, internal carotid artery, vertebral artery on both sides (- $P < 0.05$, $P < 0.001$). At the same time, differences in the LSK from healthy individuals were significant. The most often stenosis of the lumen of the vessels of the magician met in patients with 3 groups, while they most often observed multiple stenosis of vessels.
Conclusions
1) Doppler of the main arteries of the head is informative to determine the forecast of brain ischemia in patients with type 2 diabetes with chronic kidney disease. 2) Linear blood flow rate was reduced in all groups of patients with type 2 diabetes with chronic kidney disease.

DOI: 10.1530/endoabs.81.EP452

EP453

"The prognostic efficiency of the N-terminal fragment of the Brain natriuretic peptide in the diagnosis of chronic heart failure in patients with type 2 diabetes"

Zamira Khalimova[1] & Shakhnoza Yusupova[2]
[1]Republican Specialized Scientific Practical Medical Center of Endocrinology of Public Health Ministry named by acad. Ya.Kh. Turakulov, Department of Neurendocrinology, Tashkent, Uzbekistan; [2]Andijan State Medical Institute, Department of Endocrinology, Andija, Uzbekistan

The purpose of the study is to study the prognostic role of NT¬proBNP in patients with diabetes mellitus type 2 associated chronic heart failure (CHF).
Material and research methods
For the period 2015-2021, 185 patients were identified as an object of study, and 185 patients based on the materials of their preparations into therapeutic and prophylactic institutions of Andijan from 30 years and older. Patients were distributed to 3 groups: 1 Group are patients with DM 2 type + CHF - 65 patients, 2 Group are patients with DM 2 type without CHF - 60 patients, 3 Group - these are patients with CHF without DM 2 type - 60 patients Patients were fulfilled with general, biochemical, hormonal, genetic blood tests, as well as ECG, ECHC and other instrumental research.
Results of the study
The average values of NT-proBNP were significantly different in all groups and at the same time they were significantly higher in the group of patients with DM2 + CHF compared with the parameters of the patients with insulated CHF. We selected median levels of NT-proBNP in increasing NT-proBNP treads ranging from 125 to 250 pg / ml, from 250 to 500 pg/ml and above 500 pg/ml.
Conclusions
Increasing the concentration of NT-proBNP in all patients of DM 2 with CHF, as well as the high sensitivity and specificity of the test dough, the value of this marker for the diagnosis of CHF in patients with a 2-type diagnosis. The dynamics of their concentration, mainly NT-proBNP, can help in assessing the effectiveness of the therapy and the need for dose of drugs.

DOI: 10.1530/endoabs.81.EP453

EP454

"Hormonal characteristic of patients with diabetes mellitus 2 types of associated chronic heart failure"

Shakhnoza Yusupova[1] & Zamira Khalimova[2]
[1]Andijan State Medical Institute, Hospital therapy and endocrinology department,, Andijan, Uzbekistan; [2]Republican Specialized Scientific Practical Medical Center of Endocrinology of Public Health Ministry named by acad. Ya.Kh. Turakulov,, Tashkent, Uzbekistan

The purpose of the study is to study the clinical and hormonal features of diabetes mellitus 2 (DM) associated chronic heart failure (CHF).
Material and research methods
For the period 2015-2021, 185 patients were identified as an object of study, and 185 patients based on the materials of their preparations into therapeutic and prophylactic institutions of Andijan from 30 years and older. Patients were distributed to 3 groups: 1 gr. are patients with DM 2 type + CHF - 65 patients,2 gr. are patients withDM 2 type without CHF - 60 patients, 3gr - these are patients with CHF without DM 2 type - 60 patients. Patients were fulfilled with general, biochemical, hormonal, genetic blood tests, as well as ECG, ECHC and other instrumental research.
Results
The average values of the N-terminal fragment of the Brain natriuretic peptide (NT-proBNP) were reliably different in all groups, and at the same time they were significantly higher in the group of patients with DM 2 + CHF compared with the parameters of patients with insulated CXN. In the study of the aldosterone, elevated average values were found in all groups, in patients with CHF, the indicators are reliable higher than in the group of patients with DM 2 type, in the group of patients with DM 2, in combination with CHF, the indicators were the highest, reliably distinguish from indicators of patients with DM 2 type and unreliable in comparison with the CHF Group. Renin levels in groups were significantly higher than the upper limit of the norm lying. However, it should be noted that in the DM 2 + CHF group, the indicators statistically significantly exceeded the indicators in the first two groups.

Conclusions
1) Chronic hyperglycemia and activation of RAAS are pathogenetic factors that are aggravated by chronic heart failure in patients with 2-type diabetes. 2) Increasing the concentration of NTproBNP in all patients of the 2-type diabetes with concomitant CHF, as well as high sensitivity and specificity of the test proves the value of this marker for the diagnosis of CHF.

DOI: 10.1530/endoabs.81.EP454

EP455

"The Level of awareness of the risk of developing coronary heart disease of patients with type 2 diabetes mellitus complicated by cardio-renal syndrome"

Kamola Alimova
Republican Specialized Scientific Practical Medical Center of Endocrinology of Public Health Ministry named by acad. Ya.Kh. Turakulov, Tashkent, Uzbekistan

The purpose of the study is to study the Level of awareness of the risk of developing coronary heart disease (CHD) of patients with type 2 diabetes mellitus complicated by 4 type cardio-renal syndrome.
Material and methods
We examined in total for the period from October 1, 2021 to December 1, 2021 - 25 patients suffering from type 2 diabetes mellitus with chronic renal disease (CRD) and chronic cardial insufficiency (CCR). The average age of 33.3% of patients was within 50-59 years, and in 46.7% - from 60 to 69 years. The research methods included: 1) general clinical (study of endocrine, neurological status, anthropometry, height (sm), weight (kg), BMI, waist circumference (WC), hip circumference (HC), waist-hip ratio 2) instrumental (ECG, roentgen of thorax, ultrasound of internal organs 3) biochemical tests (Hb1AC, glycemic profile, urea, creatinine, lipid spectrum, coagulogram),4) hormonal blood tests (insulin, C-peptide etc.)
Results
When patients learned about the risk of CHD: before the diagnosis of DM 2 is 20%, in the process of investigation the diagnosis of DM 2 - 6.7%, shortly after the DM 2 was revealed - 20%, a few years after the DM 2 was identified in 40%, when the diagnosis of cerebro-vascular disease (CVD) is 6.7%, does not know - 6.7%. The risk levels of the development of the heart complications (HC) were the following: low -20%, average - 33%, more average - 27%, high - 13%, below average - 7%. Among the suffering diseases were: arterial hypertension - 53.3%, arrhythmia -40%, kidney disease -13.7%, stroke -6.7%.
Conclusion
1 of the 3 respondents suffering from the DM 2 rated their level of risk of developing CVD low, while diabetes a history of already high risk of CVD. 40% of the respondents received information on the risk of the development of the CVD several years after the diagnosis of the diagnosis of the DM 2. All respondents talked with the attending physician about the DM 2 and the risk of CVD. Nevertheless, at the time of the survey, all of them had CVD.

DOI: 10.1530/endoabs.81.EP455

EP456

Plasmalogen levels are associated with the severity of diabetic neuropathy

Nilufar Akhrarova[1], Talat Saatov[2], Munojat Salimova[3], Mehriniso Khamraeva[4], Bakhodir Zaynutdinov[2] & Zulaykho Shamansurova[2,5]
[1]City Specialised Outpatients Clinic, Endocrinology, Tashkent, Uzbekistan; [2]Institute of Biophisics and Biochemistry at the NUUz, Metabolomics, Tashkent, Uzbekistan; [3]City Specialised outpatients Clinic, Physiotherapy, Tashkent, Uzbekistan; [4]City Specialised Outpatients Clinic, Cardiology, Tashkent, Uzbekistan; [5]Tashkent Pediatric Medical Institute, Endocrinology, Tashkent, Uzbekistan

Backgrounds
Diabetes mellitus is a complex disease accompanied by the development of complications. In addition to the classic hyperglycemia and dyslipidemia, a number of other factors are involved in the pathogenesis of complications. Plasmalogens disturbances participates in nerve tissue degeneration.
Materials and methods
In 76 people with DM2 plasma and erythrocytes membranes plasmalogenes measured and compared according to diabetic neuropathy.
Results
Blood plasma plasmalogenes and erythrocytes membranes plasmalogens level shown decreased in patients with DM2 in compare with people without diabetes. When results analysed according to severity of diabetic nephropathy Blood plasma and erythrocytes membranes plasmalogens levels showed linkage. Blood plasma plasmalogens level were significantly differs between the groups and shown in 2.4 and 3.1 times lower in DN1 and DN2 groups. Whereas erythrocytes membranes plasmalogenes were more lower and showed lowering in DN1 groups in 3.6 times and DN2 groups in 4.2 times.
Conclusion
Blood plasma and erythrocytes membranes plasmalogens have linkage with severity of DN and involved into pathogenesis of neuropathy by neurodegeneration.

DOI: 10.1530/endoabs.81.EP456

EP457

Lipid metabolism in patients with type 1 diabetes mellitus accompanied by ischemic heart disease

Gulnora Artykbaeva & Talat Saatov
Institute of Biophysics and Biochemistry under MirzoUlugbek National University of Uzbekistan, Laboratory of metabolomics, Tashkent, Uzbekistan

Cardio-vascular disorders (CVD), ischemic heart disease (IHD) and myocardial infarction (MI) heading the line are the main cause of death among patients with diabetes mellitus (DM). DM has been proved to be an essential risk factor for IHD and MI to be instrumental in regarding all patients as belonging to the CVD high risk group. Dysfunction of adipocytes, insulin resistance, hyperinsulinemia, hyperglycemia and dyslipidemia seen in DM are the triggers for the cascade of hemodynamic and neuro-humoral responses underlying the atherosclerotic damages of vessels of various location with clinical manifestation in the form of IHD. The work was initiated to study lipid metabolism parameters in patients with the IHD- accompanied type 1 diabetes mellitus.
Materials and methods
We examined 10 patients with type 1 DM and 14 patients with type 1DM and IHD. 12 donors were included in the control group. Concentrations of lipids, triglycerides (TG), total cholesterol (TC) and high density lipoproteins (HDP) cholesterol were analyzed in all groups.
Results and discussion
Significant increase in concentrations of total lipids and TC could be seen in all patients being more pronounced in the IHD-accompanied type 1 DM. Concentrations of total lipids in patients with the accompanied pathology were the highest (11.42 $\pm$ 0.61 versus 5.2 $\pm$.33 g/l in the controls). Total cholesterol concentrations were approximately equal in all groups of patients to be 226.0 $\pm$ 11.3 mg% in patients with type 1 DM and 223.0 $\pm$11.8 mg% in those with DM and IHD ($P < 0.05$) while the concentrations of TG and HDL cholesterol changed by presence of IHD. The most pronounced changes in the serum TG concentrations could be seen in patients with IHD-accompanied type 1 DM (232.8 $\pm$ 26.0 mg%), as compared to those in patients with DM but not IHD (211.3 $\pm$ 14.3 mg%)($P < 0.05$) and the controls (137.8 $\pm$ 1.9 mg%). The reduction in HDL cholesterol could be seen both in patients with type 1 DM (36.3 $\pm$ 2.26 mg%, $P < 0.05$) and those with the pathology-accompanied disease (33.9 $\pm$ 1.8 mg%, $P < 0.001$) to significantly differ from the parameters in the controls (59.7 $\pm$ 0.8 mg%). Thus, the increase in concentrations of total cholesterol, TC, TG paralleling reduction in HDL cholesterol could be seen characteristic of patients with type 1 DM. IHD was demonstrated to be the confounding factor for DM course due to metabolic and pro-atherogenic changes, as well as formation of risk factors, to name arterial hypertension, obesity and dyslipidemia.

DOI: 10.1530/endoabs.81.EP457

EP458

Are diabetes mellitus and parkinson's disease linked?: a case report

Gorgi Khaoula, Echchad Lamya, Rifai Kaoutar, Iraqi Hinde & Gharbi Mohamed El Hassan
Ibn Sina University Hospital, Endocrinology and Metabolic Diseases, Rabat, Morocco

Introduction
Parkinson's disease is considered the most common chronic neurodegenerative disease that often affects the elderly, rarely the young. Meanwhile, Diabetes mellitus is the most common chronic metabolic disease. Because of the increase

in the prevalence of diabetes and neuro-vegetative diseases, we can wonder about the relationship between the two diseases. We report the case of a patient with type 2 diabetes mellitus associated with young onset Parkinson's disease
Case
A 44-year-old female patient, has been followed for type 2 diabetes mellitus for 5 years under Metformin and insulin with a history of Parkinson disease diagnosed 2 years ago in front of resting tremor, slowness of movements and muscular rigidity. She was put on L-Dopa with favorable clinical evolution.
Discussion & conclusion
The possibility of a relationship between Parkinson's disease and T2DM has been well studied. A few epidemiological studies have shown that diabetes is a major risk factor that accelerates the deterioration of motor function or cognitive status. T2DM shares some common pathogenic traits with PD. For example, high levels of immune cells, cytokines and chemokines have been described in pancreatic islets of patients with T2DM, while microglia activation seems to play a central role in PD progression. Similarly, the role of mitochondrial dysfunctions and oxidative stress in both T2DM and PD is now well established.

DOI: 10.1530/endoabs.81.EP458

EP459

An inaugural diabetic ketoacidosis revealed by Fournier's gangrene

Gorgi Khaoula, Echchad Lamya, Rifai Kaoutar, Iraqi Hinde & Gharbi Mohamed El Hassan
Ibn Sina University Hospital, Endocrinology and Metablic Diseases, Rabat, Morocco

Introduction
Fournier's gangrene (FG) is a rare but life-threatening disease. Although originally thought to be an idiopathic process, FG has been shown to have a predilection for patients with diabetes, HIV, alcoholism and other immunocompromised states. We report the case of a patient who presented an inaugural diabetic ketoacidosis revealed by Fournier's gangrene
Observation
A 38-year-old male patient with a smoking history, presented to the emergency department for intense perineal pain associated with a fever. The physical assessment had revealed a tachycardia of 120 bpm, blood pressure 110/60 mmHg, a high respiratory rate 24 per minute & a temperature of 39°C. The perineum was swollen and necrotic. An abdominal CT scan was performed which showed air bubbles at the perineal area extended to the retroperitoneal space and to the scrotal region. In the other hand the biological assessment was in favor of an elevated plasma glucose level of 4 g/l, metabolic acidosis and urine ketones.C-reactive protein level was at 235 mg/l with white blood cell count 18 per mm^3. The diagnosis of a Fournier's gangrene associated with an inaugural diabetic ketoacidosis was made. Management with intravenous fluids, insulin infusion and aerobic/anaerobic broad-spectrum antibiotics were started followed by surgical debridement without any complications.
Discussion & conclusion
Fournier's gangrene is a fulminant form of infective necrotizing fasciitis of the genital, perianal and perineal regions, which commonly affects men, but can also occur in women and children. Diagnosis should be prompt with early surgical intervention, along with antibiotics and good supportive care. Proactive management of diabetic and immunosuppressed patients with perineal infections is of extreme importance to prevent the development of the condition in the first place as this condition in the presence of such comorbidities is associated with high mortality

DOI: 10.1530/endoabs.81.EP459

EP460

Long-term diabetes complications

Chaima Sdiri, Yosra Htira, Skander Msolly, Maryam Cheikhrouhou, Zohra Hadj Ali, Hedfi Imene, Chaima Jemai & Feika Ben Mami[1]
Institut De Nutrition, Tunis, Tunisia

Introduction
The chronic hyperglycemia related to inadequately controlled diabetes is involved in the onset of degenerative complications, responsible for disabilities. The objective of the present study was to determine the long-term complications observed in hospitalized patients with diabetes.
Methods
We used a prospective study conducted in the department of diabetology in the National Institute of Nutrition (Tunisia). This work was carried out on the medical records of hospitalized patients. Diabetics with less than 10 years of diabetes evolution were not included.
Results
We collected 48 patients: 18 men and 30 women. the majority have type 2 diabetes (79%). For the type 1 diabetic group, the mean age was 35.2 ± 10 years and the mean glycated hemoglobin (HbA1c) level was 9 ± 1%. The mean age of type 2 diabetes (T2DM) was 65.7 ± 8.4 years and the mean HbA1c level was 10.7 ± 1.5%. Almost the half of T2D patients (49%) had diabetic retinopathy. It was minimal, moderate and proliferative in 35%, 18% and 47% of the cases, respectively. In type 1 diabetics (T1DM), retinopathy was observed in 70% of patients. In this case, minimal, moderate and proliferative retinopathy were found in 58%, 28% and 14% of the cases, respectively. Diabetic nephropathy was present in 47% of T2DM and in 10% of T1DM. Peripheral neuropathy was mentioned in 26% of T2DM and in 10% of T1DM. For the T2DM group, macroangiopathy affected 39% of hospitalized patients: 21% had coronary artery disease, 13% had chronic arterial occlusive disease of the lower extremities and 5% had a history of ischemic stroke. We did not found similar anomalies in the T1DM group. In the present data, no significant correlation was observed between the onset of chronic diabetic complications and the HbA1c level or age of diabetes (P = NS).
Conclusion
The prevalence of diabetes-related complications is increasing but often underestimated. Early screening of these complications may allow a better management.

DOI: 10.1530/endoabs.81.EP460

EP461

Correlation between pulse wave velocity and retinopathy in type 2 diabetes

Chayma Besrour[1], Rojbi Imen[1], Ben Ahmed Habib[2], Mekni Sabrine[1], Mchirgui Nadia[1], Ben Nacef Ibtissem[1] & Khiari Karima[1]
[1]Hospital Charles Nicolle, Endocrinology, Tunis, Tunisia; [2]Hospital Charles Nicolle, Cardiology, Tunis, Tunisia

Introduction
Diabetic retinopathy (DR) is a serious complication of diabetes that affects 50% of patients with type 2 diabetes. It represents the first cause of blindness. The aim of this study was to examine the relationship between diabetic retinopathy and arterial stiffness.
Methods
We conducted a prospective study including 249 diabetic patients without macroangipathic complications, between July 2020 and May 2021. Using a SphygmoCor®XCEL device, we measured arterial stiffness directly by the carotid to femoral pulse wave velocity (cfPWV).
Results
The mean age of the study population was 57.53 $\pm$ 9.34 years (139 women and 110 men). The mean duration of the disease was 10.2 years. Diabetic retinopathy (DR) was found in 24.1% of the patients. Among them 26.7% had proliferative DR. CfPWV $>$ 10 m/s was found in 95% of the patients with DR. In this group, cfPWV was at 15.34 $\pm$ 2.94 m/s VS 13.10 $\pm$ 2.56 m/s in patients without diabetic retinopathy ($P < 0.001$). Moreover, in patients with DR, we did not find a correlation between cfPWV and the stage of the retinopathy ($P = 0.108$).
Conclusion
Arterial stiffness is often increased in type 2 diabetes. And It is more increased in the presence of retinopathy. Microvascular disorders of the retina including DR were associated with cardiovascular disease, highlighting the relationship between microvascular abnormalities and atherosclerosis specifically and arterial stiffness overall.

DOI: 10.1530/endoabs.81.EP461

EP462

Correlation between pulse wave velocity and neuropathy in type 2 diabetes

Chayma Besrour[1], Rojbi Imen[1], Ben Ahmed Habib[2], Mekni Sabrine[1], Mchirgui Nadia[1], Ben Nacef Ibtissem[1] & Khiari Karima[1]
[1]Hospital Charles Nicolle, Endocrinology, Tunis, Tunisia; [2]Hospital Charles Nicolle, Cardiology, Tunis, Tunisia

Introduction
Diabetic neuropathy (DN) is the most common complication of diabetes affecting up to 50% of patients with type 2 diabetes. Carotid to femoral pulse wave velocity (cfPWV) is an independent cardiovascular marker of morbidity and mortality and is considered the gold standard in the assessment of arterial stiffness. The aim of

this study is to examine the relationship between diabetic neuropathy and arterial stiffness.
Methods
We conducted a prospective study including 249 diabetic patients without macroangipathic complications, between July 2020 and May 2021. Using a SphygmoCor®XCEL device, we measured arterial stiffness directly by the carotid to femoral pulse wave velocity (cfPWV).
Results
The mean age of the study population was 57.53 ± 9.34 years (139 women and 110 men). The mean duration of the disease was 10.2 years. Diabetic neuropathy (DN) was found in 27.7% of the patients. CfPWV > 10 m/s was found in 94.2% of the patients with DN. In this group, cfPWV was at 14.56 ± 2.99 m/s VS 13.29 ± 2.68 m/s in patients without DN ($P = 0.001$).
Conclusion
This study shows that arterial stiffness is higher in type 2 diabetic patients with diabetic neuropathy than in those without diabetic neuropathy. Indeed, increased aortic stiffness can directly damage microcirculation, including vasa nervorum, by increasing the transmission of larger and harmful pulsatile pressure waves due to loss of normal aortic buffer function. More importantly, diabetic neuropathy has been shown to be a major risk factor for cardiovascular disease. Thus, diabetic neuropathy and macroangiopathy might have common pathogenic mechanisms.

DOI: 10.1530/endoabs.81.EP462

EP463

Correlation between pulse wave velocity and hypertension in type 2 diabetes

Chayma Besrour[1], Rojbi Imen[1], Ben Ahmed Habib[2], Mekni Sabrine[1], Mchirgui Nadia[1], Ben Nacef Ibtissem[1] & Khiari Karima[1]
[1]Hospital Charles Nicolle, Endocrinology, Tunis, Tunisia; [2]Hospital Charles Nicolle, Cardiology, Tunis, Tunisia

Introduction
People with high blood pressure have a greater risk of developing diabetes, and people with diabetes also have an increased risk of high blood pressure. These two associated pathologies can increase cardiovascular risks and cause other repercussion such as arterial stiffness. The aim of this study is to examine the relationship between pulse wave velocity and hypertension in type 2 diabetes.
Methods
We conducted a prospective study including 249 diabetic patients without macroangipathic complications, between July 2020 and May 2021. Using a SphygmoCor®XCEL device, we measured arterial stiffness directly by the carotid to femoral pulse wave velocity (cfPWV).
Results
The mean age of the study population was 57.53 ± 9.34 years (139 women and 110 men). The mean duration of the disease was 10.2 years. The mean systolic blood pressure was at 138.9 ± 17.2 mmHg and the mean diastolic blood pressure was at 78.7 ± 9.8 mmHg. High blood pressure was found in 54.2% of the patients. Among them 33.3% had a controlled blood pressure under treatment. In this group, cfPWV was at 14.66 ± 2.83 m/s VS 12.43 ± 2.29 m/s in patients without hypertension ($P < 0.001$). Moreover, the presence of arterial stiffness multiples by 8 the risk of hypertension (Odds Ratio = 8).
Conclusion
Both diabetes and hypertension are known to be causes for arterial stiffness and their association increases more this risk. Therefor a well-controlled blood pressure and glycemic level is necessary to slow down this process.

DOI: 10.1530/endoabs.81.EP463

EP464

Predicting factors of insulin requirement in gestational diabetes mellitus

Zeineb Zemni[1], Daii Raja[2], Haifa Abdesselem[1], Emna Bornaz[1], Chaima Sdiri[1], Nadia Alaya[1], Kamilia Ounaissa[1], Fatma Boukhayatia[1], Imen Sebaii[1], Ryme Yahyaoui[1], Asma Ben Brahim[1] & Chiraze Ammrouche[1]
[1]National Institute of Nutrition of Tunis, Outpatient Department and Functional Explorations, Tunis, Tunisia; [2]National Institute of Nutrition of Tunis, Department C, Tunis, Tunisia

Background
The management of gestational diabetes mellitus (GDM) is based on nutrition therapy associated to insulin therapy in second intention if glycemic targets are not achieved. The aim of this study was to assess predictive factors of insulin requirement in a group of pregnant women with GDM.
Methods
We conducted a retrospective study at the Outpatient Department and functional explorations, in the National Institute of Nutrition of Tunis, between April and June 2021. Clinical and biological data were collected from medical observation records.
Results
The study included 110 pregnant women with GDM. Mean age of patients was 33.4 ± 5 years. Diagnosis of GDM was based on pathological 75 g oral glucose tolerance test (OGTT) in 60% of patients and pathological fasting blood glucose in 40%, with a mean term of discovery of 22.75 ± 7.55 weeks of gestation. Nearly to one-third (33.6%) of the patients required initiation of insulin therapy. The mean term of insulin therapy instauration was 27.27 ± 5.55 weeks of gestation with a mean time between diagnosis of GDM and insulin therapy of 4.76 ± 3.94 weeks. Insulin therapy was initiated during the first week of follow-up in 16.6%. Insulin therapy was initiated with short-acting insulin, NPH insulin and basal bolus pattern in 54.1%, 13.5% and 32.4% of cases respectively. Univariate analysis showed a significant association between level of education ($P = 0.031$), sedentarity ($P = 0.013$) and the need for insulin therapy. Glycated hemoglobin (A1c) was higher in women with insulin therapy ($P = 0.018$). We did not find a statistically significant association between insulin use and history of GDM, early discovery of GDM, maternal age, and fasting blood glucose. Multivariate analysis showed that predictive factors for insulin therapy were A1c (OR = 4.34) and personal history of miscarriages (OR = 3.67).
Conclusion
Pregnant women who develop gestational diabetes treated with insulin are at increased risk of developing type 2 diabetes in the future. That's why postpartum management is essential based on long-term screening and diabetes prevention strategies.

DOI: 10.1530/endoabs.81.EP464

EP465

Are type 2 diabetic insulin-requiring elderly satisfied?

Fatma Zaouali, Najoua Lassoued, Arfa Sondos, Alaya Wafa & Sfar Mohamed Habib
Taher Sfar University Hospital, Endocrinology Department, Mahdia, Tunisia

Introduction
Glycemic control in elderly diabetics is a challenge. Treatment Satisfaction reflects this control.
Objectives
To assess insulin treatment satisfaction and to determine the factors associated with insulin treatment satisfaction among type 2 diabetic elderly.
Methods
A cross-sectional study on 86 type 2 diabetic insulin dependent elderly recruited from the outpatient endocrinology consultation during June and July 2021.We applied the Diabetes Treatment Satisfaction Questionnaire (DTSQ) and geriatric assessment scores.
Results
Three quarters of the patients were satisfied with the insulin therapy. Satisfied patients had significantly less history of hospitalization and more regular follow-up. Diabetic neuropathy medications were significantly less taken by satisfied patients. The number of daily insulin injections was significantly higher among unsatisfied patients. Diabetic foot was significantly more frequent among unsatisfied patients. Satisfied patients were significantly less depressed, more independent in both basic and instrumental activities of daily living, without memory impairment, in better nutritional status and not falling. Higher DTSQ scores were associated with regular follow up (β 7.92, 95% CI 1.83 to 34.3). Lower DTSQ scores were associated with the history of hospitalization (β 0.12, 95% CI 0.02 to 0.58), the taking of medications for diabetic neuropathy (β 0.07, 95% CI 0.09 to 0.51), the high number of insulin injections (β 0.43, 95% CI 0.19to 0.97) and the presence of diabetic foot (β 0.17, 95% CI 0.01 to 0.38).
Conclusions
Risk factors for patients' insulin dissatisfaction should be detected early and managed appropriately to improve patients'satisfaction and consequently their well-being.

DOI: 10.1530/endoabs.81.EP465

EP466

Insulin analogs: do patients know their treatment advantages and modalities?

Emna Bornaz, Radhouen Gharbi, Lina Ghram, Marwa Chiboub, Hajer Kandara, Manel Jemel & Ines Kammoun
Institut De Nutrition, Tunis, Tunisia

Introduction
In Tunisia, the prescription of insulin analogs is increasingly « automatic » by practicians, convinced by this treatment superiority over human insulin in diabetes management. The aim of our study is to determine whether the analogs prescription modalities and advantages are known by the patients, and to assess the factors associated with this knowledge.
Patient and Methods
We conducted a retrospective study including 65 diabetic patients attending the National Institute of Nutrition and on insulin analogs. Information was extracted from medical record and patients interviews.
Results
Fourteen patients had type 1 diabetes, and 51 had type 2 diabetes. Prescription of analogs (primary or switch from human insulin) was the doctor initiative in 86.2% of cases, and was the patients' in 13.8%. The motivation of this prescription (ie advantages over human insulin) was explained to the patients by the practician in 60.7% of cases. In 58.5% of cases, the patients knew that analogs are more flexible,% 49.2 knew that analogs cause less hypoglycemia, and 10.8% that its injection (insulin pen, solely available to analogs in Tunisia) was less painful than syringe. The percentage knowing the fast analog latency and action duration were respectively 74.2% and 48.5%. There was a statistically significant association between the patient knowledge about hypoglycemia risks and the doctors explanations ($P = 0{,}00$). This knowledge was associated with a better diabetes management: less hypoglycemia ($P < 0{,}001$) a better HbA1C. (9.62 vs 8.81, $P = 0{,}019$). 98.5% of patients manifested their satisfaction with analogs and their desire to keep their prescription.
Conclusion
A substantial proportion of diabetics on analogs didn't know their advantages and characteristics. This ignorance was partly due to lack of communication with their doctors. Improving this knowledge will lead to a better management of this treatment, and will help to have a better glycemic control.

DOI: 10.1530/endoabs.81.EP466

EP467

Metformin adherence and its impact on diabetes control

Elyes Kamoun[1,2], Meriem Yazidi[1,2], Sahar Abidi[1,2], Nadia Khessairi[1,2], Yasmine Mouelhi[1,2], Ibtissem Oueslati[1,2] & Melika Chihaoui[1,2]
[1]Hospital Rabta, Department of Endocrinology, Tunis, Tunisia; [2]Faculté de Médecine de Tunis, Tunis, Tunisia

Introduction
Metformin is the first-line treatment of type 2 diabetes mellitus. Poor adherence can be lead to poor glycemic control. The aim of our study was to determine the level of metformin adherence and its link with glycemic control in type 2 diabetic patients.
Methods
We performed a cross-sectional study including 273 patients with type 2 diabetes taking metformin for at least three years. We assessed metformin adherence using the Girerd questionnaire in its Tunisian version. The level of adherence was considered good, medium or poor. Diabetes was considered controlled when HbA1c was less than 7%.
Results
The mean age was 60 ± 8.22 years. Mean duration of metformin treatment was 10 ± 5.5 years, with extremes ranging from 3 to 40 years. Mean HbA1c was 8.7 ± 1.8% with extremes ranging from 5.6% to 15.7%. The diabetes was controlled in 18.3% of patients. The compliance was good in 7.3% of patients, medium in 48% of patients and poor in 44.7% of patients. When comparing mean HbA1c in all three adherence categories, there was a near statistically significant difference between the three categories ($P = 0.058$). HbA1c was higher in patients with poor treatment adherence compared to patients with good or medium level of adherence (8.98 ± 1.96% vs 8.46 ± 1.7%, $P = 0.02$). Duration of diabetes was lower in patients with poor adherence (9.7 years vs 11.1 years, $P = 0.045$).
Conclusion
Poor adherence to metformin treatment is frequent in type 2 diabetic patients. It is associated with a poorer glycemic control and should be targeted in therapeutic education programs.

DOI: 10.1530/endoabs.81.EP467

EP468

Painful fat necrosis as a consequence of insulin application - an unsolvable problem?

Sanja Borozan, Emir Muzurovic & Snezana Vujosevic
Clinical Centre of Montenegro, Department of Endocrinology, Podgorica, Montenegro

We report a case of 39–year-old female presented with painful, scaling skin lesions on insulin application sites. She was diagnosed with type 1 diabetes mellitus (T1DM) at the age of 21 years and treated with intensified conventional insulin therapy. Three months before hospital admission, she suddenly started to feel pain at insulin injection sites, followed by oval subcutaneous deposits and skin ulcer in the further course. Identical local changes repeated after subcutaneous use of every available type of both human insulin and insulin analog. Patient past medical history was significant for surgically treated cervical cancer, cervical disc herniation and unilateral hip replacement due to femoral head osteonecrosis. On physical examination, multiple skin lesions in a form of scabs with maximal diameter of 7 mm, were present in bilateral upper arm and anterior abdominal region, and along the thighs. Her insulin injection technique was observed and estimated as adequate. Clinical, biochemistry and radiological assessment was performed as the biopsy of skin lesions. An insulin pump was inserted, but after a few days the same changes occurred at the site of catheter application. She is currently being treated with insulin parenterally.

DOI: 10.1530/endoabs.81.EP468

EP469

Impact of COVID-19 lockdown on glycemic control in diabetic patients hospitalized in emergency months

Rim Rachdi, Nadia Ben Amor, Olfa Lajili, Faten Mahjoub, Ramla Mizouri, Rym Ben Othman, Berriche Olfa & Jamoussi Henda
The National Institute of Nutrition in Tunis, Tunisia, Diabetology Department A, Tunisia

Introduction
The global pandemic spread of SARScov2 has led to a heavy medical and socio-economic toll since December 2019. Patients suffering from chronic diseases were particularly affected during the lockdown period due to difficulties in accessing care. The aim of our study was to evaluate the impact of the 2-month lockdown introduced in Tunisia in March 2020 on diabetic patients' glycemic control.
Materials and methods
Retrospective study involving 54 diabetic patients hospitalized through the emergency room in June 2020, one month after lockdown, in the diabetology department "A" at the National Institute of Nutrition in Tunis. Glycemic control, lipid balance as well as microvascular complications of diabetes were noted for each patient before and after lockdown (in January 2020 and June 2020).
Results
Median age was 54.72 years [20-87 years]. The sex ratio (M/F) was 0,5. 74% of patients had type 2 diabetes and 26% had type 1 diabetes. Median diabetes duration was 15.5 years [2-38 years]. 20.37% of patients were on oral antidiabetic drugs (ADO), 59.26% were on insulin, and 20.37% were on a combination of insulin and ADO. 53.7% were hypertensive and 66.66% had dyslipidemia. Patients were hospitalized for unbalanced insulin-deficient diabetes in 59.27%, for switching to insulin in 20.37%, diabetic ketosis in 16.66% and for unstable type 1 diabetes with severe hypoglycemia in 3.7%. Average fasting blood glucose increased from 9.35 mmol/l before lockdown to 13.24 mmol/l ($P < 10^{-3}$). Mean HbA1C value of lockdown (10.92%) was much higher than of pre lockdown (8.5%; $P < 10^{-3}$). 3.7% of patients had developed mild nonproliferative retinopathy and 1.85% saw their pre-existing retinopathies worsen. 18.52% of patients had worsened their 24-hour microalbuminuria and developed at least moderate renal impairment. Worsening of LDL cholesterol levels was observed in 38.88% of patients. The main diabetes complications aggravating factors found were non-compliance with hygienic-dietary measures during the lockdown period (83.33%), as well as non-compliance and non-availability of medications related to patients' absenteeism at the consultation (61.11%).
Conclusion
COVID-19 lockdown was associated with a deterioration in glycemic control and diabetes complications mainly due to non-adherence to the diet and lack of access to care.

DOI: 10.1530/endoabs.81.EP469

EP470

Mitochondrial diabetes: from diabetes to syndrome

Celia Gallego Díaz, Álvaro Romero Porcel, E Arturo Cuellar Lloclla & María Victoria Cózar León
Hospital Virgen de Valme, Endocrinología y Nutrición, Sevilla, Spain

Anamnesis
We report the case of a 54-year-old man who consulted for weight loss. He had been diagnosed with diabetes more than 20 years ago with good glycemic control (currently HbA1c 6.9%), no obesity, hypertension, or dyslipidaemia. A history of chronic pancreatitis and retinitis pigmentosa with eyelid ptosis. He maintains regular treatment with metformin, sitagliptin, repaglinide, ASA, Kreon and Pregabalin.
Complementary test
In reference to the chief complaint, there had not been any changes in his eating habits, his glycaemic control was in range, there were not abnormalities in CT scans, abdominal ultrasound, and faecal occults blood test. Subsequently, he was admitted for constitutional syndrome, and an echoendoscopy was requested where a hypoechogenic lesion measuring 28x27 mm was observed in the head of the pancreas with FNA showing signs of cytological atypia. A radical pancreaticoduodenectomy was performed with a diagnosis of pancreatic adenocarcinoma with areas of squamous differentiation (G3pT4 N0, Mx). During hospitalisation the patient presented palpitations, with paroxysmal EKG conduction with right bundle branch block, and a permanent pacemaker was implanted.
Discussion
We assessed the different clinical profile and discussed a mitochondrial disease known as Kearns-Sayres Syndrome. It starts in childhood with a classic triad of palpebral ptosis, retinitis pigmentosa and progressive external ophthalmoplegia, associated with sensorineural deafness, myopathies (progressive neuralgic pain and generalised muscle weakness), cardiac conduction disturbances, CNS involvement (cerebellar ataxia, bilateral facial weakness, etc.), digestive disorders (pancreatitis, diarrhea, etc.), and endocrinopathies (diabetes, delayed puberty...) and kidney failure. The aetiology of diabetes is due to an A3243g mutation affecting the mitochondrial MTTL1 gene. This gene encodes Leucine transfer RNA, which results in an attenuation of cytosolic ADP/ATP levels, resulting in a resetting of the glucose sensor in the pancreatic B-cell, producing less insulin. There is a high clinical variability based on the percentage of mutated DNA. In the beginning, usually under 40 years of age, there is insulin reserve, but it usually progresses to insulin dependence and treatment with metformin is not recommended due to the risk of lactic acidosis.
Conclusion
Our patient underwent a muscle biopsy, which was positive for specific alterations of fibres with mitochondrial proliferation.

DOI: 10.1530/endoabs.81.EP470

EP471

Correlation of knowledge and self-care with glycemic control in people with diabetes

Smaragdi Boulazeri[1], Anastasia Ntikoudi[1], Anna Kavga[1], Martha Kelesi[1], Polyxeni Mangoulia[2], Eleni Evangelou[1], Athanasios Tsartsalis[3], John Komninos[3], Andromachi Vryonidou- Bompota[4] & Eugenia Vlachou[1]
[1]University of West Attica, Nursing, Greece; [2]Evangelismos General Hospital, Athens, Greece; [3]Athens Naval Hospital, Endocrinology Department, Athens, Greece; [4]Korgialenio- Benakio General Hospital, Endocrinology Department, Athens, Greece

Introduction
Diabetes mellitus (DM) is a disease that shows a rapid increase over the recent years and is a major cause of morbidity and mortality. Thus new ways of prevention and treatment are needed and constantly being developed. As a lifelong challenge, DM is likely to affect one's life in a variety of ways. It requires daily planning and decision making. Self-care is a vital component of the disease. Knowledge consists of information about the disease and its management, which makes people with DM capable to carry out self-care activities. Knowledge about DM, its course and its treatment and how all of these factor work together are prerequisites for an sufficient level of self-care.
Aim
The aim of this study was to investigate the relationship between knowledge and self-care of people with DM in accordance with their glycemic control.
Materials and Methods
This is a cross-sectional study with a sample of 98 people with type 1 and type 2 DM, aged 18-50 years old. A convenience sample was used, and the data were collected through anonymous questionnaires.
Results
The average score of people's knowledge regarding the diabetes disease showed a good level of knowledge. The results showed a moderate level of knowledge of the participants in insulin use. People with better knowledge of insulin use, younger people, people with lower body mass index, and people with shorter duration of diabetes appeared to have better level of knowledge in physical activity. Regarding the level of care of the lower extremities, a moderate level of care was observed. The average overall medication score showed a fairly good level of compliance with the treatment. It was also found that the average overall nutrition score was relatively good. In terms of physical activity, it was found that the average overall score was low, which indicates a low level of physical activity of the participants.
Conclusion
These results indicate the need to improve education of people with diabetes, in subjects related to the disease in order to enhance their capacity for self-care. Factors that have been shown to influence both the level of knowledge and the self-care activities need to be considered in the individualized diabetes education.

DOI: 10.1530/endoabs.81.EP471

EP472

Abstract withdrawn

DOI: 10.1530/endoabs.81.EP472

EP473

Oral health related behavior and knowledge in adult patients with diabetes: a questionnaire study

Meriam Dalhoum, Zohra Hadj Ali, Bani Ines, Htira Yosra & Ben Mami Faika
National Institute of Nutrition, Department C, Tunis, Tunisia

Diabetes is a common disease with concomitant oral manifestations that impact dental care.
Purpose
To investigate oral health awareness, oral hygiene and behavior in adults with diabetes.
Subjects and methods
This study involved interviews with a sample of 30 patients with diabetes type 2 followed in the C department of the National Institute of Nutrition in Tunis using a questionnaire study on oral health behavior and awareness.
Results
The mean age of our patients was 53 ± 7 years, with a sex ratio M/F = 0.43. The average duration of diabetes was 10 ± 8 years. The majority of respondents (59.4%) visited a dentist once a year, but oral care varied: 67.2% reported brushing at least once a day, whereas only 4.3% flossed daily. Awareness of oral health risks was limited, only 22% of the participants answered correctly about oral health knowledge items related to diabetes and 74.1% had never received any oral health advice related to their diabetes.
Conclusions
Many adults with diabetes have poor awareness of oral care and health complications associated with diabetes, and are receiving limited advice. Health professionals should take the opportunity to educate patients with diabetes and to promote proper oral health behaviors.

DOI: 10.1530/endoabs.81.EP473

EP474

Daytime sleepiness in patients with diabetes

Meriam Dalhoum, Zohra Hadj Ali, Bani Ines, Htira Yosra & Ben Mami Faika
National Institute of Nutrition, Department C, Tunis, Tunisia

Excessive daytime sleepiness (EDS) is commonly considered a cardinal sign of sleep apnea; however, the mechanism underlying the association is unclear.

Purpose
The purpose of this study is to investigate the daytime sleepiness in patients with diabetes.
Methods
Participants were 30 adults with type 2 diabetes (T2DM) followed in the C department of the National Institute of Nutrition in Tunis. Subjective sleepiness was assessed using the Epworth Sleepiness Scale (ESS).
Results
The mean age of our patients was 60±11 years, with a sex ratio M/F=0.48. The average duration of diabetes was 17±4 years. Obesity was present in 83.4% of patients. The mean glycated hemoglobin was 10.8% and the frequency of hypertension was 73%. This study showed that most patients (43.2%) presented a mild daytime sleepiness. People who scored highly on the ESS (4.9%) were more likely to have poor glycemic and blood pressure control and a higher body mass index than those with low scores (34.1 vs 31.8 kg/m^2).
Conclusions
Sleep abnormalities and daytime sleepiness are frequent in T2DM and it is associated with decreased diabetes self-management. We suggest that diabetic patient should be more thoroughly investigated for symptoms of daytime sleepiness.

DOI: 10.1530/endoabs.81.EP474

EP475

Prophylactic gonadectomy in A young phenotypic female with turner syndrome 45,XO/46,XY mosaicism: a case report

Sofia Ouhessaine, Nassim Essabah Haraj, Siham El Aziz & Asma Chadli
UHC Ibn Rochd, Endocrinology, Diabetology, Nutrition and Metabolic Diseases, Casablanca, Morocco

Introduction
Turner syndrome is a chromosomal disorder that affects an estimated 1/2500 female live births. An estimated subset of 6-12% of all Turner Syndrome patients will be a mosaic with Y-chromosomal elements. It is recognized that a Turner female possessing Y chromosome material has an increased risk of developing gonadoblastoma, a precursor to dysgerminoma. Consequently guidelines recommend prophylactic gonadectomy in Turner females.
Obsevation
We present the case of a 17-year old female, followed for mosaic turner syndrome, who underwent prophylactic gonadectomy. Patient was followed for 4 years, the diagnosis was initially suspected in front of a failure to thrive, presence of Nevi on the face, and primary amenorrhea. Karyotype study was ordered and revealed a mosaic pattern of 46,X/45,X—70% of the cells containing Y chromosome material. The clinical examination finds the stigmata of the classic Turner Syndrome, wide neck with a low hairline, a high palate and a bradymetacarpus. An exploratory laparoscopy performed showed bilateral ovarian strips. Prophylactic gonadectomy was organized, by laparoscope. The post-operative follow-up was simple, with anapath, bilateral ganadic dysgenesis without signs of malignancy.
Conclusion
Early gonadectomy has been recommended in mosaic Turner females with Y-chromosomal material as a consequence of high risk of gonadoblastoma in infants as early as 5 months old.

DOI: 10.1530/endoabs.81.EP475

EP476

Can Alopecia Areata predict the appearance of autoimmune diabetes in a patient with autoimmune polyglandular syndrome type 2?

Ana Silvia Corlan & Mihaela Vlad
University of Medicine and Pharmacy "Victor Babes", Endocrinology, Timisoara, Romania

Autoimmune polyglandular syndrome type 2 can be associated with alopecia areata. We present herein a case of a female patient, 42 years old, who suffered from autoimmune thyroid disease with hypothyroidism and autoimmune adrenalitis and who was recently diagnosed with alopecia areata. She accused sudden, asymptomatic hair loss, which she noticed 3 months ago, accompanied by a burning sensation in her scalp. Her menstrual cycles were normal. The clinical examination identified smooth, circular, discrete areas of complete hair loss on her scalp. Her physical exam was otherwise normal. Her medication included 88 mcg Synthroid/day and 20 mg hydrocortisone daily. The laboratory investigations identified normal thyroid function, decreased levels of cortisol (the patient was feeling well, her blood pressure was normal), normal electrolytes, normal renal and hepatic function, normal levels of serum testosterone (in the female normal range). The glycemic profile showed normal fasting glucose, with a HbA1c of 5.2%. A suspicion of alopecia areata was raised and the patient was sent to a dermatological evaluation. The dermoscopy confirmed the diagnosis of alopecia areata. Data in the literature point to the fact that there are human leukocyte antigen alleles, that are high risk for alopecia areata. Epidemiological studies show that a history of autoimmune disease increases the risk of alopecia areata. Specific associations mentioned in the literature are: alopecia areata with thyroid disease, vitiligo, rheumatoid arthritis. Given the fact that autoimmune polyglandular syndrome type 2 (as is the case of our patient) associates autoimmune diabetes in 30-52% of cases, we decided to test for diabetes autoantibodies. The test detected increased levels of glutamic acid decarboxylase (GAD-65). Studies point to the fact that antibodies, in particular antibodies anti-GAD, are also present in a percentage of nondiabetic patients, that do not develop diabetes over many years. But given the association with multiple other autoimmune diseases, the patient must be carefully followed, to detect diabetes onset in an early stage, preventing life-threatening complications. Literature data suggest that alopecia areata protects against type 1 diabetes in predisposed individuals (it is the reason, why our patient at risk didn't develop clinical diabetes). In conclusion, the appearance of alopecia areata in a patient with autoimmune thyroid and adrenal disease, who is at increased risk of autoimmune diabetes, could protect against the development of rapidly progressive type 1 diabetes.

DOI: 10.1530/endoabs.81.EP476

EP477

Globoid cell leukodystrophy: case report and literature review

Fatima Zahra Outtaleb[1], Amal Tazzite[2], Bouchaib Gazzaz[2,3] & Hind Dehbi[2,4]
[1]Ibn Rochd University Hospital, Laboratory of Medical Genetics, Casablanca, Morocco; [2]Faculty of Medicine and Pharmacy. Hassan II University, Cellular and Molecular Pathology Laboratory, Casablanca, Morocco; [3]Royal Gendarmerie, Genetics Analysis Institute, Rabat, Morocco; [4]Ibn Rochd University Hospital, Laboratory of Medical Genetics, Casablanca, Morocco

Krabbe disease, also known as globoid cell leukodystrophy, is an autonomic recessive genetic disorder caused by *GALC* mutations. *GALC* gene codes for galactosylceramidase, which is a lysosomal enzyme. This disorder can occur during early childhood, between the ages of 1 and 8 years old (later onset form) or during adulthood; its prevalence is estimated at 1/100 000. Nevertheless, in most cases, this disorder occurs during childhood. With this case report, our aim is to attempt to describe both clinical features and evolution of this rare defect. A 5-year-old non-consanguineous female with a good psychomotor development has been showing psychomotor regression including generalised hypotonia, loss of both speech and walking since age 3. This patient no dysmorphia and no organomegaly and she had no fever. Genetic testing revealed the presence of a compound heterozygote mutation in *GALC* gene— c.865G>C and c.195G>C confirming diagnosis of globoid cell leukodystrophy. Both parents received genetic counselling in order to determine the risk of reiteration and to offer prenatal diagnosis in case of any future pregnancy. Regarding patients with later onset globoid cell leukodystrophy (occurrence between 1 and 8 years of age), as is the case we are currently reporting, initial symptoms usually include eating difficulties and irritability. Then hypertonic episodes including myoclonic seizures occur in association with development regression. During the final stage of this disorder, hypotonia, blindness and deafness appear. Diagnosis can be stablished based on reduced galactosylceramidase enzymatic activity or by genetic testing for mutations in *GALC* gene. Death usually occurs 2 to 7 years after initial symptoms begin. For patients with either early childhood or later onset forms of this disorder, the only therapeutic option is hematopoietic stem-cell transplantation which slows down development of this disease. These facts provide new light on the need for genetic cancelling in order to provide pre-symptomatic diagnosis to at risk relatives. Furthermore, reporting of new cases will help to better unravel the phenotype-genotype correlation of *GALC* gene variants.

DOI: 10.1530/endoabs.81.EP477

EP478

Metabolic and hemodynamic disorders in obese patients with true and pseudo-resistant hypertension

Anna Shalimova[1,2], Ganna Isayeva[1], Olena Burakoska[1], Iryna Komir[1], Maryna Vovchenko[1] & Kostyantyn Prosolenko[2]
[1]L.T. Malaya Therapy National Institute of the National Academy of Medical Sciences of Ukraine, Complex Risk Reduction of Chronic non-Communicable Diseases, Kharkiv, Ukraine; [2]Kharkiv National Medical University, Internal Medicine N1, Ukraine, Ukraine

Objective
to conduct a comparative assessment between metabolic and hemodynamic parameters in obese patients with true and pseudo-resistant (due to different causes) hypertension.
Materials and methods
The study included 302 patients with uncontrolled hypertension and obesity. Initial treatment efficacy was assessed 3 months after dual therapy was administered. Those patients who did not reach target blood pressure (BP) in dual therapy were transferred to triple therapy. Among patients who received triple therapy, 69 people did not reach target BP (they received the fourth drug spironolactone). All patients were additionally examined 6 months after the initiation of antihypertensive therapy.
Results
A comparative assessment of office BP, ambulatory BP monitoring (ABPM) and home self-measurement of BP was carried out between non-resistant and resistant patients: at the initial stage of enrolling patients, there was no significant difference in BP levels between non-resistant and subsequently resistant patients; after 3 months of follow-up (after prescribing double fixed combinations), there was a significant difference in the indicators of both office and out-of-office BP in resistant and non-resistant patients; despite the achievement of target BP levels after 6 months of therapy (double or triple fixed combinations in non-resistant patients and triple therapy + spironolactone in resistant patients), in the presence of resistance, both office, home and most ABPM indicators were significantly higher than in non-resistant patients. If at the stage of enrolling patients into the study and 3 months after the start of therapy there was no significant difference in BP levels between patients with true and pseudo-resistance, then after 6 months of antihypertensive therapy, patients with true resistance had significantly higher levels of office systolic BP (SBP, $P < 0.01$) and 24 h average SBP according to ABPM data ($P < 0.05$) compared with pseudo-resistant patients. Obese patients with true resistance had also significantly lower body mass index (BMI) and low-density lipoprotein cholesterol (LDL-cholesterol, $P < 0.05$) as well as higher levels of aldosterone and SBP ($P < 0.05$) compared with pseudo-resistant patients.
Conclusions
Even when target BP levels in antihypertensive therapy are achieved, obese resistant patients are characterized by higher levels of office and out-of-office BP, compared with non-resistant patients. Compared with pseudo-resistance, the presence of true resistance in obesity is associated with higher SBP and aldosteron levels, as well as lower BMI and LDL-cholesterol.

DOI: 10.1530/endoabs.81.EP478

EP479

A new rehabilitation complex for muscle strength deficit correction and movement disorders in case of obesity

Valeriia Vasileva & Larisa Marchenkova
National Medical Research Center for Rehabilitation and Balneology, Department of Somatic Rehabilitation, Reproductive Health and Active Longevity, Moscow, Russian Federation

Aim
The Aim of the study was evaluation of effectiveness a new complex included aerobic and physical training, kinesiohydrotherapy, balance therapy on changes in muscle strength and movement disorders in patients with obesity.
Materials and methods
The study group included 40 patients aged 58 [53;66] y.o. with a BMI $\geq$ 30 kg/m^2. The control group included of 40 people aged 57 [54;63] y.o. with BMI $\geq$ 30 kg/m^2. Study methods included anthropometry, functional tests, and dynamometry.
Results
In research it was a significant decrease in body weight (from 106.03 [83;145] to 102.8 [80;141] kg), BMI (from 39.2 [30.12;49.1] to 38.1 [29.4;46.7] kg/m^2), decreased WC (from 109 [105;125.8] to 107 [98.8 12] cm), HC (from 127 [112.3;139.8] to 121 [109.5;133.5] cm), decreased pain syndrome (from 5 [3;7] to 2.5 [1;4.75] points), increased arm strength (in right arm from 20 [14.25;34] to 30 [19;42], in left arm from 19.5 [14.25;29.5] to 22 [18;30.75] daN). Conditioning and coordination abilities improved significantly in the main group according to the functional tests: "Up and go test" (from 7.9 [7.1;8.9] to 7.4 [6.5;8.3] sec.), back muscle strength (from 5[5;5] to 5[5;5]), static and dynamic abdominal muscle endurance (from 12.04 [9.47;17.13] to 16.07 [10.69;27.7] sec. and from 31[21;37.25] to 39 [29.5;46.5] sec, and back and (from 14.94 [5.8775;22.205] to 18.41 [9.745;31.335] times and from 8 [5;14] to 10 [8;23], times, respectively); Fukuda test scores (from 65 [56;76.75] to 72 [61;82] reps), One leg standing test (from 13.9 [5.38;32.15] to 18.61 [8.6125;38.1575] sec. for the left) and closed eyes (from 3.45 [2.16;6.38] to 3.975 [2.715;5.82] seconds for the right and from 4.12 [1.3;8.61] to 4.31 [2.16;8.13] seconds for the left).
Conclusions
A new complex including aerobic and strength training, kinesiohydrotherapy, and balance therapy showed significant effects on body weight reduction, body volume reduction, and muscle strength improvement in obese patients. A new integrated method results in a longer maintenance of the achieved effect when controlling the long-term results after 3 months and 1 year compared with the group that received only the 2-component program.

Keywords
obesity, kinesiohydrotherapy, balance, rehabilitation, coordination training, muscle strength.
DOI: 10.1530/endoabs.81.EP479

EP480

Age aspects and body mass index in patients with toxic hepatitis

Oksana Prokopchuk[1,2], Ihor Hospodarskyy[2], Nadiia Gavryliuk[2], Svitlana Danchak[2] & Olha Kozak[2]
[1]Ternopil National Medical University, Department of Higher Nursing Education, Patient Care and Clinical Immunology, Ternopil, Ukraine; [2]Ternopil National Medical University, Ternopil, Ukraine

Background
Over the last year the social consequences of obesity has become significant, with weight-based stigmatization and prejudiced common outcomes. Toxic hepatitis is one of those diseases that has obese as comorbidity in different age groups. The pervasiveness of prejudice toward obese in patients with toxic hepatitis makes it imperative that scientists have access to valid and reliable measures to assess weight bias.
Objectives
Age groups structuring and examination of patients with toxic hepatitis for obesity detection as one of the hepatic fibrogenesis triggers.
Methods
124 patients with toxic liver disease were examined. The body mass index (BMI, Kettle index) was calculated using anthropometric indicators. For all our patients BMI was interpreted using standard weight status categories (classification of BMI adopted by the WHO (1997). The value of BMI in the range of 18.5-24.9 kg/m^2 should be considered optimal - normal or healthy weight; reduced BMI or underweight $\geq$ 18.5; overweight - 25.0-29.9; obesity I degree - 30,0-34,9; obesity II degree - 35,0-39,9; grade III obesity - $\geq$ 40 (kg / m^2). The age standards were interpreted using adopted by the WHO/Europe, according to which the young age is 25-44, the average age - 44-60, the older age - 60-75, the elderly age - 75-90, people aged 90 and over considered as long-lived. However, it should be noted that the last age category among the examined patients was not presented.
Results
The examination revealed that the following changes were observed in BMI: 52.8% of patients were with normal weight, 39% were overweight, obesity I degree was detected in 8.1% of patients. Age structuring of BMI is given in the table.

Characteristics	Young age n = 8(%)	Average age n = 56(%)	Elderly age n = 52 (%)	Old age n = 7 (%)
1	**2**	**3**	**4**	**5**
BMI kg/m^2 18,5-24,9	7(87,5)	31(55,4)	24(46,2)	3(42,9)
BMI kg/m^2 25,0-29,9	1(12,5)	22(39,3)	23(44,2)	2(28,6)
BMI kg/m^2 30,0-34,9	-	3(5,4)	5(9,6)	2(28,6)

Conclusions
Obesity of varying degrees was found in 47.2% of patients with toxic hepatitis in all age groups. The most numerous was group of average age ($n = 56$), the smallest in number was group of old age patients ($n = 7$). These data should be taken into account when choosing and prescribing adequate treatment, nutrition should always be considered among physicians in the liver and obesity fields, who have an important role to play in improving the quality of life for so many individuals afected by these pathologies.

DOI: 10.1530/endoabs.81.EP480

EP481

Prevalence of non alcoholic fatty liver disease and fibrosis in morbidly obese patients undergoing bariatric surgery

Rahma Khalaf, Faten Mahjoub, Nadia Ben Amor, Olfa Berriche & Henda Jamoussi
National Institute of Nutrition, Department A, Tunisia

Background
Patients undergoing bariatric surgery have a higher prevalence of non alcoholic liver fatty disease (NAFLD) than the general population; however, its assessment and the accurate staging of fibrosis are often complicated because noninvasive tests are not very accurate in patients with morbid obesity, and liver biopsy cannot be performed as a routine exam.
Aim
The aim of this study was to determine the prevalence of non alcoholic fatty liver disease and fibrosis in patients undergoing bariatric surgery.
Methods
This is a monocentric prospective descriptive study including 40 morbidly obese patients before bariatric surgery. NAFLD was diagnosed by ultrasound and alterations in liver enzyme levels (aspartate aminotransferase (ASAT), alanine aminotransferase(ALAT) and yGlutamylTransferase (yGT)). Fibrosis score used was the fibrosis-4 (FIB-4) index.
Results
The mean age was 38.18 $\pm$ 10.03 years, 35 (87.5%) were females, mean body mass index (BMI) was 47.13 $\pm$7.73 kg/m^2 and mean waist circumference was 134.64 $\pm$ 20.39 cm. Mean triglyceride level was 1.8 $\pm$ 1.67 mmol/l [0.41-7.67]. Mean serum levels of liver enzymes ASAT, ALAT and yGT were respectively 25.29 $\pm$ 12.11 UI/l [10-54], 26.82 $\pm$ 14 UI/l [14-58] and 28.11 $\pm$ 15.6UI/l [8-55]. Mean 25 OH vitamin D level was 17.02 $\pm$ 13.61 ng/ml [8.1-64.8] .Ultrasound was abnormal in 26 patients (65%). NAFLD was associated with triglyceride levels ($P = 0.034$). However, age ($P = 0.5$), body mass index ($P = 0.44$), hypertension ($P = 0.7$), diabetes ($P = 0.4$), ASAT levels ($P = 0.6$), ALAT levels ($P = 0.1$),ASAT/ALAT($P = 0.053$) and yGT levels ($P = 0.4$) and Vitamin D levels ($P = 0.05$) were not associated with NAFLD. Mean FIB-4 index was 0.74 [0.19-3.76]. Of the study population, 92.1% of patients had a FIB-4 index <1.3, 5.3% had a FIB-4 index between 1.4 and 2.67 and 2.6% of patients had a FIB-4 index >2.67. FIB-4 index >1.3 was associated with ALAT levels ($P = 0.005$), vitamin D levels ($P = 0.038$) and yGT($P = 0.03$).However, no association was found with ASAT levels ($P = 0.1$), yGT ($P = 0.3$), HOMA2-insulin resistance ($P = 0.9$), age ($P = 0.3$), BMI ($P = 0.56$) and waist circumference ($P = 0.4$).
Conclusion
Vitamin D status were associated with NAFLD and advanced fibrosis in morbidly obese patients. Therefore, routine screening of 25OH vitamin D deficiency have important therapeutic implications in this population. FIB-4 index ruled out advanced fibrosis in most of our study cases.

DOI: 10.1530/endoabs.81.EP481

EP482

The effect of laparoscopic mini-gastric bypass on the compensation of carbohydrate metabolism in patients with morbid obesity and type 2 diabetes

Natalya Mazurina, Ekaterina Ershova, Kseniya Komshilova & Ekaterina Kim
Endocrinology Research Centre, Therapeutic Endocrinology, Moscow, Russian Federation

Objective
Sustained weight loss is a highly effective strategy to treat and prevent the development of type 2 diabetes (T2D). Bariatric surgery leads to significant weight loss, which ensures the achievement of remission of diabetes mellitus and other obesity-related comorbidities.
Aim
The aim of this study was to estimate glycemic profile of patients with morbid obesity and T2D after laparoscopic mini-gastric bypass (LMGB).
Methods
We conducted a retrospective study of obese patients admitted to the Endocrinology Research Center between February 2019 and December 2020. We included 45 adults (41 women and 4 men, median age 57.5 years) with diabetes mellitus type 2 (median duration of disease 8 years, 5 newly diagnosed) and morbid obesity (BMI>40 kg/m^2). Anthropometric (BMI) and metabolic (fasting plasma glucose (FPG), glycosylated hemoglobin (HbA1c), C-peptide) parameters were determined before surgery and at 6, 12 months after. Statistical analysis was performed with the use of Statistica v. 13.3 (TIBCO Software Inc., Palo Alto, CA, USA). Data is presented by medians and interquartile ranges (Median, (25;75)). There were carried out a comparative analysis of three dependent groups for quantitative data using the Friedman criterion, pairwise comparison of groups for quantitative data using the Wilcoxon criterion. The initial critical level of significance in testing statistical hypotheses was assumed to be 0.05.
Results
In the studied group the baseline median BMI was 51 kg/m^2 (44.3; 55.6), FPG 7.4 mmol/l (6.6; 9.0), HbA1c 7.2% (6.5; 8.5), C-peptide 4.5 ng/ml (4.3; 5.1). 6 months after LMGB the median BMI was 38.6 kg/m^2 (35.5; 42.1), FPG 5.3 mmol/l (4.9; 6.2), HbA1c 5.5% (5.3; 6.2), C-peptide 2.5 ng/ml (2.3; 3.9); 1 year after - BMI 31.6 kg/m^2 (28.65; 34.2), FPG 4.9 mmol/l (4.4; 5.3), HbA1c 5.7% (5.1; 5.9), C-peptide 2.2 ng/ml (1.9; 3.2). Comparing three groups differences in HbA1c levels were revealed ($n = 11$, $P < 0.001$). Difference between groups of 6 and 12 months after LMGB ($n = 10$, $P > 0.05$) was significantly less than before LMGB and 6 months after ($n = 23$, $P < 0.001$), before and 12 month after LMGB ($n = 18$, $P < 0.001$) in further pairwise comparison.
Conclusion
Weight loss was accompanied by a significant improvement of carbohydrate metabolism. A more pronounced decrease in body weight and improvement of metabolic parameters were observed in the first 6 months after surgery.

DOI: 10.1530/endoabs.81.EP482

EP483

Hypoglycemia after gastric bypass

Coskun Ates, Erhan Hocaoglu, Ensar Aydemir, Filiz Mercan Saridas, Özen Öz Gül, Soner Cander, Canan Ersoy & Erdinc Erturk
Uludag University Faculty of Medicine, Endocrinology and Metabolic Diseases, Bursa, Turkey

Introduction
Today, approximately 33% of the world population is either overweight or obese. National Health and Nutrition Examination Survey (NHANES) results show that, when 20 years and older American adults are examined, it is seen that 33% of them are overweight, 35.7% of them are obese, and 6.3% of them are morbidly obese (1). Roux-en-Y gastric bypass is a restrictive and malabsorptive combined method and is a complicated operation. Cases of endogenous hyperinsulinemic hypoglycemia developing an average of 5-6 years after the operation have been reported (2). We aimed to present a case of severe hypoglycemia after Roux-en-Y gastric bypass.
Case
A 27-year-old female patient had a sleeve gastrectomy in 2015 and a Roux-en-Y gastric bypass operation in 2018. She lost 76 kg after the operation. His hypoglycemia started one year after Roux-en-Y gastric bypass. The patient, who has tremors, sweating, and palpitations, especially 2-4 hours after the meal, states that his capillary blood sugar is 24 mg/dl. Therefore, the patient sometimes applied to the emergency room. The patient was interned at Bursa Uludağ University in 2019. At the 15th hour of the 72-hour fasting test, blood glucose was: 20 mg/dl Insulin: 19.2 pmol/l c-peptide: 7 ng/ml. At the 2nd hour of the mixed meal test, blood glucose was 47 mg/dl while insulin: was 43.4 pmol/l. Computed tomography (CT) was performed on the patient. The pancreas was normal in CT. Islet abnormalities after Roux-en-Y gastric bypass surgery were considered in the patient. The patient received acarbose and metformin treatments for three months, but to no avail. Then liraglutide was started. After a month, the controlled hypoglycemia continued, and isoptin and acarbose were added to his treatment. However, the patient's complaints continued. Thereupon, Octreotide LAR 20 mg was started. The patient whose hypoglycemia improved is being followed up.
Conclusion
It is necessary to be careful about hypoglycemia developing after Roux-en-Y gastric bypass. Also, we should consider the long-term results of bariatric surgery

when making an operational decision. Octreotide therapy may be an alternative to pancreatectomy in hypoglycemia developing after gastric bypass.

References
1. Forse RA, Betancourt-Garcia MM, Kissee MC. Epidemiology and discrimination in obesity. In: *The ASMBS textbook of bariatric surgery*. Springer; 2020. p. 3–14.
2. Service GJ, Thompson GB, Service FJ, Andrews JC, Collazo-Clavell ML, Lloyd RV Hyperinsulinemic hypoglycemia with nesidioblastosis after gastric-bypass surgery. *N Engl J Med*. 2005; **353** (3):249.

DOI: 10.1530/endoabs.81.EP483

EP484

Quality of life, anxiety-depressive disorders and their assessment in patients with metabolic syndrome

Olga Moskalenko & Eduard Kasparov
Federal Research Center «Krasnoyarsk Science Center» of the Siberian Branch of the Russian Academy of Sciences, Russian Federation

This article discusses the assessment of quality of life, psychological state and anxiety-depressive disorders in patients with metabolic syndrome. It is known that the prevalence of metabolic syndrome in different countries is about 30% and varies from included criteria. The problem of the quality of life of obese and overweight patients is relevant and socially significant.

Research Methods

The authors present the results of a study of 70 patients with MS and 36 apparently healthy volunteers who do not have concomitant diseases and are not obese. The study was conducted on the basis of the clinic of the Federal Research Center. Patients were examined, anthropometric parameters were determined (waist circumference, body weight) with an assessment of the quality of life (SF-36 questionnaire). The level of anxiety and depression was determined by the hospital anxiety and depression scale HADS.

Results

Analysis of the results revealed that most of the quality of life indicators were statistically significantly different in patients with metabolic syndrome relative to the control group. Thus, the indicators of the level of QoL are significantly higher in healthy individuals than in patients with obesity. Differences in all groups are significant ($P \leq 0.05$). It was found that the average level of parameters "physical functioning" decreased by 19.2% ($P < 0.05$), "role functioning" by 34.2% ($P < 0.05$), "general health" by 14.7% ($P < 0.05$), "vitality" by 16% ($P < 0.05$), "emotional functioning" by 53.1% ($P < 0.05$). The assessment of the level of anxiety and depression in patients with MS corresponded to the subclinically expressed level, and the level of depression exceeded the control group by 19%. The level of QoL in patients with obesity is significantly lower than in healthy individuals.

Conclusion

Assessment of the quality of life of patients with obesity and overweight is one of the most important factors in the integrative assessment of the condition of such patients. I would like to note that the higher the patient's body weight, the lower his physical condition and the more pronounced concomitant diseases. Patients with MS are characterized by a decrease in quality of life indicators, subclinically expressed anxiety-depression. Patients require correction of psychological disorders, which will reduce the level of anxiety and depressive disorders, which will further improve the quality of life.

DOI: 10.1530/endoabs.81.EP484

EP485

Correlation between Type-1 diabetes and obesity

Subhash Kumar[1], Anand Shankar[2], Shaibal Guha[3] & Amit Kr Das[4]
[1]Diabetes and Obesity Care Center, Diabetes, Patna, India; [2]Shankar Diabetes Care and Research, Patna, India; [3]Positive Health Care Center, Patna, India; [4]SHMC Muzaffarpur, Diabetes, Muzaffarpur, India

Introduction

Increase in global childhood obesity is considered to be one of the detrimental problems all across the world. It is well known that about every 1 in every 300-500 infants suffers from Type-1 Diabetes Mellitus. Obesity has been directly associated with elevation of blood sugar and HbA1c.

Objective

This study investigates the prevalence of obesity in Type-1 DM and the distribution of sex, age and its correlation with HbA1.

Methods

Transversal revision of Type-1 DM anthropometric measurements from patients at a selected general hospital in Bihar. Sex, age, weight, values of HbA1c were reviewed.

Results

Among the selected 60 subjects, 6 (10% participants) were underweight with BMI below 15 kg/m^2, 18 (30% participants) were also underweight, however, their BMI falls between 15 to 16 kg/m^2. 9 (15% of participants) were also underweight but in between BMI 16-18.5 kg/m^2. 24 (40% of participants) were in the normal range and their BMI was between 18.5-25 kg/m^2. HBA1c median was 9.44% with a standard deviation of 2.45%. Only one patient had a normal HbA1c value below 7%. Out of 60, 8% had between 7-8%, 22% patients had 8-9%, 22% had 9-10, 16% had 10-11, 4% had 11-12%, 14% had 12-13%, 10% had between 13-14% and 1 patient had A1c level between 14-15% which was elevated.

Conclusion

This study showed that overweight and obesity were not big issues in the Type-1 diabetic population. Both these cases are rare when the HbA1c level is high.

DOI: 10.1530/endoabs.81.EP485

EP486

Manifistation of psoriasis in patients with type 2 diabetes

Elena Brutskaya-Stempkovskaya [1], Alla Shepelkevich[2] & Yuliya Dydyshka[2]
[1]Belarusian State Medical University, Jeneral Medicical Practice, Minsk, Belarus; [2]Belarusian State Medical University, Endocrynology, Minsk, Belarus

Background

It is known that the prevalence of skin diseases in patients with type 2 diabetes (T2D) is increased including psoriasis. Patients with T2D and psoriasis have an increased risk of psoriasis exacerbations. The study of the psoriasis manifestation features in patients with T2D can help to reduce the number of exacerbations, their severity and duration.

Aims

To study the influence of T2D on the psoriasis manifestation and exacerbation.

Materials and Methods

We studied hospitalized patients with T2D and psoriasis in dermatological clinic during 5 years ($n = 47$) - the main group. Comparison group 1- patients with psoriasis without T2D ($n = 40$), comparison group 2 - patients with T2D without psoriasis ($n = 37$). Patients were excluded: with the psoriatic arthritis, GFR ≤ 45 ml/min/1.73 m^2.

Results

Patients of the main group (women-53.2%, men-46.8%, mean age 61.0$\pm$7.7 years), comparison group 1 (women-55%, men- 45%, mean age 60.5$\pm$7.5 years), comparison group 2 (women-54%, men-46%, mean age 62.0$\pm$7.8 years) were same in clinical, anthropometric, anamnestic and laboratory data (AST, ALT, total cholesterol, creatinine, $P > 0,05$). Patients of the main group and comparison group 1 differed in serum glycaemia ($P = 0.005$), HbA1c ($P = 0.009$). Patients of the main group had an increase HbA1c (11.8 (7.9-12.3)) compared with the comparison group 2 (6.8(6.1-7.3), $P = 0.006$) in the exacerbation of psoriasis period. All patients of the main group were ranked into groups depending on the HbA1c level. HbA1c $<$ 7.0% was detected in 8.5% ($n = 4$) of patients with T2D and psoriasis, HbA1c 7.0-8.5% -in 31.9% ($n = 15$), HbA1c $>$ 8.5% - in 59.6% ($n = 28$) cases. Thus, result of the study indicates a decrease in glycemic control in 91.5% patients of the main group for a period of at least 3 months before the psoriasis exacerbation.

Discussion

Result of the study indicates a decrease in glycemic control in patients with T2D and psoriasis before the psoriasis exacerbation. There is probably a correlation between psoriasis exacerbation and low glycemic control in patients with T2D and psoriasis.

DOI: 10.1530/endoabs.81.EP486

EP487

Neurodegeneration type and severity have linkage with plasma insulin in DM patients

Talat Saatov[1], Timur Alimov[2], Elvira Ibragimova[1], Takhir Ishankhodjaev[3], Zafar Ibragimov[3], Gulnora Artikbaeva[3], Mukhammadjon Mustafakulov[1], Dilnoza Saidova[3] & Zulaykho Shamansurova[1,4]
[1]Institute of Biophisics and Biochemistry at the NUUz, Metabolomics, Tashkent, Uzbekistan; [2]Republican Specialised Scientific Practical Medical Centre of Hematology, Tashkent, Uzbekistan; [3]Institute of Biophisics and Biochemistry at the NUUz, Tashkent, Uzbekistan; [4]Tashkent Pediatric Medical Institute, Tashkent, Uzbekistan

Background
In Pathogenesis of Neurodegeneration in Diabetes Mellitus (DM) addition to insulin resistance, glycemic control and blood plasma lipid levels existing other mechanisms were proposed. We investigated plasma insulin level in patients according to severity of diabetic neuropathy.
Materials and methods
In 32 people with DM2 glycemia, HbA1c, blood plasma insulin, blood total cholesterol, triglycerides, Low Density Lipoproteins (LDLP) levels were measured and compared regarding to DN severity by stages in DN1 and DN2 groups.
Results
People with DN1 and DN2 have the same age and disease duration. Glycemia and HbA1c level were also comparable between groups. Although, body weight and BMI (in 1.32 times), blood total cholesterol (in 1.3 times), triglycerides (in 1.32 times), LDLP (in 1.4 times) levels were significantly higher in DN2 group than DN1, blood plasma insulin was higher in DN2 group and suggested about involvement of insulin resistance into pathogenesis of DN. However, people in DN2 group used metformin with combination of sulfonilureas, whereas DN1 group mostly used metformin for lowering blood sugar.
Conclusion
DM2 patients with severe DN have higher BMI, blood lipids and plasma insulin level. Plasma insulin level have a linkage with DN severity in DM2 and play a role in the development of neurodegeneration.

DOI: 10.1530/endoabs.81.EP487

EP488

Salvage nephrectomy for a severe acute emphysematous pyelonephritis with septic shock: a case report

Maatougui Jasser[1], Raboudi Mehdi[1], Chayma Besrour[2], Ouertani Haroun[2] & Ghozzi Samir[1]
[1]The Military Hospital of Tunis, Urology, Tunis, Tunisia; [2]The Military Hospital of Tunis, Endocrinology, Tunis, Tunisia

Introduction
Emphysematous pyelonephritis is associated with high mortality rate. It is seen in patients with a long-standing diabetes. We report a case of a women presenting a septic shock following a severe acute right emphysematous pyelonephritis and requiring salvage nephrectomy.
Case report
A 52-year-old female presented fever with right flank pain. She had a long history of uncontrolled diabetes. Physical examination revealed a with high fever (39°) with tender right loin. Basic investigations reported high blood sugar (33 mmol/l) with HbA1c at 13.2%. Urinary labstix showed negative results for ketones. Biology found renal failure (Creatinine 243 μmol/l) with an hyperleukocytosis (23 × 109/l) and thrombocytopenia (85 × 109/l). kidney, ureter, and bladder (KUB) X-ray revealed no significant abnormality. Ultrasonography showed a right kidney with hydronephrosis upon a 8 mm lumbar ureteral calculus. Left kidney was normal. The diagnosis of acute obstructive right pyelonephritis has been established and antibiotherapy using cefotaxime, amikacin injection and insulin has been immediately started. A double J stent has been also inserted to drain right renal cavities. Despite those measures, our patient continued to be febrile, without improvement of biological parameters. Rapidly, she became sleepy with persistent hypotension, tachycardia and deterioration of renal function. Computed tomography, urgently performed, showed a right emphysematous pyelonephritis (stage III) with gas replacing almost all renal parenchyma and extrarenal extension to pararenal space (Figures 1). Based on the clinical and radiological features, Urologists has performed an urgent right salvage nephrectomy. The removed kidney was gangrenous. She had an uneventful recovery during 5 days in intensive care unit. She received imipenem for 21 days. Renal and tests and CBC normalized. Blood sugar became normal with insulin.
Conclusion
Emphysematous pyelonephritis occurs mostly in patients with diabetes and a predilection for females. It has a high fatality rate. Therefore, aggressive medical with early surgical intervention is recommended.

DOI: 10.1530/endoabs.81.EP488

EP489

Ptosis and type 1 diabetes: fortuitous association?

Ramla Mizouri, Rym Ben Othman, Nadia Ben Amor, Faten Mahjoub, Selma Mohsen, Rihab Yamoun, Berriche Olfa & Jamoussi Henda
Institut National de Nutrition de Tunis, Service A, Tunis, Tunisia

Introduction
Diabetes is the cause of ophthalmological complications that are all the more severe when the balance of diabetes is precarious. Among the non-retinal ocular targets of diabetes is damage to the optic nerve. The diagnosis of diabetic mononeuritis should only be made after excluding other causes of neuropathy.
Observation
We report the case of a patient referred to our service for equilibration of diabetes. This is a 59-year-old patient, type 1 diabetic for 30 years, coronary stent 6 years ago. In addition, the patient presents a ptosis of the right eye which appeared two weeks ago. As part of the exploration of this symptomatology, a brain scan and a brain MRI were requested. The scan came back with no abnormalities. MRI showed moderate thickening of the optic nerve consistent with optic neuritis. The etiological investigation was continued by serological, enzymological and immunological tests. CMV and HIV serologies were negative. The angiotensin converting enzyme level was normal. Polymorphonuclear anti-cytoplasm antibodies and native anti-DNA antibodies also came back negative. On biology, he had a fasting blood sugar level of 25.1 mmol/l and a glycated hemoglobin of 12.9%. The patient was put under hygieno-dietetic rules, metformin and insulin therapy. The evolution was marked by the normalization of the glycemic figures after one week of hospitalization.
Conclusions
Optimal glycemic control reduces the risk of diabetic retinopathy but also of the occurrence of other ocular pathologies, in particular oculomotor damage and damage to the optic nerve responsible for reduced visual acuity.

DOI: 10.1530/endoabs.81.EP489

EP490

Association between severe COVID-19 pneumonia and characteristics of type 2 diabetes patients

Olfa Lajili, Zouaoui Chadia, Rim Rachdi, Bchir Najla & Haroun Ouertani
The Military Hospital of Tunis, Endocrinology and Nutrition Department, Tunis, Tunisia

Introduction
COVID-19 caused by SARS-COV-2 infection can lead to multi-organ injuries and significant mortality in severe and critical patients, especially among those individuals with type 2 diabetes. The aim of our study was to assess associations between severe COVID-19 pneumonia and clinical and biological characteristics of patients with type 2 diabetes.
Methods
This was a retrospective and descriptive study including 40 Tunisians patients hospitalized for severe form of covid 19. The study was conducted the Military Hospital of Tunis during a period of 3 months (April -June 2021). The diagnosis was retained by a positive RT-PCR test and by the radiological aspect on the chest scanner. Statistics were performed using SPSS 20.
Results
The averge age was 71 ± 8.57 years [58-85 years]. A male predominance was noted (71.4%). The averge BMI was 28.8 ± 5.6 kg/m^2. Two thirds of the patients were overweight and 35.7% were obese. The average duration of diabetes was 11.4 ± 4.3 years. Hypertension and dyslipidemia were noted in 71.4%, 28.6% of cases. Two thirds of our population (78.6%) were treated with oral antidiabetics et 21.4% with insulin. The mean CRP was 94.7 ± 42.3 mg/l. Dimer tests were positive in 43% of patients and 7.1% had cytolysis. Patients had severe COVID-19 pneumonia (> 50%) in 21.4% of cases. The average length of hospital stay was 12.4 ± 7.6 days. Patients with severe pneumonia had a longer length of hospital stay ($P < 0.001$) and a tendency to have a longer duration of diabetes ($P = 0.06$). Furthermore, we did not noted an association between age, BMI, insulin treatement and CRP level, and severe COVID-19 pneumonia ($P = 0.4$, $P = 0.6$, $P = 0.7$ and $P = 0.5$ respectively).
Conclusion
Our study showed that severe COVID-19 pneumonia was associated with length of hospital stay in patients with type 2 diabetes. Further studies need to be done, to understand the relationship between severe COVID-19 pneumonia and characteristics of patients with type 2 diabetes, to provide special treatment for this high-risk population.

DOI: 10.1530/endoabs.81.EP490

EP491

Sulphonylureas induced hypoglycemia: a negleted cause of focal encephalopathy

Leonor Lopes, Carlos Bello, Maria Clotilde Limbert & João Sequeira Duarte
Hospital Egas Moniz, Endocrinology, Portugal

Introduction
Sulphonylureas (SU) are an effective therapy for type 2 diabetes (T2DM). As insulin secretagogues, hypoglycemia is a potencial adverse effect. Hypoglycemia may cause neuroglycopenic brain injury, which can mimetize stroke and infections of the central nervous system.
Case Report
The authors report the case of an autonomous 71 year-old woman, with medical history of hypertension and T2DM, treated with enalapril and gliclazide, that was admitted in the Emergency Room after being found unresponsive at home. The first medical evaluation revealed: GCS 14, hypertension (172/85mmHg) and capillary blood glucose of 28 mg/dl. Complete neurological exam showed left hemiparesis and aphasia, being stroke the most probable diagnosis.Patient was admitted to the Neurology floor. No ischemic lesion or hemorrhage were found in two separate cerebral MRIs. All other exams were normal, including: holter, cardiac ultrasound, carotid doppler, EEG and lumbar puncture. Blood workup was unremarkable, without signs of infection or inflammatory disease. A1C hemoglobin was 5.7%. All symptoms and deficits remitted after SU discontinuation. After excluding differential diagnosis, it was assumed the diagnosis of neuroglycopenia with focal neurological deficits caused by treatment with SU.
Conclusion
Nowadays, with the development of new antidiabetic drugs, the use of SU has been reduced. The risk of SU induced hypoglycemia is relevant, mainly in the elderly. Cognitive and mental impairment are the most frequent symptoms of hypoglycemia. In rare cases, hypoglycemic encephalopathy with focal deficts may occur. Being a reversible cause of injury, its peremptory diagnosis is relevant.

DOI: 10.1530/endoabs.81.EP491

EP492

Diabetic muscle infarction: a case study

Ons Maaoui[1], Sabrine Mekni[1], Senda Ben Rebai[1], Imen Rojbi[1], Youssef Lakhoua[1], Nadia Mchirgui[1], sahar agerbi[2], Soumaya Chargui[2], Nada Sallemi[2], Ibtissem Ben Nacef[1] & Karima Khiari[1]
[1]Hospital of charles Nicolle, Endocrinology, Tunisia; [2]Hospital of Charles Nicolle, Nephrology, Tunisia

Introduction
Diabetic muscle infarction (DMI) is a rare complication of long-standing, poorly controlled diabetes, and it's more common in patients with micro-vascular complications. Herein, we present a case of DMI occurring in patient on hemodialysis.
Case presentation
A 44-year-old man on maintenance hemodialysis presented with an acutely painful and swelling in his left calf. He had a 21-year history of poorly controlled type one diabetes, with micro-vascular complications (nephropathy and retinopathy). On physical examination: his skin was pale, his temperature was 37°c, his heart rate was 80 beats per minute and his blood pressure was 150/80 mmHg. His left calf was swollen and tender with no edema or inflammatory signs. Biochemical findings showed: C-reactive protein (CRP) 42 mg/l, CPK 179 U/l (39-308) and LDH 382 U/l (140-280). A Doppler ultrasound showed no sign of deep vein thrombosis, but demonstrated edema of the superficial tissues which prompted the practice of an MRI showing thickening of the lateral gastrocnemius muscle with edema. It is the seat of a lack of enhancement extending over 3 cm with the interposition of a few fibers of marked enhancement. The thickening and muscle edema was more important in the posterior compartment of the leg. It also showed edematous infiltration of fascia and subcutaneous cellulitis without significant enhancement and minimal fatty degeneration of the different muscle compartments of the leg. The patient was put on analgesics and activity restriction in the acute phase followed by gradual mobilization.
Conclusion
Diabetic muscle infarction is a rare and under-reported condition that should be suspected in any diabetic dialysis patient who develops a painful, swollen muscle.

DOI: 10.1530/endoabs.81.EP492

EP493

Quality improvement project; Recognition and management of Hyperosmolar Hyperglycemic State (HHS)

Adnan Adnan, Tahir Omer & Abaid-Ur Rehman
Northampton General Hospital, United Kingdom

Introduction
Hyperosmolar Hyperglycemic State (HHS) is an uncommon and potentially fatal complication of diabetes. HHS is a medical emergency with high mortality. Therefore, it needs to be managed promptly and carefully utilising nationally agreed guidance. Delays in recognition and challenges in management may lead to poor outcome.
Aim and Targets
The primary objective is to improve the recognition and management of HHS. The project was set to the standards of the HHS guideline produced by the Joint British Diabetes Societies (JBDS) in August 2012. Our target is to improve adherence with this national guidance by at least 50% by May 2022.
The Project
A retrospective audit was undertaken initially to understand the current local care of patients admitted with HHS. this was conducted in a single district general hospital. Data were collected from the medical notes of patients with a diagnosis coded as "Hyperosmolar Hyperglycemic State/HHS" in the proceeding 12 months. The data clearly demonstrated that the current local practice falls short of the JBDS recommendation for HHS. This spanned from identification to management (rehydration, insulin therapy and monitoring) of HHS.
Intervention
A number of interventions to increase awareness and improve the management of patients admitted with HHS were applied simultaneously. In addition to teaching sessions for clinicians working in acute medical admission wards, an HHS prescription chart was introduced with details about the diagnostic criteria and further management of HHS and possible metabolic complications based on the JBDS guideline. This was structured in an easy step by step approach.
Discussion and conclusion:
HHS is an uncommon medical emergency and sometimes it's the first presentation of Type 2 diabetes. Moreover, it usually co-presents with other medical conditions (infections, vascular events etc) which makes the recognition more challenging. A second audit to gauge the degree of improvement the interventions contributed to the care of patients with HHS is currently being prepared. This will contribute to further interventions to the already established prescription charts and education sessions as deemed required. This project provides a useful learning opportunity for quality improvement and patient safety contributing to better patient care.

DOI: 10.1530/endoabs.81.EP493

EP494

Clinical cardiovascular autonomic neuropathy (CAN) and amputations - a sinister combination for the quality of life in diabetes

Daniel Cosma[1], Cristina Alina Silaghi[2] & Horatiu Silaghi[3]
[1]Horezu City Hospital, Diabetes, Nutrition and Metabolic Diseases Outpatient Clinic, Horezu, Romania; [2]"Iuliu Hatieganu" University of Medicine and Pharmacy, Endocrinology Department, Cluj-Napoca, Romania; [3]"Iuliu Hatieganu" University of Medicine and Pharmacy, 5th Department of Surgery, Cluj-Napoca, Romania

Introduction
Diabetic autonomic neuropathy (DAN) and CAN as one of its most common manifestations are serious complication of type 1 and type 2 diabetes mellitus leading to a significant increase in morbidity and mortality.
Case presentation
A 51-year old male, diagnosed with T2DM for 25 years, complicated by stage III diabetic polyneuropathy, proliferative retinopathy and several amputations on both feet, treated with Metformin (2g/day), Glargine (26 IU/day) and Aspart (21 IU/day), was admitted in our center for: neuropathic ulceration on the plantar surface of the 4th metatarsal head, hyperglycemia on self-monitoring, dry mouth, nocturnal enuresis (3 times/night), blurred vision and deep muscle cramps in the calves with insidious onset, lasting for 15-20 minutes and alleviated by Cilostazol administration. One year prior to current admission, he was diagnosed with Monckeberg sclerosis. On admission: altered general status, BP = 120/80 mmHg, Pulse = 88b/min, symptomatic orthostatic hypotension, rhythmic cardiac sounds with stage III holosystolic murmur on the entire cardiac area, diminished peripheral pulses, multiple ecchymosis after insulin injection in the right lumbar region, bilateral plantar hyperkeratosis, interdigital maceration at the level of the 3rd and 4th space of the left foot. Lab exams revealed: inflammatory syndrome,

iron deficiency anemia, hypocalcaemia and poor glycemic control (A<ce:inf>1</ce:inf>c = 10.19%). The foot surgeon removed the affected soft tissue including the 4th metatarsal joint of the left foot. Under antibiotic therapy with Clindamycin (i.v) and Ciprofloxacin, α-lipoic acid, benfotiamine, aspirin, atorvastatin, cilostazol and iron substitution, the clinical evolution was slowly favorable. The plague culture was negative, possible in the context of prior Amoxicillin Clavulanate administration before hospital admission. Given his clinical presentation, a Cardiosys evaluation was performed, which confirmed the CAN diagnosis. In order to decrease the number of the symptomatic orthostatic episodes, 0.1 mg/day of Fludrocortisone was initiated under 24 h BP monitoring. The therapeutic education with emphasis on carbs ingestion, blood glucose self-monitoring and foot care was resumed.

Conclusions

This case illustrates typically the negative impact of peripheral and clinical CAN association on the quality of life (QoL). Unfortunately, the poor prognosis in this case relies mostly in the lack of adherence to the medical therapy and foot care.

DOI: 10.1530/endoabs.81.EP494

EP495

The prevalence of diabetic peripheral neuropathy among the futsal players participating in the DiaEuro 2017 Championship

Daniel Cosma[1], Cristina Alina Silaghi[2] & Horatiu Silaghi[3]
[4]Horezu City Hospital, Diabetes, Nutrition and Metabolic Diseases Outpatient Clinic, Horezu, Romania; [2]"Iuliu Hatieganu" University of Medicine and Pharmacy, Endocrinology Department, Cluj-Napoca, Romania; [3]"Iuliu Hatieganu" University of Medicine and Pharmacy, 5th Department of Surgery, Cluj-Napoca, Romania

Objectives

To assess the prevalence of diabetic peripheral neuropathy (DPN) among futsal players participating in the 2017 edition of the European Futsal Championship for people with diabetes (DiaEuro).

Methods

In this cross-sectional study were included 94 amateur/professional futsal player, from 9 European countries. The evaluation was made based on the data extracted from the standard medical certificate completed by each player's diabetologist. The official participation criteria were: age ≥ 18 years old, a diagnosis of diabetes and no other severe comorbidities that could contraindicate this type of sport.

Results

Of 94 subjects, 90 (95.74%) had type 1 diabetes, 3 (3.19%) had type 2 diabetes, and one player had type 3c diabetes secondary to chronic pancreatitis. 3 players were on oral medication, one was on diet therapy and 90 players (95.74%) were under insulin treatment as follows: 78 (82.97%) on a basal bolus regimen and 12 (12.76%) on insulin pump. Regarding the diabetes microvascular complication, 2 (2.12%) individuals were diagnosed with DPN and 3 (3.19%) with retinopathy and 6 (4.31%). Furthermore, only one subject out of the 2 with DPN received treatment with alpha-lipoic acid for his condition.

Conclusions

In our analysis of 94 amateur/professional futsal players with diabetes, we found a prevalence of 2.12% of DPN.

Parameter	Interval (min-max)	Mean	STDEV
Age (years)	18 - 55	27.74	±8.23
Diabetes duration (years)*	1 – 39	12.21	±7.34
Last A_1c (%)*	5.3 -10.5	7.31	±0.99

The general characteristics of the study population; *Data were available for 91 subjects; STDEV = standard deviation; A1c = glycated hemoglobin

DOI: 10.1530/endoabs.81.EP495

EP496

Metabolic complications of obese Tunisian adults

Zeineb Zemni[1], Olfa Lajili[2], Nadia Ben Amor[1], Emna Bornaz[1], Ben Ali Khaoula[3], Eya Safi[3], Ramla Mizouri[1], Ryme Ben Othmen[1], Faten Mahjoub[1], Olfa Berriche[1] & Henda Jamoussi[1]
[1]National Institute of Nutrition of Tunis, Unit of Obesity Research, Tunis, Tunisia; [2]Military Hospital of Instruction of Tunis, Department of Hygiene, Tunis, Tunisia; [3]Military Hospital of Instruction of Tunis, Endocrinology Department, Tunis, Tunisia

Introduction

Obesity is a major health problem through its numerous complications especially metabolic complications associated with cardiovascular risk. The aim of our work was to describe the clinico-metabolic profile of obese Tunisian adults.

Methods

This was a descriptive cross-sectional study involved 174 obese patients who consulted between July and December 2020 at the Obesity Unit of the National Institute of Nutrition in Tunis.

Results

The average age was 45.21 ± 13.88 years with a female predominance of 75.3%. All patients were obese with an average BMI of 40.2 ± 7 kg/m^2. Obesity was visceral in 100% of cases with a mean waist circumference of 121.05 ± 14.4 cm (men 123.93 ± 14.01 cm vs women 120.11 ± 14.45 cm).Arterial hypertension was noted in 47.13% of our population of which 15.85% were not known hypertensive. Dyslipidemia was found in 54.6% of cases of which 45.26% were unknown. Carbohydrate tolerance disorders was found in 67.81% of cases devised as follow: 37.36% prediabetes; 24.71% diabetes and 5.17% unknown diabetes. Hyperuricemia was found in 33.3% of cases. No patients were symptomatic. Waist circumference Was significantly correlated with BMI (r = 0,62;P < 0,001)), as was triglycerides (r = 0,16; P = 0,039).

Conclusion

In our study metabolic disorders were of incidental discovery in many patients. Their treatment must be specific, it should not be limited to weight loss, and the early detection of these abnormalities and their management will improve the cardiovascular prognosis of patients.

DOI: 10.1530/endoabs.81.EP496

EP497

Metabolic profile of morbid obesity compared to moderate and severe obesity: What particularities?

Soumiya Berrabeh[1], Lamiae Zarraa[1], Achwak Alla[1], Salma Derbel[1], Ouafae Elmehraoui[1], Tahri Abir[1], Dounia Zerrouki[1], Siham Rouf[2,3] & Hanane Latrech[2]
[1]Mohammed VI University Hospital Center Oujda, Faculty of Medicine and Pharmacy Oujda, University Mohammed First Oujda, Endocrinology-Diabetology and Nutrition Department, OUJDA, Morocco; [2]Mohammed VI University Hospital Center Oujda, Faculty of Medicine and Pharmacy Oujda, University Mohammed First Oujda, Morocco, Endocrinology-Diabetology and Nutrition Department, Laboratories of Epidemiology, Clinical Research and Public Health, OUJDA, Morocco; [3]Faculty of Medicine and Pharmacy of Oujda, Mohamed the First University, Laboratory of Epidemiology, Clinical Research and Public Health, Oujda, Morocco

Introduction

The prevalence of obesity is increasing in the world. It constitutes a major risk factor associated with diabetes, hypertension, dyslipidemia and cardiovascular diseases. The aim of our work is to compare the metabolic profile of morbid obesity with that of moderate to severe obesity.

Patients and methods

It is a Retrospective, descriptive and analytical study, including 63 obese patients, followed at the endocrinology, diabetology and nutrition department of the CHU Mohamed VI Oujda. The patients were divided into two groups: Group 1 (G1: moderate to severe obesity): 37cases (BMI:30 to 40 kg/m^2), Group 2 (G2: morbid obesity): 26 cases (BMI ≥ 40 kg/m^2). Collected data were analysed using SPSS V24 software.

Results

The mean age of the patients was 30.5 ± 16.9 years in G1 and 39.8 ± 12.5 years in G2. A female predominance was noted in the 2 groups with a Sex-ratio F/M (G1) :2.7 and (G2):7.6. The mean BMI in G1 was 35 ± 2.9 kg/m^2 and 47.8 ± 5.9 kg/m^2 in G2. The mean waist circumference was higher in G2 (165.6 cm vs 111.2 cm). The prevalence of diabetes and pre-diabetes was 35.2% and 43.3% (G1) vs 30.7% and 38.5% (G2) respectively (P = 0.05). The prevalence of hepatic steatosis was higher in G2 compared to G1 (69.2% vs 48.6%) but without significant difference (P = 0.5).The mean uricemia was 54 ± 14.5 mg/l (G1) and 65.3 ± 12 5 mg/l (G2). In contrast, the prevalence of dyslipidemia was higher in G1 (32.4%) compared to the group having morbid obesity (26.9%) with a highly significant difference (P = 0.008).

Discussion/Conclusion
Obesity is an excess of body fat with harmful consequences for health. It has been defined as a disease by the World Health Organization since 1997 in view of its epidemic dimension and its somatic, psychological and socio-economic repercussions. The main metabolic complications of obesity are associated with the phenomenon of insulin resistance and are included in the metabolic syndrome. Several studies suggest that despite a greater accumulation of fat, morbid obesity is not characterized by a more deleterious metabolic profile than moderate and severe obesity. The results of our study are also in line with those of the literature, which show that the severity of obesity is not significantly correlated with metabolic risk.
Keywords
Morbid obesity, moderate and severe obesity, metabolic profile
DOI: 10.1530/endoabs.81.EP497

EP498

How to treat severe obesity due to binge eating in children?
Amalia Ioana Arhire[1,2]
[1]Elias Hospital, Endocrinology, Diabetes and Nutrition Department, Bucharest, Romania; [2]Kilostop Junior Nutrition Clinic, Endocrinology, Diabetes and Nutrition Department, Bucharest, Romania

Introduction
As the incidence of pediatric obesity is gaining pandemic levels, with children and teenagers developing obesity complications similar to the adult population, a rapid evaluation and treatment is necessary. We present such a case.
Case report
A 12-year-old male with a medical history of binge eating, treated by Topiramate, since the age of 11 and 3rd degree obesity, complicated with JNC stage II hypertension, NASH and dyslipidemia was referred to our clinic for nutritional assessment and treatment. He was referred by a colleague endocrinologist that evaluated his obesity for endocrinological causes, which were excluded. The clinical examination:Showed normal pubertal Tanner stage (P1G2), BMI 37.3 kg/m^2, height of 155 cm (75th centile), 51.4%fat, 205% obesity degree from the 95th centile, normal muscle mass of 23.7 kg, BP 150/90 mmHg and a waist circumference of 120 cm.
Laboratory
Dyslipidemia with HDL= 30 mg/dl, TG= 133 mg/dl:, insulin resistance HOMA-IR: 6, blood glucose= 82.5 mg/dl, an inflammatory status with a VSH=21, fibrinogen = 357, 25-OH vitamin D of 17 ng/ml, TSH of 2,71, normal salivary cortisol, IGF1, FSH, LH < 0.3, testosterone of 0.16 nmol/l and a prolactin of 293 mcUI/ml. The abdominal ultrasound showed liver steatosis. The basal metabolic rate (indirect calorimetry) - low of 1600 kcal (85%), correlated with the low muscle mass. The cardiology consult found normal ECG, JNC stage II hypertension, septal left ventricular hypertrophy and indicated treatment with Lisinopril 10 mg per day. We began a hypocaloric Mediterranean diet (400 calories daily deficit), moderate physical activity (45-60 minutes), low sodium intake, but the patient didn't lose weight for the first month of nutritional monitoring, so Liraglutide was introduced, with a 0.6 mg /day regimen, with dose titration every 2 weeks to avoid adverse effects, to a dose of 2.4 mg per day. He received Omega 3(2000 mg) and 2000 UI vitamin D per day. After 1 month of diet and Liraglutide, the binge eating improved, he lost 2% of body fat and the BP normalized. Also, the eating disorder improved.
Conclusion
The metabolic syndrome that complicates obesity is a frequent condition in adults with increasing incidence in children. As more and more children develop severe complicated obesity, before the age for bariatric surgery, more pharmacological treatment is needed and clear and standardized cut-offs for the metabolic syndrome definition is necessary.
DOI: 10.1530/endoabs.81.EP498

EP499

Lipid profile of the obese: about 100 cases
Rym Ben Othman[1], Ramla Mizouri[2], Amany Amorri[3], Nadia Ben Amor[1], El Amri Abir[3], Berriche Olfa[2], Faten Mahjoub[1] & Jamoussi Henda[3]
[1]Faculty Of Medicine of Tunis, Tunisia; [2]Institut National de Nutrition de Tunis, Tunisia; [3]University of Tunis El Manar, Tunisia

Obesity is a major public health problem. It is a privileged provider of a constellation of metabolic abnormalities, particularly lipids, increasing the risk of morbidity and mortality and hampering the quality of life of the obese.
Material and methods
We conducted a prospective study on 100 obese patients recruited at the Human Obesity Research Unit at the National Institute of Nutrition in Tunis. Our patients benefited from an assay of fasting insulinemia and a complete lipid profile including the assay of cholesterol, triglycerides, HDL-cholesterol with calculation of LDL-cholesterol and non-HDL-cholesterol.
Results and Statistical Analysis
The average age of our population is 37 $\pm$ 10.8 years. The average BMI is 38 $\pm$ 6.7 kg/m^2 with extremes of 30 and 67 kg/m^2. Mean fasting insulinemia is 24.7 $\pm$ 20.1 µU/ml with extremes of 5.3 and 146 µU/ml. One-third of obese people have high fasting insulin levels. Hypertriglyceridaemia is noted in 19% of obese patients. 29% of obese people have hypercholesterolemia. More than a quarter of obese people (27%) have low HDL-cholesterol levels below 1.03 mmol/l (0.4 g/l). On the other hand, 14% of patients have an HDL-cholesterol level greater than or equal to 1.55 mmol/l (0.6 g/l). The average non-HDL cholesterol is 3.35 $\pm$ 0.9 mmol/l (1.3 $\pm$ 0.36 g/l). The average LDL-cholesterol of 2.81 $\pm$ 0.85 mmol/l (1.09 $\pm$ 0.33 g/l) with extremes of 1 and 6 mmol/l (0.39 and 2.32 g/l). Hyper LDLemia was discovered in 29.3% of obese patients. The duration of evolution of obesity is positively and significantly correlated with the elevation of cholesterolemia ($P = 0.001$), LDL-cholesterol ($P = 0.002$) and non-HDL-cholesterol ($P = 0.001$). The rise in fasting insulinemia is positively and statistically correlated with the rise in cholesterolemia ($P = 0.001$), LDL-cholesterol ($P < 10-3$), non-HDL-cholesterol ($P < 10-3$). A negative and statistically significant correlation was also noted between fasting insulinemia and HDL-cholesterol ($P = 0.02$).
Conclusion
The lipid profile of the obese is highly atherogenic. It is distinguished by a variety of lipid abnormalities dominated by elevated LDL-cholesterol, total cholesterol and triglycerides with hypo-HDLemia justifying their early management in order to improve their cardiovascular prognosis.
DOI: 10.1530/endoabs.81.EP499

EP500

Comparative study of epidemiological, clinical and paraclinical characteristics between a group of complicated obese versus uncomplicated obese: about 400 cases
Fatma Mnif, Mariem Souissi, Dhoha Ben Salah, Khouloud Boujelben, Kawthar El Arbi, Mouna Mnif, Nabila Rekik Majdoub, Mouna Elleuch, Nadia Charfi & Mohamed Abid
Hedi Chaker Hospital, Sfax, Tunisia

Introduction
Obesity, through its complications, influences the functional and vital prognosis. The search for these complications constitutes a major axis of the management of the obese patient, independently of the weight loss. The objective of this work is to focus on the different complications of obesity and to identify, through a comparative study between two groups of obese patients, complicated versus uncomplicated, the different predictive factors of the occurrence of these different complications, especially arterial hypertension and cardiovascular complications.
Patients and methods
This is a retrospective comparative study of 400 obese patients, hospitalized and followed in the endocrinology and diabetology department of the Hedi Chaker Hospital in Sfax. These patients were subdivided into 2 groups: G1: 264 patients with at least one complication of obesity and G2: 136 uncomplicated obese patients.
Results
The mean age of our complicated patients was significantly higher than that of the uncomplicated ones (46.29$\pm$17.377 years versus 33.97$\pm$12.08 years), ($P = 0.0001$). A significant female predominance was noted in our complicated and uncomplicated obese groups ($P = 0.0001$). 78.7% of group 1 and 86% of group 2 had a family history of obesity ($P = 0.05$). Anthropometric parameters (weight, BMI, waist circumference (WC) waist circumference/hip circumference (WC/TH) and systolic and diastolic blood pressure values were significantly higher in the complicated obese group. It was noted that high BMI positively influences the occurrence of hypertension, cardiovascular, respiratory and osteoarticular complications. In addition, high waist circumference was significantly involved in the development of hypertension, hyperlipidaemia and cardiovascular, respiratory, skin and osteoarticular complications. Lean body mass and fat mass are significantly higher in our complicated obese than in our uncomplicated obese. The saturated fatty acid (SFA) intake in% is significantly higher in uncomplicated obese patients. The comparison between G1 and G2 regarding metabolic parameters shows that these are higher in G1 than in G2. Only alanine aminotransferase (ALT or SGPT) was higher in G2 than in G1.
Conclusion
The knowledge of the factors influencing the occurrence of these complications could help us to better treat them but especially to better prevent them. The treatment of obesity and its complications is certainly a challenge for all health care providers today, but prevention is still the best way to fight against this burden.
DOI: 10.1530/endoabs.81.EP500

EP501

Assessment of depression in diabetics with erectile dysfunction (ED): 37 cases

Kolsi Boulbaba[1], Rihab Ben Abdallah Kolsi[2], Mohamed Dammak[3], Khouloud Boujilbéne[3], Kawthar Elarbi[3], Asma Zargni[3], Faten Hadj Kacem[3] & Mohamed Abid[3]
[1]CHU Hedi Chaker Sfax Tunisia, Endocrinology and Diabetology, Sfax, Tunisia; [2]Faculty of Sciences of Sfax, FSS Tunisia, Biology, Tunisia; [1]CHU Hedi Chaker Sfax Tunisia, Endocrinology and Diabetology, Sfax, Tunisia

Introduction
Diabetes is a disease that can slowly be. Among its complications, erectile dysfunction can appear. Be careful, these problems can be warning signs. These problems can be warning signs, especially cardiovascular, but they also have significant psychological retention.
Materials and methods
Prospective study on 37 diabetic patients collegiate in the department of Endocrinology CHU Hedi Chaker Sfax Tunisia. All patients are assessed for erectile function by the International Index (IIEF 5) and screened for depression using the Beck Scale (BDI).
Results
The majority of our hospitalized patients (80.5%) were between 45 and 70 years old. As well as 60.25% of diabetics had diabetes evolving for more than 16 years. The mean blood glucose at young was 18 mmol/l with HbA1c at 9%. Only 20% had a normal sex life. Erectile dysfunction is found in 72% of cases; it is severe in 8% of patients, moderate in 12% of cases, mild to moderate in 22% of cases and mild in 30% of cases. Concerns are all the more frequent as the diabetic disease is old, and especially poorly controlled, 77% of poorly controlled diabetics are subject to erectile disorders against 64% for those whose pathology is under control. According to the Beck Scale (BDI), 54% of our patients had experienced a feeling of sadness, of which 14% were unable to cope.
Conclusion
When the chronic complications of diabetes are already present, almost 75% of patients also have erectile dysfunction. A consequence that alters the quality of life. Only 25% of nurses are interested in the psychological side of diabetics with erectile dysfunction, of which 70% encourage them to consult a psychiatric hospital.

DOI: 10.1530/endoabs.81.EP501

EP502

Obesity and lifestyles related to diabetes during COVID-19 pandemic

Virgínia Regufe
Faculty of Medicine of the University of Porto, Porto, Portugal

Diabetes is mainly a consequence of the lifestyle of the current population, characterized by an increase in obesity, sedentarism and a highly caloric diet, added to which is an ageing population. Prevention and its treatment consist in following an adequate diet, practising physical exercise regularly and maintaining normal weight, factors which are achieved through the adoption of healthy lifestyles. However, weight loss remains a problematic issue among diabetics, mainly due to the fact that the diabetic individual neither understands nor incorporates the need for significant alterations in his lifestyle. The current COVID-19 pandemic has drawn, once again, our attention to the problem of obesity. This study depicts the analysis of residents in a neighbourhood in greater Porto, Portugal. The data collection derived from the answers of a questionnaire highlighted the existence of various factors that contribute to the development of obesity over a long period of time, being behavioural patterns one of the most impactful causes as they are related to our lifestyle. Repeated lockdowns were responsible for a decrease in the practice of physical activity and changes in the eating habits of the Portuguese population in general, resulting in an increase in the consumption of fizzy drinks, fried and fast food, processed meals, frequent intake of food and, consequently, weight gain. The present pandemic has also contributed to a rise in a sedentary behaviour exemplified by prolonged periods of time spent watching TV or on other technological gadgets (cell phone, laptop, etc.), attending online classes and working from home, aspects which increase the risk of obesity and diabetes. Smoking, the lack of physical activity and a poor diet also add to the increase in weight and poor glycemic control. There are, however, lifestyle alteration programs which include a variety of procedures to overcome obstacles regarding weight loss. In fact, significant changes in lifestyle appear to be associated with a greater weight loss e better glycaemic control.

DOI: 10.1530/endoabs.81.EP502

EP503

Inadequate iodine intake in lactating women in the inland area of norway

Tonje Eiane Aarsland[1, 2], Siri Kaldenbach[3, 4], Beate Stokke Solvik[1, 2], Kjersti S. Bakken[1, 2] & Tor Arne Strand[2, 5]
[1]Innlandet Hospital Trust, Lillehammer, Norway, Women's Clinic, Lillehammer, Norway; [2]University of Bergen, Department of Global Public Health and Primary Care, Bergen, Norway; [3]Innlandet Hospital Trust, Lillehammer, Norway, Department of Paediatric and Adolescent Medicine, Lillehammer, Norway; [4]University of Oslo, Clinical Medicine, Oslo, Norway; [5]Innlandet Hospital Trust, Lillehammer, Norway, Research Department, Lillehammer, Norway

Background
Many studies in Norway have found inadequate iodine status in pregnant and lactating women, but no studies have been undertaken in a random, population-based sample. Globally, the main strategy to eliminate iodine deficiency is iodization of salt. However, this is not compulsory in Norway, where the current legislation only permits iodization up to 5 µg per gram of salt. To reach the Nordic Nutrition Recommendation (NNR) of 200 µg/day iodine, supplements are recommended to lactating women who do not cover their needs through food sources. In Norway, the main iodine sources in the diet are milk and lean seafood. A study in 130 lactating women in 2018 revealed that mild-to-moderate iodine deficiency was common in the inland area of Norway. Considering the importance of iodine for infant development, more information on iodine status in lactating women is needed.
Objective
This study aimed to evaluate iodine status and intake in a random sample of lactating women and their infants in the inland area of Norway.
Methods
From April 2020 to October 2021, 366 mother-infant pairs were recruited in a cross-sectional study through public health care centers. Urine samples from the mothers and children and breast milk samples were collected for analysis of iodine concentration. Data on habitual and recent iodine intake was collected using food frequency questionnaire (FFQ) and 2 x 24-h dietary recall (24HR), respectively.
Results
Urinary iodine concentration (UIC), breast milk iodine concentration (BMIC) and data from FFQ are pending analyses. Recent use of iodine-containing supplements was reported by 30.1 % of the women. Including supplements, the estimated 24 h median (IQR) iodine intake was 125 (70.8, 233.45) µg/day. Excluding supplements, the 24 h median (IQR) iodine intake was 100.1 (65.05, 161.5) µg/day. According to the 24 HR, the food sources that contributed the most to the iodine intake were milk and dairy products, carbonated mineral water from a specific water source in Larvik (Norway), lean fish, whey cheese and eggs. More than two-thirds of the 24HR (68.2 %) had an estimated iodine amount below the NNR recommendation for lactating women.
Conclusion
We found inadequate iodine intake in lactating women in the inland area of Norway. Milk, lean fish, eggs, and a specific type of carbonated mineral water were important iodine sources in the diet. The study indicates that a large proportion of lactating women in Norway may need iodine-containing supplements due to a low dietary iodine intake.

DOI: 10.1530/endoabs.81.EP503

EP504

Metabolic burden in mediterranean patients with schizophrenia and psychotic disorders

AbdelMouhaymen Missaoui[1], Salem Jdira[2], Oumeyma Trimeche[1], Houda Hsine[2], Wafa Abbes[2] & Ines Khochtali[1]
[1]Fattouma Bourguiba University Hospital, Endocrinology Departement, Monastir, Tunisia; [2]Gabes Regional Hospital, Department of Psychiatry, Gabes, Tunisia

Introduction
Mortality among patients with schizophrenia and psychotic disorders(SAPD) is two to threefold higher than in the general population and is widely attributed to cardiovascular and metabolic morbidity.
Objectives
We aim to highlight the metabolic profile of Mediterranean patients diagnosed with SAPD.
Methods
We conducted a descriptive and analytical cross-sectional study involving 55 patients who attended the psychiatry department at Gabes regional hospital, Tunisia, from 2019 to 2020. SAPD were diagnosed according to the DSM-5. MetS was defined based on the 2005-IDF criteria.

Results
The mean age was 46.8±11.1 years with a male predominance(74.5%). The majority were single(54.5%), from rural areas(52.7%), low-educational backgrounds(65.5%), and low-socioeconomic status households(74.5%). Addictive behaviors were reported in 49.1% mainly tobacco(45.5%). Suicidal behavior was noticed in 9.1%. Schizophrenia and schizoaffective disorder were the leading diseases in 72.8% and 16.4%, respectively. Obesity was the most common metabolic comorbidity in 30.9%. Dyslipidemia, diabetes, and hypertension were recorded in 20.0%, 14.5%, and 1.8%, respectively. The prevalence of MetS was 29.1%. MetS was significantly associated with female gender ($P=0.046$) and atypical antipsychotics prescription ($P=0.018$).
Conclusions
Patients with SAPD are five times more prone to develop MetS than healthy patients. Increased insulin resistance was substantiated in antipsychotic-naive patients. Besides common genetic predispositions to both MetS and schizophrenia suggested by some researchers, this population often has a poor lifestyle, little physical activity, and an unhealthy diet. That could be partially related to negative symptoms of psychotic disorders and drug-induced sedation. Second-generation antipsychotics seem to increase the risk of insulin resistance, obesity, and diabetes by the antagonism at serotonin 5-HT2c receptors.

DOI: 10.1530/endoabs.81.EP504

EP505

Hepatic steatosis and cardiovascular risk in type 2 diabetes

Ines Bani, Zohra Hadj Ali, Meriam Dalhoum, Yosra Htira & Feika Ben Mami
National Institute of Nutrition of Tunisia, Department C, Tunis, Tunisia

Introduction
Non-alcoholic fatty liver disease (NAFLD), is a frequent cause of chronic liver disease and is widely associated with metabolic syndrome. When associated with diabetes, it can increase the risk of cardiovascular events. The aim of this study is to evaluate the relationship between hepatic steatosis and the occurrence of cardiovascular events in patients with type 2 diabetes.
Method
It is a retrospective study, including 184 type 2 diabetic patients, conducted in the department C of the National Institute of Nutrition of Tunis during the year 2021. The diagnosis of hepatic steatosis was retained by an abdominal ultrasound.
Results
Our population was composed of 66 men and 118 women. The mean age of the patients was 61 +/- 10 years, and the average duration of diabetes was 13 +/- 8 years. The prevalence of NAFLD was 29.3%. A clear female predominance was noted in patients with NAFLD(77.8%). Diabetic patients with NAFLD had dyslipidemia in 88.9%. The majority of patients had poorly controlled diabetes with a mean HB1AC of 10.4 +/- 2%. The average body mass index of these patients was 35+/- 5 kg/m^2. Hepatic steatosis is positively correlated with coronary artery disease ($P=0.016$) and high blood pressure ($P=0.000$). Morever a significant association was noted with hyper uricemia ($P=0.021$) and obesity ($P=0.000$).
Conclusion
The coexistence of type 2 diabetes and NAFLD increases the occurrence of cardiovascular events and disturbs the glycemic balance of diabetic patients, which underlines the importance of screening for this hepathopathy.

DOI: 10.1530/endoabs.81.EP505

EP506

Clinical and biochemical outcomes of sodium-glucose co-transporter-2 (SGLT2) inhibitors in type 2 diabetes mellitus patients as a fourth oral anti diabetic medicine

Muhammad Saleem, Nanik Ram & Sajjad Ali Khan
Aga Khan University Hospital, Section of Diabetes, Endocrinology and Metabolism and Department of Medicine, Aga Khan University Hospital, Karachi, Pakistan. , Karachi, Pakistan

Objectives
to evaluate the clinical and biochemical effects of (SGLT2) inhibitors as a fourth oral anti-diabetic drug in patients with type 2 diabetes mellitus (T2DM).
Patients (Materials) and Methods
In a tertiary hospital in Karachi, Pakistan, a retrospective assessment of patient medical records was conducted from January 1, 2017 to December 31, 2020.A total of 100 patients (mean age [Standard Deviation]: 53.8 [9.63] years) with poorly controlled T2DM were included. Data was collected before the SGLT-2 inhibitor was added, as well as three and six months after the medicine was started. Weight, Body Mass Index, blood pressure (BP), HbA1c, SGPT, and Creatinine were measured at the start and during the study
Results
There was a significant reduction in HbA1c (P-value < 0.001) with (Mean Reduction [Standard Deviation]) 0.81[1.02] % at 3 months and 1.07[1.11] % at 6 months, Weight (P-value < 0.001) with (MR [SD]) 1.83[2.32] kg at 3 and 4.02[6.04] kg at 6 months, BMI with 0.69[0.95] kgm-2 at 3 months and 2.13[3.41] kgm-2 at 6 months of follow up. Systolic Blood Pressure showed significant reduction (P-value < 0.05) of 5.9[15.76] mmHg at 3 months and 6.37[18.33] mmHg at 6 months. Mild variation in creatinine and SGPT was also noted.
Conclusions
SGLT-2 is a safe and effective oral anti-diabetic medicine that can help individuals with diabetes who are currently using glucose-lowering or anti-diabetic medications. These medications can be used as an alternative to injectable insulin for people who do not want to use it, and they can help diabetic patients stick to their regimen.
Keywords
SGLT2 Inhibitors, T2DM, Weight loss

DOI: 10.1530/endoabs.81.EP506

EP507

Verapamil can be used as a type 2 diabetes mellitus saviour and stopping the need for insulin in uncontrolled type 2 diabetes mellitus

Mahmoud Younis
Egypt Ministry Of Health, Endocrinology, Kafr Elsheikh, Egypt

Introduction
Diabetes mellitus is not just a disease as it is already known, the matter is more complicated, and it is considered as an assembly of metabolic defects with end result of hyperglycemia. verapamil can decrease the expression of thioredoxin-interacting protein (TXNIP), which is recognized as an important factor in pancreatic beta cells. verapamil could enhance beta cell mass and function.
Materials and methods
160 type 2 diabetes mellitus and hypertensive patients into 2 parallel groups. Each group had 80 patients, 50 males and 30 females. All patients were monitored in a private clinic. All the patients Lied between 30-60 years old. All patients are on maximum doses of glimepiride, sitagliptin, metformin and empagliflozin but are uncontrolled on this combination with hba1c more than 8. The first group received verapamil 240 mg as substitute or added to the present hypertension therapy for 6 months. The second group was still on hypertensive therapy but received lantus 20 units added to the oral therapy. We measured hba1c and c-peptide levels in the 2 groups at the start of the trial and after 6 months of the trial.
Results
The results show a statistically significant difference in hba1c in group 1 patients before and after 6 months of treatment with verapamil With P value less than 0.0001. The results show statistically significant difference in hba1c in group 2 patients with P value less than 0.0001. The results show significant differences in c-peptide levels in group 1 patients before and after 6 months of treatment of verapamil. The results show non-significant differences in c-peptide levels in group 2 patients before and after 6 months treatment of basal insulin with b value 0.9822. The results show significant difference in hba1c after 6 months of treatment of verapamil vs. basal insulin with b value less than 0.0001. Results also show that verapamil can increase c-peptide levels after 6 months of treatment.
Conclusion
Verapamil could be used as a type 2 diabetes saviour by increasing beta cell mass and function.
Key words: type 2 diabetes mellitus, verapamil, (TXNIP), beta cells

DOI: 10.1530/endoabs.81.EP507

EP508

Therapeutic optimization of type 2 diabetes: what role of the pharmacist?

Asmaâ Memou[1], Derouicha Matmour[2], Habiba Fetati[1], Nadjet Fatima Zohra Mekaouche[1], Fatma Boudia[1] & Houari Toumi[1]
[1]Faculte De Medicine D'Oran, Pharmacie, Oran, Algeria; [2]College of Medicine Taleb Murad, Pharmacie, Sidi Bel Abbès, Algeria

Introduction
Type 2 diabetes is a chronic disease whose management is characterized by the complexity of its therapeutic axes (methods of taking, storage of drugs, adverse effects, compliance with treatment, etc.), which requires the patient to be well informed to avoid the onset of complications. Faced with this issue, the pharmacist could make a real contribution.
Goal
The objective of this work was to assess what role the pharmacist could play in the therapeutic optimization of type 2 diabetes.
Matherials and methods
We conducted a descriptive study in patients with type 2 diabetes over a period of 03 months. We used a questionnaire comprising 04 parts: knowledge of antidiabetic drugs, assessment of compliance (Morisky's questionnaire), drug iatrogenism and treatment monitoring.
Results
The study was carried out on 60 patients. Analysis of the results showed that 36.6% of patients on insulin did not master the injection technique, 51.7% did not know how to store the drugs and 40% were poor observers.
In addition, 66.7% exhibited adverse effects, 25% exhibited at least one drug interaction and 26.7% did not master the technique of self-monitoring of blood glucose.
Discussion
Our study revealed the existence of several gaps in these patients in terms of knowledge and proper use of their treatment and monitoring of their disease. This emphasizes the need for pharmacist involvement in therapeutic education programs for these patients in order to optimize their therapeutic management.
Keywords
type 2 diabetes, anti-diabetic drugs, pharmacist, compliance, therapeutic education.

DOI: 10.1530/endoabs.81.EP508

EP509

Is Semaglutide superior than Liraglutide in patients with type 2 diabetes on insulin therapy? - case presentation

Ivana Mickovski, Daniela Buklioska-Ilievska, Radmila Milosheska & Taner Hasan
City General Hospital 8 September, Skopje, North Macedonia

Type 2 diabetes (T2DM) is a chronic and progressive disease associated with microvascular and macrovascular complications leading to increased morbidity and mortality. Insulin remains the cornerstone therapy for longer-duration T2DM and b-cell failure. Glucagon-like peptide-1 receptor agonists are a class of multifactorial T2DM medications that have been shown to improve numerous risk factors for diabetes-related complications, including glycemic control, reduction in body weight and a low risk of hypoglycaemia. Improvements in glycaemic control confer a reduced risk of long-term diabetes-related complications. We reported here a case that provides the efficacy and safety of once-weekly semaglutide vs once daily GLP-1 RAs in obese patient with T2DM inadequately controlled on insulin therapy (Insulin Aspart + OADs). Improvements in glycaemic control were greater with once-weekly semaglutide 1 mg than with once-daily liraglutide 1.8 mg, resulting in a longer time to treatment intensification with insulin therapy. Together with lifestyle modifications and physical activity we achieved better glycemic control without severe or blood glucose-confirmed symptomatic hypoglycemia (plasma glucose level below 3.1 mmol/l), HbA1c, FPG, and body weight in patient who is receiving insulin therapy. Also with this therapy we achieved reduction in his lipoprotein metabolism because he could not tolerate any statins. Overall, the case presented here summarized the benefit of once-weekly semaglutide 1.0 mg as an add-on to insulin therapy as the most efficacious GLP-1 RA in terms of further reductions in HbA1c, body weight, BMI in patient with T2DM, insulin therapy and GLP-1RA injections. The reasons for switching to semaglutide from liraglutide included a need to reduce HbA1c or weight further, decreased frequency of administration and cardiovascular protection.
Keywords: Type 2 diabetes, obesity insulin therapy, GLP 1 RAs, lifestyle modifications

DOI: 10.1530/endoabs.81.EP509

EP510

A weight loss of 20 kg on liraglutide

Mohamed Hamid Abdillahi, Mohamed Ali Boutheina, Aicha Ahmed Mohamed, Kaoutar Rifai & Mh Gharbi
Chu Ibn Sina, Rabat, Morocco

Introduction
Liraglutide is a glucagon-like peptide 1 (GLP-1) receptor agonist, approved for the treatment of adult patients with type 2 diabetes mellitus of a particular interest in the significant improvement of glycaemic, systolic blood pressure and lipid control with their impact on weight, making it possible to avoid this infernal spiral of weight gain-increased insulin resistance.
Observation
55-year-old female patient, known diabetic for 10 years, put on metformin 2 g. Before liraglutide: the patient had grade 2 obesity (Weight = 102 kg, BMI = 37.5 kg/m^2). HbA1c = 8.4%, Total cholesterol = 2 g/l, LDL = 1.4 g/l, HDL = 0,36 g/l. After 18 months of liraglutide 1.8 mg/j and metformin 2 g : weight loss of 20 kg (weight = 82 kg, BMI = 29 kg/m^2). HbA1c = 6.5%, Total cholesterol = 1,5 g/l, LDL = 0.8 g/l, HDL = 0,42 g/l
Discussion
Incretins are digestive tract hormones secreted in response to oral carbohydrate intake. They stimulate the secretion of insulin, inhibit that of glucagon, slow down gastric emptying and increase satiety, thus allowing weight loss. These molecules have pleiotropic effects enriching current therapy, with associated weight loss, allowing better control of diabetes. We report in this case a significant weight loss with an improvement of glycaemic and lipid control without any episode of hypoglycemia.
Conclusion
At a time of epidemics of chronic diseases such as obesity associated with type 2 diabetes, recent therapeutic options focusing on several targets are emerging, such as GLP-1 analogues.
References
Forte Marques, & all. (2015). Analogues du GLP-1 vs inhibiteurs du SGLT-2 pour les diabétiques de type 2 obèses. Revue Médicale Suisse, 11(477), 1227–1233.
Halimi, S. (2013). Prise en charge du diabète de type 2. Presse Médicale, 42(5), 861–870.

DOI: 10.1530/endoabs.81.EP510

EP511

Association between cortisol/DHEA-S ratio and inflammatory indicators in patients with non-functioning adrenal incidentalomas

Joanna Kowalska[1], Iwona Zielen-Zynek[1], Justyna Nowak[1], Aleksander Włodarczyk[2], Bartosz Hudzik[1, 3] & Barbara Zubelewicz-Szkodzińska[1,2]
[1]Department of Metabolic Diseases Prevention; School of Public Health in Bytom, Bytom, Poland; [2]Department of Endocrinology, Piekary Medical Center, St. Luke's Local Hospital in Piekary Śląskie, Poland; [3]3rd Department of Cardiology, School of Medicine with the Division of Dentistry in Zabrze, Medical University of Silesia in Katowice, Silesian Center for Heart Diseas, Zabrze, Poland

Introduction
It is well known that DHEA and DHEA-S has and impact on lipid metabolism, cardiovascular system and others. De Castro et al. showed that cortisol/DHEA-S ratio was an independent predictor of long-term mortality in patients with sepsis. Chronic inflammation is an important factor in cardiovascular diseases development that reduce quality and life expectancy. CVDs are more common in patients with adrenal incidentaloma than in general population. Literature data on the cortisol/DHEA-S ratio are contradictory, there are no scientific studies in the group of patients with endocrinopathies, including adrenal incidentalomas.

Aim
The aim of the study was to evaluate inflammation indicators – old one: insulin, CRP and new one: PLR (*platelet-lymphocyte ratio*), MPVLR (*MPV-to-lymphocyte ratio*), NLR (*neutrophil-lymphocyte ratio*), SII (*systemic immune-inflammation index*) in group of patients with non-functioning adrenal incidentalomas.
Material and methods
The study included 150 patients with non-functioning adrenal incidentalomas hospitalized in Endocrinology City Hospital in Piekary in 2016-2019. The exclusion criteria were mainly: other adrenal disorders (e.g. secreting adrenal adenomas, overactive adrenal cortex), decompensated diabetes defined as HBA1C% > 7, kidney failure as eGFR < 60 ml/min/1,73 m^2 liver failure as bilirubin > 2 mg/dl, INR > 1,5 and albumins < 3,5 g/dl, severe inflammation, treated cancer disease. Morphology parameters, cortisol and DHEA-S concentration (taken from the patient's medical record) were used to calculate inflammatory indicators and cortisol/DHEA-S ratio, CRP and insulin concentration was also taken from medical record.
Results
Most of the respondents (n = 150) were women (72.67%). The median age was 62 years in women, 66 years in men (P = 0.00), cortisol concentration at 8 a.m. was 278.62 nmol/l in women, 320 nmol/l in men (P = 0,00), DHEA-S was 78,8 μg/dl in women, 102,5 μg/dl in men (P < 0,05), CRP was 1,69 in women, 1,5 in men (P > 0,05), MPVLR 5,33 in women, 5,32 in men (P = 0,00). There was negative correlation observed (P < 0,05) between cortisol/DHEA-S ratio and: CRP (r = -0,21), insulin (r = -0,18). There was no signifficant correlation (P > 0,05) demonstrated between analyzed cortisol/DHEA-S ratio and new inflammation indicators: MPVLR, SII, PLR, NLR.
Conclusion
There is association between cortisol/DHEA-S ratio and old inflammation indicators but not between cortisol/DHEA-S ratio and new ones in studied group of patients with non-functioning adrenal incidentalomas. There is a necessity to enlarge the studied group to confirm obtained results.

DOI: 10.1530/endoabs.81.EP511

EP512

Omega 6 and 3 intake in depressive patients

Rym Ben Othman[1], Amel Gamoudi[2], Ramla Mizouri[3], Nadia Ben Amor[1], Insaf Loukil[1], Cyrin Souissi[1], Olfa Berriche[1], Feten Mahjoub[1] & Henda Jamoussi[1]
[1]INNTA, A, Tunis, Tunisia; [2]Faculty of Medicine Of Tunis, A, Tunis, Tunisia; [3]University of Tunis El Manar, Nutrition, Tunis, Tunisia

Background
several studies show a ralation between the lack of omega 6 and 3 and the developpement of depression. in other hand, there is a modification in the food behaviors in case of depression which can lead to the persistance of symptoms so the intake of omega 6 and 3 should be assessed for every depressive patient
Methods
50 patients whith depression were involved in our study. They were recruited from outpatient department in a psychiatric hospital Razi. The severity of depressive symptoms were assessed by HAD and PHQ9. A food history coupled with the frequency of consumption of foods rich in alphalinolenic acid, alphalinoleic acid, eicosapentaenoic acid, docosahexaenoic acid were carried out in order to assess the typical eating habits of patients. Food quantity was estimated using a photographic manual in order to assess food portions and quantification of intakes. The estimate of the daily intakes of EPA (eicosapentaenoic acid), DHA (docosahexaenoic acid) and alpha linolenic acid (GA C18: 3) was made manually based on data from the table of food composition (CIQUAL 2016). We compared the intakes of our poulation compared to the ANCs of the general adult population.
Results
The mea nage of the population is 45 year old. There were 34 women for 16 men. The average BMI was 28.2 Kg/m^2. The study of consumption shows lipids intake about 36% of total energy intake (TEI). The monounsatured fatty acid about 15.62% of TEI and poly unsatured fatty acid 11.62 % TEI. The intake was unsuffisient for 46% of population for linolenic acid, 86% for EPA, 76% for DHA, 38% for omega 3 and 16% for omega 6. According to HAD more is the intake in omega 3 and linoleic acid less are the severity of symptoms (P = 0.03 and 0.002) and according to PHG9 score the depression was more severe if the intake of linoleic acids was low (P = 0.04).
Conclusions
the omega 3 and 6 intake are important to assess to improve patient symptoms and ensure faster healing.

DOI: 10.1530/endoabs.81.EP512

EP513

Nutritional status in patients with heart failure and its relation with cardiac function

Carlos Manuel Alzás Teomiro[1], Ana maría moyano sánchez[1], Concepción Muñoz Jiménez[1], Soraya Leó n Idougourram[1], José Ló pez Aguilera[2], Manuel Crespín[2], María José Molina Puerta[1], María Ángeles Gá lvez Moreno[1] & Aura Herrera Martínez[1]
[1]Reina Sofía University Hospital, Endocrinology and Nutrition, Córdoba, Spain; [2]Reina Sofía University Hospital, Cardiology, Córdoba, Spain

Background
Heart failure (HF) has a rising incidence and is one of the most prevalent diseases worldwide. Serum NT-proBNP and systolic ejection fraction correlate with the severity and prognosis of this condition. The nutritional evaluation of patients with HF, who usually have normal weight, overweight or obesity, has acquired a novel approach due to the incorporation of novel techniques (bioelectrical impedance, nutritional ultrasonography), and functional tests.
Objective
To evaluate the relation between nutritional parameters (bioimpedance, adipose and muscle ultrasound) and clinical outcomes. in patients with HF
Methods
Patients with at least one hospital admission during the previous year were included. Anthropometric, biochemical, ultrasound, cardiac and functional tests were collected. Statistical analysis was performed with SSPS v.24.
Results
Thirty-eight patients (72.2% males; 44.4% with type 2 diabetes) were included; 36.2% presented at least one episode of acute myocardial infarction; mean systolic ejection fraction measured by echocardiogram was 37.35%. During the previous 12 months, 39.5% of patients required more than one admission due to HF, with a mean length of stay in hospital of 5 days. In our cohort, the incidence of overweight/obesity and malnutrition reached 75% and 58.3% respectively. Decreased phase angle (< 5.5) was observed in 60% or the patients. Fat and lean mass measured by bioelectrical impedance correlated with systolic ejection fraction (P < 0.05). This cardiac biomarker also showed a positive correlation with the adipose tissue measured in rectus femoris nutritional ultrasonography (Spearman's rho + 0.384; p < 0.05). Serum NT-proBNP levels correlated with body cell mass (BCMe) measured by bioelectrical impedance, calf circumference, albumin, prealbumin and LDL cholesterol levels (p < 0.05).
Conclusions
Nutritional and cardiac parameters are correlated in patients with HF. Routine nutritional evaluation and early nutrition intervention, if required, should be implemented in order to improve the clinical outcome in these patients. Prospective, interventional studies should be performed.

DOI: 10.1530/endoabs.81.EP513

EP514

25(OH)D vitamin D status and anthropometric parameters among patients hospitalized in geriatric department

Justyna Nowak[1], Marzena Jabczyk[1], Bartosz Hudzik[1, 2] & Barbara Zubelewicz-Szkodzińska[1,3]
[1]Department of Metabolic Disease Prevention; Faculty of Health Sciences in Bytom, Medical University of Silesia, Bytom, Poland; [2]3rd Department of Cardiology, Faculty om Medical Science in Zabrze, Medical University of Silesia, Silesian Center for Heart Diseases, Poland; [3]Department of Endocrinology, Piekary Medical Center, St. Luke's Local Hospital in Piekary Slaskie, Poland

Introduction
Vitamin D deficiency is observed across all age groups and both sexes. Moreover vitamin D deficiency is common in elderly especially along elderly patients. Elderly people are prone to develop of vitamin D deficiency caused by various factors such as deceased dietary intake, impaired intestinal absorption, reduced sunlight exposure, impaired skin synthesis as well as impaired hydroxylation in the liver and kidneys. Vitamin D deficiency may leads to rickets, osteoporosis,

osteomalacia and furthermore increase the risk of cardiovascular diseases, type 2 diabetes, mental illness and many others.
Aim
We have set out to investigate status of vitamin D among patients over 60 years hospitalized at the geriatric department.
Material and methods
The study was carried out with 422 patients. From the study was excluded patients with marked physical and/or mental impairment, liver disorders, decompensated thyroid disorders, cancer, as well as people using medications such as glucocorticosteroids or/and using of vitamin D supplement. Finally to the study was included 242 patients (172 females, 70 males). All patients provided consent before included to the study. Venous blood samples were collected after overnight fasting. The serum level of 25-hydroxyvitamin D (ng/ml) was measured by enzyme-linked immunosorbent assay (ELISA). Anthropometric parameters and body impedance analysis were measure on the morning.
Results
The mean serum 25(OH) vitamin D concentration among total patients was 14.88 ± 5.95 ng/ml, among women group was 14.41 ± 6.19 ng/ml, among men group was 16.06 ± 5.16 ng/ml. The mean serum 25(OH) vitamin D concentration was higher among patients aged 60-74 years in comparison to patients aged 75 years and over (16.24 ± 6.18 ng/ml vs 14.22 ± 5.73 ng/ml), $P = 0120$. Most of elderly patients 79.8% ($n = 193$) had vitamin D deficiency defined as 25(OH)D $\leq$ 20.0 ng/ml. Suboptimal vitamin D concentration ($>$20.0-30.0 ng/ml) was observed in 19.0% ($n = 46$) study group and adequate of vitamin D concentration ($>$ 30.0 ng/ml) had 1.2% ($n = 3$) patients. The mean value of BMI was 28.15 ± 5.50 kg/m^2 (men 27.52 ± 4.76 kg/m^2; women 28.41 ± 5.77 kg/m^2), mean of body fat in % was 33.56 ± 9.59 (man 26.93 ± 7.80; women 36.26 ± 8.93) mean of muscle mass in kg was 43.30 ± 8.25 (men 52.47 ± 6.63; women 39.57 ± 5.45). Vitamin D concentration was 14.84 ± 5.50 ng/ml among obese patients (BMI $\geq$30.0 kg/m^2), 15.32 ± 6.00 ng/ml among overweigh patients (BMI 25.0-29.0 kg/m^2) and 4.00 ± 6.00 ng/ml among patients with normal weight (18.5-24.9 kg/m^2), $P = 3480$.
Conclusion
Vitamin D was observed in geriatric patients irrespective of age, gender and body mass. Proper vitamin D supplementation should be recommended in this group of people.

DOI: 10.1530/endoabs.81.EP514

EP515

Diplopia, a sign of diabetes: A case report

Ramla Mizouri, Rym Ben Othman, Nadia Ben Amor, Faten Mahjoub, Abir El Amri[1], Amany Amorri, Berriche Olfa & Jamoussi Henda
Institut National de Nutrition de Tunis, Service A, Tunis, Tunisia

Introduction
Diabetes mellitus is the leading cause of neuropathy worldwide. Non-retinal diabetic complications including oculomotor damage represent 1 to 3% of ocular manifestations of diabetes. The affected oculomotor nerves are essentially the external oculomotor nerve (VI), the common oculomotor nerve (III), and more rarely, the pathetic nerve (IV).
Observation
We report the case of a patient referred to our department for additional management of recently discovered diabetes. This is a 44-year-old patient with a history of Buerger's disease with amputation of both right toes. The clinical examination showed binocular diplopia with left horizontal nystagmus and damage to the external oculomotor nerve VI on the left. As part of the exploration of this diplopia, a CT scanner and an angioscanner were performed. They were normal and showed no signs of an ischemic stroke. A cerebral MRI and a lumbar puncture were strictly normal. On biology, we found a fasting blood sugar at 7 mmol/l and a glycated hemoglobin at 8.9%. The patient started diet and metformin. The evolution was marked by the progressive remission of diplopia after glycemic control after six weeks.
Conclusions
Our observation illustrates the interest of screening for diabetes in the face of damage to the oculomotor nerves. The evolution is favorable spontaneously after few weeks, but the recurrence on the same side or on the contralateral side is possible.

DOI: 10.1530/endoabs.81.EP515

EP516

Treatment Induced Neuropathy in Diabetes: Case Report

Chin Voon Tong & Poh Shean Wong
Melaka Hospital, Medicine, Melaka, Malaysia

Introduction
Treatment-induced neuropathy of diabetes (TIND) is a small fibre neuropathy precipitated by rapid correction of chronic hyperglycemia.
Methods
We report two patients who developed TIND after rapid improvement of glycaemic control.
Results
21-year-old gentleman, underlying type 2 DM diagnosed since 2017. He was not compliant to insulin therapy and defaulted follow up. His Hba1c ranged from 16.6%-19%. In July 2020, he was admitted for diabetic ketoacidosis and dengue fever. He was discharged with basal bolus insulin. Within a month after discharge, he experienced severe lower limb pain. The pain worsened at night and affected his sleep. On examination, he had increased pinprick sensation over bilateral lower limb dermatomes. Hba1c was reduced markedly to 8.9%. His urine biochemistry revealed proteinuria. He was started on Gabapentin and Vitamin B1, B6 and B12. His insulin dose was reduced. A month later, his neuropathic symptoms had much improved. His subsequent neurological examination revealed reduced pinprick sensation at gloves and stocking distribution. Nerve conduction study (NCS) revealed symmetrical length dependent sensory motor predominantly axonal polyneuropathy, suggestive of diabetic neuropathy. 36-year-old lady, diagnosed with type 2 DM since 2016 and was started on Sitagliptin/Metformin. Nevertheless, she defaulted her follow up and medication. In September 2020, she was admitted for diabetic ketoacidosis with Hba1c $>$ 14%. She was discharged with basal bolus insulin. During follow up, she complained of severe lower limb pain since discharge, with pin and needle sensation, worsened at night. Her neurological examinations were unremarkable. Hba1c had been reduced substantially to 8.7%. She was commenced on Gabapentin and Amitriptyline. One month later, her neuropathic symptoms improved markedly. NCS showed symmetrical length dependent sensory motor axonal polyneuropathy, suggestive of diabetic neuropathy.
Conclusion
These 2 cases highlight the importance of early detection and timely management of this distressing and potentially debilitating condition. The condition may be prevented by gradual titration of glycaemic control treatment, especially in long standing poorly controlled diabetic patients.

DOI: 10.1530/endoabs.81.EP516

EP517

Trigger finger complicating diabetes: a case report

Kamel Farah, Khaoula Gorgi, Manal Azriouil, Kaoutar Rifai, Hind Iraqi & Mohamed Hassan El Gharbi
Ibn Sina University Hospital, Endocrinology and Metabolic Diseases, Rabat, Morocco

Introduction
Trigger finger is a stenosing tenosynovitis in which constriction of the tendon sheath is associated with the presence of a nodule on the flexor tendon of the finger. This is an often unrecognised complication in the diabetic patient. We report the case of a diabetic patient with a complication of trigger finger.
Observation
A 55 year old female patient, known to be diabetic for 10 years and treated with a basal-bolus insulin therapy regimen. Her evolutionary profile is marked by several episodes of ketoacidosis decompensation. Her diabetes is complicated by chronic renal disease at the stage of proteinuria, and proliferating diabetic retinopathy. The clinical examination found limited mobility in flexion and extension of the fourth finger of the right hand, with a palpable nodule on the flexor tendon of the finger. Biological findings: HbA1c: 9%, renal function and lipid profile were correct. The patient had unbalanced diabetes complicated by microangiopathy and a trigger finger. The therapeutic management is based first on glycemic control and therapeutic education then we proposed corticosteroid injections, with a good evolution.
Discussion
Trigger finger is an often unrecognised tenosynovitis in the diabetic patient. It can occur during flexion or extension. The nodule is palpable on the flexor tendon of the affected finger. In diabetes, trigger finger occur in 4-10% of cases, and their occurrence is correlated with the length of time the patient has had diabetes, but not with its control. In a study of young insulin-dependent diabetic patients, this symptom was noted in 5% of patients and no controls.Treatment is based on

corticosteroid injections in the first instance. If this fails, percutaneous needle lung resection may be performed. A recent meta-analysis has shown that patients treated with percutaneous methods have fewer failures and are more satisfied than those treated with corticosteroid injections.Finally, surgical treatment should only be proposed in case of failure of medical treatment and in case of significant impact but with 45% of side effect.
Conclusion
Our clinical case illustrates one of the osteoarticular complications linked to diabetes, which is frequent but often unrecognized; it is the 'trigger finger'; it is however at the origin of an important functional handicap. A multidisciplinary management should be proposed to these patients while remembering that the first treatment of these manifestations is generally a better glycemic balance.

DOI: 10.1530/endoabs.81.EP517

EP518

Correlation between pulse wave velocity and nephropathy in type 2 diabetes

Chayma Besrour[1], Rojbi Imen[1], Ben Ahmed Habib[2], Mekni Sabrine[1], Mchirgui Nadia[1], Ben Nacef Ibtissem[1] & Khiari Karima[1]
[1]Hospital Charles Nicolle, Endocrinology, Tunis, Tunisia; [2]Hospital Charles Nicolle, Cardiology, Tunis, Tunisia

Introduction
Nephropathy is a kidney complication that affects up to 50% of people with diabetes during their lifetime. Diabetes is the first cause of kidney failure. The aim of this study was to examine the relationship between diabetic nephropathy (DN) and arterial stiffness.
Methods
We conducted a prospective study including 249 diabetic patients without macroangipathic complications , between July 2020 and May 2021. Using a SphygmoCor®XCEL device, we measured arterial stiffness directly by the carotid to femoral pulse wave velocity (cfPWV).
Results
The mean age of the study population was 57.53 $\pm$ 9.34 years (139 women and 110 men). The mean duration of the disease was 10.2 years. Diabetic nephropathy (DN) was found in 34.5 % of the patients. The mean microalbuminuria was 48.58 $\pm$ 86.67 mg/g of creatinuria. CfPWV $>$ 10 m/s was found in 96.5 % of the patients with DN. And the mean microalbuminuria in patients with cfPWV $>$ 10 m/s was 52.36 $\pm$ 90.17 mg/g of creatinuria. In this group, cfPWV was at 14.38 $\pm$ 2.70 m/s VS 13.25 $\pm$ 2.81 m/s in patients without DN ($P = 0.002$). We did not find a correlation between cfPWV and the stage of the nephropathy. Moreover, the presence of arterial stiffness multiples by 5 the risk of diabetic nephropathy (Odds Ratio $= 5$).
Conclusion
This study shows that arterial stiffness is higher in type 2 diabetic patients with diabetic nephropathy than in those without diabetic nephropathy. Indeed, an elevated microalbuminuria is a marker of arterial stiffness in the general population and in the diabetic and hypertensive population. Several studies have investigated the relationship between arterial stiffness in type 2 diabetics, but there is little information regarding the relationship between cfPWV and microalbuminuria.

DOI: 10.1530/endoabs.81.EP518

EP519

'Relationship between of the quality of life indicators and neuromarker S100 in patients with type 2 diabetes mellitus on program hemodialysis'

Alisher Kholikov[1] & Urmanova Yulduz[2]
[1]Republican Specialized Scientific Practical Medical Center of Endocrinology of Public Health Ministry named by acad. Ya. Kh. Turakulov, Department of Hemodyalisis, Tashkent, Uzbekistan; [2]Tashkent Pediatric Medical Institute, Department of Endocrinology, Tashkent, Uzbekistan

The purpose of the study
is to assess the quality of life of patients with type 2 diabetes before treatment with hemodialysis using the WHO Brief Questionnaire for the Assessment of Quality of Life (WHOQOL-BREF) and the Hamilton Depression Scale, taking into account the degree of neuromarker S100.
Material and methods
We examined in total for the period from January 1, 2018 to January 1, 2021 - 90 patients suffering from type 2 diabetes mellitus with chronic renal failure (CRF) on programmed hemodialysis.
Results
We analyzed 90 cases of grade 5 diabetic nephropathy who were on programmed hemodialysis. Of these, women -43, men -47. The obtained results also confirm the literature data that patients with type 2 diabetes mellitus have low quality of life indicators before programmed hemodialysis. According to the degree of chronic brain ischemia (CBI), patients were divided into 3 groups: 1 gr. - 36 (40.0%) patients with diabetic nephropathy (DN) 5 stage with CBI 1 degree; 2 gr. - 32 (35.5%) patients with DN 5 stage with CBI 2 degree; 3 gr. - 22 (24.4%) patients with DN 5 stage with CBI 3 degrees. A reliable difference between the mean values of S100 in the blood in patients 2 and 3 groups compared with the rate indicators was detected. In addition, in 2 and 3 groups of patients revealed direct correlation with the quality of life in 3 questionnaires - WHOQOL-BREF), MMSE test and Hamilton depression scales.
Conclusions
Assessing the quality of life using the WHOQOL-BREF scale, determining the level of anxiety and depression, as well as the MMSE test must act as the criteria for the clinical and functional severity of the state and the effectiveness of the treatment of therapy in patients with CRF in the conditions of therapy with various methods.

DOI: 10.1530/endoabs.81.EP519

EP520

Obesity and diabetes mellitus as predictors of adverse course of COVID-19 infection

Yuliya Dydyshka[1,2], Alla Shepelkevich[1], Mariya Efremava[1], Veranika Lobashova[2] & Elena Brutskaya-Stempkovskaya[1]
[1]Belarusian State Medical University, Minsk, Belarus; [2]Republic Center of Endocrinology and Medical Rehabilitation, Endocrinology Department, Minsk, Belarus;

According to WHO epidemiological data, there are more than 650 million obese people in the world, the medical and social significance of which is determined by the development and aggravation of insulin resistance. Accumulation of experience in the treatment of patients with COVID-19 infection has demonstrated that obesity and diabetes mellitus are important risk factors affecting the clinical severity of inflammatory disease - for impaired function of β-cells along with a cytokine storm and the release of contrainsular hormones.
The aim of the study was to identify phenotypic parameters that affect the prognosis of the course of COVID-19 infection by analyzing data on the features of the manifestation and course of the disease in patients with endocrine and metabolic risks.
Materials and methods
The main group consisted of 15 patients with confirmed COVID-19 infection, a history of type 1 or type 2 diabetes mellitus, or increased fasting glycemia (more than 5.5 mmol/l in capillary blood and 6.1 mmol/l in venous blood) and/or any hyperglycemia (more than 11.1 mmol/l). Comparison group - patients with confirmed COVID-19 infection without dysglycemia. All patients had a severe course of the disease, requiring transfer to the intensive care unit and resuscitation.
Results and discussion
The main group consisted of 7 (47%) men and 8 (53%) women. It was found that in the main group BMI (31.6 (29.0–33.8) vs. 26.0 (24.0–31.0), $U = 60$, $P = 0.045$) and the number of days of hospitalization (17, 6 (14.0–21.1) vs. 14.4 (10.0–18.0), $U = 67$, $P = 0.033$) is significantly higher than in the control group, which confirms overweight and obesity as risk factor for adverse course of COVID-19. Patients with DM have a low percentage of lymphocytes (18.48 (19.0–27.0) vs. 29.0 (16.2–37)%, $U = 51$, $P = 0.042$) and a level of leukocytes (4.6 (3.4–7.9) vs. 5.9 (4.2–9.0) $*10^9$/l, $U = 68$, $P = 0.035$), increased levels of C-reactive protein (62.5 (27,0–120.0) vs. 41.0 (22.5–50.9) mg/l, $U = 69$, $P = 0.045$), procalcitonin (0.14 (0.1–0.2) vs. 0.1 (0.08–0.11) ng/ml, $U = 65$, $P = 0.05$) and IL-6 (38.4 (19.0–70.0) vs. 15.0 (9.0–39.0) pg/ml, $U = 53$, $P = 0.04$) compared with patients without diabetes. In the main group of patients, hyperglycemia was first detected in 61.1% of patients, which may indicate COVID-19 as a significant risk factor for the manifestation of DM.
Conclusions
Patients with diabetes have a worse prognosis for COVID-19 due to a complex of associated conditions that increase the risk

DOI: 10.1530/endoabs.81.EP520

EP521

India epidemiological mapping study- attempt at early screening - early intervention

Bharat Saboo[1], Abhishek Shrivastav[2], Aniket Inamdar[3], J Jayaprakash Sai[4], Ajoy Tewari[5], Dhruvi Hasnani[6], Vipul Chavda[6], Dr S S Dariya[7] & Rupam Choudhary[8]
[1]Prayas Diabetes Center, Indore, India; [2]R R Hormone Clinic, Jabalpur, India; [3]Samarpan Clinic, OmerGa, India; [4]Apollo Sugar Clinic, Hyderabad, India; [5]Jai Clinic and Diabetes Care Centre, Lucknow, India; [6]Rudraksha Institute of Medical Sciences, Ahmedabad, India; [7]SMS Hospital, Jaipur, India; [8]Apollo Diabetes Clinic, Dispur, India

Background
Hypertension is the most important chronic condition leading to cardiovascular complications in India. Lack of awareness and epidemiological data is the reason for inertia for primordial, primary and secondary prevention. Education, region epidemiological mapping and early screening and intervention can help benefit the population in terms of cardiovascular morbidity and mortality.
Aims & Objectives
To gather, analyze and intervene a large population for early screening, primary and secondary prevention for hypertension.
Patients/Materials & Methods
A team of doctors, nurse, educator and MSW gathered together to understand the prevalence and the incidence of diabetes and Hypertension at rural and sub-urban areas under 9 consultants at different geographical areas of India. Collection of anthropometric data and medical history along with education of the population was done. Further analysis and follow up with Lab parameters was advised to those with newly detected hypertension. They consulted those with preexisting and uncontrolled hypertension and the therapy was up titrated at the consultant's discretion. Screened population was from 30 to 88 years of age
Results
No. of sites: 9 Population screened: 346 Male- 189; Female: 157. Median Age: 46 Newly detected Hypertensive: 66 Pre-existing Hypertensive: 142 Undetected HTN is more common in females, Rural area and those with T2DM.
Discussion & Conclusion
Hypertension is Far More prevalent than what it seems in Indian Population, the need is to emphasize screening amongst those found at more risk of having undetected hypertension, Also healthcare workers should focus more emphasis on educating those with undetected HTN so that they can get themselves screened early and get treated. As this subset of patient often go undetected and suffer long-term consequences

DOI: 10.1530/endoabs.81.EP521

EP522

Gut microbiota genera regarding carbohydrate metabolism status and GLP-1 treatment

Jana Caudet-Esteban[1], María Trelis-Villanueva[2,3], Matilde Rubio-Almanza[1], Rosa Cámara-Gómez[1] & Juan Francisco Merino-Torres[1,2]
[1]La Fe University and Polytechnic Hospital, Endocrinology , València, Spain; [2]University of Valencia-Health Research Institute La Fe, Joint Research Unit on Endocrinology, Nutrition and Clinical Dietetics, València, Spain; [3]University of Valencia, Aea of Parasitology, Department of Pharmacy and Pharmaceutical Technology and Parasitology, Valencia, Spain

Introduction and Objetive
The composition of human gut microbiota is an emerging field of research and is currently regarded as pathophysiologically linked to obesity. However, we still lack a thorough understanding of what constitutes health and disease in this subject. We present herein a descriptive study of the gut microbiota composition among Spanish morbidly obese subjects, clustered regarding the carbohydrate metabolism status (CHMS) displayed.
Methods
Stool samples were collected from type II-III obese subjects to perform metagenomic analysis of the intestinal bacterial community. This analysis was realized by the Sequencing and Bioinformatics Service of the Foundation for the Promotion of Health and Biomedical Research of Valencia Region, according to their own protocol. To compare the differences in the relative abundance (RA) of taxa between groups, we employed SPSS v22 and performed the Wilcoxon rank sum test.
Results
Stool samples were obtained from 56 obese subjects (64% women) of 48.1($\pm$9.8) years old and BMI 45.6($\pm$6.6) kg/m^2. 22 subjects presented a normal CHMS, 15 had prediabetes and 19 suffered diabetes mellitus (DM). When comparing the microbiota composition regarding the CHMS, no differences were found in the Shannon nor Chao1 alpha-diversity indexes. At phylum level, no differences were detected either in the RA of *Firmicutes, Bacteroidetes, Proteobacteria, Actinobacteria* nor *Verrrucomicrobia*. At genus level, subjects with a normal CHMS presented higher RA of *Faecalibacterium* ($p=0.032$) and *Clostridium* ($p=0.026$) and lower of *Escherichia* ($p=0.038$), with no differences in *Akkermansia*. Among DM patients, 15 were treated with a GLP-1 agonist (GLP-1A): compared to the rest of the participants, these subjects displayed higher RA of the phylum *Proteobacteria* ($p=0.044$), higher RA of the genera *Parabacteroides* ($p=0.034$) and *Escherichia* ($p=0.002$), and lower RA of *Clostridium*($p=0.007$). In the DM subgroup, patients treated with GLP-1A displayed higher RA of *Bacteroides* spp. ($p=0.027$) and lower of *Prevotella* spp. ($p=0.009$) than the rest of diabetic subjects.
Conclusions
In this small study performed in severely obese subjects, significant differences were found in the RA of the genera *Faecalibacterium*, *Clostridium*, *Escherichia, Bacteroides* and *Prevotella* in regards of the CHMS and the use of GLP-1A. Further research is needed to ascertain whether a pathophysiological relationship between these phenomena exists.

DOI: 10.1530/endoabs.81.EP522

EP523

HbA1c evaluation predicting hyperglycaemia and avoiding morbidity in steroid initiation

Philip Maher[1] & Maeve Durkan[2]
[1]University College Cork, Cork, Ireland; [2]Bon Secours Hospital Cork, Endocrinology and Internal Medicine, Cork, Ireland

Introduction
Steroids can precipitate significant hyperglycemia and Diabetes Mellitus in vulnerable populations including DM, pre-DM and the elderly. Steroid risks include deterioration in DM, glucose toxicity, HONK and HHS. This may be avoided by a simple screening HbA1c, which could prompt a 'safeguard algorithm' for the patients including instruction in glucose monitoring. The 'at risk' cohort is identified, and a surveillance regime is implemented.
Methods
We conducted a pilot study, assessing the prevalence of HbA1c screening pre-steroids commencement. This was a prospective study, identifying all patients (medical, surgical and oncological admissions/inpatients) in the BSH Cork, commencing oral steroids from July 19 – August 1, 2021. We reviewed if any had HbA1c screening within the preceding three months.
Results
Of all inpatients, 49 were commenced on steroids. 8/49 (16%) patients had an HbA1c measurement pre-treatment, ranging from 45-134 mmol/mol.
Discussion
The results highlight low level HbA1c testing pre steroids. 94% of steroid induced hyperglycemia develops within 48 hours of initiation (1), when most patients are still inpatients. 41/49 patients were not tested and are at risk for steroid induced hyperglycemia. Of those tested, all were in 'at-risk category' (HbA1c $\geq$ 42mmol/mol). This may suggest a limitation in our study, in so far as, all those tested may have been known to be hyperglycaemic and the true screening value may be lower. Nonetheless, a simple HbA1c will identify those 'at-risk' for targeted glucose monitoring on steroids, ideally in hospital. This may minimize the risk of readmission and morbidity with HONK/HHS.
1. Fong AC, Cheung NW. The high incidence of steroid-induced hyperglycaemia in hospital. Diabetes Res Clin Pract. 2013;

DOI: 10.1530/endoabs.81.EP523

EP524

Insulin resistance: in type 1 diabetes

M'ballou Camara[1], Fatiha Ettalibi[1], Sana Rafi[1], Ghizlane EL MGHARI[1] & Nawal EL Ansari[1]
[1]CHU Mohammed VI, Endocrinology, Diabetes, Metabolic Diseases and Nutrition, Marrakech, Morocco

Introduction
Insulin resistance is one of the characteristic abnormalities of type 2 diabetes. Recently it has been recognized that type 1 diabetes may also present with insulin

resistance of varying intensity. We report a case of insulin resistance in a patient with type 1 diabetes.
Observation
The patient was 23 years old, with a history of type 1 diabetes since the age of 20, with positive antibodies against GAD (glutamate acid decarboxylase), revealed by a cardinal syndrome with inaugural ketosis on discovery under high dose insulin: mixtar30 (70IU at 08:00 - 30IU at 12:00 - 64IU at 20:00) and Actrapid: (5IU at 08:00 - 38IU at 12:00 - 34IU at 20:00), no diabetic heredity. The admission examination revealed a stable conscious patient with hyperglycemia between 2.53 and 3.23 g/l, systolic pressure at 132 mmhg, body mass index (BMI) at 22 kg/m^2 with a waist circumference (WC) of 77 cm. Biology showed normal transaminases: ALT 38U/l, ASAT 33U/l, GGT 12UI/l, total cholesterol 1.67 g/l, LDL 1.28 g/l, HDL 0.61g/l, Triglycerides 1.36 g/l, management consisted of the introduction of oral antidiabetic drugs: metformin 2 g, empagliflozin 10 mg/d, in combination with insulin. The evolution was marked by the improvement of the glycemic figures with reduction of the doses of insulin, currently under: mixtard30: (24UI at 08 h-00-24UI at 20 h) metformine 2g/d and jardiance 10 mg/d.
Discussion
Insulin resistance is mainly related to type 2 diabetes. Recently it has been recognized that type 1 diabetes may also present insulin resistance of variable intensity. The pathophysiology of this insulin resistance is not known. Hypotheses have been put forward, notably a deficit in muscle oxidative phosphorylation. In our case, the high doses of insulin and the chronic imbalance despite the respect of the injections and the dietary rules pushed us to evoke insulin resistance. The improvement of the glycemic figures after the setting on ADO in particular metformin and the recourse to lesser doses of insulin reinforced our diagnosis. Insulin resistance remains rare in type 1 diabetics and the pathophysiological mechanisms have not yet been elucidated, but it should be considered when faced with profiles of type 1 diabetics who remain in chronic imbalance under very high doses of insulin.

DOI: 10.1530/endoabs.81.EP524

EP525

Neurognic osteoarthropathy: place of Biphosphonates (one case report)
Lionel Stève Kamgain Simeu, Mjabber Amal, Nassim Essabah Haraj, Siham El Aziz & Asma Chadli
Ibn Rochd University Teaching Hospital, Endocrinology, Diabetology, Metabolic Dieases and Nutrition, Casablanca, Morocco

Introduction
Charcot's foot is a rare and extremely serious complication of diabetic neuropathy resulting in foot deformities through the non-infectious destruction of bones and joints. Its diagnosis is very difficult, it is often evoked in front of the persistence of inflammatory signs in spite of a well conducted antibiotic therapy.
Case report
59-year-old patient, T2DM for 3 years on Metformin, active smoker for 20 years. Reports for 1 week the progressive installation of a red and painful swelling of the dorsal surface of the right foot without any notion of obvious trauma or signs of infection.
Clinical examination
Overweight patient with a BMI of 26 kg/m^2. On the right foot, hot and painful red tumefaction on the dorsal side of the foot, without ulceration, without pus or serum. Disturbed monofilament test without other neurological signs, on mixed feet with neuropathic predominance classified as stage 2-IWGDF and stage 0A-TEXAS, with perceived and symmetrical pulses, an SPI at 0.9.
Paraclinical findings
Glycemia: 1.43 g/l
Urine dipstick: Negative
CRP: 213 mg/l (<6)
Procalcitonin: 0.19 ng/ml (0.5)
Uricemia: 67 (35-72) mg/l
GFR $=$ 78 ml/min
HbA1c: 7.8%
X-rays of the right foot (F/P): No osteitis.
MRI of the right foot: osteoarthropathy without bone lysis associated with tendinosynovitis.
The patient benefited from a total discharge by removable boot and alendronic acid at a rate of 70 mg/week for 6 months and diabetes balance with a good evolution.
Conclusion
The management of Charcot's foot remains complex and often requires multidisciplinary management. The use of bisphosphonates in the control of inflammation during the acute phase has been reported in the literature. It remains a promising therapeutic alternative and has its place in the control of inflammatory signs.

DOI: 10.1530/endoabs.81.EP525

EP526

Does the initial daily insuline dose vary with the amount of glycated hemoglobin
Zeineb Zemni, Wissal Ghamgui, Daii Raja, Rihab Yamoun, Amal Salem, Salma Abadlia, Imen Hedfi, Chaima Jemaii, Yosra Htira & Faika Ben Mami
National Institute of Nutrition of Tunis, Department C, Tunis, Tunisia

Introduction
Insulin therapy remains a treatment of last resort for type 2 diabetic patients with uncontrolled diabetes with oral antidiabetic. The aim of this study was to find a correlation between the initial dose of insulin and the glycated hemoglobin (A1c) level.
Methods
We conducted a cross sectional study. We included 63 patients with type 2 diabetes hospitalized for a switching to insulin in the C department of diabetology and nutrition at the National Nutrition Institute in Tunis, during 3 months. We correlate the initial daily insuline dose and the A1c level using the Spearman test.
Results
The mean age of patients was 58.75$\pm$ 12 years ,43% were men and 57% were women. The average duration of diabetes was 9,27$\pm$ 6 years. We found a statistically significant correlation between the initial daily insuline dose and the A1c level ($r = 0{,}66$; $P = 0.000$).
Conclusion
Our results showed a positive correlation between A1c level and initial insulin dose, which encourages us to consider insulin treatment in time to avoid the need for high doses and to minimize side effects.

DOI: 10.1530/endoabs.81.EP526

EP527

Effective treatment of allergy to the insulin excipient meta-cresol with desensitization therapy in type 1 diabetes mellitus: a case report.
Ameni Terzi, Meriem Yazidi, Anis Grassa, Nadia Khessairi, Wafa Grira, Ibtissem Oueslati & Melika Chihaoui
La Rabta University Hospital, Department of Endocrinology, Tunisia

Introduction
Insulin allergy is a clinical challenge in the management of type 1 diabetes mellitus since there is no other therapeutic alternative. The specific cause of insulin allergy can be related to insulin itself or to additives including zinc, protamine and meta-cresol. The manifestations range from localized reactions to systemic severe anaphylaxis. We here present the case of a generalized allergy to insulin excipient meta-cresol, in a type 1 diabetic patient successfully handled by desensitization therapy.
Case-presentation
A 35 years old female with a medical history of seasonal allergic sinusitis and type 1 diabetes mellitus for 4 years on insulin glargine and insulin aspart, presented to our department for the development of generalized urticaria, erythema and pruritus. Symptoms started since diabetes diagnosis, but the intensity and frequency of these reactions increased recently. Symptoms occur 10-30 minutes after insulin injection. Antihistamine treatment improves partially the condition. The allergic reaction persisted with the other types of insulin (regular human insulin, NPH-insulin, detemir, glulisine). Immunological evaluations revealed negative results for specific immunoglobulin E to latex and protamine. Anti-human insulin IgE antibodies (CAP) were inferior to 0,1 kU/l. Skin prick testing revealed a hypersensitivity to the all types of insulins stated above. Because the patient had an allergic reaction to all available insulin and meta-cresol was the only excipient common to all tested insulin types, a presumed allergy to the excipient meta-cresol was diagnosed. We started desensitization therapy to glargine following Joselyn Rojas's protocol using subcutaneous insulin injection with simultaneous intravenous regular insulin infusion associated to premedication with corticosteroid and H1 antagonist. Subsequently, we conducted desensitization to aspart insulin adopting Füsun

Erdenen's protocol. Seen 1 month later, the patient didn't require antihistamines anymore with tremendous allergic symptoms relief.
Conclusion
Allergy to insulin excipient meta-cresol in a type 1 diabetic is unusual and represents a substantial challenge warranting a stepwise approach to be diagnosed and managed. Specific immunotherapy should be considered as a key treatment option.

DOI: 10.1530/endoabs.81.EP527

EP528

Should the Fracture Risk Assessment tool be used without Bone Mineral Density in elderly patients having type 2 diabetes mellitus ?

Malak Belkhiri[1], Boubaker Fadia[1], Houda Ben Salem[1], Mouna Brahem[2], Houcem Mrabet[1], Alaya Wafa[1], Zantour Baha[1], Mohamed Younes[2] & Sfar Mohamed Habib[1]
[1]Taher Sfar University Hospital, Internal Medicine and Endocrinology Department , Tunisia; [2]Taher Sfar University Hospital, Rheumatology, Tunisia

Introduction
Osteoporosis and diabetes are two chronic diseases with increasing prevalences, particularly among elderly. Their coexistence results in socio-economic burdens. Clinical and paraclinical assessment for fracture risk among diabetic eldery patients are necessary to implement in clinical practice. Appropriate tools shoud to be determined and tested.
Objective
To assess comorbidities and fracture risk in elderly patients having type 2 diabetes mellitus (T2DM).
Methods
A cross-sectional study was conducted between December 2020 and January 2021 among 31 patients having type 2 diabetes and aged over 65 years in the department of Endocrinology at the UHC Taher Sfar in Mahdia, Tunisia. Patients with risk factors for secondary osteoporosis weren't included. Fracture risk of the population study patients was assessed using the FRAX tool
Results
Our population study included 16 women and 15 men having T2DM. The mean age was calculated at 69.5 $\pm$ 4.5 years. The most frequent comorbidities encountered were : overweight (26 patients), dyslipidemia (23 patients), hypertension (20 patients), osteoarthritis (21 patients), and history of (a)previous fracture(s) (8 patients). The median of A1c was situated at 9,73%. The median duration of diabetes was of 14,7 years (1–30 years). Twenty seven patients were treated with antidiabetics presenting a potential hypoglycemic risk. Chronic complications of T2DM were found among 28 patients. Bone Mineral Density (BMD) results showed osteopenia in 13 cases (41,9 %) and osteoporosis in 3 (9,7 %). Without including BMD, the Fracture risk of the population study patients assessed using the FRAX was estimated at 11.09% $\pm$ 6.28, whereas FRAX including results of the BMD estimated it at 9.91% $\pm$ 4.26. The risk of fracture using FRAX was higher in our population study without considering the results of the BMD. The BMD therefore underestimated the fracture risk in our diabetic elderly population.
Conclusion
Osteoporosis should probably be considered as a complication of diabetes rather than a comorbidity to encourage clinicians to prevent bone demineralisation and risk of falls leading to fracture specially among eldery patients. Appropriate tools should be used to detect osteopenia, osteoporosis and fracture risk among diabetic 2 patients, since having usually an associated metabolic syndrome. BMD was reported by studies underestimating osteoporosis among T2DM. FRAX tool should probably be used without including BMD to better estimate the risk of fractures the elderly diabetic population. Other contolled essays are needed and testing of new appropriate tools seems relevant.

DOI: 10.1530/endoabs.81.EP528

EP529

Risk factors associated with symptomatic hypoglycemia in type 2 diabetes mellitus patients

Aniket Inamdar
Samarpan Clinic, Internal Medicine, Omerga, India

Background
Diabetes mellitus is an emerging global epidemic and is the main illness threatening human health in 21st century. The target clinical outcomes in patients with type 2 diabetes mellitus (T2DM) is good control of HbA1C less than 7 %. However, aggressive treatment is needed to achieve this target in some patients. But this aggressive treatment predisposes patients to a higher risk of hypoglycemia that become a major hurdle in achieving glycemic goal in these patients. Hypoglycemia is one of most feared complication of diabetes treatment and the very important barrier in achieving tight glycemic control in diabetes patients.
Objective
To describe characteristics of the patients with T2DM presenting with hypoglycemia and identify the predisposing factors of hypoglycemia in them.
Materials and Methods
This cross-sectional study was conducted in a hospital in rural India from January 2021 to November 2021. Venous plasma glucose was measured in all patients with T2DM presented with signs-symptoms of hypoglycemia, patients having biochemically confirmed hypoglycemia (venous plasma glucose $<$70 mg/dl) were selected for the study. Proper history was taken from patients and their relatives to obtain the demographic and clinical data including hypoglycemic symptoms.
Results
Fourty three with T2DM were included in the study among whom 60% were female, 56% aged $\geq$60 years, 90% lived in rural and sub-urban areas, 52% had diabetes for $\geq$10 years, and 25% took insulin. Hypertension was the most common (55%) co-morbid condition followed by ischemic heart disease (23%) and CKD (13%).28% patients presented in unconscious state. Their mean plasma glucose at presentation was 51 mg/dl. Skipped meal was the most common precipitating factor followed by drug overdose and other medical illness such as CKD. More than half had (51%) hypoglycemic episodes in the preceding 12 months. Self-monitoring of blood glucose (SMBG) was done in only 7% patients.
Conclusions
Hypoglycemia is the most common and often treatment-limiting serious adverse effect of diabetes therapy. Despite being potentially preventable, hypoglycemia in type 2 diabetes incurs substantial personal and societal burden. Awareness of hypoglycemia and its timely management at home needs to be emphasized. Patient education regarding hypoglycemic signs and symptoms, regular meal timings, proper exercise, regular follow ups and self-monitoring of blood glucose (SMBG) and sick days care are of utmost importance to prevent hypoglycemia.

DOI: 10.1530/endoabs.81.EP529

EP530

Degenerative complications of diabetes during the switch to insulin

Amal Mehrzi, El Amri Abir, Amorri Amani, Berriche Olfa, Mahjoub Faten, Ben Amor Nadia, Ben Othmen Rim, Mizouri Ramla & Jamoussi Henda
Tunisian Institute of Nutrition, The A Department of Diabetology and Nutrition, Tunis, Tunisia

Introduction
Type 2 diabetes is a chronic, silent disease. Patients with diabetes could experience complications during the evolution of their disease. We studied the presence of degenerative complications during the initiation of insulin.
Methods
Cross-sectional study including a group of patients with type 2 diabetes requiring a switch to insulin, hospitalized at the A department of Diabetology and Nutrition in the National Institute of Nutrition of Tunis between July 2021 and December 2021. The data was collected by consulting medical records.
Results
We included 50 patients with type 2 diabetes hospitalized for a switch to insulin, 44% were men, 56% were women, with an average age of 51 years, the averge duration of diabetes was 6 years, 10% had diabetes for less than a year. We found that 32% of the patients had diabetic retinopathy, 18% had diabetic nephropathy, 40% had diabetic neuropathy, 10% had a history of stroke, 2% had a history of transient ischemic attack, 20% had a coronary diseace, 4% suffered from chronic obliterative arterial disease of the lower limbs.
Conclusion
In our study degenerative complications were present during the initiation of insulin. This could be explained by the therapeutic inertia in type 2 diabetes. The switch to insulin when indicated is necessary to prevent degenerative complications of diabetes.

DOI: 10.1530/endoabs.81.EP530

EP531

Type 1 diabetes, metabolic syndrome and cardiovascular risk

Mohamed Abdellahi Mohamed Ahmed, Dhoha Ben Salah, Siddiqa Soomauroo, Mouna Elleuch, Mouna Mnif, Nabila Mejdoub, Faten Haj Kacem Akid & Mohamed Abid
CHU Hedi Chaker Sfax, Department of Endocrinology and Diabetology, Tunisia

Introduction
Metabolic syndrome (MS) is responsible for the increased cardiovascular risk in type 2 diabetics, but few studies have looked at the metabolic syndrome in type 1 diabetics. The aim of This study is to evaluate the prevalence of microvascular and macrovascular complications and evaluate the cardiovascular risk among patients with T1DM associated with metabolic syndrome.
Materials and Methods
Retrospective study which included 36 type 1 diabetics, hospitalized in the diabetology endocrinology department CHU Hedi Chaker in Sfax, with a metabolic syndrome from 1997 to 2018, MetS was defined according to the NCEP-ATP III criteria.
Results
The average age of our patients was 53 years (extremes: 26-80). a female predominant is noted (21 men vs 15 women) with a sex ratio of H/F to 1,4. Diabetes duration average was 15 years. Metabolic syndrome occurred after an average duration of diabetes of 13.7 years (E: 1-35). HTA was present in 21 patients (58.3%). The mean BMI was 26 kg/m^2, 19.7% of patients were obese. The average waist circumference was 95.5 cm. an android distribution of fat was present in 3 women. The mean total cholesterol level was 7 mmol/l, that of triglycerides was 3.3 mmol/l. hypertriglyceridaemia was present in 17 cases. The average HDL cholesterol level was 0.6 g/l. hypoHDLemia was present in 20 cases. The DM consisted of 3 criteria in 22 cases, 4 criteria in 11 cases and 5 criteria in 3 cases. In the majority of cases, it was the combination of dyslipidemia, HTA plus diabetes (80%). Therapeutically, the average dose of insulin used was 0.8 IU/kg/day (0.2-1.4). The combination of an insulin sensitizer was required in 3 cases. Hepatic steatosis was present in 8 cases. Microvascular complications were present in all patients with retinopathy (74%) and nephropathy (86%). Macrovascular complications, such as coronary insufficiency, were present in 20% of cases. The Cardiovascular risk is very high in all patients.
Conclusion
The prevalence of metabolic syndrome during type 1 diabetes is increasing. Its presence indicates an increased risk for micro- and macrovascular complications. A comprehensive management including lifestyle modification might reduce their risk of micro and macrovascular complications in adults with T1DM and MetS.

DOI: 10.1530/endoabs.81.EP531

EP532

A case of idiopathic postprandial syndrome in a middle-aged nigerian woman

Damilola Jesuyajolu[1], Abdulhafeez Mohammed[2], Charles Okeke[3] & Armstrong Nicholas[4]
[1]First Graceland Hospitals, Ajah, Nigeria; [2]Top Medics Hospital, Kwara State,, Nigeria; [3]EYN Primary Healthcare Center, Adamawa State, Nigeria; [4]Umaru Shehu UltraModern Hospital, Maiduguri, Borno State, Nigeria

Introduction
Not much has been reported about Idiopathic Postprandial syndrome, especially in Africa. Many cases are often wrongly diagnosed as reactive hypoglycemia. Idiopathic postprandial syndrome refers to signs and symptoms of hypoglycemia in the absence of low blood sugar occurring after meals and is of unknown cause.
Clinical case
We report a case of Idiopathic Postprandial Syndrome in a 44-year old woman living in Nigeria. We present a 44-year-old woman who had been having recurrent hypoglycemic symptoms, which included dizziness, body weakness, lightheadedness, restlessness, headaches, and fatigue after she eats a meal (Postprandial) for a year. Blood glucose is normal during episodes, and extensive examinations and investigations yielded no other cause.
Discussion
Idiopathic postprandial syndrome (IPS) is a condition in which an individual experiences symptoms of hypoglycemia without having biochemical evidence. The major difference between idiopathic postprandial syndrome (IPS) and hypoglycemia is that IPS may present with only symptoms of low blood sugar without the other components of Whipple's triad. These symptoms usually occur within a few hours of eating and the exact cause is not known. Managing the possible identified triggers, dietary modification and the use of alpha-glucosidase inhibitors have been seen to improve the condition. Much work still needs to be done to identify the exact etiology of the syndrome.
Keywords: Postprandial syndrome, hypoglycemia, idiopathic postprandial, adrenergic symptoms, Whipple's triad

DOI: 10.1530/endoabs.81.EP532

EP533

Effect of a high calorie diet on the ileum histology of Psammomys Obesus

Asma GUEZIL[1], Zineb Bellahreche[2], Benmessaoud- Mesbah Ouahiba[1] & Koceir El hadj Ahmed[1]
[1]University Of Science And Technology Houari Boumediene, Bioenergetics and Intermediary Metabolism Team, Laboratory of Biology and Organism Physiology,, Bab Ezzouar, Algeria; [2]University Of Science And Technology Houari Boumediene, Nutrition & Metabolism, Department of Biology and Physiology of Organisms, Bab Ezzouar, Algeria

Obesity is associated with low-grade systemic inflammation, indeed the production of pro-inflammatory cytokines by mesenteric adipose tissue has been implicated in the pathogenesis of inflammatory diseases of the small intestine: duodenum, jejunum and ileum. This is the main site of intestinal inflammation. The objective of this work is to study the effect of a high calorie diet on the histology of the ileum in *Psammomys obesus*. The animals were captured in the area of Beni Abbes, in the Algerian Sahara .11 *Psammomys obesus* were divided into two groups, a control group ($n=5$) fed with the halophile plant containing (0.4 Kcal/g), and the second group ($n=6$) subjected to a high calorie diet (3.85kcal/g) for 12 weeks. A part of the ileum was fixed in bruin's solution and was sliced at 3 mm thickness then stained with masson trichrome. Our results show that the high calorie diet induced significant increase on body weight gain compared to control group. Histological analysis shows an increase in muscularisis thickness in high calorie diet group compared to the control one. Furthmore in the submucosa we observed the presence of fat cells and lymphoid infiltration in high calorie diet group, we also observed fibrosis in conjonctive tissue. These results show that our animal could be a model of inflammation and nutrient-induced fibrosis of the ileum. We conclude that a high calorie diet induces inflammatory lesions in ileum that may affect enteroendocrine cells involved in the control of feeding and metabolic pathways related to obesity.

DOI: 10.1530/endoabs.81.EP533

EP534

Esophagogastroduodenoscopy Findings in a group of morbidly obese patients undergoing bariatric surgery

Rahma Khalaf, Faten Mahjoub, Nadia Ben Amor, Olfa Berriche & Henda Jamoussi
National Institute of Nutrition, A, Tunisia

Background
Studies of morbid obese patients undergoing bariatric surgery (BS) have revealed that obesity is related with an increased prevalence of endoscopic and histologic gastritis. Performing esophagogastroduodenoscopy (EGD) prior to BS allows the detection and treatment of Helicobacter pylori (H.pylori) infection which is considered to be limiting access to bariatric surgery.
Aim
The aim of this study was to determine the prevalence of gastric lesions and Helicobacter pylori (Hp) infection in a group of morbidly obese patients referred for endoscopy prior to bariatric surgery.
Methods
This is a monocentric prospective descriptive study including 40 morbidly obese patients undergoing EGD before BS. Preoperative data included Age, gender, BMI, comorbidities, upper digestive symptoms, EGD findings and H.pylori infection assessed during a histopathological examination.
Results
EGD was performed in 40 patients. Only 30 patients underwent bariatric surgery:79.3% had sleeve gastrectomy and 21.4% had bypass surgery. The mean age was 39.49 $\pm$ 8.41 years, 35(85.7%) were females, with a mean body mass index of 48.39 $\pm$7.03 kg/m^2. Of the study population,42.9% had hypertension,

20% had type 2 diabetes, 28.6% had dyslipidemia, 8.6% had hypothyroisidm, 65.7% had obstructive sleep apnea syndrome, 14.3% had hypochromic microcytic anemia and 28.6% had vitamin D deficiency. The overall upper digestive symptoms prevalence was 48.5%, with the most frequent being gastroesophageal reflux disease (37.1%), followed by constipation (11.4%). Regarding endoscopic findings, 45.5% presented no endoscopic lesions. Pathological findings were detected in 61.11% of asymptomatic patients. Of the study population, 35.5% presented hyperemic gastropathy, 18.5% erosive gastropathy, 15.6% had hiatus hernia, 21.9% had peptic oesophagitis and 16.1% had cardial beance. No patient had duodenal or gastric ulcer. On histopathological examination, 40.7% presented no lesions, 59.3% ($n=24$) had chronic non atrophic gastritis and no patient had intestinal metaplasia or dysplasia. H.pylori was present in 20 (50%) patients. All patients with H. pylori infection had chronic gastritis of variable severity. There was no significant association between H.pylori infection and age ($P=0.8$), gender ($P=0.6$), BMI ($P=0.38$), hypochromic microcytic anemia ($P=0.1$), vitamin D deficiency ($P=0.67$).
Conclusion
EGD with histological analysis plays an important role in the pre-surgical evaluation in BS, with a high rate of pathological findings in asymptomatic patients.

DOI: 10.1530/endoabs.81.EP534

EP535

Prevalence of metabolic syndrome in obese children and adolescents

Eya Safi, Berriche Olfa, Ben Ali Khaoula, Rim Rachdi, Olfa Lajili, Imen Ouderni, Nadia Ben Amor, Faten Mahjoub & Jamoussi Henda
National Nutrition Institute, A, Tunis, Tunisia

Introduction
The metabolic syndrome is a major public health problem. Its prevalence is constantly increasing, especially in children and adolescents. Our objective was to determine the prevalence of metabolic syndrome in a population of obese children and adolescents.
Method
This is a descriptive cross-sectional study including 47 children and adolescents recruited at the obesity unit of the National Institute of Nutrition in Tunis. Each patient underwent anthropometric measurements, clinical examination, metabolic and hormonal assessment.
Results
The mean age of the population was 14.04 $\pm$ 2.55 years. Females were predominant in 57.4% of cases. The mean body mass index (BMI) was 34.34 [26.27-46.28] kg/m^2. All patients had abdominal obesity with a mean waist circumference of 111.93 $\pm$ 12.47 cm. The mean HOMA index was 9.03 $\pm$ 4.97. Type 2 diabetes and hypertension were present in 2.1% and 8.5% of obese patients respectively. Hypertriglyceridemia was found in 13.3% of cases. Almost two thirds of the patients (64.4%) had hypoHDLemia and more than one third had impaired glucose tolerance (40.4%). Hyperuricemia was noted in 18 patients (35.6%). Almost half of our sample (48.9%) had a metabolic syndrome. This syndrome was found in 15 girls (57.7%) and 7 boys (36.8%) but without significant difference ($P=0.17$). It was positively correlated with age and BMI but not significantly ($P=0.26$ and $P=0.44$ respectively). Metabolic syndrome was independent of uricemia ($P=0.7$). It was positively and significantly correlated with the HOMA index ($P=0.015$).
Conclusion
The metabolic syndrome was frequent in our population justifying prevention, screening and early and adequate management of obesity, from childhood, in order to decrease the risk of metabolic and cardiovascular complications.

DOI: 10.1530/endoabs.81.EP535

EP536

The role of hypothalamus mediators in energy imbalance.

Feruza Khaydarova[1] & Maftunakhon Latipova[1]
[1]Republican Specialized Scientific-and-Practical Medical Centre of Endocrinology, Tashkent, Uzbekistan

Obesity is considered a chronic metabolic disease that occurs at any age. Regulation of body weight in the body is carried out through complex interaction of a complex of interrelated systems that control the body's energy system. Energy imbalance is the cause of obesity and overweight, in which the supply of energy from food exceeds the energy needs of the body. Obesity is closely related to impaired appetite regulation, and hypothalamus is a key place of neural regulation of food consumption. The nucleus of the hypothalamus is connected and interdependent on receiving, integrating and sending hunger signals to regulate appetite.
Purpose of The Study
To identify markers of food behaviour.
Materials and Methods
The screening was carried out to identify eating disorders in 200 men and women aged 18 to 35 years with overweight and obesity and to check the effects of Orexin A and Neuropeptide Y markers. A questionnaire and questionnaires were conducted with over 200 people aged 18 to 35 years. Questionnaires were for abnormal eating habits and hidden depression (Zung Anxiety Rating Scale-ZARS). Anthropometry is measured by waist circumference, hip circumference, body mass index, weight, height. Based on the results of the collected data, were divided three groups: People with obesity; People with overweight; Control group of healthy people.
Results
Of the 200 analysed persons, 86% had eating disorders. Of these, 60% of eating disorders were associated with childhood. According to the result ZARS: Normal condition was about 37%, mild depressive disorder 20%, moderate depressive disorder 25% and 18% of people suffered from severe depressive disorder without knowing it. First group of people with obesity had eating disorders, moderate and severe depressive disorder, second group was overweight with mild depressive disorder. According to laboratory data, the first group had the lowest concentration of Orexin A and Neuropeptide Y in blood serum.
Conclusion
Overweight and obesity are the first signal of many diseases. Prevention and detection of these problems will avert various illness, including type 2 diabetes. Obesity aetiology is associated with eating disorders wich leads to anxiety conditions and signal transmission of the orexinorghetic system of the hypothalamus.
Keywords: obesity, energy imbalance, hypothalamus, orexin A, neuropeptide Y.

DOI: 10.1530/endoabs.81.EP536

EP537

Biochemical parameters in laboratory diagnostics of metabolic syndrome

Olga Moskalenko & Edward Kasparov
Federal Research Center «Krasnoyarsk Science Center» of the Siberian Branch of the Russian Academy of Sciences, Russian Federation

MS, is defined by a combination of abnormalities, such as obesity, arterial hypertension, elevated blood sugar and cholesterol levels, type 2 diabetes mellitus and is not a disease, but represents a group of risk factors that often occur together, increasing the likelihood of severe disease. It is well known that the main reasons for the increase in the incidence of MS is a decrease in physical activity with a high-calorie diet.
The aim of the study
Assessment of biochemical parameters in the pathogenesis of MS.
Materials and methods
70 MS patients and 45 practically healthy volunteers were examined at the clinic of the Research Institute of MPS. The glucose level was determined by the glucose oxidant method, lipid profile assessment, the use of standard test systems. Insulin was determined by enzyme immunoassay using the DRG test system. All study participants signed an informed consent approved by the ethics committee of the Federal Research Center. Statistical data processing was carried out using the application packages 'Statistica for Windows 8.0'.
Results
The main diagnostic criterion for MS is abdominal obesity, it is important to find out the cause of obesity, which may be associated, for example, with diseases of the endocrine system, in combination with a number of additional symptoms confirmed by tests. It is known that insulin resistance is one of the most important links in the pathogenesis of MS, and the calculated coefficient HOMA-IR was used to assess it. This coefficient is of the greatest diagnostic value and has received wide practical application at the present time. The calculation of HOMA-IR revealed an almost 2-fold increase in this indicator in patients with MS ($P<0.05$), which is a predictor of the risk of developing vascular and diabetic complications. The level of NEFA in patients with MS was increased in 97% of cases and was almost 2 times higher than the normal values. Also, in patients with

MS, there was an increase in the content of insulin and glucose in the blood in comparison with the control group ($P<0.05$).
Conclusion
The study shows that early diagnosis of MS is important for providing timely medical care and lifestyle correction and preventing the development of severe vascular and diabetic complications.

DOI: 10.1530/endoabs.81.EP537

EP538

Vologdàs Regional Diabetes Center - equal care for everyone

Nina Kholmskaia[1] & Valentina Victorovna Kalugina[2]
[1]Vologdàs Regional Diabetes Center, Vologda, Russian Federation; [2]North-Western State Medical University named afterv I.I. Mechnikov, Endocrinology named after academician V.G. Baranov, Saint Petersburg, Russian Federation

Vologda is situated in the North-Western region of Russian Federation. It is mostly rural – about 30% of population lives in remoted villages. One can compare Vologdàs region with Greece – same amount of land area (approximately 140000 m2), but the population density is 10 times less (8 per km2 and 85 per km2 respectively). The Vologdàs region population is approximately 1151000, the amount of Diabetes patients is 42 000 (3,7% of overall population). The territory is divided into 28 subregions with endocrine care available in 5 subregions. That is why there is an issue of equal access to specialized care for people with diabetes. Vologdàs Regional Diabetes Center was established in 2016. Diabetes center is armed with Diamobile on which multidisciplinary team (consisted of Endocrinologist, Cardiologist, Neurologist, Ophthalmologist, Podiatrist and nurse-educator) reaches every part of the region. 50000 consultations were made by multidisciplinary team. During the consultation patienès treatment plan, diet and physical activity are revised. Special attention is paid to the detection of Diabetes complications. Center specialists are cooperating with the main Vologdàs, Moscoẁs and Saint Petersburġs hospitals. The Diabetes registry is maintained by general practitioners and endocrinologists. Before the Center opening the data about Diabetes patients in the region was scarce and inconsistent. Thanks to the multidisciplinary team every bit of data acquired is included into Diabetes registry now, which led to better understanding of prevalence, morbidity and mortality, complications and Diabetes druġs distribution throughout the region. The results of data processing are clearly indicating the improvement of medical care quality. There is a great improvement in Diabetes compensation – 15% of patients have 1% reduction in HbA1c level per 1 year. Type 2 Diabetes Mellitus patienès life expectancy has increased from 72 to 74 years (Vologda region total population average –70,7 years). The percentage of patients treated with insulin is about 23%, the proportion of insulin analogues – 90%. 78% of type 2 Diabetes Mellitus patients have metformin as monotherapy or as a part of combination therapy. Consistent with current guidelines the main emphasis is on life quality improvement and avoiding cardiovascular mortality using SGLT2 inhibitors and GLP-1 agonists.
In the COVID-19 era there is an urgent need for switching to online visits. The most important future direction for Center is partial shift to online consultations. In order to achieve this goal a special application is being developed.

DOI: 10.1530/endoabs.81.EP538

EP539

High prevalence of pre-diabetes and diabetes in asymptomatic patients attending an endocrine clinic in a tertiary care institute in Colombo.

Ishara Ranathunga, J P Naveenkumar, T G Athukorala, Manilka Sumanatilleke & Noel Somasundaram
NHSL, Colombo, Sri Lanka

Background and Objectives
The prevalence of pre-diabetes and diabetes has risen exponentially in the recent past. Though the symptomatic patients frequently undergo testing for the diagnosis of the disease, asymptomatic individuals are not routinely subjected to diagnostic testing. Thus, data on asymptomatic people are still lacking. We have studied the prevalence of pre-diabetes and diabetes in asymptomatic subjects attending the Endocrinology clinic in a tertiary care institute in Sri Lanka.
Methods
A descriptive cross sectional study was conducted from January to August 2020 at the Endocrinology Unit of the National Hospital of Sri Lanka. Systematic sampling was done recruiting non diabetic patients aged more than 40 years, attending the clinic for other endocrine diseases. After obtaining informed written consent, the data was collected using an interviewer administered questionnaire. Pre-diabetes or diabetes was diagnosed according to the ADA-2020 diagnostic criteria.
Results
The study enrolled hundred and nine patients. The mean age was 53.9 years (range 40-76) and 90.8% were females. The mean weight was 62.1 (SD = 11.3) kg and BMI was 26.6 (SD = 4.6) kg/m^{-2}. Forty six percent had a family history of first degree relative being affected with type 2 diabetes. All the patients were asymptomatic of classic symptoms of hyperglycemia. Patients were evaluated with fasting blood glucose levels and HbA1c values. Forty nine patients (45%) were diagnosed with diabetes or pre-diabetes with either one or both values being impaired range. Out of that, six patients (5.5%) were diagnosed with type 2 diabetes and 43 patients (39.4%) were diagnosed with pre-diabetes. Out of the patients diagnosed with pre-diabetes and diabetes ($n=49$), sixty four percent did not had a family history of first degree relative being affected with type 2 diabetes. Out of the pre-diabetes and diabetes patients 32% had their BMI < 25 kgm^{-2}.
Conclusions
The prevalence of pre-diabetes and diabetes are much higher than expected in asymptomatic individuals. Hence, the likely patients should be regularly screened to diagnose asymptomatic phase of the disease. This is important as the prevalence has escalated in the immediate past, and diagnosing and treating early will improve long term outcome of the disease. Further large scale studies including community studies are needed to recognize the current prevalence and the rising trend both in urban and rural regions.

DOI: 10.1530/endoabs.81.EP539

EP540

The Evaluation of the quality of life questionnaire of patients with autoimmune polyglandular type 2 syndrome

Zamira Khalimova[1] & Gulzoda Negmatova[2]
[1]Republican Specialized Scientific Practical Medical Center of Endocrinology of Public Health Ministry named by acad. Ya.Kh. Turakulov,, department of neurendocrinology, Tashkent, Uzbekistan; [2]Samarkand State Medical Institute, Department of Endocrinology, Samarkand, Uzbekistan

The purpose of the study is to assess the quality of life of patients with autoimmune polyglandular type 2 syndrome using the questionnaire.
Material and research methods
Under our observation there were the following 2 groups of patients: 1 gr. - patients with PAI with AIT (primary adrenal insufficiency and autoimmune thyroid) - 25 patients, 2 gr. - PAI with DM 1 (type 1 diabetes mellitus type 1 - 30 patients, as well as 20 healthy persons of the appropriate age and gender. The study used generally crystal and clinical and biochemical methods of research, hormonal blood tests (TSH, free thyroxine, antibodies to TPO, cortisol), immunological studies (antibodies to thyroid gland, to the pancreas, to adrenal glands), and instrumental research methods (ECG, ultrasound of internal organs, thyroid gland, genital organs, neurophthalmologic, radiographic - MSCT of adrenal glands, statistical techniques, as well as the quality of life of patients with ADDIQOL. AddoQol consists of 30 questions with the estimate of each question in 6 points. At the same time, the patient must be selected in each question 1 answer: 'Yes' or 'no'. If the patient is gaining more than 15 points with the answer 'Yes', then this indicates a low quality of life [1].
Research results
The assessment of the quality of life (QoL) on the AddOQOL questionnaire showed that the middle score of patients 1 of the group was 18 $\pm$ 0.95, and in healthy - 2.35 $\pm$ 0.54 ($P<0.05$). The average score in patients 2 groups amounted to 19.6 $\pm$ 1.06 ($P<0.05$).
Conclusions
QoL patients in patients with APS 2 type of both groups has significantly lagging behind QoL in healthy faces.

DOI: 10.1530/endoabs.81.EP540

EP541

Rickettsiosis in diabetics: a Case Report

Kadiri Chaimae & Lachkar Hassan
Hôpital Cheikh Zayd, Endocrinology, Rabat, Morocco

Introduction
Rickettsia diseases are infectious, re-emerging, polymorphic, potentially fatal diseases that are widespread worldwide. These are diseases caused by strict intracellular bacteria with a Gram-negative stain associated with arthropods, mainly ticks, but also lice, fleas and other mites. In diabetics, adequate and early management is essential given the risk of developing malignant Mediterranean spotted fever.
Observation
We report the case of a 69-year-old patient, known to be type 2 diabetic for 13 years, well balanced on 1 g/d of metformin (HBA1C at 6.9%) and who consulted for a fever associated with a generalized rash evolving since 1 week with intense myalgia and asthenia. Clinical examination revealed a maculopapular rash and a pressure ulcer spot. Laboratory workup demonstrated thrombocytopenia, lymphopenia, inflammatory syndrome with elevated CRP, hepatic cytolysis and glycemic imbalance. The treatment consisted of antibiotic therapy and insulin therapy with good clinical and biological progress.
Discussion and conclusion
The diabetic subject can present a polymorphic clinical picture of rickettsioses associating an infectious syndrome which is sometimes severe, a skin rash and a disturbance of the biological assessment with thrombocytopenia and hepatic cytolysis as the case of our patient. This observation underscores the value of early and adequate management in diabetics in order to avoid multisystem involvement that can be life-threatening.

DOI: 10.1530/endoabs.81.EP541

EP542

Leo-Bueger's disease: a rare cause of gangrene in diabetics

Kadiri Chaimae & Lachkar Hassan
Hôpital Cheikh Zayd, Endocrinology, Rabat, Morocco

Introduction
Leo Burger's thromboangiitis obliterans 'TALB' is a rare inflammatory, segmental and occlusive disease affecting small and medium-sized arteries and the veins of the extremities of the limbs. It is more common in males and its major aggravating factor is smoking.
Observation
We present the case of a 66-year-old patient with a history of chronic smoking at a rate of 25 packs per year, known type 2 diabetic for 10 years, well balanced under hygieno-dietetic measures alone (HBA1C = 6.5 %) without degenerative complications and who consults for necrosis of the right big toe associated with plantar claudication and right plantar erythema. Clinical examination revealed acute distal ischemia of the right lower limb with abolition of the distal pulses on the right and gangrene in the right big toe. The inflammatory, lipid and hemostasis assessment as well as the immunological assessment and viral serologies (HIV, HCV, and HVB) are negative. Vascular imaging shows an occlusion of the right superior popliteal artery. The patient underwent a femoropopliteal bypass with strict discharge and local care combining cleanings and excision of necrotic tumor tissue. Amputation of the right big toe is indicated. Psychological and medical support is in place to obtain smoking cessation.
Discussion and conclusion
The diagnosis of TALB is a diagnosis of elimination evoked in the absence of specific markers and identified etiological factors and which must be considered in the well-balanced diabetic patient with chronic smoking hence the interest of a overall burden of diabetics aimed both at balancing diabetes but also at correcting other cardiovascular risk factors, in particular smoking cessation, as is the case for our patient.

DOI: 10.1530/endoabs.81.EP542

EP543

Type 1 diabetes in autoimmune polyendocrinopathy

Sanaa Bammou, Severin N'Koua, Sana Rafi, Ghizlane El Mghari & Nawal El Ansari
Mohamed VI University Hospital Center, Department of Endocrinology, Diabetology, Metabolic Diseases Nutrition, Marrakech, Morocco

Introduction
Type 1 diabetes is accompanied by a high frequency of autoimmune diseases.
The aim
of this study is to determine the different epidemiological, clinical, immunological and therapeutic aspects of Type 1 Diabetes in Autoimmune Polyendocrinopathy and to analyze the results obtained.
Patients and methods
This is a retrospective study of 44 patients with type 1 diabetes, suffering from Autoimmune Polyendocrinopathy and followed in the Department of Endocrinology, Diabetology, Metabolic Diseases Nutrition the CHU Mohammed VI or in the consultation dedicated to type 1 diabetes.
Results
A total of 44 patients were included in the study. Of these patients, 32 females and 12 males. The average age at the discovery of type 1 diabetes was 12.77 ± 6.26 years. Only one patient had type 1 APS associating chronic mucocutaneous candidiasis, hypoparathyroidism, adrenal insufficiency, exocrine pancreatic insufficiency and type 1 diabetes. A APS type II was found in 14 patients, 2 of whom had Schmidt syndrome. 17 patients had APS type 3: 15 patients had Hashimoto's disease and type 1 diabetes, 1 patient had Hashimoto's disease, celiac disease and type 1 diabetes, only one patient had Graves-Basedow disease associated with diabetes type 1. 12 patients had a APS type 4 associating type 1 diabetes and celiac disease. Therapeutic management is based on replacement therapy, synthetic antithyroid drugs, gluten-free diet with education and monitoring of patients and their family members.
Discussion
APS-1, or APECED syndrome, is the rarest of the autoimmune polyendocrinopathy. The discovery of the syndrome dates back to 1929, when Torpe and Handley described the association of hypoparathyroidism and chronic candidiasis. Type 2 autoimmune polyendocrinopathy is the most frequent: i It mainly affects the adrenal cortex, the endocrine pancreas, the thyroid, the ovary, the anterior pituitary, possibly associated with digestive disorders (Biermer's disease, celiac disease), cutaneous (vitiligo, alopecia areata), rheumatological (rheumatoid arthritis). PAI 3 is a rare disease defined by the association of autoimmune dysthyroidism with type 1 diabetes, celiac disease, vitiligo or other autoimmune disease, in the absence of adrenocortical involvement and hypoparathyroidism according to the Neufeld classification. Autoimmune polyendocrinopathy type 4 is a diagnosis of elimination, which associates at least two of the organ-specific autoimmune endocrine syndromes that cannot be attributed to APS2 or APS 3 .
Conclusion
In any patient with autoimmune disease, regular follow-up is indicated in order to detect the outbreak of possible Autoimmune Polyendocrinopathy Syndrome.

DOI: 10.1530/endoabs.81.EP543

EP544

Hospitalization in a diabetes unit

Chaima Sdiri, Yosra Htira, Skander Msolly, Maryam Cheikhrouhou, Zohra Hadj Ali, Chaima Jemai, Hedfi Imene & Feika Ben Mami
Institut De Nutrition, Tunis, Tunisia

Introduction
Diabetes is a chronic disease. Its management may require frequent hospitalization. The aim of our study was to determine hospitalization reasons in the diabetic department of The National Institute of Nutrition of Tunis.
Method
It was a prospective study conducted in the department of diabetology in the National Institute of Nutrition in Tunis for three months. The study was carried out on the medical records of hospitalized patients.
Results
We included 90 patients with diabetes with a sex ratio (M/F) of 0.7 and a mean age of 51.7 ± 17.7 years. The majority were type 2 diabetics (72%). The mean age of diabetes was 12.7 ± 8.8 years [0;34]. Smoking concerned 11% of patients. A history of hospitalization in the department was found in 36% of the cases. Chronic diabetic imbalance was the most frequent reason of hospitalization (72%): the initiation of insulin therapy was necessary in 35% of the cases. Emergency hospitalization was indicated in 22% of patients with diabetes and it was correlated significantly with type 1 diabetes ($P = 0.004$) among whom 11% were hospitalized for diabetic ketosis and 11% for severe hypoglycemia. Among hospitalized women with diabetes, 6% were pregnant. The average length of hospital stay was 5.2 ± 2.4 days [2;15]. Hypertension, dyslipidemia, dysthyroid, obesity and coronary artery

disease were found in 52%, 53%, 11%, 40% and 11% of the cases, respectively.
Conclusion
Our study showed a high rate of hospitalization among patients with diabetes outside of a genuine emergency. Therapeutic and dietary education is an essential pillar in the management of all diabetic patients to achieve a good glycemic control while keeping a regular ambulatory follow-up.

DOI: 10.1530/endoabs.81.EP544

EP545

Pegylated Interferon induced Latent Autoimmune Diabetes Mellitus of Adults(LADA) in acute setting is not uncommon

Gideon Mlawa[1,2], Chrisopher Smith[1, 3], Janessa Bell[3], Hassan Rehmani[3], Mahamud Bashir[1], Shrini Patel[3], Haythum Elsayed[3], Muhammad Saleem[3] & Musarat Hussain[3]
[1]Queen's Hospital, London, United Kingdom; [2]Queen's Hospital, Diabetes and Endocrinology/Acute Medicine, London, United Kingdom; [3]Queen's Hospital, Acute Medicine, London, United Kingdom

Background
Pegylated interferon-alpha (IFN-α) is licensed as an antiviral, immunomodulatory and anti-proliferative therapy, but may induce autoimmune conditions including Type 1 diabetes Mellitus/latent Autoimmune Diabetes of Adults (LADA).
Case Report
A 50-year-old male presented with a 3-week history of polyuria, polydipsia and weight loss. Following review by his General Practitioner he was found to have an elevated serum glucose (55.4 mmol/l). Inpatient treatment with intravenous fluids was given alongside initiation of Metformin and Gliclazide. Further investigations revealed HbA1c 170 mmol/l and positive Anti-GAD antibody titer, confirming a diagnosis of LADA, therefore, Insulin detemir was commenced and Gliclazide was stopped. He has polycythemia Vera being treated with peginterferon alfa-2a 135 mg fortnightly, and a history of ischemic heart disease, stroke and an implantable cardioverter-defibrillator. He was taking peginterferon alpha-2a for 4 years prior to diagnosis of LADA.
Discussion
Polycythaemia Vera is a myeloproliferative disorder with Pegylated interferon-alpha as possible treatment option. Pegylated interferon-alpha therapy may be associated with onset of Diabetes mellitus, which can be acute, slow or fulminant. In our case, LADA presented 4 years after initiation of treatment. The pathogenesis of pegylated induced autoimmune diabetes is unclear. It has been proposed that pegylated interferon may shift the Th1/Th2 balance to a Th1-predominant state, resulting in an induction of Th1-type cytokines which leads to an accelerated destruction of β-cells within the pancreas as demonstrated by Murine models. Additional studies have reported high levels of anti-GAD antibodies in patients a few months after initiation of pegylated interferon treatment.
Conclusion
This case highlights causal relationship between Pegylated interferon-alpha and Type 1 autoimmune diabetes/lADA. It's recommended that pre-treatment HbA1c is measured alongside regular serum glucose and GAD antibodies during the course of treatment with Pegylated Interferon-alpha to ensure timely diagnosis and management of diabetes.

DOI: 10.1530/endoabs.81.EP545

EP546

Case report: The HAIR-AN syndrome

Sanaa Bammou, Sana Rafi, Ghizlane EL Mghari & Nawal EL Ansari
Mohamed VI University Hospital Center, Department of Endocrinology, Diabetology, Metabolic Diseases Nutrition, Marrakech, Morocco

Introduction
The HAIR-AN syndrome, which consists of hyperandrogenism (HA), insulin resistance (IR) and acanthosis nigricans (AN), is an underdiagnosed endocrinopathy.
Observation
We report the case of Miss A.M., 24 years old, admitted for exploration of hyperandrogenism. Anamnesis: the patient reported polyuropolydipsic syndrome and the notion of weight gain without eating disorders, making a total of 28 kg in 6 months. This period is also marked by the onset of amenorrhea, increased body and facial hair, increased pigmentation of skin, increased sweating and alopecia. Upon presentation to the Endocrine clinic, examination of the patient revealed
- Severe hirsutism scored at 34 according to the Ferriman and Gallowey score, associated with acne and seborrhea
- Homogeneous obesity without male musculature
- Acanthosis nigricans was positive at the flexor surfaces, neck, axillae, cubital fossae the base of the neck.
- buffalo hump

Investigations showed
follicle stimulating hormone (FSH), luteinizing hormone (LH), and prolactin (PRL) are within normal limits. She had normal estradiol level, and testosterone level of 0.5 mg/l, 4 androstene-dione and 17 OHP within the standards. low-dose dexamethasone suppression test returned to negative at 0.35 mg/dl, 2 normal 24-hour urinary free cortisol (UFC), UFC the first at 31.85 mg/24 h, the second at 42 mg/24 h and salivary cortisol was normal level of 0.6 ng/ml. Ultrasound of the pelvis revealed that the left ovary measured 18.8 cm^3 with several anechoic cystic formations, number$>$ 10 of infracentimetric size, The right ovary measured 13.7 cm^3 in volume, seat of several anechoic cystic formations number$>$ 10 of infracentimetric size concluding to an aspect in favor of a bilateral ovarian dystrophy. The metabolic impact assessment showed hypertriglyceridemia level of 2.02 g/l and diabetes with an HBA1c 6.8%. From a therapeutic, the patient was started hygiene and dietary measures with metformin for her blood sugar, and to help in enhancing the peripheral insulin action., cyproterone acetate associated with ethinyl estradiol.
Discussion
The HAIR-AN syndrome is one of the most underdiagnosed clinical entities in endocrinology. The reason for this is that women with hyperandrogenism are not usually screened for insulin resistance and acanthosis nigricans. It probably accounts for 1%-3% of women with hyperandrogenism. Barbieri and Ryan have described the salient features of this syndrome.
Conclusion
The HAIR-AN syndrome can cause profound psychological distress manifested by morbidity, depression and a sense of worthlessness which may require long-term psychological support.

DOI: 10.1530/endoabs.81.EP546

EP547

Familial hypercholesterolemia: a case report

Gorgi Khaoula, Kamel Farah, Lamya Echchad, Rifai Kaoutar, Iraqi Hinde & Gharbi Mohamed El Hassan
Ibn Sina University Hospital, Endocrinology and Metabolism Disease Department

Introduction
Familial hypercholesterolemia is an autosomal dominant genetic disease linked to a mutation in 3 genes involved in the catabolism of LDL particles. It is characterized by an exclusive increase in low-density lipoproteins (LDL). It is associated with a high risk of premature cardiovascular complications. We report the case of a patient with familial hypercholesterolemia.
Case
44-year-old patient, From a first-degree consanguineous marriage, with a history of: hypertension under treatment, deaths at an early age as well as hypercholesterolemia in the family. Her history of the disease dates back to the age of 7 years with the appearance of cutaneous xanthomas and xanthelasmas. The diagnosis of hypercholesterolemia was retained following family screening at the age of 33 years, treated with Rosuvastatin 40 mg. The evolution was marked by the development of severe coronary artery disease requiring double coronary bypass surgery. Clinical examination found tendon and skin xanthomas and xanthelasma. The biological work-up showed LDL-C: 5.41 g/l, HDL-C: 0.34 g/l, triglycerides (Tg): 0.88 g, total cholesterol (TC): 5.93 g/l, Lipoprotein electrophoresis (LPE) found: clear appearance, LDL: 83.3%, HDL: 12.5%, VLDL: 4.2%, ApoB measuring: 3.14 g/l. The diagnosis of familial

hypercholesterolemia in the patient was retained: in view of the familyhistory of the first-degree relative with early coronary disease, the personal history of early coronarydisease, the presence of tendinous xanthomas, and the LDL-C level above 3.3 g/l according to the Dutch Lipid Clinic Network Score. The workup showed multiple bilateral atheromatous plaques in the carotid arteries and in the arteries of the lower limbs. The management of the patient consisted of a reinforcement of hygienic and dietary measures, with a combination of Rosuvastatin 40 mg per day, Ezetimib 10 mg per day and IPCSK9. The genetic study is essential but not available in Morocco, a cascade screening is proposed in her family.
Discussion & Conclusion
Familial hypercholesterolemia is often underdiagnosed and undertreated. The diagnosis is made according to the Dutch Lipid Clinic Score, which take into account LDL c levels, personal and/or family history of cardiovascular disease and clinical signs of dyslipidemia. Early diagnosis is important to treat the disease as early as possible and prevent cardiovascular complications.

DOI: 10.1530/endoabs.81.EP547

EP548

Methods to measure the mitochondrial toxicity in mouse kidney stem cell by toxicant

Minsu Lee, KangMin Kim, Jimin Lee, YongIn Kim & Eui-Bae Jeung
Chungbuk National University, Laboratory of Veterinary Biochemistry and Molecular Biology, College of Veterinary Medicine, Cheongju, Rep. of South Korea

Mitochondria play an important role in generating energy, and they are essential to cell survival. Mitochondria have varieties of functions, such as regulating intracellular calcium concentration and signal transduction, controlling hormone synthesis, inflammatory responses, and free radicals. In particular, this research is interested in the mitochondria in kidney tubular cell. Since mitochondria in tubular cells play an important role in supplying energy, removal of waste and reabsorption of nutrients in the blood, control of blood pressure, and maintenance of homeostasis. Mitochondrial damage may occur by drugs or related chemicals for the treatment of various diseases. Therefore, it may be related to mitochondrial dysfunction. Following experiment was conducted to investigate the relation between kidney and mitochondrial dysfunction. First, five drugs known to be toxic and two non-toxic chemicals to mitochondria were selected. After treatment with mouse kidney stem cells, the specific concentration of cell viability (IC_{50}) was selected for each drug. The results of doxorubicin, a representative mitochondria toxicant, treated on the cell, confirmed that the expression of Mn-SOD increased according to the increasing concentration of doxorubicin. Result of performing an analysis using MitoSOX red staining to confirm the relationship between mitochondrial toxicity and reactive oxygen species (ROS), it was found that the level of ROS according to the concentration of a toxic drug was relatively increased compared to that of a non-toxic drug.

Acknowledgement
This research was supported by grants (20183MFDS525) from the Ministry of Food and Drug Safety in 2021.

DOI: 10.1530/endoabs.81.EP548

EP549

Abstract Withdrawn

DOI: 10.1530/endoabs.81.EP549

EP550

Correlation between the markers of peripheral arterial disease, albuminuria, dyslipidemia with the change in HbA1c in patients with T2DM

Ragini Rohatgi, Pooja Kudkar & Daisy Alfred
Rohit Diabetes Centre, Mumbai, India

Introduction
We explored utility of ankle-brachial index (ABI), toe brachial index (TBI), Albumin Creatinine Ratio (ACR), Low Density Lipoprotein Cholesterol (LDL-C) in context with change in HbA1c
Methods
We conducted an observational study in 25 T2DM on standard care in real world setting
Results
The mean follow up (months) was 19.2 ($\pm$6, range 12). The mean age (years) was 57 ($\pm$12, 95% CI 52 to 63). Initially 36% (9/25) had HbA1c $<$ 7% which increased by 16% with an addition of four patients with HbA1c $<$ 7%, 52% (13/25). Additional four patients achieved LDL-C $<$ 100 mg/dl, 72% (18/25) increase to 88% (22/25). Initially, TBI Left was within range (0.5-0.75) in 8% patients (2/25) which increased to 16% (4/25). ACR was unchanged with $<$ 30 in 80% of patients (20/25). There was a decrease in the number of patients with target range of ABI- right and left from 80% (20/25) to 68% (17/25) and 72% (18/25) to 68% (17/25) patients, respectively. There was no significant corelation between the change in HbA1c and change in LDL (r -0.14, 95% CI -0.51 to 0.26, $P=0.47$ ns), ABI- right (r -0.18, 95% CI -0.54 to 0.22, $P=0.36$ ns), ABI- left (r 0.25, 95% CI -0.15 to 0.59, $P=0.21$ ns), TBI- right (r -0.14, 95% CI -0.15 to 0.26, $P=0.48$ ns), TBI- left (r -0.32, 95% CI -0.63 to 0.08, $P=0.11$ ns), ACR (r 0.06, 95% CI -0.34 to 0.44, $P=0.77$ ns). Table: Change in markers
Conclusion
The change in HbA1c was independent of the change in the markers of peripheral arterial disease and nephropathy. The results need corroboration with larger studies.

DOI: 10.1530/endoabs.81.EP550

Table 1

		Mean	SD	95% CI	p value	Mean change
HbA1c (%)	Baseline	8.3	2.2	7.3 to 9.2	0.081 ns	-0.97
	Follow up	7.3	1.4	6.7 to 7.9		
LDL (mg/dl)	Baseline	84.8	39.3	68.5 to 101.1	0.08 ns	-17
	Follow up	67.5	30	55.1 to 79.9		
ABI-Right	Baseline	1.19	0.10	1.14 to 1.23	0.68 ns	0.014
	Follow up	1.2	0.13	1.15 to 1.26		
ABI-Left	Baseline	1.21	0.11	1.16 to 1.26	0.29 ns	0.37
	Follow up	1.57	1.75	0.85 to 2.3		
TBI-Right	Baseline	1.02	0.28	0.91 to 1.14	0.62 ns	-0.044
	Follow up	0.98	0.34	0.84 to 1.12		
TBI-Left	Baseline	1.09	0.25	0.99 to 1.19	0.039	-0.15
	Follow up	0.94	0.25	0.84 to 1.04		
ACR	Baseline	32.52	50.2	11.7 to 53.2	0.97 ns	-0.5
	Follow up	32.03	51.4	10.7 to 53.2		

EP551

Dopplerography and neuromarker BDNF indicators correlation in patients with diabetic neuropathy at the later complications stage'

Telman Kamalov & Olimkhon Alimkhanov
Republican Specialized Scientific Practical Medical Center of Endocrinology of Public Health Ministry named by acad. Ya.Kh. Turakulov, Tashkent, Uzbekistan

The purpose of the study is to study the correlation bond indicators of ultrasonic doppler and neuromarker BDNF in blood in patients with diabetes mellitus type 2 (DM 2) with diabetic neuropathy at the later complications stage
Material and research methods
A study was conducted 215 patients with DM 2, of which 160 persons suffering from diabetic neuropathy (DNP) in the late complications stage. The following groups of patients were formed: 1 gr. - patients with DM2 type without DNP - 55 patients, 2 gr. - Patients of the DNP in the stage of late complications - 160 patients. In the study, the patients were subjected to clinical and biochemical methods of the study (Glycemia, HBA1C, Alt, Ast, Bilirubin, Urea, Creatine, BDNF, etc.), as well as instrumental examination methods - ECG, Electroneuromyography, Doppler Vessels of the lower extremities, and etc
Research results
Revealed significant correlations of BDNF levels and a number of laboratory and instrumental indicators. A correlation bond with a level of HBA1C and doppler indicators in both groups of patients was detected. In this case, the connection with the glycemia on an empty stomach was unreliable. All the above data indicate the need for timely adequate conservative therapy of chronic wound defects of the lower limbs in patients with DM 2, developing the prevention measures for their recurrence and organizing long-term observation of patients with high risk of development of this complication of diabetes.
Conclusions
The correlation relationship with a level of glycated hemoglobin, blood flow rate in the femoral artery, in the leg, the pulsation index in the tibial artery and the index of resistance in the femoral artery

DOI: 10.1530/endoabs.81.EP551

EP552

'The Echocardiography data of patients with type 2 diabetes mellitus complicated by cardio-renal syndrome'

Kamola Alimova
Republican Specialized Scientific Practical Medical Center of Endocrinology of Public Health Ministry named by acad. Ya.Kh. Turakulov, Department of Diabetic Nephropathy, Tashkent, Uzbekistan

The purpose of the study is to study the Echocardiography dataof patients with type 2 diabetes mellitus complicated by 4 type cardio-renal syndrome
Material and methods
We examined in total for the period from October 1, 2021 to December 1, 2021 - 25 patients suffering from type 2 diabetes mellitus with chronic renal disease (CRD) and chronic cardial insufficiency (CCR). The research methods included: 1) general clinical (study of endocrine, neurological status, anthropometry 2) instrumental (ECG, roentgen of thorax, ultrasound of internal organs 3) biochemical tests (Hb1AC, glycemic profile, urea, creatinine, lipid spectrum, coagulogram),4) hormonal blood tests (insulin, C-peptide etc.)
Results
We analyzed 25 patients with type 2 diabetes mellitus complicated by chronic renal disease III and chronic heart insufficiency (CHI). Of these, women -13, men -12. Biochemical blood tests have shown that urea and creatinine were reliably elevated in all patients. The Echocardiography investigation showed dysfunction of left ventricle and cardiomyopathy. According to the classification of cardio-renal syndrome, we distributed patients to 2 groups: 1 group – 15 patients with 2 type of cardio-renal syndrome. 2 group with 4 type of cardio-renal syndrome.
Conclusions
In the diagnosis of cardio-renal syndrome, the assessment of the indicators of central hemodynamics plays an important role. Patients with type 2 diabetes mellitus complicated by cardio-renal syndrome have dysfunction of left ventricle and cardiomyopathy

DOI: 10.1530/endoabs.81.EP552

EP553

'The results of the Echo-cardiographic investigations in patients with diabetic foot syndrome and chronic heart failure'

Telman Kamalov[1] & Muzaffar Khaydarov[2]
[1]Republican Specialized Scientific Practical Medical Center of Endocrinology of Public Health Ministry named by acad. Ya.Kh. Turakulov of Diabetic Foot Syndrome, Tashkent, Uzbekistan; [2]Andijan State Medical Institute of Surgery Diseases, Andijan, Uzbekistan

The purpose of the study is to study the echo-cardiographic disorders in patients with diabetic foot syndrome (DFS) and chronic heart failure (CHF)
Material and methods
The study was conducted in 62 patients with SDS treated in the department of surgical diseases and civil defense of the Andijan State Medical Institute in 2019 - 2021. The following groups of patients were formed: 1 gr - patients with DM 2Type and the neuroichemic form of DFS and HSN-31 patients, 2 groups - patients with diabetes mellitus type 2 (DM 2Type) and neuroichemic DFS form without CHF -31 patients, 3 gr. - A group of control, 20 healthy persons of the appropriate age and gender. All 50 patients were exposed to surgical treatment. In a study, patients were subjected to clinical and biochemical methods of research, functional tests, as well as instrumental methods of examination, doppler vascular vascular methods, bacteriological analysis of separated from the wound, as well as statistical techniques.
Results
In the 1st group of patients, the average value of the fraction of the left ventricle emissions (LVE) were in the range of 41.5 $\pm$ 2.2 compared with the 2nd group of 56.3 $\pm$ 3%; ($P<0.001$). The indexed finite-systolic volume of LV was reduced only in patients 1 of the group (43 $\pm$ 8 ml/m against 57 $\pm$ 9 in 2 groups; $P<0.05$). The value of the anterograde shock volume was also reliably below in 1 group of patients (39 $\pm$ 9 vs 49 $\pm$ 11 ml in 2 group; $P<0.05$). Cardiac output and the heart rate were also reliably reduced in 1 group (4.4 $\pm$ 0.5 vs 5.7 $\pm$ 0.6 l/min; $P<0.05$ and 1.23 $\pm$ 0.26 vs 1.72 $\pm$ 0.29 l/m 2; $P<0.005$, respectively).
Conclusions
In patients with diabetic foot syndrome and chronic heart failure reliable decrease in echo-cardiographic indicators was revealed.

DOI: 10.1530/endoabs.81.EP553

EP554

'The Hemodynamic indicators in patients with diabetic foot syndrome and chronic heart failure'

Telman Kamalov[1] & Muzaffar Khaydarov[2]
[1]Republican Specialized Scientific Practical Medical Center of Endocrinology of Public Health Ministry named by acad. Ya.Kh. Turakulov, Tashkent, Uzbekistan; [2]Andijan State Medical Institute, Department of Surgery Diseases, Andijan, Uzbekistan

The purpose of the study is to study the Hemodynamic indicators in patients with diabetic foot syndrome (DFS) and chronic heart failure (CHF)
Material and methods
The study was conducted in 62 patients with SDS treated in the department of surgical diseases and civil defense of the Andijan State Medical Institute in 2019 - 2021. The following groups of patients were formed: 1 gr - patients with DM 2 Type and the neuroichemic form of DFS and HSN-31 patients, 2 groups - patients with diabetes mellitus type 2 (DM 2 Type) and neuroichemic DFS form without CHF -31 patients, 3 gr. - A group of control, 20 healthy persons of the appropriate age and gender. All 50 patients were exposed to surgical treatment. In a study, patients were subjected to clinical and biochemical methods of research, functional tests, as well as instrumental methods of examination, doppler vascular vascular methods, bacteriological analysis of separated from the wound, as well as statistical techniques.
Results
In the 1st group of patients, the average central systolic pressure was significantly higher (168/96 $\pm$ 7.2 mm hg. in comparison with the 2nd group of 126.3 $\pm$ 3 6; ($P<0.001$). Peripheral blood pressure was increased only in patients 1 groups (162/92 $\pm$ 4.2 mm hg. against 118/66 $\pm$ 3.6 mm hg. in group 2; $P<0.05$). The value of the daily blood pressure was also reliably higher in 1 group of patients (171/98 $\pm$ 4.3 vs 129/82 $\pm$ 11.2 mm. In 2 groups; $P<0.05$).

Conclusions
In patients with the syndrome of the diabetic foot of the neuro-ischemic form with chronic heart failure, reliable deterioration of hemodynamic indicators was revealed.

DOI: 10.1530/endoabs.81.EP554

EP555

'Biochemical indicators in patients with type 2 diabetes mellitus in hemodialysis'

Mokhira Teshabekova[1]
[1]Republican Specialized Scientific Practical Medical Center of Endocrinology of Public Health Ministry named by acad. Ya.Kh. Turakulov, Tashkent, Uzbekistan

The purpose of the study is to study biochemical indicators in patients with type 2 diabetes in hemodialysis
Material and methods
The study was carried out in 30 patients with type 2 diabetes mellitus (DM 2) treated in the Diabetic Nephropathy Department 2019 - 2021. Healthy volunteers ($n=$ 20) amounted to a control group. The paper included general-clinical, clinical and biochemical, hormonal, immunological methods of blood testing, as well as instrumental methods of I investigation -ultrasound of internal organs, ECG, ECHO-ECG, indicators of the quality of life of patients (questionnaire), as well as statistical techniques.
Results
We analyzed 30 patients with type 2 diabetes mellitus, complicated by chronic kidney disease CKD V degree and receiving hemodialysis. Of these, women -12, men -18. The average age of patients amounted to 56.3/675 years, respectively, among men and women. Biochemical blood tests have shown that urea and creatinin were reliably increased in all patients of the group, while in the control group they were within the normal range ($P<0.05$). The average pulmonary filtration rate in these patients was less than 20 ml/min/1.73 m2, which indicated the need for substantive renal therapy.
Conclusion
In patients with DM 2 associated with the CKD, the average temperature of the glomerular filtration rate in these patients was less than 20 ml/min/1.73 m2, which indicated the need for substitution renal therapy.

DOI: 10.1530/endoabs.81.EP555

EP556

'The renal dysfunction indicators of the patients with severe complications of diabetic foot syndrome(ulcer, gangrene, amputation) and chronic kidney disease'

Khamidulla Shokirov & Telman Kamalov
Republican Specialized Scientific Practical Medical Center of Endocrinology of Public Health Ministry named by acad. Ya.Kh. Turakulov, of Diabetic Foot Syndrome, Tashkent, Uzbekistan

The purpose of the study is to study the results of the biochemical investigation of the patients with diabetic foot syndrome and chronic kidney disease (CKD).
Material and research methods
A study was conducted 60 patients with diabetes mellitus type 2 (DM 2) with diabetic foot syndrome (DFS) in the late complications stage accociated with chronic kidney disease. All observed patients will be divided into 3 groups:
1 gr. - 20 patients with DFS, complicated by ulcers, gangrene and amputation and in combination with HBP 4-5 stages on hemodialysis
2 gr. - 20 patients with DFS, complicated by ulcers, gangrene and ammputation in combination with CKD 4-5 stages without hemodialysis
3 gr - 20 patients with DFS, complicated by gangrene and amputation, without CKD.
A group of control will be 20 healthy faces. The investigationn methods included biochemical (bilirubin, lipid spectrum, ALT, AST, blood sugar, HbA1C, urea, creatinine, etc) and instrumental (: ECG, MRI of foots, Dopplerography of the legs vessels, ultrasound of the internal organs, etc)investigation
Results
Patients with 1 and 2 groups have revealed a reliable increase in urea levels and creatinine in the blood. The average of the blood urea in group 1 reached 15.6 mmol/l, in the second 26, 5 mmol l, in group 3 - 3.4 mmol/l (normally 2.1 - 8, 2 mmol/l). The average blood creatinine values were 167, 8 mcmol/l in group 1, 188, 7 mcmol/l in 2 groups and 35.6 mcmol/l in 3 groups in men (normally 77-127 in men and 44-96 мcmol/l in women). The average value of creatinine in women group reached 101, 4 mcmol l, in group 2 - 126.7 mcmol/l and in group 3 - 49 mcmol/l.. The value of the HbA1C achieved in groups of values 9, 2%, 10, 4% and 10, 6%, respectively.
Conclusions
In patients with diabetic foot syndrome and CKD IV-V st. without hemodialysis, reliably worst indicators were revealed in comparison with patients with DFS and CKD IV-V st without hemodialysis and patients with DFS without CKD.

DOI: 10.1530/endoabs.81.EP556

EP557

'Anamnestic indicators in patients with severe complications of diabetic foot syndrome (ulcer, gangrene, amputation) with chronic kidney disease of various stages'

Khamidulla Shokirov[1] & Telman Kamalov[2]
[1]Republican Specialized Scientific Practical Medical Center of Endocrinology of Public Health Ministry named by acad. Ya.Kh. Turakulov, of Diabetic Foot Syndrome, Tashkent, Uzbekistan; [2]Republican Specialized Scientific Practical Medical Center of Endocrinology of Public Health Ministry named by acad. Ya.Kh. Turakulov,, Tashkent, Uzbekistan

The purpose of the study is to study the anamnestic indicators in patients with severe complications of diabetic foot syndrome with chronic kidney disease of various stages
Material and research methods
A study was included 85 patients with DM 2 with diabetic foot syndrome (DFS) in the late complications stage accociated with chronic kidney disease (CKD). All observed patients will be divided into 4 groups:
1 gr. - 22 patients with DFS, complicated by ulcers, gangrene and amputation and in combination with CKD 4-5 stages on hemodialysis
2 gr. - 21 patients with DFS, complicated by ulcers, gangrene and amputation in combination with CKD 4-5 stages without hemodialysis
3 gr - 22 patients with DFS, complicated by gangrene and amputation, without CKD.
4 gr - 20 patients with DFS, without severe complications, with the initial stage of CKD.
A group of control will be 20 healthy faces. The investigationn methods included biochemical and instrumental investigation
Results
In group 1, 12 men were observed (average age 56, 5 years) and 10 women (average age 52, 6 years). The duration of the DM 2 was 24/25 years, respectively, on the floor. The duration of HD (hemodialysis) was 25/26 months, respectively. In group 2, 10 men were observed (the average age 59, 5 years) and 12 women (average age 58, 6 years). The duration of the DM 2 was 25/27 years, respectively, by the sex. The duration of the HD was 24/28 months, respectively. In the group 3, 13 men were observed (average age 52, 2 years) and 9 women (average age 53, 6 years). The duration of the DM 2 was 18/16 years, respectively, on the sex. All diabetic polyneuropathy was diagnosed. In the 4th group, 11 men were observed (average age 53, 8 years) and 9 women (average age 58, 6 years). The duration of the DM 2 was 15/12, respectively, on the sex.
Conclusions
1. Patients 1 and 2 groups have noted the worst values of clinical and demographic indicators. 2. It is necessary to conduct further research in groups.

DOI: 10.1530/endoabs.81.EP557

EP558

Characteristics of dyslipidemia in a group of patients with diabetes

Amal Mehrzi, Saadi Wiem, Abdesslem Haifa, El Amri Abir, Sebai Imen, Ouneissa Kamilia, Yahyaoui Rim, Ben Brahim Asma & Amrouche Chiraz
[1]Tunisian Institute of Nutrition, The Day Hospital Department, Tunis, Tunisia

Objective
Dyslipidemia represents an added factor of cardiovascular risk for patients with diabetes. The objective of this work was to study the characteristics of dyslipidemia in a group of patients with diabetes.
Methods
Cross-sectional study including a group of patients with diabetes associated with dyslipidemia, during a period of 6 months, admitted in the day hospital unit of the National Institute of Nutrition of Tunis. The data was collected by consulting medical records.
Results
We included 58 patients with an average age of 57 ± 11 years and a female predominance (69%). The average duration of diabetes was 14 ± 7 years. Patients were on insulin therapy in 84% of cases. Mean glycated hemoglobin (HbA1c) was 9.4±1%. Arterial hypertension, dysthyroidism, coronary artery disease and renal failure were found in 62%, 13%, 14% and 4% of cases respectively. Pure hypercholesterolemia was noted in 58% of patients while 42% had mixed dyslipidemia. Mean cholesterolemia was 4.6 ± 1 mmol/l, mean triglyceridemia was 1.5 ± 0.6 mmol/l. The average HDL-cholesterol level was 1± 0.2 mmol/l. Mean LDL-cholesterol was 1.1± 0.3 mmol/l.
Conclusion
Lipid abnormalities are frequent in diabetes, hence the importance of systematic screening and adequate therapeutic management in order to improve cardiovascular prognosis.

DOI: 10.1530/endoabs.81.EP558

EP559

Treatment adherence in Type 2 Diabetes: Experimental study research project

Virgínia Regufe
Faculty of Medicine of the University of Porto, Porto, Portugal

Summaries
Treatment adherence in Type 2 Diabetes: Experimental study research project
Diabetes is a metabolic disease brought about by high levels of glicose in the blood over a long period of time. It's a disease which shows an increasing incidence, mainly in developed countries. When untreated, diabetes can cause several acute complications, such as ketoacidosis, hyperglycemic hyperosmolar state or even death. Prevention and treatment consist in maintaining adequate eating habits, doing physical activity regularly and keeping a normal weight. The development of type 2 diabetes prevention projects in the community is regarded as a significant opportunity of promoting health, whereby health professionals play a vital role in its implementation. This project is integrated in "Doctoral Program in Metabolism – Clinic and Experimental" and its aim is to evaluate the efficiency of a Therapeutical Education Program in the treatment adherence in Type 2 diabetes carriers. An experimental, quantitative study is going to be conducted among individuals with Type 2 diabetes, who are being followed by health professionals at a university hospital located in Porto, Portugal. The population will be submitted to randomization and separated into experimental and control groups. Randomization will be done through random number selection per site. The evaluation of results will be carried out by responding to a questionnaire entitled "Treatment adherence in diabetes", both prior and posterior to the implementation of the program. It is expected that the results garnered from the questionnaire will prove that the adoption of Therapeutical Education Programs by the population will improve the rates of treatment adherence in diabetes.

DOI: 10.1530/endoabs.81.EP559

EP560

Long-term-high-fat/high-carbohydrate-diet-induced subcutaneous adipose tissue inflammation in gerbil model (Gerbillus tarabuli)

Zineb Bellahreche[1], Asma Guezil[2] & Yasmina Dahmani[1]
[1]University Of Science And Technology Houari Boumediene, LBPO/Nutrition & Metabolism, Department of Biology and Physiology of Organisms, Faculty of Biological Sciences, Algiers, Algeria; [2]University Of Science And Technology Houari Boumediene, Bioenergetics and Intermediary Metabolism team, Laboratory of Biology and Organism Physiology, Algiers, Algeria

Obesity results from an imbalance between energy intake and expenditure. The WHO has considered it as a chronic disease which is associated with many complications, such as insulin resistance, metabolic syndrome, etc. It is defined as an abnormal or excessive accumulation of body fat that can harm health. The distribution of this fat (visceral and subcutaneous), the size of the adipocytes and the inflammatory state of the adipose tissue are of great importance in the progression of this disease. The objective of this work is to study the effect of a long-term high-fat/high-carbohydrate diet (HFHC) on the subcutaneous adipose tissue histology of the gerbil. *Gerbillus tarabuli*, nocturnal desert rodents, is native to North Africa (south western Algeria). Our study involved 12 animal divided into 2 groups. Control group: gerbils received a natural diet (carrots and lettuce) and HFHC group: experimental animals were fed a high-fat/high-carbohydrate diet (barley, dried date and butter). After 20 weeks, gerbils were decapitated, their body weight measured, and subcutaneous adipose tissues were fixed in 10 % formalin solution for 24 h, dehydrated in graded ethanol, embedded in paraffin and stained with hematoxylin-eosin for microscopic observation. Our results show a significant increase in the final body mass induced by the HFHC diet. The histological examination revealed changes in the structure of subcutaneous adipose tissue (expansion, inflammation, and fibrosis) in HFHC group. Indeed HFHC diet increased both the accumulation of macrophages in visceral adipose tissue and in subcutaneous adipose tissue with the presence of significant vascularization and connective tissue deposition in the latter. Thus, we suggest that adipose tissue remodeling can affect all adipose tissues in the gerbil model submitted to long-term HFHC diet.

DOI: 10.1530/endoabs.81.EP560

EP561

Source of folic acid in obesity patients in the Odessa region (Ukraine)

Maria Zhygalina-Hritsenyuk & Anatoly Gozhenko
Research Institute for Transport Medicine, Odessa, Ukraine

Introduction
Obesity is known to be a disease of civilization. Both genetic and environmental factors play a role in the development of obesity. In the vast majority of cases, the main factor is eating disorders and hypodynamy. The modern human exceeds daily food demand mainly due to saturated fats and refined carbohydrates, with lack of fibre and vitamin. We decided to test the source of folic acid, because this vitamin is part of the folate cycle as a coenzyme to reduce homocysteine levels. At high levels of homocystein, the risk of cardiovascular disease, stroke, Alzheimer's disease and osteoporosis increases. Cardiovascular diseases are the main cause of death in Ukraine. The goal of the work is to study the source of folic acid depending on the body mass index in the inhabitants of the Odessa region.
Methods
Fifty-six persons (16 men and 40 women) aged from 20 to 65 living in the Odessa region were examined. Height, weight, and BMI were measured. Folic acid was determined with an immunochemical method with electrochemiluminescent detection of the test system Cobas 6000; Roche Diagnostics (Switzerland).
Results
Based on the determination of the level of folic acid in the blood, 19.6% of the surveyed inhabitants of the Odessa region had a deficiency of this vitamin. In the obesity group, the rate was 32 per cent. Folic acid deficiency can be nutritional (insufficient use of deciduous green and/or abuse of coffee) or genetically induced (folate cycle polymorphism), and further research is needed, with the development of deficit correction techniques.

DOI: 10.1530/endoabs.81.EP561

EP562

Cardio-metabolic profile of morbid obesity compared to moderate and severe obesity

Zeineb Zemni[1], Emna Bornaz[1], Nadia Alaya[2], Olfa Lajili[1], Rihab Yamoun[2], Eya Safi[3], Ben Ali Khaoula[3], Nadia Ben Amor[1], Ramla Mizouri[1], Ryme Ben Othman[1], olfa Berriche[1], Faten Mahjoub[1] & Henda Jamoussi[1]
[1]National Institute of Nutrition of Tunis, The Unit of Obesity Research, Tunisia; [2]National Institute of Nutrition of Tunis, Outpatient Department and Functional Explorations, Tunis, Tunisia; [3]Military Hospital of Instruction of Tunis, Endocrinology Department, Tunis, Tunisia

Introduction
Obesity is the disease of modern society whose prevalence continues to increase. The aim of this study was to compare the cardio-metabolic profile of morbid obesity with that of moderate to severe obesity.
Methods
It was a retrospective study conducted at the obesity unit of the national institute of nutrition in Tunis including 174 obese patients We divided the population into two groups. Group 1 (G1) with morbid obesity including 83 patients and group 2 (G2) with moderate to severe obesity including 91 patients. Morbid obesity is defined by a BMI $\geq$ 40 kg/m^2 and moderate to severe obesity is defined by a BMI between 30-39.9 kg/m^2. Clinical and biological data were collected from medical observation records.
Results
The mean age of our patients was 42.22 years in G1 and 47.93 years in G2 ($P=0.006$). A female predominance was noted in both groups, sex ratio M/F (G1): 0.18 and (G2): 049. A significant association was found between female gender and morbid obesity ($P=0.008$). The study of the metabolic profile did not find any significant difference in the prevalence of diabetes between the two groups but dyslipidemia was higher in G2 ($P=0.024$). The mean waist circumference was higher in the morbidly obese group (127.7 cm VS 114.99 cm) ($P<0.001$). No significant difference was found between the biological parameters of the two groups. Regarding cardiovascular complications, there was no significant difference between the two groups in the prevalence of heart failure, hypertension, and stroke. Joint complications such as gonalgia and low back pain were higher in G1 ($P=0.015$). Sedentary lifestyle was higher in the morbidly obese group (69.88% vs. 51.65%) with a significant difference between the two groups ($P=0.014$). The prevalence of eating disorders (the presence of at least one disorder) was higher in G1 (89.16% vs 74.73%) ($P=0.014$).
Conclusion
Our study showed that despite higher body fat, morbid obesity is not characterized by a more severe cardio-metabolic profile compared to moderate and severe obesity.

DOI: 10.1530/endoabs.81.EP562

EP563

Diabetic ketoacidosis in pregnant women with type 1 DM and Covid 19

Jesus Manuel Cornejo Dominguez, Almudena Lara Barea, Isabel María Mateo Gavira & Cristina Lopez Tinoco
Hospital Universitario Puerta del Mar, Cádiz, Spain

Introduction
Diabetes is a recognized risk factor for the development of complications in COVID-19 infection, with an increased incidence of ketoacidosis observed in patients admitted to hospital.
Case Reports
We present the case of a patient with type 1 DM complicated by diabetic retinopathy and unplanned pregnancy (pregestational Hba1c 9.1%). In follow-up during pregnancy: progression of retinopathy and fetal renal pyeloectasia in morphological ultrasound at 20 weeks, HbA1c second trimester 6.8%. Consultation in the Obstetrics Emergency Room of a 29+4 week pregnant woman due to emetic symptoms of 3 days of evolution, showing ketoacidosis (fasting plasma glucose 287 mg/dl, pH 7.11 bicarbonate 5.7 mmol/l and ketonuria), and starting intravenous insulin and fluid therapy. In case of suspicion of COVID-19 contact, PCR Sars-CoV-2 is performed, which is positive. Cardiotocographic record (CTG) on admission: pattern according to gestational age and adequate fetal HR, limited variability in some section that recovers spontaneously. No sustained decelerations. Non-dynamic. Free Style Libre (previous 14 days): average glucose 155 mg/dl, GMI 7.0%, CVC 41.7%, time on target 65%, above target 29%. Although the patient did not present respiratory symptoms or vital compromise, it was decided to admit her to the intensive care for treatment and monitoring of ketoacidosis and obstetric control with continuous CTG. At 24 h, uterine dynamics is evident in the CTG, for which she receives tocolytic treatment with atosiban to inhibit contractions, magnesium sulfate and betamethasone for fetal lung maturation and a slight worsening of glycemic control. After intensifying intravenous insulin therapy, optimal fasting plasma glucose levels for pregnancy were achieved, but refractoriness in the control of ketoacidosis and intermittent oral tolerance prevented withdrawal of the insulin perfusion. On the 11th day of admission (current gestation of 31+1 weeks) there was evidence of CTG, loss of fetal well-being and uterine dynamics, deciding to carry out an urgent caesarean section that proceeded without complications. After this, correction of ketoacidosis and improvement of oral tolerance were achieved, with withdrawal of intravenous insulin therapy and transfer to a conventional ward without complications.
Conclusions
We present this case emphasizing the importance of multidisciplinary management of diabetic ketoacidosis during pregnancy and the role that COVID-19 infection may have played.

DOI: 10.1530/endoabs.81.EP563

Endocrine-Related Cancer

EP564

Clinical features and survival outcomes of patients with ectopic Cushing's syndrome: a single-center study

Olga Golounina[1], Liudmila Rozhinskaya[2], Svetlana Arapova[2], Michael Pikunov[3], Patimat Khandaeva[2], Valentin Fadeyev[1], Evgenia Marova[2] & Zhanna Belaya[2]
[1]I.M. Sechenov First Moscow State Medical University of the Ministry of Health of the Russian Federation (Sechenov University), Moscow, Russian Federation; [2]The National Medical Research Center for Endocrinology of the Ministry of Health of the Russian Federation, Moscow, Russian Federation; [3]The National Medical Research Center of Surgery named after A.V. Vishnevsky of the Ministry of Health of the Russian Federation, Moscow, Russian Federation

Objective
To analyze long-term treatment outcomes and to determine prognostic factors affecting the survival of patients with ECS.
Matherials and methods
Retrospective, observational study on 147 patients (88 women, 59 men) with ECS diagnosed between 1990 and 2021. Various imaging studies were performed on all patients to find the source of ACTH producing neuroendocrine tumor (NET). Multivariable analysis was performed using a Cox proportional hazards model to define the independent prognostic factors.
Results
The median age at diagnosis was 40 years [28;54]. 89 patients (60,5%) had bronchopulmonary NET, 15 (10,2%) – thymic carcinoid, 5 – pancreatic NET, 6 – pheochromocytoma, 1– cecum NET, 1– appendix carcinoid tumor, 1 – medullary thyroid cancer and 29 (19,7%) patients had an occult NET. Mean time to diagnosis was 31 months, 11 patients (7,5%) had a cyclic course of disease. The most common complications in the active stage of disease were arterial hypertension (83,7%), osteoporosis with low-energy fractures (60%), type 2 DM (56,5%), cardiovascular disease (52,4%). The median follow-up period of patients was 36 months [11;73] with a maximum follow-up of 379 months. To the present date, the primary tumor was removed in 94 (63,9%) patients. Regional and distant metastases were revealed in 32 (21,8%). At the time of last observation, 62 patients (66%) had achieved stable remission, 12 (12,8%) had relapsed and received treatment with somatostatin analogs ($n=9$) or ketoconazole ($n=1$), and 38 patients (25,9%) had died from multiple organ failure ($n=22$), pulmonary embolism ($n=5$), sudden cardiac death ($n=2$), acute cerebrovascular accident ($n=2$), COVID-19 ($n=3$), complications of surgery ($n=2$), hip fracture ($n=1$), unknown cause ($n=1$). Bilateral adrenalectomy was performed on 45 patients (30,6%): due to occult tumor in 16 patients and incurable stage of disease in 29 patients. Multivariate analysis revealed that negative predictive factors for survival were: age $\geq$51 years at diagnosis, $P<0,001$ (HR 5,513 (2,286–13,293)), localization of NET in the pancreas, $P=0,013$ (HR 5,771 (1,473–23,176)), occult tumors, $P=0,006$ (HR 3,670 (1,461–9,216)) and LNSC $\geq$108,4 nmol/l, $P=0,009$ (HR 4,205 (1,433–12,334)). Bronchial NET, $P=0,006$ (HR 0,272 (0,109–0,684)) was a positive predictor of survival.
Conclusion
The survival rate ofECS is up to 75% over a mean follow-up of 36 months in spite of severe multiple complications associated with hypercortisolism. The severity of hypercortisolism, NET localization and occult tumors are negative factors associated with high mortality. Consequently, more aggressive treatment of

hypercortisolism is potentially beneficial for survival in patients with extremely high LNSC.

DOI: 10.1530/endoabs.81.EP564

EP565

Analysis and prognostic significance of miRNAs in papillary thyroid carcinoma

Romena Laukienė[1] & Laima Ambrozaityte[2]
[1]Vilnius University Hospital Santaros Klinikos, Center of Endocrinology, Vilnius, Lithuania; [2]Vilnius University Hospital Santariskiu Clinics, Department of Human and Medical Genetics, Institute of Biomedical Sciences, Vilnius, Lithuania

Background
Papillary thyroid carcinoma (PTC) is the most frequently occurring endocrine malignancy, with an increasing rate of incidence over the last three decades. Generally, PTC has an excellent prognosis with a relatively low mortality rate, but a small portion of PTC patients suffers from an aggressive form of the disease with tumor invasion and metastasis. Analysis of miRNAs expression data may improve perioperative decision making for patients with PTC.
Aim of the study
To settle the diagnostic utility of specific miRNAs in the preoperative assessment of thyroid nodules.
Methods
One hundred thyroid fine needle aspiration (FNA) samples with suspected thyroid carcinoma were collected in the prospective molecular study at Vilnius University hospital Santaros klinikos. The expression level of the selected five miRNAs (miR125a, miR146b, miR200b, miR221, miR4324) was verified by real-time PCR in 36 non-malignant nodule aspirate samples, 34 PTC without lymph node metastases (LNM) samples and 30 PTC with LNM samples.
Results
The relative expression levels of four miRNAs differed significantly between benign and PTC groups ($P < 0.05$). The relative expression levels of two miRNAs differed significantly between PTC without LNM and PTC with LNM groups ($P < 0.05$). A 16.002-fold increase in the value of miR146 increases the probability (odds ratio) that the disease will be cancerous without metastasis rather than benign (95% CI [4.188; 61.148]). A 4.187-fold increase in the value of miR146 increases the odds (odds ratio) that the disease will be cancerous with metastasis rather than benign (95% CI [1.692; 10.366]). A 31.917-fold increase in miR4324 value increases the odds (odds ratio) that the disease will be cancerous with metastases rather than benign (95% CI [5.966; 170.765]). A one-fold increase in miR4324 value increases the odds (odds ratio) that the disease will be cancerous with metastasis by 8.301 times more than non-metastatic (95% CI [2.155; 31.977]).
Conclusions
Our study showed that the expression analysis of four miRNAs (miR125A, miR221, miR146B and miR4324) could improve the accuracy of fine-needle thyroid node biopsy, which would allow a better differentiation of malignant from benign thyroid nodules. Analysis of miRNA expression levels and detection of miRNAs in FNAB can be used for the pre-operative diagnosis of thyroid cancer. To translate these data into clinical application, large cohort studies are required to examine the prognostic and diagnostic value of miRNAs.

DOI: 10.1530/endoabs.81.EP565

EP566

Immunotherapy induced glycemic dysregulation - characterization and proposed mechanisms beyond beta-cell autoimmunity

Ruth Percik[1,2] & Bernice Oberman[3]
[1]Sheba Medical Center, Division of Endocrinology, Diabetes and Metabolism, RAMAT GAN, Israel; [2]Tel Aviv University, Sackler Faculty of Medicine, Tel Aviv, Israel; [3]Gertner Institute for Epidemiology and Health Policy Research, RAMAT GAN, Israel

Aim
Check-point inhibitors have revolutionized cancer treatment while introducing a new spectrum of immune-related adverse effects. Hyperglycemia is frequently observed shortly after initiation of immunotherapy. While immune-mediated type 1 diabetes mellitus is currently the only defined condition associated with post-immunotherapy hyperglycemia, it includes only a small fraction of cases (an estimated prevalence of 0.5%). This study was aimed to determine factors associated with glycemic dysregulation following immunotherapy.
Methods
A retrospective study, using the MD-Clone interface, including data from the electronic medical records of all cancer patients treated with checkpoint inhibitors between January 2015 and January 2021.
Results
Among 3384 patients treated with immunotherapy during the study period, a statistically significant increase in glucose levels was observed after the initiation of immunotherapy [mean of maximum glucose levels during the month before immunotherapy 132.3 $\pm$ 55.8 mg/dl vs 139.8 $\pm$ 64.6 in the month after immunotherapy (P-Value < 0.001)]. Glycemic dysregulation was significant among patients treated with glucocorticoids as part of an anti-emetic regimen in protocols combining chemotherapy and immunotherapy or managing immune-related adverse events ($n = 2168$). Mean of maximal glucose level was 136.4 $\pm$ 59 mg/dl during the month before immunotherapy and 145.6 $\pm$ 68 mg/dl one month after immunotherapy ($P < 0.001$)]. Among patients who were not treated with glucocorticoids ($n = 1216$), glycemic dysregulation was not found to be significant.
Conclusions
Concomitant glucocorticoid therapy is the primary determinant of post-immunotherapy hyperglycemia. Evaluation of the possibility of a distinct, reversible, autoimmune damage to beta cells would require a prospective study with a dynamic assessment of the beta-cell reserve.

DOI: 10.1530/endoabs.81.EP566

EP567

Association of tissue miRNA (MiR-146b, -21, -221, -222, -181b) expression and the overall survival of papillary thyroid carcinoma patients

Aistė Kondrotienė[1], Albertas Dauksa[2], Diana Pamedytytė[3], Mintautė Kazokaitė[1], Aurelija Žvirblienė[3], Dalia Daukšienė[1], Vaida Simanavičienė[3], Raimonda Klimaitė[1], Rasa Verkauskienė[1] & Birute Zilaitiene[1]
[1]Institute of Endocrinology, Medical Academy, Lithuanian University of Health Sciences, Kaunas, Lithuania; [2]Institute of Digestive Research, Medical Academy, Faculty of Medicine, Lithuanian University of Health Sciences, Kaunas, Lithuania; [3]Institute of Biotechnology, Life Sciences Center, Vilnius University, Vilnius, Lithuania

Introduction
Improper management of papillary thyroid carcinoma (PTC) patients results in potentially higher fatal outcomes due to a lack of relevant prognostic markers, inadequate periodic individualized risk assessments and/or insufficient initial treatment. MiR-146b, -21, -221, -222, -181b are potential biomarkers for risk stratification in PTC.
Aim
The aim of our study was to analyze expression levels of five miRNA molecules (miR-21; miR -221; miR -222; miR -146b; miR -181b) in PTC formaline-fixed paraffin embedded (FFPE) tissue samples and evaluate their relation with the overall survival of PTC patients.
Methods
We analyzed expression of miR-221, miR-222, miR-146b, miR-21, miR-181b in FFPE PTC tissue samples of 312 patients and evaluated their relationship with the overall survival of these patients. To evaluate the association of survival rate after thyroidectomy with miR expression pattern, PTC patients were divided into two groups with high and low PTC tissue miRs expression. Patients with miR expression levels below the median values (miR-146b = 2.59; miR-21 = 1.16; miR-221 = 0.79; miR-222 = 2.04; miR-181b = 0.00048) were assigned as having low expression levels, and patients with miR above or equal to median values were assigned as having high expression levels.
Results
The median follow-up time of PTC patients was 152 (IQR 60) months. 35 deaths were recorded till the end of study. Kaplan–Meier curves estimating the overall survival of PTC patients after thyroidectomy according to high/low tissue expression levels of miR-146b, -21, -221, -222, -181b were compared using the Log rank test, however no statistically significant differences were found ($P = 0.479$; $P = 0.583$; $P = 0.383$; $P = 0.995$; $P = 0.516$). Kaplan–Meier plots for miR-146b paired with miR-221 (median survival 141.7 months (IQR 18)), and miR-146b, miR-221, miR-21 panel (median survival 138 months (IQR 12.75)) compared by the Log-rank test demonstrated significant differences in survival curves for miR-146b, miR-21 and miR-221 panel ($P = 0.019$).

Conclusion
Higher expression of miR-146b, miR-21 and miR-221 is associated with a decreased overall survival of PTC patients.

DOI: 10.1530/endoabs.81.EP567

EP568

New insights into armadillo repeat-containing 5 gene: originated in gene mutation, suffering protein property alteration, culminate in function inactivation

Minmin Han[1], Xiaoming Cao[2], Xueming Lin[3], Xiao Lv[2], Ruizhi Xue[2], Chunduo Zhang[2], Bingjun Chen[2], Jian Zhang[1], Mengnan Li[1] & Yunfeng Liu[1]
[1]First Hospital of Shanxi Medical University, Endocrinology, Taiyuan, China; [2]First Hospital of Shanxi Medical University, Urology, Taiyuan, China; [2]First Hospital of Shanxi Medical University, Urology, Taiyuan, China

Introduction
As a tumor-suppressor gene, armadillo repeat-containing 5 (ARMC5) gene regulates steroidogenesis and cell apoptosis in manner of second-hit model. Mutations of ARMC5 gene will disturb its normal function, leading to reduced cortisol synthesis and cell apoptosis, which is acknowledged as a frequent cause of primary bilateral macronodular adrenal hyperplasia (PBMAH). Not until another somatic ARMC5 mutation occur in germline mutation carriers, will they manifest as PBMAH. The underlying pathogenesis has always been of great interest among researchers, however, still remains mystery.
Matherials and methods
This study was conducted in a Chinese family with hereditary PBMAH, including four members from two generations. Gene test was conducted in the blood samples and adrenal tissues. In vitro experiments were introduced to explored gene expression of wild type and mutants at transcription and translation levels. Further investigations were conducted to trace the subcellular location, degradation pathway and stability of wild type and mutant protein.
Results
Gene test discovered one germline (mutant 1: c.337dupG, p.A113Gfs*7) and two somatic (mutant 2: c.1157G>A; p.W386X, mutant 3: c.1900G>T, p.E634X) ARMC5 gene mutation sites. In vitro experiments indicated significantly increased mRNA levels of all the mutants along with significantly increased protein content of mutant 2 and 3 than that of wild type, however, the mutant 1 protein cannot be detected with western blot. Extensive subcellular localization experiment demonstrated that wild type protein was localized in both cytoplasm and nucleus, while, the mutants were accumulated primarily in the nucleus. As regard to protein degradation pathway experiment, it proved that wild type and mutant 1 protein were degraded through ubiquitin-proteasome pathway and lysosomal pathway, respectively. Based on the different degradation rate of wild type, mutant 2, and mutant 3, we inferred that the protein stability of the mutant 2>wild type>mutant3.
Conclusion
This study discovered three novel ARMC5 gene mutation sites which extended the spectrum of the mutation. In vitro experiments demonstrated significant differences at transcription and translation levels between the wild type and mutants. In addition, mutant protein presented different subcellular location, degradation pathway, and stability compared with that of wild type. Taking the lead from these findings, we inferred that these protein property alterations might influence its normal function, leading to PBMAH progression.

DOI: 10.1530/endoabs.81.EP568

EP569

Novel pathogenetic mutation of MEN1 gene causing hyperparathyroidism, pancreatic glucagonoma, adrenal adenoma, and collagenomas

Rosa Pitino[1], Davide Vimercati[1], Francesca Pizzolitto[1], Edoardo Luigi Maria Mollero[1], Tommaso Daffara[1], Alice Ferrero[1], Renzo Boldorini[2], Marina Caputo[1, 3] & Flavia Prodam[1,3]
[1]Endocrinology, Università del Piemonte Orientale, Department of Translational Medicine, Novara, Italy; [2]Pathology Unit, Novara Medical School, Department of Health Sciences, Novara, Italy; [3]Department of Health Sciences, Università del Piemonte Orientale, Novara, Italy

Background
Multiple endocrine neoplasia type 1 (MEN1) is a rare hereditary autosomal dominant tumor syndrome caused by inactivating mutations of the tumor suppressor gene *MEN1* which encodes the protein menin. It is characterized by the occurrence of tumors involving two or more endocrine glands, primarily parathyroid, entero-pancreatic, and anterior pituitary, as well as non-endocrine neoplasms. Glucagonomas occur in fewer than 3% of patients with MEN1, causing hyperglycemia, skin rash (necrolytic migratory erythema), weight loss, anemia, and stomatitis.
Case report
In March 2019 a 35-year-old Pakistani woman underwent surgical removal of 2 overactive parathyroid glands causing primary hyperparathyroidism diagnosed after a pelvic fracture and the identification of brown tumors. After surgery, she was lost at follow-up. In August 2020, she was admitted to Emergency Department for fever, weight loss, and new-onset diabetes mellitus causing polyuria and polydipsia without ketoacidosis. Glucagon was at the upper limits of normal (252 pg/ml) and abdominal MRI revealed a neuroendocrine tumor (10 mm in the pancreatic tail) and left adrenal adenoma, confirmed by a 68Ga-DOTATOC-PET, that showed 4 areas of abnormal uptake in the pancreatic tail, body, and head, and in left adrenal gland. Duodenocephalopancreatectomy and left adrenalectomy were performed; histological examination revealed the presence of multiple well-differentiated G1 neuroendocrine tumors (Ki67<3%) with intensive positive IIC for glucagon, and adrenal adenoma. The post-surgical period was complicated by cava vein thrombosis, typical of glucagonoma, and endocarditis. The study of other endocrine glands showed the persistence of primary hyperparathyroidism due to hyperplasia of the remnant parathyroid glands confirmed by Sesta-MIBI-scintigraphy; pituitary function and MRI were normal. Dermatological investigation showed cutaneous collagenomas. Genetic testing identified a novel missense *MEN1* heterozygous pathogenetic variant c.703T>C-p.(Cys235Arg) in exon 4. The patient was monitored by MRI, 68Ga-DOTATOC-PET, and FDG-PET and no significant abnormal uptakes have been identified until now, however, she developed skin lesions suspected for necrolytic migratory erythema and she is in a close follow-up. Genetic inheritance is under investigation.
Conclusion
The clinical behavior of MEN1 depends on histological features of the tumors, the type, and degree of hormone hypersecretion and the risk of tumor recurrence. Some authors described a potential genotype-phenotype correlation, but this link remains debated. Current clinical guidelines recommend that index case and their relatives should be included in a screening program to reduce morbidity and mortality. Our case of a new pathogenetic mutation associated with glucagonoma underlines the need for a closer follow-up and surveillance with an interdisciplinary approach.

DOI: 10.1530/endoabs.81.EP569

EP570

Insulinoma in a patient with a crest syndrome

Jesus Manuel Cornejo Dominguez, Maria Isabel Mateo Gavira, Laura Larrán Escandón, Maria del Mar Roca Rodriguez & Isabel Torres Barea
Hospital Universitario Puerta del Mar, Cádiz, Spain

Introduction
Insulinomas are pancreatic neuroendocrine tumors (PNET), characterized by insulin hypersecretion syndrome with the development of hypoglycemia. The incidence of the tumor is 3-10 cases per million inhabitants. The average age of onset is 40-50 years old, being more frequent in women.
Case Reports
We present a clinical case of a patient with CREST syndrome and difficult-to-control hypoglycemia. Female patient, 81 years old, with a history of CREST syndrome (calcinosis, Raynaud's phenomenon, esophageal dysmotility, sclerodactyly, and telangiectasia) with multiple complications (esophagitis with scleroderma, vasculitis, nail ulcers) and hypertension. The patient is transferred to the Emergency Department in February 2020 due to loss of consciousness coincident with fasting plasma glucose 27 mg/dl. She had no history of diabetes, previous episodes of hypoglycemia, or apparent intake of hypoglycemic drugs. She was admitted to the Endocrinology Service for study. Refers to asthenia anorexy and weight loss of about 5 kg in the last two months which attributes to dental intervention., although it recognizes significant intake of fast-absorbing sugars. At baselane, insulin 3.2 mcUi/ml, proinsulin 5.8 pmol/l, HbA1c 3.8%, beta hydroxybutyrate <1, C-peptide 1.92 ng/ml, negative oral antidiabetics and anti-insulin antibodies, coinciding with fasting plasma glucose 35 mg/dl. After analytical confirmation of endogenous hyperinsulinism, we started treatment with fluid therapy, requiring a contribution of 1500 ml of 10% dextrose fluid daily to

keep fasting plasma glucose in range. Abdominal CT with intravenous iodinated contrast in basal phase evidenced a 12x15 mm hypodense lesion in the tail of the pancreas with enhancement in the portal phase suggestive of insulinoma. Given clinical and radiological suspicion of insulinoma and given the impossibility of suspending intravenous glucose fluid, treatment with diazoxide it was considered. Initially presents good tolerance and evolution, with progressive reduction of the requirements of intravenous glucose. However, after 6 days of treatment, he develops picture of pruritic skin lesions that do not disappear on pressure compatible with erythroderma. Evaluated by allergy service confirming allergy to diazoxide, started treatment with steroids. Consequently, the treatment was discontinued., being the evolution of the lesions favorable. In the absence of a medical therapeutic alternative, finally required surgical treatment. Distal pancreatectomy with a pathological result of a low-grade neuroendocrine tumor compatible with insulinoma. After surgery, he maintains excellent glycemic control, without hypoglycemia. Nonetheless, the patient presented a torpid postoperative period (acute renal failure, cavitary pneumonia with therapeutic bronchoscopy, respiratory failure with invasive mechanical ventilation) and she finally died.

DOI: 10.1530/endoabs.81.EP570

EP571

Clinical characteristics and survival of a cohort of patients presenting with bone metastases from differentiated thyroid cancer

Ana Piñar Gutiérrez, Ana R. Romero Lluch, Suset Dueñ as Disotuar, Irene De Lara-Rodriguez & Elena Navarro
Virgen del Rocío University Hospital, Sevilla, Spain

Introduction
Bone metastases (BM) are rare in differentiated thyroid cancer (DTC). They determine the quality of life and survival of these patients. Our objective was to evaluate the characteristics, survival and prognostic factors of a cohort of patients with BM from CDT.
Methods
Retrospective descriptive study. Patients with BM from DTC diagnosed between 1980-2021 were included. Qualitative variables are shown as n(%); quantitative variables as median and interquartile range. Survival and prognostic factor analysis was performed using the Kaplan-Meier method and univariate tests.

Table 1

Variable	Result
BM diagnosis at initial evaluation	13(48%)
BM diagnosis during follow-up	14(52%)
Time until BM appearance (months)	*151(78-234)*
Thyroglobulin at diagnosis, after thyroidectomy (ng/ml)	1000(195-7743)
T	
1-2	*8(30%)*
3-4	14(51%)
N1	9(33%)
Multiple BM	22(81,5%)
BM location	
Spine	*20(74%)*
Pelvis	*10(37%)*
Cranial	*5(18%)*
Rib cage	*4(15%)*
Upper limbs	*3(11%)*
Lower limbs	*4(15%)*
Metastases in other locations	19(70,3%)
Skeleton-related events	
Bone fractures	*7(26%)*
Spinal cord compression	*7(26%)*
Pain	*10(37%)*
Treatment with I131	*19(70,4%)*
I131 Uptake in BM	*10(37%)*
Antiresorptive treatment	10(37%)
BM Surgery	4(15%)
Palliative radiation therapy	9(33%)
Treatment with Tyrosine-kinase inhibitors	7(26%)

Results
N = 27. Women = 17(63%). Follicular carcinoma = 13(48%). Follow-up time (months) = 72(34-222). Age at diagnosis = 62(55-73). Exitus = 18(66,7%). Suvival at 1 and 5 years was 68.5% and 43.5% respectively. No independent risk factors for increased risk of death were found.
Conclusions
In our case series, 5-year survival was slightly lower than that reported in the scientific literature. This may be due to the fact that 48% presented with BM in the initial evaluation, although it has not been possible to prove it given the low number of cases. No other prognostic factors were found, possibly for the same reason.

DOI: 10.1530/endoabs.81.EP571

EP572

Clinical case of ACTH ectopic syndrome associated with small cell lung cancer (SCLC)

Malika Kozhemzharova[1], Anna Bazarova[1], Zhanar Kamitbekova[2], Natalya Pavlova[2] & Asem Baisalova[3]
[1]Astana Medical University, Nur-Sultan, Kazakhstan; [2]Multidisciplinary city hospital No1, Nur-Sultan, Kazakhstan; [3]National Research Cardiac Surgery Center, Nur-Sultan, Kazakhstan

Introduction
Ectopic Cushing's syndrome (ECS) is a rare disease caused by ACTH secretion by extrapituitary neuroendocrine tumors, characterized by high mortality. Despite the clinical sings of Cushing's syndrome, difficult access to reliable clinical examinations, leads to a delay in diagnosis and the choice of optimal treatment tactics. Small-cell lung cancer patients with ECS have a very poor prognosis.
Case report
A 35-year-old woman was hospitalized in the endocrinology department with complaints of dry mouth, thirst, hypertension (up to 170/100 mmHg). The patient also had signs of heart failure due to concomitant congenital heart disease, diabetes mellitus type 2 (T2DM) and obesity. During the year, she was repeatedly examined due to the presence of clinical manifestations of Cushing's syndrome. Physical examination: centrapetal obesity with fat deposits around the face, neck and upper back, BMI = 41.8 kg/m^2, hyperpigmentation in the neck, axillary and inguinal region, reddish-blue stretch marks on the arms, abdomen, buttocks. Laboratory evaluation revealed high levels of ACTH in the blood – 229,3 pg/ml (reference 7,2-63,3), and cortisol in daily urine 3600.8 μg/24 h (normal 58 - 403), and a decrease in potassium levels to 1.1 mmol/l, fasting glucose - 12 - 21 mmol/l. CT scan of the thoracic segment revealed a dense focus of the X segment of the right lung, metastatic character is not excluded. Abdominal CT revealed hyperplasia of both adrenal glands, multiple liver formations. PET-CT (18F-fluorodeoxyglucose): metabolically inactive formation of the lower lobe of the right lung, multiple metabolically inactive hypodense liver formations, moderately pronounced splenomegaly. The tumor marker Pro Gastrin Releasing Peptide (ProGRP) in blood was significantly increased - up to 5000 pg/ml (reference 0-46), which can increase in small cell lung cancer. Somatostatin analogues and steroidogenesis blockers (Ketoconazole) were used to treat the disease, but cortisol levels did not decrease. The primary tumor during life could not be identified, death occurred due to lung and cardiovascular failure. The histological examination at post-mortem autopsy revealed the lung neuroendocrine tumor with signs of malignancy and multiple metastatic lesions of the liver.
Conclusion
Despite the availability of modern imaging diagnostic methods, the search for the primary focus and the treatment of ACTH-ectopic syndrome present considerable difficulties and often require long-term follow-up and an interdisciplinary approach. Although the prognosis for this type of tumor is unfavorable, timely diagnosis using lung tissue tumor markers and PET could help clarify the diagnosis at an earlier stage of the process.

DOI: 10.1530/endoabs.81.EP572

EP573

Postoperative prediction of tumor recurrence in patients with nonfunctional pancreatic neuroendocrine tumors

Helena Olearska[1], Anna Sowa-Staszczak[1], Marta Opalinska[2], Anna Kurzyńska[1] & Alicja Hubalewska-Dydejczyk[1]
[1]Chair and Department of Endocrinology, Jagiellonian University Medical College, Kraków, Poland; [2]Nuclear Medicine Unit, Department of

Endocrinology, Oncological Endocrinology and Nuclear Medicine, University Hospital, Kraków, Poland

Introduction
Pancreatic neuroendocrine tumors (pNETs) are a heterogeneous group with various treatment options depending on grading, staging, and presence of symptoms related to hormonal secretion. Their incidence significantly increased over the past decade and nowadays constitutes 30% of all NETs of the gastrointestinal tract. Despite the evidence of a different malignancy potential of PNETs G2, postoperative management is the same in all patients.
Aim
The purpose of the study was to determine possible predictors of postoperative tumor recurrence in patients with nonfunctional pNET G2.
Materials and methods
We identified 165 patients diagnosed with pancreatic neuroendocrine tumors. 47 of them with locally advanced or metastatic pNET G2 were included in the study.
Results
Relapse occurred in 37.93% of patients operated with intention to treat, with the mean time to progression equaling about 2 years. In this group based on preoperative CT examinations, the average largest dimension of the tumor was estimated to be over twice bigger in comparison to patients with no recurrence (46.71 mm vs 22.89 mm), which was confirmed by postoperative histopathological examination (53.83 mm vs 34.36 mm). In over 80% of patients with the disease relapse, the average largest dimension of tumor equaled 25 mm or more, whereas in the group without relapse only 55.65% of patients had lesions of this size. Ki-67 varies significantly (metastatic 8.8% vs disease recurrence 6.78% vs no recurrence 5.15%). Both progression and recurrence were associated with the primary location of the tumor in the pancreatic tail. Interestingly, about 50% of patients were symptomatic in all three groups.
Conclusions
Based on the analyzed material it seems that lesions with the largest dimension equaling 25 mm or more and a higher Ki-67 may be a predictor of the disease recurrence. Patients' complaints, important for the management of disease, seem to be unrelated to the possible PNET G2 relapse. The unequivocal confirmation of these findings requires further observation.

DOI: 10.1530/endoabs.81.EP573

EP574

Pregnandiene-structures coupled with anti-inflammatory moieties as inhibitors of the 5α-reductase activity

Marisa Cabeza[1], Juan Soriano[2], Eugene Bratoeff[3] & Yvonne Heuze[1]
[1]Departamento de Sistemas Biológicos y de Producción Agrícola y Animal, Universidad Autónoma Metropolitana-Xochimilco, Mexico; [2]Departamento de Patología del Hospital General de México, Mexico; [3]Departamento de Farmacia, Universidad Nacional Autónoma de México, Mexico

Proliferative inflammatory atrophy and prostatic intraepithelial neoplasia are the first signs of prostate cancer. This inflammatory etiology, together with the infiltration of immune cells, could lead to the binding of the cytokines with cancer cells, forming a population that could initiate tumor growth. [1] Androgens also play an essential role in prostate tumor growth, as is well documented. [2] Androgen deprivation therapy is currently the gold standard for hormone-sensitive metastatic prostate cancer patients.[3] These data have inspired researchers to improve therapy for this disease. Previously, our group prepared a new series of hybrid compounds based on a 5,16-pregnadiene scaffold linked to anti-inflammatory drugs. These derivatives showed important antiproliferative properties. [4] In the present study, we identified the effect of five 5,16-pregnadiene derivatives bound to anti-inflammatory drugs (**M1-5**) as inhibitors of the 5α-reductase enzyme activity. This enzyme has been recognized as responsible for forming intraprostatic dihydrotestosterone from testosterone. Dihydrotestosterone has also been associated with prostate cell proliferation [5], so blocking this enzyme and preventing prostate inflammation could improve therapies for this disease. Derivatives of **M1-5** were tested as inhibitors of 5α-reductase activity by incubating radiolabeled testosterone in the presence or absence of these compounds. A fraction of the human prostate membrane and NADPH were added to this medium. Subsequently, the compounds formed were separated and identified by thin-layer chromatography. Compounds **M1-3** and **M5** inhibited *in vitro* formation of dihydrotestosterone, with the highest activity for **M1-2**, with IC_{50} values of 24.2 and 0.26 nM, respectively. However, **M3** and **M5** showed IC_{50} values too much higher, 15.8 and 6.06 μM, than **M1-2**, respectively, and **M-4** no-displayed activity. Previously, our group demonstrated the inhibitory effect of 5,16-pregnandiene on 5α-reductase activity [6]. This 5, 16 pregnandiene effects was completely diminished by indomethacin moiety attached to this compound, as shown in the **M4** derivative.
Reference List
1. Packer JR, Maitland NJ. The molecular and cellular origin of human prostate cancer. Biochim Biophys Acta. 2016;1863(6 Pt A):1238-60.
2. Culig Z, Santer FR. Androgen receptor signaling in prostate cancer. Cancer Metastasis Rev. 2014;33(2-3):413-27.
3. Nevedomskaya E, Baumgart SJ, Haendler B. Recent Advances in Prostate Cancer Treatment and Drug Discovery. Int J Mol Sci. 2018;19(5).
4. Garrido M, González-Arenas A, Camacho-Arroyo I, Cabeza M, Alcaraz B, Bratoeff E. Effect of new hybrids based on 5,16-pregnadiene scaffold linked to an anti-inflammatory drug on the growth of a human astrocytoma cell line (U373). European Journal of Medicinal Chemistry. 2015;93(0):135-41.
5. Ma C, Yoshioka M, Boivin A, Gan L, Takase Y, Labrie F, et al. Atlas of dihydrotestosterone actions on the prostate transcriptome *in vivo*. Prostate. 2009;69(3):293-316.
6. Cabeza M, Heuze I, Bratoeff E, Ramírez E, Martínez R. Evaluation of new pregnane derivatives as 5alpha-reductase inhibitor. Chem Pharm Bull (Tokyo). 2001;49(5):525-30.

DOI: 10.1530/endoabs.81.EP574

EP575

Somatostatin analogues in the treatment of metastatic paraganglioma

Joao Roque[1], Catarina Regala[2], Tiago Silva[2, 3] & Valeriano Leite[2,3]
[1]Centro Hospitalar Universitário Lisboa Norte - Hospital de Santa Maria, Endocrinology, Diabetes and Metabolism, Lisbon, Portugal; [2]Instituto Português de Oncologia de Lisboa Francisco Gentil, Endocrinology, Diabetes and Metabolism, Lisboa, Portugal; [3]Universidade de Lisboa, Faculty of Medicine, Portugal

Introduction
Paraganglioma (PGL) is a neuroendocrine tumor derived from extra adrenal autonomic paraganglia with a germinal mutation rate of 30%. Metastatic paraganglioma (MPGL) can only be predicted after evidence of secondary lesions and it can occur in up to 50% of cases. Clinical course is remarkably variable, but 5-year overall survival is generally around 50%. Treatment options include surgical resection, chemotherapy, radiotherapy, and ^{123}I-MIBG. Being a neuroendocrine tumor, PGL usually express somatostatin receptors but somatostatin analogues have been seldomly used in metastatic PGL and its efficacy is not well demonstrated.
Clinical case
We present a 45yr female patient with a 1-month history of right thoracic pain associated with homolateral back pain and upper limb paresthesia. Thoracic CT identified a 6 cm lesion on the right lung apex, with extensive invasion of posterior thoracic wall, D1 and D2 vertebral bodies and vertebral canal. Urinary normetanephrine was markedly increased (7719 pg/ml, RR $<$600). Tissue biopsy allowed the diagnosis of aggressive PGL with Ki-67 of 15%. PET ^{68}Ga-DOTANOC was unremarkable except for the previously known lesion. After alfa-blockade, surgery was performed and then followed by ^{123}I-MIBG (200 mCi). Post-treatment scintigraphy and PET ^{68}Ga-DOTANOC identified residual tumor without distant metastasis. After 4 years of loss of follow-up, symptoms returned, and both ^{123}I-MIBG scintigraphy and PET ^{68}Ga-DOTANOC identified a 7 cm thoracic lesion and additional bone lesions on multiple vertebrae and iliac bone. The patient underwent a second surgical procedure but had tumor progression 4 months later. Stereotaxic radiotherapy with 49 gray was then given. However, the following PET ^{68}Ga-DOTANOC showed new metastatic bone lesions and so we decided to start lanreotide 120 mg every 28 days. After 6-months, all previously known lesions were stable but a new slightly increased uptake was seen at the pleura. So that, we increased lanreotide frequency to every 3 weeks. Since then, 18 months have passed with no evidence of disease progression and she is still on this treatment regimen.
Discussion
To date, metastatic PGL can only be cured by surgical resection. Chemotherapy, radiotherapy and ^{123}I-MIBG are used for disease control. Most recently, peptide receptor radionuclide therapy has shown promising results. Somatostatin analogues such as lanreotide are currently used on gastroenteropancreatic neuroendocrine tumors but its role in PGL treatment is still unclear. This case shows an extraordinary response of MPGL to lanreotide, raising interest in this potential therapeutic weapon for a subset of patients who have still few treatment modalities available.

DOI: 10.1530/endoabs.81.EP575

EP576

Panhypopituitarism and diabetes insipidus due to metastatic breast cancer

Diana Cuconu[1], Cristina Stancu[1] & Corin Badiu[2]
[1]National Institute of Endocrinology, Thyroid Related Disorders, Bucharest, Romania; [2]'Carol Davila' University of Medicine and Pharmacy, Endocrinology, Bucharest, Romania

We report the case of a 36 years old female, with personal history of breast cancer, treated with neoadjuvant chemotherapy, breast sectorectomy and then chemotherapy and radiation therapy 2 years ago. She was continuously monitored by her oncologist, disease free for over a year, with recent CT scan that showed no particular lessions suggestive for secondary disease. Meanwhile, she got pregnant and delivered at term a healthy baby. She was admitted 3 months postpartum with intense headache, weight loss, fatigability and low blood pressure. She mentioned hydric intake of aproximate 6 l/day and similiar diuresis during pregnancy. No visual field defects were found at the neurological examination. The initial blood tests revealed panhypopituitarism and central diabetes insipidus and adequate substitution was started. Her blood pressure normalized, but headache persisted without response to pain medication. The magnetic resonance imaging was suggestive for pituitary metastasis and cytologic evaluation of CSF obtained by lumbar puncture was inconclusive. Transsphenoidal surgery was performed and histopatologic exam confirmed a metastatic carcinoma.

Discussion

Although rare, metastatic pituitary spread should always be taken into consideration in a patient with personal history of malignancies and signs and symptoms suggestive of pituitary involvement. Breast cancer is the most likely source of pituitary metastasis in women, while in men lung cancer is usually encountered. Hematogenous tumor spread explains why neurohypophysis is first affected, with early development of polyuria-polydipsia syndrome and diabetes insipidus that precedes anterior pituitary deficiencies. Once diagnosis is made, treatment is difficult and implies correct substitution of hypopituitarism, surgical removal of pituitary lesion, systemic chemotherapy and radiation therapy.

Conclusion

Pituitary metastasis is a rare cause of hypopituitarism and diabetes insipidus associated with a poor prognosis and a median survival rate after diagnosis of 10 months.

DOI: 10.1530/endoabs.81.EP576

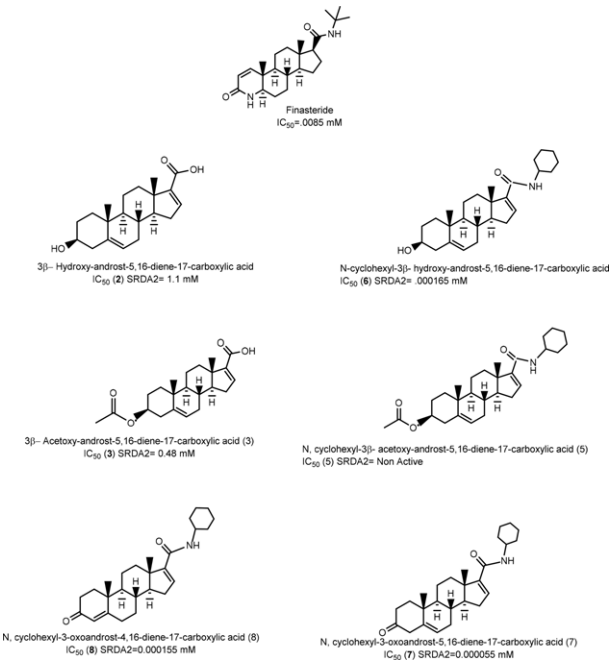
EP577

Novel steroidal derivatives preventing prostate dihydrotestosterone synthesis

Marisa Cabeza[1], Juan Carlos López-Lezama[2], Juan Soriano[3], Norma Valencia-Islas[2] & Yvonne Heuze[1]
[1]Departamento de Sistemas Biológicos y de Producción Agrícola y Animal, Universidad Autónoma Metropolitana-Xochimilco, Mexico; [2]Departamento de Farmacia, Universidad Nacional de Colombia, Colombia; [3]Departamento de Patología del Hospital General de México, Mexico

It is well-known that the increase of intraprostatic levels of 5α-dihydrotestosterone is related to the development of prostatic pathologies such as benign prostatic hyperplasia and prostate cancer. So finasteride and dutasteride-based therapies have been used to improve these diseases. These drugs are potent inhibitors of the enzyme 5α-reductase, which is found in the androgen-dependent tissues. This enzyme is responsible for converting testosterone into dihydrotestosterone in these tissues. This study aimed to identify the effect of new pregnane (**2-8**) analogs as inhibitors of 5α-reductase activity. The action of these steroidal derivatives was compared with that of finasteride. Two different experiments were performed: *in vivo* and *in vitro*. In *in vitro* experiments, we separately incubated derivatives **2-8** in the presence of radiolabeled testosterone, a membrane fraction of the human prostate as a source of 5α-reductase and NADPH. In addition, products **2-8** were also evaluated in testosterone-treated neutered male hamsters. After six days of treatment, the hamsters were sacrificed, and the weight of the prostate was determined. Finasteride was used as a reference compound in both *in vitro* and *in vivo* experiments. The results indicated that steroids **2-8** inhibited 5α-reductase activity showing **6-8** higher potency, with IC_{50} values of: 0.169, 0.105, and 0.155 nM, respectively. These IC_{50} values were lower than those determined for the reference compound finasteride (IC_{50} = 8.5 nM). However, pharmacological experiments demonstrated a non-significant difference between the weight of the prostate in castrated hamsters treated with testosterone to those treated with testosterone plus each of the novel steroids. At the same time, testosterone plus finasteride treatment effectively decreased the weight of this gland. In conclusion, derivatives **6-8** were more potent than finasteride to blockade *in vitro* dihydrotestosterone formation. Nevertheless, their lack of efficacy for decreasing the weight of the prostate could be explained based on the pharmacokinetic processes undergoing these steroids.

Table 1. A series of pregnane derivatives (**2-3**) with a 17-N-cyclohexylcarboxamide residue (**5-8**) were evaluated as blockers of 5α-reductase type 2 (SRDA2) activity. The figure shows the 50% (IC_{50} value) inhibition of enzyme produced by **2-8**. Finasteride was used as the reference compound.



DOI: 10.1530/endoabs.81.EP577

EP578

Genetic novelty in MEN1: about a tunisian family

Mnif Fatma[1], Kawthar El ARBI[1], Yosra Lajmi[2], Asma Zargni[1], Faten Haj Kacem Akid[1], Khouloud Boujelben[1], Dhoha Ben Salah[1], Nadia Charfi[1], Mouna Mnif[1], Nabila Rekik Majdoub[1], Mouna Elleuch[1], Hassen Kammoun[2], Fatma Abdelhédi[2] & Mohamed Abid[1]
[1]Hedi Chaker Hospital, Department of Endocrinology, Sfax, Tunisia; [2]Hedi Chaker Hospital, Department of Medical Genetics, Sfax, Tunisia

Introduction

Multiple endocrine neoplasia type 1 (MEN1) is a rare hereditary syndrome that should be considered when different endocrine tumors are associated in an individual or familial context. We report the observation of a Tunisian family, two sisters and a brother.

Observations

Patient1: a 31 years old female, followed for multinodular goiter, was hospitalized for a left maxillary tumefaction associated with headache and blurred vision. Investigations concluded to a maxillary epulis complicating a primary hyperparathyroidism (PHP). A macroprolactinoma was also diagnosed. The epulis completely regressed after parathyroidectomy. Patient2: a 48 years old female, was followed for asymptomatic hypercalcemia due to a PHP. The investigations showed multiple parathyroid adenomas wrongly taken radiologically and macroscopically as nodular thyroid tissue. The screening for further lesions of MEN 1 was negative. Patient3: a 41 years old male was followed for multinodular goiter. PHP was revealed by recurrent bilateral renal lithiasis. He underwent a total thyroidectomy with removal of the hyperfixing adenoma on parathyroid scintigraphy. A persistent hypercalcemia was objectified indicating a reoperation. The screening for further lesions of MEN1 was negative. The genetic

study of this family identified a new missense mutation, not described in the literature, at exon4 of the MEN1 gene in the heterozygous state.
Conclusion
Recent studies have shown that specific clinical manifestations may affect one family more than the other. Intra-familial correlations were shown to be significant only for pituitary, adrenal glands and thymus. For this family, PHP was the constant lesion.

DOI: 10.1530/endoabs.81.EP578

EP579

Bilateral localization of Leydig tumor in the testicles: Case Report

Fatima Zahra OUTTALEB[1], Amin Alami[2], Zineb Bouchbika[2], Nadia Benchakroun[2], Hassan Jouhadi[2], Nezha Tawfiq[2], Souha Sahraoui[2], Abdellatif Benider[2] & Hind Dehbi[1,3]
[1]Ibn Rochd University Hospital, Laboratory of Medical Genetics, Casablanca, Morocco; [2]Ibn Rochd University Hospital, Mohamed VI Oncology Center, Casablanca, Morocco; [3]Faculty of Medicine and Pharmacy, Hassan II University, Cellular and Molecular Pathology Laboratory, Casablanca, Morocco

Testicular cancer represents 1% of male tumors. The bilateral testicular tumors are very rare (1 to 2% of cases), with a histological predominance of 90–95% of germ cell tumors. The objectives of this case report are to describe the clinical, paraclinical and the management of a rare neoplasic disease of the testicle; the bilateral Leydig tumor of the testicles. It is a 57-year-old patient with a family history of different neoplasms, including ovarian and breast cancer in siblings, and followed since the age of 51 for a Leydig tumor of the testicle, reveled by an indolor testicular mass of the right testicle, without any clinical signs of endocrine disorders. Ultrasound scrotal found a 30 mm left testicular hypoechoic nodule, testis law without particularity, The tumor markers and hormonal explorations were normal. Extension report without anomaly. A right orchiectomy was performed. 3 years later, he presented a second localization of a Leydig tumor in the left testicle, also treated by orchidectomy. No adjuvant treatment (radio or chemotherapy) was indicated. A hormone replacement therapy was also established. Currently, the patient is followed in the oncogenetic consultation, for the identification a possible hereditary predisposition of neoplasms. The Leydig cell tumors of the testicles are typically characterized by the association of a tumor testicular and clinical and biological endocrine signs. The typical manifestations in adult include a secondary feminization. But in 10% of case, the clinical presentation is limited to the testicular mass and only the histology confirms the diagnostic. The diagnosis of the leydigioma is histological but there is no clear limit between tumor benign and malignant, therefore, orchiectomy is the standard treatment and it is only the absence of long-term metastases that will confirm the benignity, prolonged monitoring is essential.

DOI: 10.1530/endoabs.81.EP579

EP580

Solitary fibrous tumors of the pleura with Doege-Potter syndrome: a case report

Sohail Douni, Wafae Elaamadi, Safa Sabur, Mohammed Bouchikh & Achir Abdellah
CHU IBN Sina, Department of Thoracic Surgery, Rabat, Morocco

Background
Solitary fibrous tumor of the pleura is a rare primary intrathoracic tumor that arises from mesenchymal tissue. Hypoglycemia associated Solitary fibrous tumor of the pleura is referred to as the Doege-Potter syndrome and is caused by inappropriate secretion of an insulin-like growth factor II.
Case presentation
We report 70-year-old women with no particular medical history, who present a right chest pain for 1 year with fatigue. The clinical examination revealed diminished breath sounds in right lung fields, and dullness to percussion. the Lab test showed non-insulin mediated hypoglycemia. Hypoglycemia was managed firstly with corticosteroid therapy and frequent programmed nutritional intake. Scanning demonstrated a right large, well-circumscribed, homogeneous pleural mass. A transthoracic puncture was performed which came back inconclusive. Right posterolateral thoracotomy through the five intercostal space was performed for the resection of the tumor. The histopathologic examination confirmed the presence of malignant Solitary fibrous tumor of the pleura with free marginal resection. Removal of the mass solved the hypoglycemia. The patient was discharged on postoperative day 5.

DOI: 10.1530/endoabs.81.EP580

EP581

Localisation of insulinomas : the role of different imaging techniques

Wafa Belabed, Fatma Mnif, Siddiqa Soomauroo, Faten Haj Kacem Akid, Dhoha Ben Salah, Mouna Elleuch, Nabila Mejdoub & Mohamed Abid Hedi Chaker University Hospital, Endocrinology Department, Sfax, Tunisia

Introduction
The diagnosis of insulinomas is made biochemically. However, proper localization of insulinomas is essential before surgery. Therefore, we aimed to evaluate the role of different imaging techniques in the localization of insulinomas.
Case series
This case series include 10 patients with biochemically proven insulinomas. The age, gender, results of MRI, CT, EUS, are shown in Table-1. In imaging investigations, abdominal ultrasonography (AU) was normal in the 4 patients it was performed on. Abdominal CT scan was performed in all patients and found a tumor in only 6 cases. Abdominal MRI was performed in 2 patients and found a tumor in 1 case. The tumor confirmed by MRI wasn't found by other imaging means. Endoscopic ultrasound was performed in 6 patients, was normal in 2 cases and found a tumor in 4 cases. 3 tumors were only diagnosed with endoscopic ultrasound. CT scan and endoscopic ultrasound were enough to find the localization of insulinomas in 8 patients. No lesion was identifed in 1 case. All the 9 patients with confirmed pancreatic lesion underwent surgery and a diagnosis of insulinoma was made in all patients by immunohistopathological analysis. All these patients achieved cure after surgery.
Conclusion
The diagnosis of insulinoma is easily confirmed biochemically. The challenge remains in its localization as no imaging procedure was enough on its own to confirm the presence of a pancreatic lesion, confirming therefore the difficulty of pre-operative investigations

Table 1

Patient	Gender/-Age	Presence of tumor on AS	Presence of tumor on CT	Presence of tumor on MRI	Presence of tumor on EUS
1	M/18	No	**Yes**	-	-
2	M/58	-	No	-	**Yes**
3	F/40	-	No	-	No
4	M/62	-	No	No	**Yes**
5	M/38	-	**Yes**	-	**Yes**
6	F/47	No	**Yes**	-	**Yes**
7	M/28	-	**Yes**	-	-
8	F/46	-	**Yes**	-	-
9	F/56	No	No	**Yes**	No
10	M/68	No	**Yes**	-	-

DOI: 10.1530/endoabs.81.EP581

EP582

A personalised approach to tracking circulating cell free tumour derived DNA in a patient with adrenocortical carcinoma

Shailesh Gohil[1,2], Karen Page[2], Rob Hastings[2], Jacqui Shaw[2] & Miles Levy[1,2]
[1]University Hospitals of Leicester NHS Trust, Department of Endocrinology, Leicester, United Kingdom; [2]University of Leicester, Leicester Cancer Research Centre, Leicester, United Kingdom

Introduction
Adrenocortical carcinoma (ACC) is rare, with an incidence of 0.5-2 cases per million. Although generally aggressive, prognosis is highly variable and difficult to predict. Unlike other malignancies, there are no biomarkers routinely available for use in patients with ACC to help guide management. Circulating cell free tumour derived DNA (ctDNA), the proportion of circulating cell free DNA (cfDNA) originating from tumour cells, is a liquid biopsy that is quickly gaining favour as a clinically useful and superior biomarker in oncology but is only in the early stages of being investigated in ACC.
Aims
To identify and track ctDNA in a 60 year old male patient with metastatic ACC using a precision, patient specific approach.
Materials and Methods
Blood samples were collected at 5 time points over 25 months and separated into plasma and leucocytes. Paired whole exome sequencing (WES) was performed on leucocyte extracted DNA and DNA extracted from formalin fixed paraffin embedded ACC tissue. The 2 sequences were then compared to identify tumour specific somatic mutations. These mutations were used in the design of a bespoke Ampliseq™ HD ctDNA assay. cfDNA was extracted from plasma and the bespoke assay used to detect ctDNA through targeted next generation sequencing.
Results
This patient had a 14.5 cm left adrenal mass with lymph node metastases at presentation. WES identified 83 tumour specific somatic mutations including a *TP53* mutation. 22 of these mutations (including *TP53*) were chosen as targets for inclusion in the Ampliseq™ HD ctDNA panel assay. Pre-adrenalectomy, 9/22 variants were detected on ctDNA analysis with variant allele frequencies (VAF) of up to 1.16%. Post-operatively, ctDNA was initially undetectable. He was commenced on mitotane however imaging later demonstrated disease progression. ctDNA analysis at this point detected 3/22 variants with VAF up to 2.72%. He received radiotherapy for bone metastases and subsequent chemotherapy following which ctDNA was not detectable on samples 4 and 5. The *TP53* mutation was not detectable at any time point.
Discussion
We have demonstrated that ctDNA can be detected and tracked in a patient with ACC, with ctDNA dynamics mirroring progression and response. Targeting multiple, personalised variants is methodologically key to successful ctDNA detection. Only targeting mutations common in ACC, for example in *TP53*, runs the risk of missing other variants present in ctDNA. Further development is required in assay design to improve sensitivity however ctDNA is a hopeful future biomarker for patients with ACC.

DOI: 10.1530/endoabs.81.EP582

EP583

Novel peptides and cell lines to expand the tools and models to study the potential of the somatostatin system in NETs

Federica Mangili[1,2,3,4], María Trinidad Moreno Montilla[2,3,4], Pilar Salamanca Jimenez[2,3,4], Víctor García Vioque[2,3,4], Ricardo Blázquez Encinas Rey[2,3,4], Emilia Alors-Pérez[2,3,4], Giovanna Mantovani[1, 5], Erika Peverelli[1], Jö rg Schrader[6], Alejandro Ibañez Costa[2,3,4] & Justo P. Castaño[2,3,4,7]
[1]University of Milan, Department of Clinical Sciences and Community Health, University of Milan, Milan, Italy; [2]Maimonides Biomedical Research Institute of Cordoba (IMIBIC), Córdoba, Spain; [3]University of Cordoba, Department of Cell Biology, Physiology and Immunology, Córdoba, Spain; [4]Reina Sofia University Hospital, Córdoba, Spain; [5]Endocrinology Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy; [6]UKE-University Medical Center Hamburg-Eppendorf, I. Medical Department, Hamburg, Germany; [7]CIBER Physiopathology of Obesity and Nutrition (CIBERobn), Cordoba, Spain

Neuroendocrine tumors (NETs) represent a heterogeneous group of malignancies with increasing incidence worldwide, due in part to enhanced awareness and diagnosis improvements. Surgery is often effective for local disease, whereas disseminated or metastatic disease require pharmacological treatment, which is not always successful. Pancreatic (Pan-NETs) and pulmonary (Lung-NETs) neuroendocrine tumors frequently express somatostatin receptors (SSTs), providing the target for treatment with somatostatin analogs (SSAs), but a number of patients are irresponsive or become resistant to these drugs. In this context, the neuropeptide cortistatin (CST) a natural analogue of somatostatin with comparable affinity to SSTs has been highlighted as a potential endogenous anti-inflammatory player.
The aims of this study were: 1) to determine the effect of CST as compared with classic SSA on different functional parameters in Pan-NETs and in Lung-NETs cells models; 2) to characterize the somatostatin/CST/SSTs phenotype on a set of recently stablished Pan-NETs cell models. To this purpose, we evaluate cell proliferation, apoptosis, migration, colony formation and intracellular signaling on Lung-NETs (UMC-11 and NCI-H727), classical (BON-1, QGP-1), and new Pan-NETs (NT-3, NT-18 LM) and Pancreatic Neuroendocrine Carcinoma (NT-38) cell lines. We tested different concentrations (1nM-1μM) of SSAs and CST and we observed a dose-dependent effect on cell proliferation and migration, in UMC-11 and NCI-H727 cell lines. A similar result was detected in BON-1 and QGP-1, but NT-3, NT-38, NT-18LM cell lines were less responsive. Each cell model displays a unique SST expression profile, which may underlie the differential functional responses observed. Thus, we are currently exploring the particular signaling pathways involved. Altogether, this study opens original avenues to explore novel therapeutical strategies with CST in NETs and to establish and characterize new Pan-NET cell models more precisely resembling human tumors.

DOI: 10.1530/endoabs.81.EP583

EP584

Genes involved in chromatin-remodeling complex could alter the regulation of alternative splicing in lungNENs

Antonio Agraz-Doblas[1,2,3], Ricardo Blázquez-Encinas[1,2,3], Víctor García Vioque[1,2,3], Nicolás Alcalá[4], Alexandra Sexton[4], María Trinidad Moreno Montilla[1,2,3], Emilia Alors-Perez[1,2,3], pilar salamanca jimenez[1,2,3], Matthieu Foll[4], Lynnette Ferná nez Cuesta[4], Alejandro Ibañez Costa[1,2,3] & Justo P. Castaño[1,2,3,5]
[1]Maimonides Institute of Biomedical Research of Cordoba (IMIBIC), Córdoba, Spain; [2]Department of Cell Biology, Physiology and Immunology, University of Cordoba, Córdoba, Spain; [3]Reina Sofia University Hospital, Córdoba, Spain; [4]Rare Cancers Genomics Team, Genomics Epidemiology Brand, International Agency for Research on Cancer (IARC/WHO), Lyon, France; [5]CIBER Physiopathology of Obesity and Nutrition (CIBERobn), Spain

Lung neuroendocrine neoplasms (LungNENs) comprise a diverse group of rare tumors with a commonly difficult and late diagnosis, which often require complex management and treatment. The most frequently mutated genes in LungNENs have recently been identified, including known components of the chromatin-regulating pathways such as *MEN1*, *PSIP1* and *ARID1A*, which are the subject of ongoing detailed studies. In contrast, other key regulatory mechanisms, particularly posttranscriptional processes linked to RNA regulation and downstream mechanisms involving RNA regulation, remain largely unexplored. Therefore, the main objective of this study was to gain further insight into the role of chromatin-remodeling genes in LungNENs by focusing not only on their mutations but also in their potential interactions with RNA biology. To this end, we used RNAseq data from two distinct cohorts, the first one included 20 lung atypical carcinoids (EGAS00001003699) and the second cohort included 30 typical and atypical carcinoids (SRP156394). To investigate the potential impact of dysregulation of the selected genes we used a biocomputational approach, which enabled to explore the putative connections between the altered genes and other factors contributing to RNA processing, splicing and maturation. Interestingly, initial results already indicated that patients harboring mutations in genes of the chromatin-remodeling pathway also displayed a dramatic dysregulation in the expression levels of these same genes. Furthermore, a detailed examination of the association between the altered genes and particular changes in functional and gene enrichment categories revealed that the chromatin-remodeling machinery could likely modulate transcriptional activity, hence affecting crucial peripheral regulatory systems. Interestingly, samples presenting mutations in chromatin-remodeling pathway genes also showed different patterns in splicing-related genes, which may suggest a dysfunctional RNA processing. Altogether, our study supports the use of biocomputational approaches to discover new alterations in and relationships among regulatory systems, which could lead to the discovery of new biomarkers and therapeutic tools in LungNENs. Ongoing efforts are aimed at using functional assays with LungNEN cell models to better delineate these biocomputational outcomes.

DOI: 10.1530/endoabs.81.EP584

EP585

Nonpathogenic variants in genes involved in signalling pathways differ between MEN1 patients with different outcome of pancreatic tumours

Anna Skalniak, Agata Jabrocka-Hybel, Malgorzata Trofimiuk-Muldner & Alicja Hubalewska-Dydejczyk
Jagiellonian University Medical College, Chair and Department of Endocrinology, Kraków, Poland

Background
Although it is well-known that single pathogenic variants in the gene *MEN1* are responsible for the development of multiple endocrine neoplasia type 1 (MEN1), the outcome of the disease in individual patients cannot be deduced from known genetic factors, the clinical picture of other family members, nor environmental data. Encouraged by publications suggesting a possible role of the genetic background in MEN1 outcome, we performed a study that aimed at searching for pathways or biological processes in which genetic variants are identified, that might clarify the different phenotypes in MEN1 patients.
Matherials and methods
The exomes of MEN1 patients with confirmed pathogenic genetic variants in *MEN1* were sequenced on an Illumna HiSeq platform. The results served for two analyses: (1) lack or presence of pancreatic tumour, and (2) insulinoma or non-insulinoma pancreatic tumour. For each analysis, three patient pairs were available. Genetic analyses were based on genes with nonsynonymous exonic, splice-site, 5'UTR and 3'UTR variants identified in patients with the given clinical phenotype under investigation. The identified genes were interpreted for their function, gene ontology annotations, interactions, and pathways.
Results
(1) The genes identified in MEN1 patients with vs those without pancreatic tumours were annotated primarily to be involved in metabolic processes, cellular component organization or biogenesis, and biological regulation. Annotations of the individual genes included pancreas development, enteroendocrine cell differentiation, cellular detoxification, lipid metabolic process, and vitamin metabolic process. After adding interactions, the most significantly enriched pathways were BMP signalling and regulation and TGF-beta signalling pathway. (2) In insulinoma- vs non-insulinoma-patients, biological process annotations primarily indicated genes involved in metabolic processes and cellular response to stimulus. Individual gene annotations included lipid metabolic process, response to chemical, regulation of hormone levels, insulin signalling, and secretion. Together with close interaction partners, the following pathways were enriched, among others: metabolism of lipids; oxidation by cytochrome P450; synthesis of IP2, IP, and Ins in the cytosol; transcription factor regulation in adipogenesis; vitamin D receptor pathway; cytoplasmic ribosomal proteins; and selenoamino acid metabolism.
Conclusions
Although the genetic background of MEN1 is well established, we identified inherited genetic variations that differed depending on the clinical outcomes and seemed to be logically linked to the analysed symptoms. Our results give a better insight in the different clinical presentation of MEN1 patients. Analyses on other MEN1 characteristics are currently under investigation.
The project has been funded by the National Science Centre, Poland, grant no. 2015/17/N/NZ5/00129

DOI: 10.1530/endoabs.81.EP585

EP586

Papillary thyroid carcinoma and cervical cancer: what is the link?

Ihssane Abidi, Kaoutar Rifai, Iraqi Hinde & Mohamedelhassan Gharbi
University Mohammed 5 Rabat, Endocrinologie, Rabat, Morocco

Introduction
Papillary thyroid carcinoma is the most common form of thyroid cancer. It is differentiated, slow growing and usually has a good prognosis. Its risk factors are not all identified; we note exposure to radiation, particularly ionising radiation, and certain genetic mutations which are currently being explored. The aim of our work is to study the relationship between papillary thyroid carcinoma and cervical cancer.
Observation
We report the case of a 65-year-old female patient, type two diabetic and hypertensive, followed since 2016 for FIGO stage 1A2 cervical cancer revealed by a screening cervico-vaginal smear. The patient underwent a conization of the cervix with clinical, biological and radiological monitoring. The evolution was marked, 2 years later, by the appearance of a clinically suspicious thyroid nodule. Ultrasound showed a 6 mm nodule classified as tirads 5. She underwent total thyroidectomy and the result of the anatomopathological examination was in favour of a papillary microcarcinoma classified as Pt1a NxMx with low risk of recurrence. The outcome was good on L-thyroxine.
Discussion
Papillary thyroid carcinoma is often revealed by a thyroid nodule or cervical adenopathy. However, in cancer patients, it is usually revealed by a radiological image at the time of extension or follow-up. A French cohort from the hospital in Rennes showed that women with a history of uterine fibroid and/or hysterectomy are at higher risk of differentiated thyroid carcinoma. The hyperestrogenic environment could be one of the underlying pathophysiological mechanisms. (1) In our case, it is rather the papillomavirus that can possibly be incriminated.
Conclusion
Uterine pathologies are increasingly associated with the risk of incidence of differentiated thyroid carcinoma. In the light of our observation, it will be interesting to carry out a prospective study of patients followed up for cervical cancer in search of papillary thyroid carcinoma; in order to establish the link with papillomavirus.
References
(1) A. Guenego, Des antécédents d'hystérectomie et de fibrome utérin sont associés au risque d'incidence du cancer différencié de la thyroïde chez la femme dans la cohorte E3N, service d'endocrinologie, diabétologie et nutrition, CHU de Rennes, Rennes, France, Annales d'endocrinologie, Volume 77, Issue 4, September 2016, Page 287.

DOI: 10.1530/endoabs.81.EP586

EP587

Poor outcome of systemic therapy in secondary high-grade pancreatic neuroendocrine tumors

Kazhan Mollazadegan[1], Britt Skogseid[1], Johan Botling[2], Tobias Åkerström[3], Barbro Eriksson[1], Staffan Welin[1], Sundin Anders[3] & Joakim Crona[1]
[1]Uppsala University, Department of Medical Sciences, Uppsala, Sweden; [2]Uppsala University, Department of Immunology, Genetics and Pathology, Uppsala, Sweden; [3]Uppsala University, Department of Surgical Sciences, Uppsala, Sweden

Introduction
Longitudinal changes in pancreatic neuroendocrine tumor (panNET) cell proliferation correlate with fast disease progression and poor prognosis. The optimal treatment strategy for secondary panNET grade (G)3, that has progressed from a previous low- or intermediate-grade to high-grade panNET G3 is currently unknown.
Methods
This was a single center retrospective cohort study, aimed to characterize treatment patterns and outcomes among patients with secondary panNET-G3. Radiological responses were assessed utilizing the Response Evaluation Criteria in Solid Tumors version 1.1.
Results
A total of 22 patients were included and received a median of 2 (range 1-4) treatment lines in 14 different combinations. Median overall survival (OS) was 9 months (interquartile range (IQR): 4.25-17.5). For the 15 patients who received platinum-etoposide chemotherapy, median OS was 7.5 months (IQR: 3.75-10) and median progression-free survival (PFS) was 4 months (IQR: 2.5-5.5). The 15 patients who received conventional panNET therapies achieved a median OS of 8 months (IQR:5-16.75) and median PFS was 5.5 months (IQR:2.75-8.25). We observed one partial response on ^{177}Lu DOTA-TATE therapy.
Conclusion
In conclusion, this hypothesis-generating study failed to identify any promising treatment alternatives for patients with secondary panNET-G3. This demonstrates the need for both improved biological understanding of this particular NET entity and for designing prospective studies to further assess its treatment in larger patient cohorts

DOI: 10.1530/endoabs.81.EP587

EP588

Severe refractory nonislet cell tumor hypoglycemia and paraneoplastic hypercalcemia in a patient with pancreatic adenocarcinoma with neuroendocrine differentiation: a case report.

Giovanni Rossini, Alfonso Maria Di Tommaso, Donatella Rausa, Andrea Palermo, Dario Tuccinardi, Paolo Pozzilli, Nicola Napoli & Silvia Manfrini
University Campus Bio-Medico of Rome, Rome, Italy

Nonislet cell tumor hypoglycemia (NICTH) is a rare complication of malignancy characterized by overproduction of incompletely processed IGF-2 and subsequent stimulation of insulin receptors and increased glucose utilization. We report a patient with pancreatic adenocarcinoma with neuroendocrine differentiation who presented with NICTH and paraneoplastic hypercalcemia. A 51 year-old male was admitted to the ER for altered mental status and confusion. His blood glucose was 27 mg/dl and serum potassium was 3.1 mmol/l; other investigations showed increased transaminase levels and normal thyroid function. His vital signs were normal and he was taking no medication. He was treated with a 30 ml bolus of 33% dextrose solution, intravenous KCl and continuous infusion of 10% dextrose solution at 100 ml/h, achieving normoglycemia. After stopping the dextrose infusion for 2 hours, his blood glucose levels dropped again to 22 mg/dl and blood samples were taken; insulin and c-peptide levels were undetectable, cortisol was 18.5 mcg/dl and IGF-1 was 48 ng/ml (53-201). A 1 mg glucagon stimulation test was performed and blood glucose raised to 63 mg/dl at 20 minutes. Whole body CT scan revealed a pancreatic mass measuring 14x12 cm with cystic component, pathological abdominal lymphnodes and numerous liver metastases; tumor biopsy revealed a poorly differentiated adenocarcinoma with neuroendocrine differentiation (synaptophysin +, CD56 -). A diagnosis of NICTH was made and he was started on 30 mg methylprednisolone BID, hyperglucidic diet and 10% dextrose infusion was continued. Despite these therapeutic measures, other severe hypoglycemic episodes occurred and he was started on 8 mg dexamethasone BID, because of its longer duration of action, with discrete benefit. On the fourth day, he experienced a hypercalcemic crisis (blood calcium levels 14.9 mg/dl); other exams showed phosphorus 1.8 mg/dl, normal 25 (OH)vitamin D and magnesium with suppressed PTHi 15.3 pg/ml (14-65). Treatment of paraneoplastic hypercalcemia consisted of i.v. bisphosphonate infusion (zoledronic acid 4 mg) in addition to saline rehydration. In the next three days, calcium levels normalized and remained stable. A trial of octreotide was started in attempt to further reduce hypoglycemic events with no benefit. Unfortunately, the patient was not eligible for tumor debulking or chemotherapy and after seven days, he died due to multiorgan failure. This case report has shown that hypoglycemia in the setting of NICTH is difficult to manage and can be accompanied by other hormone secretory syndromes; longer acting glucocorticoids and increased carbohydrate intake may help reducing severity and frequency of hypoglycemic episodes.

DOI: 10.1530/endoabs.81.EP588

EP589

Hyperandrogenism due to ovarian stromal hyperthecosis in a woman known with PCOS

Andreea Rosu[1], Ioana Ambăruş - Popovici[1], Bianca Chiriac[1], Ilona - Beatrice Blesneac[1], Mădălina Proţop[1], Ana-Maria Patraşcu[2], Viorel Scripcariu[2, 3] & Cristina Preda[1,3]
[1]"Sf. Spiridon" Clinical Emergency Hospital, Endocrinology Department, Iasi, Romania; [2]Regional Institute of Oncology, Iasi, Romania; [3]"Gr. T. Popa" University of Medicine and Pharmacy, Iasi, Romania

Introduction
Ovarian hyperthecosis (OH) is a rare condition, reported only in case reports and small case series and is characterized by severe hyperandrogenism leading to virilisation and insulin resistance. The term hyperthecosis refers to the presence of luteinized thecal cells within a hyperplastic ovarian stroma and the pathophysiology of this remains poorly understood. Despite the fact that hyperandrogenism is a relatively common clinical problem, severe hyperandrogenism causing virilisation is rare.
Case report
a 40 year-old Caucasian woman with a prior history of PCOS presented to our department with clinical signs of hyperandrogenism (hirsutism – Ferriman-Gallwey score = 28, androgenic alopecia with temporal and anterior baldness, clitoromegaly and deepening of the voice). Menarche occurred at 14 years old with irregular menses and she reported secondary amenorrhea at the age of 30. She was known to have type 2 diabetes and hypertension. Clinical examination revealed acanthosis nigricans on armpits and groin, purple stretch marks on breasts and she was obese with body mass index of 34 kg/m^2 with moon face and buffalo hump. Hormonal profile demonstrated elevated total testosterone 4.11 nmol/l (0.29-1.67), with dehydroepiandrosterone sulfate 134.5 (60-337), 17-hydroxyprogesterone 1.82 ng/ml, low follicular stimulating hormone (FSH) 8.03 mIU/ml and luteinizing hormone (LH) 6.79 mIU/ml and a serum estradiol in the premenopausal range 53.9 pgI/ml. The results of further diagnostic test were as follows: elevated urinary free cortisol 604.8 mg/24 h (9.5-148) but with normal cortisol in overnight dexamethasone suppression test (1.32 mg/dl). Thyroid function tests and prolactin were normal. Abdominal and pelvic CT scan indicated bilateral ovarian enlargement (right ovary: 36/60/55 mm and left ovary: 38/41/57 mm) with hypodense structure on unenhanced imaging showing mild contrast uptake. She underwent laparoscopic surgery with total hysterectomy and bilateral salpingooophorectomy. Anatomopathological examination confirmed diagnosis of OH describing ovarian cortex bilaterally expanded, with multiple follicular cysts in the superficial layer and scattered luteinized cells isolated or organized in small clusters.
Discussions
Even if is a considerable overlap between hyperthecosis and PCOS making difficult to distinguish between these two conditions, testosterone levels are higher than the levels observed in PCOS and since this modified parameter is the single most important laboratory finding, imaging of the adrenal glands and ovaries must be performed. A complete medical history and full physical examination for virilisation are important hallmarks of diagnosis. Effective and timely treatment can reverse the cardio-metabolic consequences of hyperandrogenemia as well as clinical and biochemical outcomes.

DOI: 10.1530/endoabs.81.EP589

EP590

Pheochromocytomas and paragangliomas-real world data in a tertiary Greek center

Foteini Thanasoula[1], Anna Angelousi[1], Georgios Kyriakopoulos[2], Maria Yavropoulou[3], Evanthia Kassi[3, 4] & Gregory Kaltsas[2,3]
[1]National and Kapodistrian University of Athens, First Department of Internal Medicine, Unit of Endocrinology, Athens, Greece; [2]National and Kapodistrian University of Athens, Athens, Greece; [3]Laiko Hospital, First Department of Propaedeutic Clinic, Unit of Endocrinology, Athina, Greece; [4]National and Kapodistrian University of Athens, Department of Biochemistry, Athens, Greece

Purpose
Pheochromocytomas (PCs) and paragangliomas (PGLs) are rare neuroendocrine tumors arising from chromaffin cells of the adrenal medulla and the sympathetic/parasympathetic neural ganglia, respectively. Metastatic PCs/PGLs occur in about 5-26% of cases. Their management and diagnosis still remain a challenge due to their heterogeneity, the absence of guidelines and the few prognostic tools.
Aim
The aim of this study was to describe clinical and genetic characteristics of a series of PCs/PGLs patients in a tertiary center as well as to evaluate their diagnostic and therapeutic approach.
Methods
Clinical data of 50 (30 females) patients (25 with PCs and 25 with PGLs) referred to the University Hospital of Laikon were retrospectively collected and analysed.
Results
Patients' follow-up ranged from 12 to 93 months (median: 31). The 84% of PCs and 36% of PGLs were functional. Genetic analysis was performed in 50% of the total included patients ($n = 12/25$ patients with PCs and n = 15/25 with PGLs) and was found positive in both blood and tissue analysis in 12 patients (9 with SDHD/B, 2 with RET and 1 with NF-1 mutation). Genetic mutations were twice as common in PGLs (15%) compared with PCs (7%). Median PASS was 5 (min-max:4-7) for PCs and GAPP 5 (min-max:2-11) for PGLs. Median Ki-67% index levels was 3(min-max:1-18). In 96% of PCs surgery was the treatment of choice compared to 72% of PGLs. Metastatic disease ($n = 9$) or local recurrence ($n = 5$)

were found in 14/50 (28%) of patients; 25% of them with PCs and 26% with PGLs. Surgery was more often chosen (2nd line treatment) for PCs' recurrence or metastasis (37%) compared to PGLs (16%) in which systemic treatments including chemotherapy (temozolomide), radiopeptides, targeted treatment, radiotherapy or follow-up (watch and wait strategy) were applied. MSI/PDL1 expression was negative in 10 tested samples (all metastatic or progressive) and thus immunotherapy was not considered. Survival rate was 98% during the follow-up. Median progression free survival was 36 months for patients with metastatic disease, and median overall survival 96 and 48 months in patients with PCs and PGLs respectively.
Conclusion
In our series, 44.4% of patients with PCs and PGLs were diagnosed with genetic mutations confirmed in both bood and tissue analysis whereas the frequency of patients with PGLs diagnosed with pathological mutations was double compared to patients with PCs. The 28% of our cases presented local recurrence or distant metastases; however MSI/PDL1 analysis was negative and thus immunotherapy was not applicable.

DOI: 10.1530/endoabs.81.EP590

EP591

Atypical presentation of recurrence following previous resected Primary Parathyroid Carcinoma- dilemmas in follow up of this rare malignancy

Haris Khan[1], Maimoona Nawaz[2] & Isha Malik[1]
[1]North Manchester General Hospital, Crumpsall, United Kingdom; [2]Fairfield General Hospital, United Kingdom

Introduction
Parathyroid cancer is a rare endocrine malignancy and constitutes 0.005% of all cancers. It can recur in 50% of cases. The first recurrence commonly occurs within 3 years of the original diagnosis. Hypercalcaemia is the main cause of morbidity and mortality. We present a case of a 62-year-old male patient who had an atypical lung nodule recurrence with normal calcium and PTH levels, six years following resection of a functioning parathyroid cancer.
Case Report
A 62-year-old male patient was referred to endocrinology due to hypercalcaemia post resection of adenocarcinoma of the rectum. Post-bowel surgery, his serum calcium levels ranged from 3.07 to 3.71 mmol/litre (2.10-2.60), serum PTH 16.1 pmol/litre (1.2-6.9), and vitamin D3 43.6 nmol/litre (>50). A parathyroid sestamibi scan revealed right superior parathyroid adenoma and an intrathyroidal mass suspicious of parathyroid tissue. He underwent a right hemi-thyroidectomy and bilateral superior parathyroidectomy. Histology confirmed a parathyroid carcinoma in the intrathyroidal tissue with normal superior parathyroid glands. He was monitored annually by endocrinologists and surgeons. This was done by checking his serum calcium, PTH, and ultrasound neck which all remained normal. Six years following the parathyroid surgery, he was found to have an enlarging lung nodule on surveillance imaging for his rectal cancer. A CT-guided lung biopsy confirmed a parathyroid cancer metastasis. A PET CT scan and ultrasound of the neck did not reveal any evidence of local recurrence. The lung nodule was resected which confirmed a parathyroid cancer metastasis.
Discussion/Conclusions
Long-term survival is possible with recurrence of parathyroid cancer and routine surveillance can identify early recurrence. However, there is no clear consensus guidance on the follow-up of patients with parathyroid cancer. The existing guidelines recommend regular surveillance of functioning parathyroid cancer by performing serum calcium, PTH, and ultrasound neck. Our case is atypical in that the patient did not have hypercalcaemia at the time of recurrence despite the originally resected functional parathyroid cancer. If surveillance imaging for rectal cancer had not been done, the lung nodule may not have been picked up in a timely manner. This case highlights the need for lifelong follow-up for parathyroid cancer patients. Current guidelines should be reviewed to include whole-body imaging modalities to pick up early distant recurrence. Our case also highlights that recurrence of functional parathyroid cancer might not present with hypercalcaemia.

DOI: 10.1530/endoabs.81.EP591

EP592

Pheochromocytoma associated with type 1 neurofibromatosis

Chtioui Sara, Ahmed Boukhalfa, Rafi Sanaa, Ghizlane EL Mghari & Nawal EL Ansari
Med VI University Hospital Center, Endocrinology, Diabetology and Metabolic Diseases Department, Marrakech, Morocco

Introduction
Compared to normal population, patients with neurofibromatosis are at higher risk for the development of benign and malignant tumors. Pheochromocytomas are relatively rare in neurofibromatosis type 1 (NF1), and malignant ones are even rarer.
Aim of the presentation
Our aim was to report a malignant pheochromocytoma with multiple metastases in a patient with NF1.
Case report
A male patient aged 23 years old, with laparoscopically resected pheochromocytoma. He was investigated for headaches, flushing and palpitations. The diagnosis of pheochromocytoma was confirmed by elevated 24-hour urine levels of metanephrines and catecholamines. Computed Tomography Scan revealed a mass measuring 10 x 8, 2x 9,4 cm in the left adrenal gland and pulmonary metastases. The patient presented with classic clinical features of NF-1, *café-au-lait* spots and skin nodules. He was operated on and histological examination confirmed the diagnosis of pheochromocytoma with a Pass score of 9. After surgery, urinary catecholamines were high and there were diffuse pulmonary and liver metastases with Octreotide scan uptake. Somatostatin analogues and MIBG therapy are being considered.
Conclusion
The association of a malignant pheochromocytoma with neurofibromatosis type 1 although very rare should be known as pheochromocytoma and its metastases may be totally asymptomatic as in the presented case.
Key-Words : Pheochromocytoma-neurofibromatosis-malignant-catecholamines

DOI: 10.1530/endoabs.81.EP592

EP593

An analysis of blood parameter changes in cushing's syndrome - a population-based study

Jessica Mangion[1,2], Miriam Giordano Imbroll[1, 2], Sarah Craus[1, 2], Josanne Vassallo[1, 2] & Mark Gruppetta[1,2]
[1]University of Malta Medical School, Mater Dei Hospital, Department of Medicine, Msida, Malta; [2]Mater Dei Hospital, Neuroendocrine Clinic, Msida, Malta

Aim
Glucocorticoids play a significant role in inflammation and immune system disruption. Our study aimed to analyse different biochemical and blood count indices and serum inflammation-based scores in patients with all different causes of endogenous Cushing's Syndrome (CS) in a well-defined population.
Methods
Clinical records of 35 patients diagnosed with CS between 2008 and 2020 at the only central national health service hospital in Malta, were retrospectively analysed. Detailed clinical and biochemical data were obtained for each patient. Correlation and receiver operator characteristics (ROC) curve analyses were used to establish a threshold value for different variables to predict malignant CS.
Results
Malignant cause of CS (ectopic CS and adrenocortical carcinoma) had statistically significant higher cortisol, size of the tumour and lower potassium at diagnosis ($P<0.001$). Additionally, malignant causes had a lower lymphocyte count ($P=0.001$) and eosinophil count ($P=0.008$), and a higher neutrophil-to-lymphocyte ratio (NLR) ($P=0.001$), systemic immune inflammation index ($P=0.005$) and a lower lymphocyte-to-monocyte ratio (LMR) ($P<0.001$). Using Spearman's correlation, a positive correlation was noted between cortisol levels (baseline, post-ODST cortisol and 24-hour urinary cortisol) and pre-operative NLR whilst a negative correlation was observed with pre-operative LMR. Using ROC curve analysis to predict malignant cause of CS, a potassium level of < 3.05

was 75% sensitive and 100% specific (ROC-AUC 0.907, $P = 0.001$), a post-ODST cortisol level of > 841 nmol/l was 100% sensitive and 91% specific (ROC-AUC 0.981, $P < 0.001$), while a NLR ratio > 3.9 was 100% sensitive and 57.7% specific (ROC-AUC 0.885, $P = 0.001$).
Conclusion
Biochemical and blood count indices and serum inflammatory-based scores remarkably differ between benign and malignant causes of endogenous CS. Such indices can help predict the severity of disease and thus prognosis.

DOI: 10.1530/endoabs.81.EP593

EP594

New CDKN1b mutation in multiple endocrine neoplasia type 4 and brief literature review on clinical management.

Alessandro Brunetti[1], Elisabetta Lavezzi[1], Alexia Bertuzzi[2], Gennaro Nappo[3], Alice Laffi[2], Vittorio Pedicini[4], Eleonora Vitali[5], Giampaolo Trivellin[5], Gherardo Mazziotti[1] & Andrea Lania[1]
[1]Humanitas Clinical and Research Center - IRCCS, Endocrinology, Diabetology and Andrology Unit, Rozzano, Italy; [2]Humanitas Clinical and Research Center - IRCCS, Unit of Medical Oncology and Hematology,, Rozzano, Italy; [3]Humanitas Clinical and Research Center - IRCCS, Pancreatic Surgery Unit, Rozzano, Italy; [4]Humanitas Clinical and Research Center - IRCCS, Radiology Unit, Rozzano, Italy; [5]Humanitas Clinical and Research Center - IRCCS, Endocrinology Unit and Laboratory of Cellular and Molecular Endocrinology, Italy

Background
The fourth type of Multiple Endocrine Neoplasia (MEN) is a rare variant of MEN presenting a MEN1-like phenotype and originating from a germline mutation in CDKN1B. However, due to the small number of cases documented in literature, the peculiar clinical features of MEN4 are still largely unknown, and clear indications about the clinical management of these patients are currently lacking. In order to enlarge our knowledge on MEN4 and to better typify the clinical features of this syndrome, we present two more patients with a germline CDKN1B mutation developing MEN features and perform a review of the current literature about MEN4.
Case presentation
The first case is a man who was diagnosed with a metastatic ileal G2-NET at the age of 34. Genetic analysis revealed the mutation p.I119T (c.356T>C) of CDKN1B. This variant is classified as of uncertain significance according to 2015 ACMG guidelines and has been previously reported in association to early-onset pituitary adenoma. The patient was screened for pituitary and parathyroid disease without any pathological findings. The second report is a 76-year-old woman with a multifocal pancreatic G1-NET. Genetic analysis identified the CDKN1B mutation c.482C>G (p.S161C). The variant is of first description in literature in association to MEN4. It is located into the C-terminal RhoA binding domain, potentially affecting cell motility. However, in silico analysis supports that this missense variant does not alter protein structure/function and it has been currently classified as a variant of uncertain significance. Pituitary and parathyroid function resulted normal as well.
Review of literature
To date, twenty-three different mutations of CDKN1B have been described in literature in association to MEN4, including fifty-seven carriers. Forty-two of these subjects developed at least one endocrine neoplasm, while involvement of multiple endocrine organs was detected in seventeen of them. Primary hyperparathyroidism results the most frequent endocrine neoplasm (75%), followed by pituitary adenoma (≈40%) and neuroendocrine tumors (≈20%). In general, MEN 4 seems a variant with later onset, less penetrance, and milder clinical features than MEN1.
Conclusions
MEN4 patients might need a different and personalized approach in clinical management. For hyperparathyroidism, since recurrence and/or multiple parathyroids involvement appears to be rare, a less aggressive surgical approach than in MEN1 could be justified. Therefore, MEN4 carriers should be screened for neuroendocrine tumors and pituitary adenomas. Larger case series are still necessary to clarify the peculiar features of MEN4 and to establish a specific diagnostic and therapeutic standard.

DOI: 10.1530/endoabs.81.EP594

EP595

Severe psychosis: think of adrenocortical carcinoma

Kaoutar Rifai, Loubna Guissi, Wahiba Ghaffour, Hind Iraqi & Mohamed Elhassan Gharbi
Ibn Sina University Hospital, Endocrinology, Rabat, Morocco

Introduction
Adrenocortical carcinoma (AC) is a rare malignant endocrine tumor of the adrenal cortex. The psychiatric manifestations observed in AC are associated with a delayed diagnosis.
Case presentation
A 27-year-old women with medical history of severe psychosis resistant to antipsychotic medications, was hospitalized in our unit for Cushing's syndrome (CS). The physical examination revealed classical signs of CS. The Laboratory results showed 24-hour urinary free cortisol values higher than 4 times the upper limit of normal, elevated midnight serum cortisol at 86 ng/ml and no suppression of cortisol during a low-dose dexamethasone suppression. The presence of a plasma ACTH level < 3 pg/ml suggests ACTH-independent CS. Adrenal CT scan showed a 35*23 mm mass located in the left adrenal gland with an absolute washout of 28%. The patient underwent unilateral adrenalectomy. Histopathological analysis revealed adrenocortical carcinoma with a Weiss score of 4. The evolution was characterized by the improvement of psychiatric symptoms, hence the discontinuation of antipsychotic medications.
Discussion
AC is a rare malignant tumor. Its incidence is approximately 1 to 2 new cases per million per year. It occurs most often in adults between 40 and 50 years of age, with a female predominance. The prognosis is poor (five-year survival rate of less than 50%). The glucocorticoid hypersecretion observed in CS is accompanied by sleep disorders, thymic manifestations, especially depression, and cognitive disorders, but psychotic states are rare. Hypercortisolemia modulates the response of the central nervous system through the activation of membrane channels, synaptic transmission of neurotransmitters (such as serotonin, glutamate and GABA), gene transcription, synaptic plasticity, neurogenesis and apoptosis. Excessive activation of the dopaminergic system is at the basis of the pathophysiology of manic symptoms, psychotic disorders and also some forms of depression.
Conclusion
Our case illustrates the importance of a good interrogation and a careful clinical examination in all patients presenting with a psychiatric illness, in order to eliminate an organic cause which can engage the vital prognosis.

DOI: 10.1530/endoabs.81.EP595

EP596

A case of asymptomatic Pheochromocytoma with high risk of malignancy

Renata Marecek[1], Baleanu Felicia[1], Taujan Georgiana[1], Papadopoulou Blerta[1], Kosmopoulou Olga[1], Rosu Mihaela[1], Dobos Sebastian[2] & Iconaru Laura[1]
[1]Chu Brugmann Site Horta, Endocrinology, Brussels, Belgium; [2]Chu Brugmann Site Horta, General Surgery, Brussels, Belgium

Introduction
The classical triad of pheochromocytoma comprises paroxystic headache, palpitation, and diaphoresis. It is a common cause of secondary hypertension. Glycemic abnormalities are not rare. Hyperglycemia and diabetes can be the presenting features of pheochromocytoma. However, cases of hypoglycemia are also described. Malignant tumors account for about 10% of cases.
Case description
In this report, we present a case of a 41-year-old man referred to the endocrinology department for asymptomatic hypoglycemia as an incidental finding on routine laboratory screening. There was no personal or family medical

history, and patient was not taking any medication. An insulinoma was initially suspected, and patient underwent abdominal magnetic resonance imaging. The latter revealed right 24 mm hypervascular adrenal mass and normal pancreatic parenchyma. The blood pressure was normal (110/60 mmHg). The laboratory showed an elevated level of chromogranin A (322 mg/l, (N): $<$100 mg/l) and elevated urinary metanephrines (814 mg/24 h, (N): 74-297) and normetanephrines (755 mg/24 h, (N): 105-354). The fasting insulin, glucose, and c-peptides were in normal range. PET CT showed a strong surexpression of the somatostatin receptors in right adrenal mass. On a non-contrast-enhanced computed tomographic (CT) scan, density of the lesion was 35 HU. On a contrast-enhanced CT, the value was 100 HU. At this stage, a pheochromocytoma was suspected. Surgical resection was performed. The pathology confirmed a pheochromocytoma. It was described as having a high risk of malignancy because of capsular invasion, presence of nuclear atypia, up to eight mitotic figures in 10 high-power fields (hpf), presence of atypical mitoses, and confluent nodules. There was no invasion of peri-adrenal fat, vascular, lymphatic, or peri-neural tissues. The genetic tests showed no mutation in the SDH, RET, VHL, and NF1 genes. The urinary metanephrines and normetanephrines were in the normal range 2 months after the surgery.

Discussion

In conclusion, we present a case of pheochromocytoma in a patient with incidental asymptomatic hypoglycemia. Our case emphasizes that eight percent of patients with pheochromocytoma are completely asymptomatic. Histopathology results demonstrated a tumor with a high risk of malignancy because of the extensive capsular invasion. Nevertheless in literature, the only indicator of malignancy is the presence of distant metastases. Our case also highlights absence of reliable histopathologic methods to distinguish between benign and malignant tumors. However, certain histologic features are more common in malignancy, including extensive capsular invasion (as present in our patient), tumor necrosis, and vascular invasion.

DOI: 10.1530/endoabs.81.EP596

EP597

Levels to designate progressive increase in aggressiveness of medullary thyroid cancer depending on the identified mutations in the Republic of Belarus

Yuliya Dydyshka[1,2], Alla Shepelkevich[1], Victor Kondratovich[3], Tatiana Leonova[3], Alena Subach[4], Anna Portyanko[4], Andrey Gradusha[3] & Alexandra Sosedkova[3]

[1]Belarusian State Medical University, Minsk, Belarus; [2]Republic Center of Endocrinology and Medical Rehabilitation, Endocrinology Department, Minsk, Belarus; [3]Public Health Institution Minsk City Clinical Oncologic Dispensary, Minsk, Belarus; [4]N.N. Alexandrov National Cancer Centre of Belarus, Minsk, Belarus

Background

The recommended method of initial testing for MEN2A is either a single or multi-tiered analysis to detect RET mutations in exon 8, 10, 11, 13, 14, 15, and 16.

The aim of the study was to determine the relationship between the aggressiveness of the clinical course of MTC and identified mutations.

Materials and methods

The research is carried out of the program 'To develop and implement effective technologies for the diagnostic detection and observation of patients with MEN2A.' 32 patients with established medullary thyroid cancer (MTC), who underwent genetic testing, with the presence of pathogenic mutations of the RET proto-oncogene, were selected. The patients were divided into 3 groups depending on whether the mutation of the RET gene belongs to the highest, high, and medium risk levels.

Results

The number of carriers of the mutation of the highest risk level (16 exon M918T) was 2 people, which is 6.25% of the total. The median age at diagnosis is 18 years. At the time of diagnosis, the metastatic form of the disease was not detected in this group of patients. After the treatment, no recurrence of the disease was recorded in patients. In 1 of 2 patients, the presence of pheochromocytoma was established. The number of carriers of high-risk mutations was 11 people, which is 34.38%. All mutations are localized in exon 11. The average age of diagnosis is 28.7 years. At the time of diagnosis, the metastatic form of the disease was detected in 1 patient, which is 9.1%. After the treatment, remote recurrence of the disease was registered in 1 patient (9.1%), and local recurrence - in 2 patients, which is 18.2%. In 4 people (36.4%) pheochromocytoma was found. In 19 people, pathogenic mutations of the RET gene were identified, which are related to the level of moderate risk, which accounted for 59.37% of the total. Mutations in these patients are localized in exon 10 In this group of patients, MTC was diagnosed on average at the age of 41.1 years. The metastatic form of the disease at the time of diagnosis was not detected in this group. Local recurrence after the treatment was registered in 4 patients (21.05%), remote relapses in this group of patients were not registered. Pheochromocytoma was not detected in this group.

Conclusions

High-risk mutations are characterized by the earliest onset of the disease, as well as the most frequent presence of pheochromocytoma.

DOI: 10.1530/endoabs.81.EP597

EP598

Choroidal metastasis from follicular thyroid carcinoma: a case report

Sofien Affes, Ben Amor Saloua, Rekik Mona, Mariem Sehli, Kammoun Sonda & Trigui Amira

Habib Bourguiba University Hospital, Ophthalmology, SFAX, Tunisia

Introduction

Choroidal metastases are among the most common malignant ocular tumors. In the majority of cases, their origin is pulmonary in men and mammary in women. We present a rare case of choroidal metastasis from a vesicular thyroid carcinoma.

Case presentation

A 35-year-old woman presented to our department complaining of progressive vision reduction in the right eye. Six years previously, she was operated for vesicular carcinoma of the thyroid with pulmonary metastases, she was under iratherapy. The ocular examination of the right eye revealed best visual acuity to be 1/20. Intraocular pressure was 12 mmHg. Fundus examination showeda retinal detachment with the presence of an underlying yellow-orange mass. The left eye examination was normal. Ultrasonography B-scans, optical coherence tomography, fluorescein angiography and magnetic resonance imaging made the diagnosis of choroidal metastasis from thyroid carcinoma. Chest X-ray and abdominal ultrasonography were normal. Bone scintigraphy with iodine 131 showed increased uptake in the humerus and the femur, with no ocular or cerebral uptake. External radiotherapy in addition to iratherapy was proposed but refused by the patient. Then, she was lost of view. Five months later, she came back with red and sore right eye. The examination noted the increase in the size of the metastasis with extension of the retinal detachment and appearance of neovascular glaucoma. Iodine 131 scintigraphy showed ocular uptake of iodine, thus confirming the diagnosis. The iratherapy was resumed but the patient quickly died due to deterioration in her general condition.

Conclusion

Choroidal metastases secondary to vesicular thyroid carcinoma are very rare. There are few cases reported in the literature. This work describes an additional case. In all reported cases, there are bone and/or pulmonary metastases in association with choroidal metastases. Indeed, thyroid carcinomas most often metastasize to the lungs and bones. Other metastatic sites are rare and are seen in advanced stages of the disease with poor prognosis. Vesicular carcinomas of the thyroid are known to metastasize to unusual sites and are more aggressive than papillary carcinomas. The appearance of the choroidal metastasis in our patient constituted a severe evolutionary turning point of the disease.

DOI: 10.1530/endoabs.81.EP598

EP599

Co-secretory ACTH & Calcitonin tumor presented with refractory hypokalemia

Bhavna Sharma, Pratichi Joshi, Anees Fatima, Meena Lakha, Shahir Hamdulay & Elaine Hui

Northwick Park Hospital, United Kingdom

81-year-old ex-smoker presented to emergency with transient facial droop, slurring of speech and generalized weakness. He had a background of ischemic

heart disease, hypertension, and previous bladder cancer (treated 5 years ago). Examination revealed clinical signs of hypocalcaemia with no cushingoid features. Bloods revealed refractory severe hypokalemia, severe hypocalcaemia with normal phosphate, and metabolic alkalosis requiring High dependency Unit. Random cortisol done to exclude Cushing's was greater than 1750 nmol/l (unrecordable upper limit). 24-hour urinary cortisol was 18282 nmol/24 hr (normal 1-124 nmol/24 hours) with no suppression on low dose dexamethasone suppression test (>1750 nmol/l). ACTH was 352 ng/l (normal 0-50 ng/l). PTH was 19.9 pmol/l (normal 1.6-6.9 pmol/l). Vitamin D levels were sufficient. Calcitonin done due to refractory hypocalcaemia was 130 ng/l (normal <10 pg/ml). Renal MRI revealed bilateral adrenal hyperplasia and normal kidneys. Renin: aldosterone ratio done on a sample when potassium was 3.1 mmols/l revealed renin levels of 0.1 nmol/l/hr and aldosterone less than 50 pmol/l. Gut hormone profile was normal except elevated glucagon of 80 pmol/l (normal 0-50 pmol/l). CT Chest/Abdomen revealed a right sided lung 20*14 mm nodule and multiple liver lesions. MRI Pituitary was normal. PET scan did not reveal any further areas of abnormal uptake. Biopsy and immunohistochemical studies of liver lesions showed small cells with nuclear pleomorphism positive for CD56, synaptophysin and chromogranin suggestive of small cell cancer of lung origin. Refractory hypokalemia with a very high ACTH and metabolic alkalosis, is characteristic of ectopic ACTH syndrome. Refractory severe hypocalcemia was further suggestive of rare calcitonin co-secretion. He was planned for inpatient chemotherapy with dexamethasone 4 mg BD. He was stepped down to oral alfacalcidiol 500 ng once a day, calcium lactate gluconate (2.263 g + calcium carbonate 1.75 g), two tablets BD, potassium chloride 600 mg/potassium bicarbonate 400 mg (total potassium 12 mmol) tablets, two tablets TDS with magnesium aspartate (magnesium 10 mmol) BD. Unfortunately, the patient succumbed to COVID/Sepsis. Early initial medical management of ectopic ACTH and early recognition of co-secretory tumors in cases of multiple electrolyte derangements may be helpful in achieving a more positive outcome in future. A multidisciplinary management in liaison with critical care, oncology and endocrine is paramount

DOI: 10.1530/endoabs.81.EP599

EP600

Sporadic metastatic pancreatic neuroendocrine tumor in a young patient

Marius-Lucian Mitrache[1], Carmen Sorina Martin[1], Cornelia Nitipir[2] & Simona Fica[1]
[1]Spitalul Universitar de Urgenţă Elias, Endocrinology, Bucureşti, Romania; [2]Spitalul Universitar de Urgenţă Elias, Medical Oncology, Bucureşti, Romania

Background
Pancreatic neuroendocrine neoplasms (NENs) are rare tumors which can sometimes be diagnosed based on symptoms of hormone excess, but, more often, they are asymptomatic, and patients frequently present with metastatic disease. While they can occur in hereditary cancer syndromes such as multiple endocrine neoplasia type 1 (MEN1), von Hippel-Lindau (VHL), or neurofibromatosis (NF1), the majority of pancreatic NENs are sporadic
Case report
We report the case of a 37-year-old male referred to a gastroenterology clinic for nonspecific gastrointestinal symptoms. Abdominal ultrasound reported a large hepatic mass, which was confirmed with an abdominal CT scan. This prompted an ultrasound-guided hepatic biopsy, which raised the suspicion of metastatic liver disease arising from a primary pancreatic NEN. The diagnosis was confirmed with immunohistochemistry, which graded the tumor as a NET G2 based on a ki-67 of 5%, and thus the patient was referred to our department. Considering the patient's young age, biochemical screening for MEN1 was performed, but serum calcium, PTH, gastrin, insulin, IGF-1, and prolactin were normal, as were NEN-specific tumor markers. The patient also had no symptoms of hormone hypersecretion, no clinical features of VHL or NF1, and no remarkable family history. Somatostatin receptor SPECT/CT was performed, reporting a primary pancreatic NEN, with multiple metastases to the liver, abdominal lymph nodes and left adrenal gland, and portal vein invasion. The patient received monthly intramuscular lanreotide injections, in combination with a systemic chemotherapy regimen. However, owing to the unsatisfactory response of the treatment and the significant adverse reactions, the patient was recommended for Peptide Receptor Radionuclide Therapy (PRRT). Following five Lu-177-DOTATATE PRRT cycles, partial response was observed, and debulking surgery is being considered as the next therapeutic step.
Conclusions
Widespread metastatic disease is often reported in pancreatic NENs, frequently requiring multiple lines of treatment. As such, multidisciplinary teams play a pivotal role in the management of such complex cases, carefully balancing risks, benefits, the biology of the tumor, and patients' wishes.

DOI: 10.1530/endoabs.81.EP600

EP601

Hypercalcaemia in a woman with systemic lupus erythematosus: don't miss the diagnosis of gastric neuroendocrine tumor!

Selma Massanou, Asma Kefi, Khaoula Ben Abdelghani, Mounira El Euch, Syrine Sassi, Sami Turki & Ezzedine Abderahim
Service de Médecine Interne A, Hôpital Charles Nicolle, Tunis, Tunisia

Introduction
Systemic lupus erythematosus (SLE) is a chronic multisystem autoimmune disease with heterogeneous presentation. SLE can be associated with autoimmune diseases or other entities sush as neuroendocrine tumors (NET). The occurrence of gastric NET in SLE is very rare and has been described few times in the literature. Herein we report the case of SLE woman, in whom we discovered a gastric neuroendocrine tumor.
Observation
A 68-year-old woman, with a history of treated arterial hypertension and SLE, presented a hypercalcemia (2.72 mmol/l) in a routine check-up. SLE was diagnosed, 12 years before, according to the American College of Rheumatology (ACR) SLE criteria with oral ulcers, non-scarring alopecia, discoid lupus, leukopenia, thrombocytopenia, autoimmune hemolytic anemia, positive antinuclear antibodies (ANA), and low complements. She had no kidney, heart, joint, or neuropsychiatric impairment. The investigations (thyroid test, celiac serology, and digestive endoscopies) for the search of autoimmune conditions associated with her disease were initially negative or normal. She was treated with antimalarials and corticosteroids. The evolution was good and she did not present any relapses of her SLE. Given the hypercalcemia presented by our patient, after eliminating the emergencies, we began an exhaustive etiological investigation. There were no functional complaints. Our patient denied drug or toxic intake. Laboratory tests revealed normal level of phosphatemia, parathyroid hormone and vitamin D. A body scanner didn't reveal any abnormalities. A gastroscopy showed multiple millimetric fundal elevations with ulceration in the center. On histological examination, it was a well-differentiated grade 1 NET, with, on immunohistochemical study, intense and diffuse cytoplasmic staining of the tumor cells after the use of chromogranin-A. Furthermore, the fundic mucosa was atrophic with reduced glandular volume, suggesting Biermer's disease. Vitamin B12 was low (115 pg/ml), antiparietal cell antibody was positive, and anti-intrinsic factor antibody was negative. Beside, blood chromogranin-A was high (681 ng/ml). After confirming the diagnosis of Biermer's disease, NET was classified as type I. Therefore, according to The National Comprehensive Cancer Network (NCCN) guidelines, we opted for annual monitoring by fibroscopy, with monthly vitamin B12 injections in addition to endoscopic resection. The current follow-up is 2 years with a good evolution.
Conclusion
NET-SLE is a scarce association. In our observation, it occurred on a Biermer's disease, which can be part of an autoimmune manifestation associated with SLE. NET was revealed by hypercalcemia in our case, therefore we highlight the importance of an exhaustive etiological investigation of hypercalcemia especially in SLE patients.

DOI: 10.1530/endoabs.81.EP601

EP602

Ectopic Cushing's syndrome due to metastatic lung carcinoid presenting on a background of DIPNECH

Telma Moreno[1,2], Sara Ribeiro[1, 2], Ana Varela[1, 2], Paula Freitas[1,2,3] & Davide Carvalho[1,2,3]
[1]São João Universitary Hospital Center, Endocrinology, Diabetes and Metabolism, Porto, Portugal; [2]Faculdade de Medicina da Universidade do Porto - FMUP, Porto, Portugal; [3]i3S - Instituto de Investigação e Inovação em Saúde da Universidade do Porto, Porto, Portugal

Diffuse idiopathic pulmonary neuroendocrine cell hyperplasia (DIPNECH) is a relatively recent and rare disease, frequently misdiagnosed. It is characterized as a generalized proliferation of pulmonary neuroendocrine cells and is recognized as a precursor lesion for pulmonary neuroendocrine tumors, although the risk of progression to malignancy is considered low. Here we report a patient with ectopic ACTH-dependent Cushing's syndrome due to metastatic lung carcinoid tumors arising on a background of DIPNECH. A 73-year-old woman presented to the emergency department with 4 weeks of progressive lower limb edema, sudden onset of hypokalemia, refractory hypertension and de novo diabetes. She had basilar crackles on auscultation and hepatomegaly on examination. Past medical history included controlled hypertension, obesity, dyslipidemia. She was being followed in Pulmonology for chronic cough and radiological findings suggestive of DIPNECH. A thoracic CT showed diffuse mosaic attenuation with multiple bilateral lung nodules, with the largest nodules measuring 8 mm. Biopsy of the pulmonary nodules demonstrated tumorlet/typical carcinoid tumor, with evidence of DIPNECH. Severely elevated GGT prompted a cholangio-MRI that showed heterogeneous/micronodular liver parenchyma suggestive of chronic liver disease. Liver biopsy demonstrated hepatic involvement by a well differentiated neuroendocrine neoplasia expressing chromogranin and synaptophysin with a proliferative index Ki67 $< 2\%$, compatible with metastasis. The patient became increasingly confused and disoriented over the first days of hospitalization. In view of clinical suspicion of endogenous hypercortisolism, screening for Cushing's syndrome was performed. She had elevated elevated morning and midnight plasma cortisol levels (58.0 and 83.4 µg/dl, respectively) markedly increased 24-hour urinary free cortisol (3648.0 µg/day) and morning serum ACTH (167.1 ng/l). High-dose dexamethasone suppression test revealed no suppression of urinary free cortisol. A PET-Ga-68-DOTATOC was obtained showing multiple tumor lesions located at the cervical, thoracic and abdominal ganglia, lung (identified as the primary source), bone and liver with over-expression of somatostatin receptors. A PET-FDG-F18 excluded the presence of concomitant dedifferentiated/high grade metabolic lesions. Therapy with octreotide and metyrapone was initiated with a prompt and sustained decrease in serum and urinary cortisol levels. At hospital discharge, the patient was fully oriented, with controlled cortisol and potassium levels. Her vital signs were normal and peripheral edema was mild and limited to the ankles. Six months after discharge she remained clinically and imagiological stable under somatostatin analogs and metyrapone. This case describes disease progression from DIPNECH to metastatic carcinoid tumours presenting with ectopic Cushing's, highlighting the importance of long term clinical surveillance in patients with DIPNECH.

DOI: 10.1530/endoabs.81.EP602

EP603

Multiple endocrine neoplasia type 1: A case report

Meriem Adel[1], Ibtissem Ben Nacef[1], Chayma Besrour[1], Sabrine Mekni[1], Houaida Smadhi[2], Youssef Lakhoua[1], Nadia Mchirgui[1], Imen Rojbi[1] & Karima Khiari[1]
[1]Charles Nicolle Hospital, Endocrinology, Tunis, Tunisia; [2]Beja Hospital, Endocrinology, Beja, Tunisia

Introduction
Multiple endocrine neoplasia (MEN1) is a rare underdiagnosed inherited multi-tumor syndrome, affecting neuroendocrine and non-endocrine tissues. Its aspects are extremely variable with no genotype-phenotype correlation.
Case report
A 57 year old woman with a history of hypertension, presented five months before her admission with asthenia, headache and vomiting, initial biological exams revealed a central hypothyroidism. A pituitary MRI showed a sellar and suprasellar mass (3 cm of diameter) with an upper deviation of the pituitary stalk, the optic chiasma, and apparent invasion into the left cavernous sinus (knosp 2 at right; knosp1 at left) consistent with a pituitary macroadenoma. Laboratory evaluations concluded to a non-functioning pituitary adenomas with disconnection hyperprolactinemia and hypopituitarism. Ophthalmological examination revealed bitemporal hemianopsia. The patient's serum investigations revealed a primary hyperparathyroidism. Both parathyroid ultrasound and Technetium Tc-99 m sestamibi parathyroid scintigraphy were negative. The patient did not present any clinical, biological, imaging manifestations of gastro-entero-pancreatic neuroendocrine tumors. The diagnosis of MEN 1 was made and few days after, the patient had a transphenoidal adenomectomy. The surgery was complicated with a transient insipidius diabetes. 3 months after surgery, the evaluation revealed the persistence of hypopituitarism (corticotropic insufficiency, and central hypothyroidism) but a normal prolactin serum level. Pituitary MRI showed a tumor remnant. Visual field was normal.
Discussion
MEN 1, a rare endocrine syndrome, is defined by the presence of 2 or more primary endocrine tumors mainly located at parathyroid glands, anterior pituitary and gastro-enteropancreatic (GEP). Mutations of the MEN1 gene are identified as responsible for the development of this syndrome. Primary hyperparathyroidism, the most common manifestation of MEN1, presents usually in the second to the fourth decade of life. Multiple glandular disease is typical of MEN1. The most common type of pituitary adenoma in MEN1 is a prolactinoma. Conversly, non functioning adenoma are rare (5%). GEP, which are asymptomatic in 70% of cases, are the primary life-threatening manifestation of MEN1 due to their malignant potential.
Conclusion
The peculiarty of our case stems from the fact that MEN1 was revealed at an advanced age by a nonfunctionnig macroadenoma. That's why it should not be overlooked in diagnosis. In addition early recognition, multidisciplinary management and life long follow up are crucial.

DOI: 10.1530/endoabs.81.EP603

EP604

Metachronous germ cells and sex cords ovarian tumors in an adolescent girl : Hormone replacement therapy at what cost ?

Mnif Fatma, Asma Zargni, Kawthar El Arbi, Dhoha Ben Salah, Mouna Elleuch, Nadia Charfi, Mouna Mnif, Nabila Rekik Majdoub, Faten Haj Kacem Akid & Mohamed Abid
Hedi Chaker Hospital, Diabetology and Endocrinology Department, Sfax, Tunisia

Introduction
Gonadal tumors are rare in children. Because surgery is the primary treatment for ovarian tumors, ovarian salvage with fertility preservation and use of a minimally invasive surgical technique are important in children and adolescents. We report the case of an adolescent girl who was referred after bilateral annexectomy.
Observation
This is a 14-year-old girl who just had her first menses. She has been followed the last year for an ovarian tumor. She initially had a right annexectomy. The pathology examination concluded to a moderately differentiated Sertoli tumor of 11*13 mm. Two months later, she developed large ascites. Radiological explorations showed a mass of the remaining left ovary of 9*7 mm with peritoneal carcinosis classified as high risk stage IIIc. After a multidisciplinary discussion about fertility, cryopreservation of the ovarian cortex and all other preservation techniques have been discussed but they are impossible due to the high risk of recurrence upon reintroduction of the ovarian tissue. The child received 2 lines of chemotherapy followed by a left annexectomy. The surgery was considered complete and the pathology examination concluded to an ovarian teratoma. Currently, the 16-year-old patient is castrated with complete remission and no tumor recurrence. Her major complaint was the regression of secondary sexual characteristics.
Discussion-Conclusion
In the absence of high-level evidence literature, the Expert Consensus regarding hormone replacement therapy was consulted (1). Overall, the options for hormonal treatment depend on possible hormone dependence and the risk of recurrence. For germline tumors, these treatments can be used. On the other hand, a certain caution has been adopted for tumors of the sexual cords.
1- ROUSSET-JABLONSKI, Christine, SELLE, Frédéric, ADDA-HERZOG, Elodie, *et al.* Préservation de la fertilité, contraception et traitement hormonal de la ménopause chez les femmes traitées pour tumeurs malignes rares de l'ovaire: recommandations du réseau national dédié aux cancers gynécologiques rares (TMRG/GINECO). *Bulletin du Cancer*, 2018, vol. 105, no 3, p. 299-314.

DOI: 10.1530/endoabs.81.EP604

EP605

The combination of medullary thyroid carcinoma and sporadic clear cell renal cell carcinoma: coincidence or new syndrome?

Ihssane Abidi, Kaoutar Rifai, Iraqi Hinde & Mohamedelhassan Gharbi
University Mohammed 5 Rabat, Endocrinologie, Rabat, Morocco

Introduction
COVID-19 is a pandemic related to SARS-COV-2 virus infection. It is most often manifested by an influenza-like syndrome with other symptoms that are more specific such as loss of smell and taste. Its severity is highly variable, ranging from asymptomatic to severe or prolonged forms. We report the case of a 47-year-old female patient, who is being followed for hypoparathyroidism, who developed severe and persistent cramps after the COVID-19 vaccine.
Observation
This is a 47-year-old female patient with a history of high-risk papillary thyroid carcinoma since 2018, operated and irradiated. Her surgery was complicated by supplementary hypoparathyroidism. Her blood calcium was well controlled and she was asymptomatic since her supplementation with Alfacalcidol and calcium. She received the first dose of astrazeneca in July 2021, after 4 hours she developed persistent painful cramps in her extremities. Her clinical examination did not reveal any signs of hypocalcaemia and the biological dosage was 84 mg/l. As the cramps persisted, we started her on calcium and magnesium. The clinical evolution was good after 6 hours and there was no recurrence.
Discussion
COVID-19 vaccines are as well tolerated in neuromuscular patients as in the general population (1). Hypoparathyroidism is not a neuromuscular disease, but it can be caused by hypocalcaemia, which is the cause of the neuromuscular manifestations. Campesium can be seen with COVID-19 vaccines, and is generally benign and transient. The particularity of our observation is that the cramps were severe and incapacitating with the need for intravenous calcium treatment and monitoring, adding the hypoparathyroid terrain which posed a problem of differential diagnosis.
Conclusion
The vaccine against COVID-19 has become an unavoidable necessity in the face of the pandemic population. It certainly has short and long term side effects. Fragile patients must be monitored to avoid complications, particularly neuromuscular ones.
References
(1) Neuromuscular diseases and covid-19 vaccination, Recommendations of the filnemus rare diseases health sector, Version 1.0 of 4 January 2021.

DOI: 10.1530/endoabs.81.EP605

EP606

Multiple endocrine neoplasia type 2: About two Tunisian patients

Mnif Fatma, Kawthar El Arbi, Abdelmouhaymen Missaoui, Faten Haj Kacem Akid, Wafa Belabed, Dhoha Ben Salah, Nadia Charfi, Mouna Mnif[1], Nabila Rekik Majdoub, Mouna Elleuch & Mohamed Abid
Hedi Chaker Hospital, Department of Endocrinology, Sfax, Tunisia

Introduction
Multiple endocrine neoplasia type 2 (MEN2) is a rare inherited disease characterized by the occurrence of medullary thyroid cancer (MTC) either isolated or associated with pheochromocytoma, primary hyperparathyroidism (PHP), or typical morphological features. Thus, we report two cases.
Patient(1)
A 27-year-old female patient with a marfanoid appearance, had a histologically confirmed conjunctival and mucosal ganglioneuromatosis, bilateral composite pheochromocytoma (pheochromocytoma and ganglioneuroma) with multifocal and metastatic MTC. MEN2b was strongly suspected. A genetic study showed the presence of a mutation in the exon 16 (codon, M918T), in the heterozygous state, which is the most frequently associated with the MEN2b phenotype.
Patient(2)
A 46-year-old female patient presented with a complete MEN2a panel: multifocal CMT, PHP and bilateral pheochromocytoma. In addition, she had hyperpigmented indurated lesions on the upper back following intense pruritus. These lesions are reminiscent of cutaneous amyloid lichen (CAL), a rare clinical variant of 2A. The genetic study is ongoing.
Conclusion
As distinct from MEN1, each variant of MEN2 corresponds to a specific genetic mutation. It is possible to predict the patient's phenotype from the genetic study. For example, CAL occurs almost exclusively in a proportion of individuals with the codon 634 mutation. Thus clinical examination plays a crucial role in guiding the biomolecular investigation.

DOI: 10.1530/endoabs.81.EP606

EP607

Multiple endocrine neoplasia type 1: A puzzle that builds over the years

Mnif Fatma[1], Kawthar El Arbi[1], Yosra Lajmi[2], Asma Zargni[1], Faten Haj Kacem Akid[1], Hamdi Frikha[1], Dhoha Ben Salah[1], Nadia Charfi[1], Mouna Mnif[1], Nabila Rekik Majdoub[1], Mouna Elleuch[1], Hassen Kammoun[2], Fatma Abdelhédi[2] & Mohamed Abid[1]
[1]Hedi Chaker Hospital, Department of Endocrinology, Sfax, Tunisia; [2]Hedi Chaker Hospital, Department of Medical Genetics, Sfax, Tunisia

Introduction
Multiple endocrine neoplasia type 1 (MEN1) is a genetic disease that predisposes to the development of both hyperplastic and tumorous lesions of the endocrine glands, in particular parathyroid, pancreatic and pituitary. Thus we report our case.
Observation
An 18-year-old male patient was hospitalized for severe hypoglycemia mistakenly treated as epileptic seizures. The etiological investigation concluded to a benign multiple insulinoma, confirmed by the anatomopathological study. The patient was lost to follow-up and was re-hospitalized 11 years later for an intracranial hypertension related to a macro-prolactinoma of 7 cm of diameter. Prolactin level was 11300µg/l. A MEN1 was suspected. The investigation of additional associated lesions revealed a primary hyperparathyroidism. The evolution was fatal with the death of the patient in a cerebral herniation. The genetic study was not performed.
Discussion
Parathyroid tumors are the first manifestation of MEN1 in over 85% of cases. Less than 15%, the first manifestation may be an insulinoma or prolactinoma, likewise our patient. The chronology of lesion onset could differ from patient to another. The clinical presentation is usually completed over time. Thus a continuous screening of the different lesions is necessary. For our patient, the discovery of a primary hyperparathyroidism as well as a prolactinoma 11 years later make it particular.

DOI: 10.1530/endoabs.81.EP607

EP608

Clinical case: MEN1 syndrome

Ieva Meskinyte[1], Saule Cyrolyte[1], Igne Strazdiene[1], Egle Urbonaviciute[1], Raimonda Klimaite[1,2,3] & Neli Jakuboniené[1,3]
[1]Lithuanian University of Health Sciences, Lithuania; [2]Institute of Endocrinology, Medical Academy, Lithuanian University of Health Sciences, Lithuania; [3]Hospital of Lithuanian University of Health Sciences, Kauno Klinikos, Department of Endocrinology, Lithuania

Introduction
Multiple Endocrine Neoplasia Type 1 (MEN1) is a rare, autosomal dominantly inherited syndrome that causes tumors of the endocrine glands [1]. This syndrome is most commonly associated with neuroendocrine tumors of the parathyroid glands, pituitary gland and pancreas [2].
Case
A 30-year-old woman was admitted to the Hospital of Lithuanian University of Health Sciences, Kaunas Clinics for unconsciousness and significant hypoglycaemia: 1.0 - 3.04 mmol/l.
Anamnesis
In 2016, the patient was examined for infertility. Hyperprolactinemia was diagnosed. Head MRI was performed to detect pituitary microadenoma, treatment with Cabergoline 0.25 mg/week was started. In 2017, an episode of the hypoglycaemic coma was observed. Due to recurrent unspecified hypoglycaemia, the patient was admitted to the Endocrinology Department.
Laboratory tests were performed (Table 1). GTT results were within the normal range. Thyroid US: hypoechoic masses: dorsal from the left lobe, 1.6x0.5 cm and dorsal from the right lobe 2x0.4 cm - possibly parathyroid adenomas. DXA scan: T value - 2.5; Z value -2.5. Conclusion: osteoporosis.

After evaluating multiple endocrine pathologies (prolactinoma, hyperparathyroidism, hypoglycaemia), MEN1 syndrome was diagnosed with the following outcomes:

1) Microadenoma hypophysis – prolactinoma. Secondary infertility
2) Parathyroid adenomas. Primary hyperparathyroidism. Secondary osteoporosis.
3) Insulinoma. Hypoglycaemia.

Parathyroid Scintigraphy Tc-MIBI + SPECT/CT: right and left parathyroid adenomas. Head MRI: 0.6x0.6 cm hypo-enhanced area on the left side of the adenohypophysis - pituitary microadenoma, without negative dynamics. Abdominal MRI: a possible neuroendocrine tumor - insulinoma in the body and tail of the pancreas. Genetic test: sequencing of 2-4 exons of the transcript encoded by the MEN1 gene was performed. A pathogenic change in the c.446-2A> T sequence was identified, and the diagnosis of MEN1 syndrome was confirmed. The patient underwent parathyroidadenomectomia subtotal, laparoscopic surgery to remove insulinoma. An abdominal MRI was performed 6 months later and two new neuroendocrine tumors were identified in the pancreas. Confirmed during scintigraphy. The patient underwent reoperation. After 1 year, there were no signs of recurrence of insulinoma and hyperparathyroidism, test results were in normal ranges.

Conclusion

This clinical case reflects the classic manifestation of MEN1 syndrome with the typical target organs: the parathyroid glands, pancreas, and pituitary gland. In addition, secondary symptoms of these diseases were hyperparathyroidism, infertility, hypoglycaemia and osteoporosis. Multiple endocrine disorders should lead to a suspicion of a diagnosis of MEN1. Therefore, precise laboratory, imaging tests of the target organs and genetic tests should be performed.

DOI: 10.1530/endoabs.81.EP608

EP609

Diagnostic and evolutionary profiles of adrenocortical tumor, about 30 cases

Fadila Chabour & Safia Mimouni
University of Algiers, Medical, Algiers, Algeria

Adrenocortical tumor is a rare malignant tumor of adrenal location. With a poor prognosis that can be improved by rapid diagnosis and adequate early management, hence the importance to evoke this etiology in front of any atypical adrenal mass or any suggestive clinical or biological context. The objective of our modest work is to report through a retrospective study the profile of adrenocortical tumors treated in our service over a period of 13 years from 2007 to 2020. Thirty (30) patients were collected with a middle age of 45 years (27 to 74 years) with a slight female predominance of 60%. A family history of neoplasia was noted in 5 patients (16.66%) and breast neoplasia in a single patient. The most frequent mode of revelation is represented by abdominal pain observed in 56.66% of cases. Hypercortisolemia is found in 40% of cases. Morphologically, the size of the tumor varies from 66 to 180 cm with an average of 110 cm. At least one metastasis was found in 10 patients (33.33%), dominated by hepatic location. 50% of our patients benefited from surgical excision of the tumor and 6.66% underwent a biopsy only. 77% of our patients received adjuvant treatment with mitotane supplemented by chemotherapy in 30% of cases. Only two patients received adjuvant radiotherapy (6.66%). The evolution was marked by remission in 33.33% of cases with an average survival of 5 years and death noted in 50% of patients. In conclusion : Adrenal carcinoma can be seen at any age with a peak frequency in the fifties, affects both men and women with a slight female predominance. Large tumors whose treatment is surgical associated with neoadjuvant treatment in the majority of cases. Unfavorable prognosis, but optimized management can improve survival.

DOI: 10.1530/endoabs.81.EP609

EP610

Insulinoma with confusing imaging : a case report

Wafa Belabed, Fatma Mnif, Abdelmouhaymen Missaoui, Dhoha Ben Salah, Faten Haj Kacem Akid, Elleuch Mouna, Mouna Mnif, Nadia Charfi, Nabila Mejdoub & Mohamed Abid
Hedi Chaker University Hospital, Endocrinology Department, Sfax, Tunisia

Introduction

Insulinoma is a rare pancreatic tumor. It is the most frequent cause of organic hypoglycemia due to endogenous hyperinsulinism.

Case report

A 55-year-old woman was admitted in our department for the management of a recurrent hypoglycemic coma. Endogenous hyperinsulinic hypoglycemia was confirmed with a spontaneous hypoglycemia. Plasma blood glucose was 0.25 g/l concomitant to a high insulinemia of 31.5 µUI/ml ($\geq$ 3) and C-peptide level of 3.16 ng/ml ($\geq$ 0.6) In imaging investigations, abdominal CT scan and endoscopic ultrasound were both normal. A complementary nuclear imaging by Octreoscan was performed and detected the presence of 2 pancreatic lesions: one in the uncinate process and the other in the tail. Abdominal MRI was performed and concluded to the presence of a unique lesion of the pancreas tail. Our patient was then proposed for surgery of the two insulinomas. Per-operative exploration concluded to the presence of a single corporal tumor mass of the pancreas of 1.5 cm. A left pancreatectomy was then performed. Our patient had resolution of symptoms after surgery. The follow-up is 6 months to date.

Conclusion

This case highlights the difficulty of the radiological identification of small pancreatic lesions leading to a multitude of imaging investigations. Our experience also highlighted that the ^{111}In-DTPA-octreotide uptake in pancreatic uncinate process may be physiological and its interpretation must, therefore, be cautious.

DOI: 10.1530/endoabs.81.EP610

EP611

Insulinoma : a single-center retrospective analysis of 10 cases

Wafa Belabed, Fatma Mnif, Abdelmouhaymen MISSAOUI, Dhoha Ben Salah, Mouna Elleuch, Faten Haj Kacem Akid, Nabila Mejdoub & Mohamed Abid
Hedi Chaker University Hospital, Endocrinology Department, Sfax, Tunisia

Introduction

Insulinoma is a rare neuroendocrine tumor with an incidence of 1 to 4 per million person-years. It is the most frequent endocrine tumor of the pancreas and is revealed by a spontaneous hypoglycemia. This study aimed to determine the clinical characteristics, diagnostic workup, and outcome of patients with insulinoma.

Methods

This is a descriptive, retrospective study including patients with confirmed insulinoma collected over a 32-year period. We collected imaging results, medical treatment, surgical management and histologic findings.

Results

A total of 10 patients were included in this study, with a sex ratio of 1,5. The mean age was 46 $\pm$ 15,5 years. Neuroglycopenic and neurogenic symptoms were present respectively in 9 and all cases. The median duration of symptoms was 47 months (3—360). All patients fulfilled Whipple's triad. On biochemical testing, hypoglycemia occurred at a mean glucose level of 1,8 $\pm$ 0,62 mmol/l and at a mean insulin level of 18,9 $\pm$ 6,4 mUI/l. The pancreatic lesion was identified on cross-sectional imaging in 6 cases and on endoscopic ultrasound in 3 cases. No lesion was identified in 1 case. The median tumor size was 1,9 $\pm$ 1,1 cm. Insulinoma was found in the pancreatic uncinate process in 2 cases; in the pancreas body in 4 cases and in the tail in 2 cases. Multiple insulinoma were found in 1 case and was associated to multiple endocrine neoplasia type 1. Surgical procedures included 2 enucleations and 7 pancreatic resections. Histologic findings concluded to benign endocrine tumors in all cases.

All patients had resolution of symptoms after surgery. The median follow-up is 6 years to date.

Conclusion

The diagnosis of insulinoma can be difficult. The average time between start of symptoms and diagnosis is estimated to be 3 years which is consistent with our case series as well. Our experience also highlighted that in cases where cross-sectional imaging failed to localize the pancreatic lesion, Endoscopic ultrasound could be useful.

DOI: 10.1530/endoabs.81.EP611

EP612

Renal cell carcinoma revealed by acute adrenal insufficiency

Salma Abadlia, Bchir Najla, Zouaoui Chadia, Sarra Raddadi & Haroun Ouertani
Military Hospital, Endocrinology, Tunis, Tunisia

Introduction
Renal cell carcinoma (RCC) is the most common type of malignant renal tumors in adults. It is often difficult to detect it precociously since early-stage renal tumors are usually asymptomatic and non-palpable. We report a case of RCC revealed by acute adrenal insufficiency (AAI).
Case report
Mr. A.B, 46 years old, 30 pack-year smoker, with a medical history of gout treated with Allopurinol, was admitted to our department for acute adrenal insufficiency. The anamnesis revealed a significant weight loss, asthenia and melanoderma. The evolution was marked by acute abdominal pain with vomiting, leading the patient to consult our emergency department. A baseline blood sample revealed hyponatremia (127 mmol/l), hyperkalemia (6.4 mmol/l) and functional renal failure. The patient immediately received intravenous hydrocortisone hemi-succinate with hyperhydration. The diagnosis of primary AAI was confirmed by a low plasma cortisol level (99 nmol/l) in the face of high adrenocorticotropin hormone (ACTH) level (>2000 pg/ml). Adrenal computed tomography (CT) showed hypotrophic adrenal glands and a right corticomedullary renal mass (38*47*48 mm). Renal magnetic resonance imaging (MRI), performed for a better characterization of this mass, showed a right medio-renal tumor with a central necrotic zone and exophytic development, without signs of locoregional extension. A tumorectomy was performed. Anatomopathological examination revealed RCC.
Discussion
An AAI revealing a RCC has been reported in a few publications. In those cases, the adrenal insufficiency was related to bilateral adrenal metastases. However, in the present study medical imaging showed hypotrophic adrenal glands suggesting an auto-immune mecanism. Indeed, the increasing use of ultrasound, abdominal CT and more recently MRI has increased the diagnosis of renal cancers at a presymptomatic stage to nearly 70%.

DOI: 10.1530/endoabs.81.EP612

EP613

Abstract Withdrawn

DOI: 10.1530/endoabs.81.EP613

EP614

Clinical and pathological features and phenotype-genotype correlation of pheochromocytoma and paraganglioma in a highly consanguineous population

Balgees Alghamdi, Meshael Alswailem & Ali Alzahrani
King Faisal Specialist Hospital & Research Centre, Riyadh, Saudi Arabia

Context
Pheochromocytoma and Paragangliomas (PPGL) are rare neuroendocrine tumors with a strong genetic background. In this report, our objectives are to understand the molecular genetics and the genotype/phenotype correlation of these tumors in the highly consanguineous population of Saudi Arabia.
Patients and methods
We studied 88 patients with PPGL and no known family history of these tumors. We extracted DNA from peripheral leucocytes and performed PCR-based Sanger sequencing of *RET, SDHA, SDHB, SDHC, SDHD, SDHAF2, VHL, MAX* and/or *TMEM127.* The order in which these genes were selected was based on the clinical phenotype following the Endocrine Society guidelines. When no genetic alteration was found, whole exome sequencing was performed. The clinical phenotype was correlated with the underlying mutations.
Results
Of the 88 patients included in this report, 30 (34%) were males, 58 (66%) were females with a median age of 43.5 years (interquartile range 26-53.7). No mutation was found in 42 patients (47.7%). The other 46 patients (52.3%) had an underlying PPGL-predisposing genetic mutations. The most commonly mutated gene was *SDHB* (11/88), followed by *SDHD* (8/88), *RET* (6/88) and *SDHC* (3/88). There was a tendency for more locally invasive and metastatic PPGL in the patients with underlying genetic alterations, especially SDHB mutations, but this did not reach statistical significance. Although the majority of patients achieved cure (60.5%), 26 patients (29.5%) had persistent/recurrent disease. There was no difference in the final outcome between those with underlying genetic mutations and those without mutations.
Conclusions
In this study, 52.6% of PPGL carry underlying genetic mutations. *SDHB* is the most commonly mutated and associated with higher risk of locally invasive and distant metastases. There is tendency towards locally invasive and distant metastases in those carrying underling mutations but the final outcome was similar between those with and those without underlying mutations.

DOI: 10.1530/endoabs.81.EP614

EP615

Frequency of CYP1B1 gene polymorphism in obese and non-obese women with hormone-dependent endometrial cancer

Dusan Ilic[1], Sanja Ognjanovic[1], Bojana Popovic[1], Valentina Elezovic[1], Milica Opalic[2], Lena Radic[1] & Djuro P. Macut[1]
[1]Clinic for Endocrinology, Diabetes and Metabolic Diseases, Clinical Centre of Serbia, Department for Endocrine Tumors and Hereditary Cancer Syndromes, Belgrade, Serbia; [2]Clinic for Endocrinology, Diabetes and Metabolic Diseases, University Clinical Centre of Serbia, Department for Endocrine Tumors and Hereditary Cancer Syndromes, Belgrade, Serbia

Aim
There is a significant link between the increased activity of estrogen and its metabolites in endometrial carcinogenesis. Polymorphisms of the gene involved in metabolism of estrogen can modulate risk for the development of endometrial cancer. CYP1B1 plays an important role in estrogen metabolism. In our study, the frequency of three *CYP1B1* gene polymorphisms (4326 C> G, 4390 A> G and 355 G> T) were studied in obese and non-obese women with endometrioid endometrial carcinoma and healthy controls.
Methods
Genotype were determined in DNA from peripheral blood lymphocytes of 44 women with endometrial cancer and 47 healthy age-matched controls by restriction fragment length polymorphism polymerase chain reaction (RFLP-PCR).
Results
Polymorphism 4326 C>G was verified in 70.5% of women with endometrial carcinoma and 59.6% of healthy controls ($P=0.277$). In the group of women with endometrial cancer, polymorphism 4326 C>G was verified in 72.2% obese and 69.2% of non-obese women ($P=0.831$). Polymorphism 4390 A>G was verified in 38.6% of women with endometrial carcinoma and 34.0% of healthy controls ($P=0.649$). In the group of women with endometrial cancer, polymorphism 4390 A>G was verified in 27.8% obese and 46.2% of non-obese women ($P=0.218$). Polymorphism 355 G>T was verified in 43.2% of women with endometrial carcinoma and 59.6% of healthy controls ($P=0.118$). In the group of women with endometrial cancer, polymorphism 355 G>T was verified in 44.4% obese and 42.3% of non-obese women ($P=0.888$).
Conclusion
There was no statistically significant difference in the frequency of the *CYP1B1* gene polymorphism in our group of women with endometrial carcinoma and healthy controls and in women with endometrial carcinoma irrespectively of their body mass index.

DOI: 10.1530/endoabs.81.EP615

EP616

Ectopic parathyroid adenoma of the recurrent laryngeal nerve (RLN) chain lymph node

Loubna Guissi, Mohamed Hamid Abdillahi, Manal Azriouil, Kaoutar Rifai, Hind Iraqi & Mohamed Elhassan Gharbi
Ibn Sina University Hospital, Endocrinology, Rabat, Morocco

Introduction
Parathyroid adenoma can be localized in an ectopic situation, especially at the mediastinal level. The localization at the level of the RLN chain lymph node has not been reported yet.
Case presentation
A 67-year-old woman without clinical signs of hyperparathyroidism, having undergone a left isthmolobectomy for a thyroid nodule suspected of being malignant, with intraoperative discovery of lymphadenopathy of the left RLN chain lymph node. The anatomo-histopathological analysis revealed a follicular adenoma and for the lymphadenopathy a morphological appearance in favor of a parathyroid adenoma which was confirmed by immunohistochemistry.The preoperative work-up was unremarkable with a calcium level of 98 mg/l (84-102) and albuminemia at 44g/l (32-46) and phosphoremia at 37 mg/l (23-47). The diagnosis of non-functional ectopic parathyroid adenoma of the RLN chain lymph node was discovered incidentally on histological study.
Conclusion
This case illustrates an unusual location of a non-functional ectopic parathyroid adenoma of the RLN chain lymph node.

DOI: 10.1530/endoabs.81.EP616

EP617

Metastatic medullary thyroid carcinoma with diagnostic and therapeutic challenges: a case report

Hind Asbar, Hind Ouakrim, Sana Rafi, Ghizlane EL MGHARI & Nawal EL Ansari
Chu Mohamed Vi Marrakesh - Drh, Department of Endocrinology, Diabetes, Metabolic Diseases and Nutrition, Marrakech, Morocco

Introduction
Medullary thyroid carcinoma (MTC) is a neuroendocrine tumor that arises from the parafollicular C-cells of the thyroid gland with a tendency to regional and distant metastases. It is a rare tumor, making up about 3% of all thyroid malignancies. MTC occurs in both heritable and sporadic forms, early diagnosis is important as it can improve treatment outcomes. We report a case of metastatic medullary thyroid cancer with both diagnostic and therapeutic challenges.
Case presentation
37-year-old man presented with anterior cervical mass. CT scan showed a cervico-mediastinal mass measuring 29 x 56 x 66 mm, with calcitonin level at 1890 ng/l. The patient underwent total thyroidectomy, with removal of the mediastinal mass and cervical lymph nodes. The pathology revelated initially a poorly differentiated malignant tumor proliferation of thymic origin. Immuno-histochemistry was in favor of a neuroendocrine carcinoma. An anatomical-pathological re-reading revealed a medullary thyroid carcinoma aspect with secondary mediastinal location. One year later, the cervico-thoracic CT scan showed a retro clavicular mass of 31.3 mm x 26 mm x 20 mm, with intimate contact with the left common carotid artery, end intra-parenchymal micronodules measuring 4.4 mm and 4.2 mm, in favor of metastasis. The patient underwent an exeresis of the mass with surgical difficulty due to the intimate contact of the tumor with the cervical vascular axis. The patient was thereafter referred to medical oncology for systemic treatment.
Discussion
Distant metastases in MTC are observed at presentation in 7–23% of patients, they often affect multiple organs including lungs, bones and liver, and they are frequently associated with persistent disease in the neck. Calcitonin and carcinoembryonic antigen (CEA) with conventional radiographic modalities are widely used for the diagnosis, prognosis, and follow-up of MTC patients. In our case, the metastatic MTC was diagnosed with difficulty in the anatomo-pathological reading, with a loco-regional recurrence presenting a difficulty in the surgical management.
Conclusion
MTC is a rare disease with a high risk of not being cured by the initial treatment. In cases of metastasis, the approach depends on the severity and rate of progression of disease. Metastatic MTC can be treated with limited surgical resection, or medical management with tyrosine kinase inhibitors (TKIs) or another agent.

DOI: 10.1530/endoabs.81.EP617

EP618

Pro-inflammatory biomarkers in Papillary thyroid cancer

Ramesh Bangaraiahgari[1], RAmakanth Bhargav Panchangam[2], Rajesh Bangaraiahgari[3], Udaya Kumar U[4] & Sabaretnam Mayilvaganan[5]
[1]Arundathi Institute of Medical Sciences, Biochemistry, India; [2]Bhargav Endocrine Hospitals, Vijayawada, India; [3]Arundathi Institute of Medical Sciences, Anatomy; [4]Arundathi Institute of Medical Sciences, Pediatrics, India; [5]SGPGIMS, Endocrine and Metabolic Surgery, India

Introduction
Papillary thyroid carcinoma (PTC) is the most frequent endocrine malignancy. Apart from genetics, autoimmunity has been implicated in its pathogenesis. In this context, we set out study the role of Pro- inflammatory cytokines in PTC in South Indian population.
Material and methods
This prospective case-control study was conducted on surgically managed PTC patients. Institutional ethical committee approval was obtained. Diagnosis of PTC was based on imaging, fine needle aspiration cytology and later confirmed by histopathology. Exclusion criteria were subjects with any systemic or chronic inflammatory disease or any medication which interferes with the normal function of the hypothalamic-pituitary-gonadal axis. Serum samples were collected from 66 PTC subjects and 64 age matched healthy controls. Interleukin-6 (IL-6), Tumour necrosis factor-alpha (TNF-α) and high sensitive C reactive protein (hsCRP), leptin levels were measured in all serum samples. Statistical analysis was performed by one way ANOVA with Dunnet's test and Pearson correlation tests.
Results
The mean hSCRP level in PTC and controls were 18.4 $\pm$ 3.1 mg/ml and 5.5 $\pm$ 1.2 mg/ml respectively. The mean TNF-α level, IL-6 level and Leptin levels were 294 $\pm$ 30 pg/ml, 12.8 $\pm$ 4.5 pg/ml and 1.97 $\pm$ 0.7 ng/ml respectively. Serum leptin level in controls was 3.4 $\pm$1.6 ng/ml. There was statistically significant difference of all the pro-inflammatory cytokines compared to controls (P value $<$ 0.05) with negative correlation for leptin levels.
Conclusions
Our study shows raised titers of pro-inflammatory markers – IL-6, TNF-α and hsCRP, while reduced leptin levels correlated with PTC suggesting a contributory role. But, the exact immuno-modulatory role and pathogenetic mechanism needs more research.
Key words: Papillary thyroid cancer; Tumour necrosis factor; Interleukin-6; Auto-immunity; Leptin

DOI: 10.1530/endoabs.81.EP618

EP619

The different faces of a long-lasting metastasized pancreatic neuroendocrine tumor with calcitonin paraneoplastic secretion and cardiac carcinoid

Rucsandra Ilinca Diculescu[1], Iulia Florentina Burcea[1, 2], Anda Simona Dumitrascu[3], Cosmin Boldeanu[4], Madalina- Elena Iftimie[1] & Catalina Poiana[1,2]
[1]C.I. Parhon National Institute of Endocrinology, Pituitary Pathology, Bucureşti, Romania; [2]"Carol Davila" University of Medicine and Pharmacy Bucharest, Department of Endocrinology, Bucharest, Romania; [3]C.I. Parhon National Institute of Endocrinology, Bucureşti, Romania; [4]County Hospital, Brăila, Romania

Introduction
Besides medullary thyroid carcinoma (MTC), increased calcitonin serum concentrations may be due, rarely, to neuroendocrine tumour (NET) ectopic secretion, especially those of the foregut (pancreatic/lung). Patients with NETs and right-sided heart failure due to cardiac carcinoid have a worse prognosis than those presenting without.

Case presentation
We present the case of a 72-year-old female with a history of an initially considered well-differentiated non-functional pancreatic NET who underwent three surgical interventions (2008 – body and tail pancreatic excision and splenectomy, 2012 - portal vein invasion and thrombosis, 2015- removal of liver metastases). Immunohistochemistry (IHC) showed positive reactions for CK19, CK7, vimentin, chromogranin A, synaptophysin and NSE in the primary tumour, with positive chromogranin A, synaptophysin and Ki-67 of 10% in the portal vein tumour. Since the first manifestations of the carcinoid syndrome (2015) she has been treated with Octreotide LAR (maximum dose 60 mg/day). She also received chemotherapy: FOLFOX in 2015, and after a voluntary drug holiday, Irinotecan was administered between 2017-2018 and 2020-2021. After the first course of Irinotecan, radiological regression of the hepatic hilum lymph nodes and VI segment nodules (abdominal CT scan, 2016) was noted, whereas without any chemotherapy treatment (2018-2020), abdominal MRI showed progression of the hilum and hepatic nodules. In 2021, under the second Irinotecan course, tumoral growth was noticed, so chemotherapy was stopped and targeted therapy with Sunitinib was introduced. The patient developed cardiac carcinoid (elevated NT-proBNP, 239.4 pg/ml in March 2021), associating a mild tricuspid regurgitation. All neuroendocrine tumour serum markers were within the normal range from diagnosis until now, except for calcitonin serum levels, reaching levels as high as 2452 pg/ml in 2021, currently with decreasing values. The patient also associates secondary diabetes under insulin therapy, permanent levothyroxine substitutive treatment for postoperative hypothyroidism (2009, microfollicular adenoma) and secondary hyperparathyroidism due to vitamin D deficiency.
Conclusion
We presented a complex case of a patient with pancreatic NET who underwent multimodal treatment, associated with paraneoplastic calcitonin hypersecretion and cardiac carcinoid. Calcitonin-secreting NETs are rare, studies reporting that gastroenteropancreatic-NETs with high serum calcitonin have a worse prognosis that those with normal calcitonin. High calcitonin in NETs is associated with high-grade tumours, our case being of intermediate grade, further studies being needed to confirm the link between calcitonin and the clinical outcome of patients with NETs. Nozières C et al, Neuroendocrine tumors producing calcitonin: characteristics, prognosis and potential interest of calcitonin monitoring during follow-up. EJE. 2016 Mar;174(3):335-41.

DOI: 10.1530/endoabs.81.EP619

EP620

A NEM 2A with mutation in a gene outside panel ROTERC

Mohamed Abdellahi Mohamed Ahmed[1], Nabila Mejdoub[1], Guidara Souhir[2], Dhoha Ben Salah[1], Mouna Mnif[1], Faten Haj Kacem Akid[1] & Mohamed Abid[1]
[1]Department of Endocrinology and Diabetology CHU Hedi Chaker Sfax, Tunisia; [2]Faculty of Science, Sfax

Introduction
Multiple endocrine neoplasia type 2 is an inherited syndrome characterized by the characteristic combination of medullary thyroid cancer, pheochromocytoma and primary hyperparathyroidism. We report one case with phenotype-genotype mismatch.
Observation
Patient A. T is 45 years of age with a family history of thyroid bone marrow cancer (CMT) and sister brain cancer, father colon cancer, with no personal history of disease. A 60 mm long-axis left adrenaloma during a nephretic colic test with 4* normal urinary metanephrins. The diagnosis of primary hyperparathyroidism was raised in the presence of hypercalcemia: 2.9 mmol/l, Phosphoremia: 0.7 mmol/l and confirmed by normal PTH *. The topographic assessment concluded a parathyroid adenoma and a multinodular goiter. The absence of medullary thyroid cancer (CMT) decreased the probability of NEM2A but this is still possible. The patient received a left adrenalectomy. A The genetic study did not reveal any pathogenic variant or VSI.
Discussion-Conclusion
The association of pheochromocytoma, hyperparathyroidism and multinodular goiter, as well as the family history of CMT and cerebral cancer in the sister and colon cancer in the father, suggested a mutation that does not belong to the ROTERCC panel. Our observation attested to the value of conducting a genetic study for personalized medical care of patients and for establishing genetic counseling for patients and their families.

DOI: 10.1530/endoabs.81.EP620

EP621

Medullary thyroid Cancer, an experience from a tertiary care hospital of a developing country

Sajjad Ali Khan, Abdul Aziz, Umer Arif Esbhani & Muhammad Qamar Masood
Aga Khan University Hospital (AKUH), Department of Medicine and Section of Endocrinology, Karachi, Pakistan

Background
Medullary thyroid carcinoma is a rare type of thyroid cancer that is either sporadic or familial. It occasionally occurs alongside parathyroid hyperplasia and pheochromocytoma as part of MEN2A. Our aim was to study the presence and patterns of above mentioned characteristics of medullary thyroid carcinoma in our population.
Methodology
This is a retrospective study conducted in a tertiary care hospital of Pakistan in which data of medullary thyroid cancer over past 20 years was reviewed. Data from 32 patients was analyzed after fulfillment of the inclusion criteria. Their clinical, pathological, biochemical and treatment outcomes were recorded through retrospective review of their medical record files.
Results
The mean age of patients with medullary thyroid carcinoma (MTC) was 42.88 + 2.67 in our study, with male to female ratio of 2:1. 68.8% of MTC patients were sporadic and 31.2% were familial in our study. 81.3% of patients presented with neck swelling, lymph nodes were palpable in 43.8% of patients and distant metastasis were present in 25% of the patients. The rates of metastasis were highest in bones followed by lungs and liver (12.5%, 9.4%, and 3.1% respectively). Histologically, the mean tumor size was 7.62 + 3.64 with 8 (25%) having distant metastasis. Lymph node metastasis was present in 19 (59.3%) of the patients, out of which 16 had bilateral involvement. Over 50% of carcinomas in our study were unifocal, followed by bifocal (21.9%) and multifocal 3 (9.4%). Mean pre-surgery calcitonin was 11225.7 + 4043.57 which then decreased to a mean of 244.43 + 113.48 post surgery. Mean pre-surgery CEA level was 25.08 + 7.23 which then decreased to 0.0645 + 0.044 post surgery. Hyperparathyroidism was found in two patients while pheochromocytoma was found in one patient only. Two patient were positive for RET gene mutations. Total thyroidectomy was done in 26 (81.2%) of the patients while one patient had subtotal thyroidectomy followed by complete thyroidectomy as initial FNAC was Bethesda category 3. Surgery was not performed in 5 patients due to distant metastasis or palliative intent. Chemotherapy was given to only one patient while XRT was performed in two patients.
Conclusion
Medullary thyroid carcinoma usually presents in fourth decade of life with male predominance and mostly sporadic occurrence. Total thyroidectomy with subsequent serial calcitonin and CEA levels thereafter are the mainstay of treatment and follow-up.

DOI: 10.1530/endoabs.81.EP621

EP622

Refractory papillary thyroid carcinoma treated with sorafenib: an Algerian experience

Amira Bouchenna[1], Abdelghani Tibouk[1], Ghennam Brahim[2] & Ould Kablia Samia[3]
[1]Central Hospital Of Army, Anatomopathology, Algeria; [2]Central Hospital Of Army, Nucleary, Algeria; [3]Central Hospital Of Army, Endocrinology, Algeria

Introduction
5-10% of papillary thyroid carcinoma develop metastatic disease, of which about 60-70% will become refractory to radioactive iodine. Significant negative impact on the prognosis and an average life expectancy of 3 to 5 years.
Material and method
Since 2018, patients with refractory thyroid carcinoma and considered to be progressive according to the RECIST criteria have been treated with anti tyrosine Kinase type sorafenib.
9 patients treated: an anaplastic carcinoma, a medullary carcinoma and 7 differentiated carcinomas. 3 women/6 men, average age: 56 years old. Tumor regression was observed in 3 patients but stopped in 2 due to the onset of a serious side effect, with rebound phenomenon in one of them; lesion stability in 3 patients; disease progression leading to discontinuate the treatment in 3 patients.

Discussion
Refractory thyroid cancers are rare but responsible for the majority of cancer-related deaths. The use of kinase inhibitors has improved the outcome of these patients.
On the other hand, in addition to their high cost, they have a notable toxicity, responsible of major side effects impairing the quality of life, for an uncertain response. Due to the complexity of these treatments, these patients are at best managed by multidisciplinary groups.

DOI: 10.1530/endoabs.81.EP622

EP623

Hungry bone syndrome in the post-operative management of severe primary hyperparathyroidism: a case report

Loubna Guissi, Manale Azriouil, Khawla Gorgi, Kaoutar Rifai, Hind Iraqi & Mohamed Elhassan Gharbi
Ibn Sina University Hospital, Endocrinology, Rabat, Morocco

Introduction
Hungry bone syndrome (HBS) is a rare complication of parathyroidectomy for primary hyperparathyroidism. We report a case of HBS after parathyroid surgery for severe primary hyperparathyroidism.
Case presentation
A 46-year-old woman was admitted with generalized weakness and difficulty walking due to progressive worsening of low-back pain. Clinical examination revealed tachycardia at 110 bpm and chest deformity. Laboratory results revealed hypercalcemia at 185 mg/l and hypophosphatemia at 19 mg/l. The parathyroid hormone (PTH) concentration was at 4936 pg/ml (normal 15–65) and the alkaline phosphatase concentration reached478 U/l (normal 40–150). Medical treatment was initiated with rehydration, forced diuresis and intravenous infusion of biphosphonates. Ultrasound of the neck and Sestamibi scan showed a localized adenoma. The parathyroidectomy was performed and anatomopathological examination confirmed parathyroid adenoma, weighing 4 g and measuring 3*2*0.6 cm. The postoperative period was characterized by prolonged hypocalcemia, hypophosphatemia and normal PTH levels, which was consistent with the diagnosis of HBS. The patient was discharged on high doses of calcium carbonate and alfacalcidol.
Discussion
HBS refers to the rapid, profound, and prolonged hypocalcaemia associated with hypophosphatemia and hypomagnesaemia, and is exacerbated by suppressed PTH levels, which follows parathyroidectomy in patients with severe primary hyperparathyroidism and preoperative high bone turnover. Although HBS does not have a consensus definition, most resources define it as profound hypocalcemia of less than 8.4 mg/dl that persists for more than four days post-operatively. The severe hypocalcaemia is believed to be due to the greatly increased skeletal usage of calcium, thought to occur as a result of removal of the effect of high circulating parathyroid hormone (PTH) levels on bone, with immediate arrest of bone resorption in the face of continuing and enhanced bone formation. The duration of the HBS is the time taken to remineralise the skeleton, which is also mirrored by normalisation of bone turnover markers, by healing of radiological features of osteitis fibrosa cystica and brown tumours and by significant gains in bone mass. Treatment is aimed at replenishing the severe calcium deficit and at restoring normal bone turnover with the use of high doses of calcium and active metabolites or analogues of vitamin D.
Conclusion
HBS is relatively uncommon, but a serious side effect of parathyroidectomy. It can bring significant morbidity related to the consequences of hypocalcaemia in the case of patients in whom it is not recognized and corrected promptly.

DOI: 10.1530/endoabs.81.EP623

EP624

A rare case of gonadotropin independent precocious puberty in young child

Lakshman Kumar Ega[1], Rakesh Sahay[2] & Neelaveni Kudugunti[3]
[4]Osmania Medical College, Endocrinology, Hyderabad, India; [2]Osmania Medical College, Endocrinology, Hyderabad, India; [1]Osmania Medical College, Endocrinology, Hyderabad, India

Introduction
Adrenocortical carcicnoma (ACC) is a rare malignancy with overall incidence of 0.7–2.0 cases/million. It's a rare & aggressive childhood cancer with a reported incidence of 0.2– 0.3 new cases per 1 million. It has Bimodal distribution - at first decade - 85% functional & 5-6th decade of life 15-30% functional. Paediatric virilising adrenal tumours have a better prognosis after complete resection than in adults. Surgery is the mainstay of treatment. Even after complete resection, a high risk of recurrence of ACC remains. 2yrs 3months – 1st born male child brought by parents with complaints of appearance of pubic & axillary hair, enlargement of both breasts, accelerated height gain, increase in penile length without any increase in testicular size. On examination a palpable mass was noticed in right hypochondrium which was firm in consistency. A provisional diagnosis of Gonadotropin independent precocity (GIPP) due to adrenal mass lesion was made. Biochemical and Radiological evaluation was suggestive of Adrenocortical cancer. Subsequently child underwent Right adrenalectomy. Postop was uneventful and he was discharged on Day 6.
Discussion
Here is a male child with Premature development of axillary, pubic hair with features of androgenisation, Increase in penile length without Increase in testes size, with B/l Gynaecomastia, accelerated Ht gain, with palpable mass in RUQ which Implies -Precocious Puberty of Peripheral origin (Gonadotropin Independent) due to Adrenal neoplasm.
Conclusion
Though ACC is a rare cause of GIPP in paediatric age group, this entity should be considered in differential diagnosis.

DOI: 10.1530/endoabs.81.EP624

Environmental Endocrinology

EP625

The development of a GLP protocol for the measurement of 17β-estradiol and testosterone in the H295R steroidogenesis assay, Test No 456

Carol Murray[1], Angela McIntyre[1], Connor McKeever[1], Rebecca White[1], Rachel McBrinn[1], Victoria Light[2], Susan Brown[1], Aron Robinson[1], Graeme Clark[1] & Tilly Bingham[3]
[1]Concept Life Sciences, Dundee, United Kingdom; [2]Concept Life Sciences, Bradford, United Kingdom; [3]Concept Life Sciences, Chapel-en-le-Frith, United Kingdom

Regulators are concerned about the potential for environmental chemicals such as agrochemicals and their metabolites to perturb hormone systems. This has led to recommendations for the testing of potential endocrine disrupting chemicals[1]. The Steroidogenesis H295R assay is an *in vitro* cell model used to investigate compound effects on steroid hormone biosynthesis, specifically 17β-estradiol (E2) and testosterone (T). The human H295R adreno-carcinoma cell line expresses genes that encode for all the key enzymes for steroidogenesis and thus forms one of the required OECD *in vitro* tests (TG456) for the assessment of potential endocrine disrupting chemicals[2]. Although it is possible to assess hormone levels with ELISA we elected to perform the TG456 assay with LC-MS/MS hormone detection, avoiding the test item interference issues reported for immunoassay-based readouts. We describe herein the implementation of a robust GLP bioanalytical method for the detection of testosterone and 17β-estradiol in the steroidogenesis assay, to LLOQ levels of 10 pg/ml for each hormone. This method has been used to correctly identify inducers and inhibitors of T and E2 production while remaining unresponsive to a negative chemical. We present the impact this has on assay performance with respect to the proficiency items and discuss the benefits of the optimised bioanalytical protocol on Test No 456 performance.
References
1. Guidance for the identification of endocrine disruptors in the context of Regulations (EU) No 528/2012 and (EC)No 1107/2009. European Chemical Agency (ECHA) and European Food Safety Authority (EFSA) with thetechnical support of the Joint Research Centre (JRC)Niklas Andersson, Maria Arena, Domenica Auteri, Stefania Barmaz, Elise Grignard, Aude Kienzler, Peter Lepper, Alfonso Maria Lostia, Sharon Munn, Juan Manuel Parra Morte, Francesca Pellizzato, Jose Tarazona, Andrea Terron and Sander Van der Linden DOI https://doi.org/10.2903/j.efsa.2018.5311
2. Test No. 456: H295R Steroidogenesis Assay, https://www.oecd.org/env/test-no-456-h295r-steroidogenesis-assay-9789264122642-en.htm

DOI: 10.1530/endoabs.81.EP625

EP626

Clinical and demographic analysis of the structure of telemedicine "doctor-patient" consultations of the Endocrinology Research Centre

Anna Gorbacheva, Oksana Logvinova, Anna Eremkina & Natalia Mokrysheva
Endocrinology Research Center, Moscow, Russian Federation

Rationale
The COVID-19 pandemic has accelerated the development of telemedicine technologies. Today there is evidence of the successful use of telemedicine in various areas of healthcare, particularly in endocrinology. At the same time, there is not enough information for efficient integration of telemedicine into the routine management of patients.
Aim
The aim of this work was a clinical and demographic analysis of "doctor-patient" telemedicine consultations (TMC) conducted at the Endocrinology Research Centre (Moscow, Russian Federation) in 2020-2021.
Materials and Methods
A cross-sectional, single-centre, retrospective study was conducted. The study included all patients who received at least one TMC at the Endocrinology Research Centre in 2020-2021. Clinical and demographic information was analyzed (gender, age, region of residence, disease code according to ICD-10). All patients signed an informed consent for the telemedicine consultation. The received data were processed using the Microsoft Office software.
Results
In 2020, 1548 TMC were held, in 2021 - 4180 TMC. Among adults, women predominated in the structure of TMC (83-86%), among children there is a tendency towards equivalent appeals for boys and girls (in 2021 - 45% and 55%, respectively). The median age of adult patients in 2021 was 38 years [31;53], among children - 11 years [7;14]. In 2020, residents of 74 regions of the Russian Federation applied for TMC, in 2021 - of 82 regions. There is a tendency for patients from the Central, Volga, Southern and North Caucasian federal districts to predominate in the structure of TMC. In the nosological structure of TMC among adults diseases of the thyroid gland (35.2%), parathyroid glands (6.8%), diabetes mellitus types 1 and 2 (5.8%), ovarian dysfunction (5.6%) and obesity (4.7%) predominated. In children, TMC the most frequent nosologies were type 1 diabetes mellitus (49.8%), thyroid diseases (13.9%), adrenogenital disorders (5%), and polyglandular dysfunction (4.3%).
Conclusion
TMC proved to be in demand in patients with a variety of endocrinopathies. It is important to analyze both the TMC market and the effectiveness of remote counseling for various nosologies in order to determine the place of telemedicine in the modern healthcare structure and introduce TMC into the system of clinical recommendations.

DOI: 10.1530/endoabs.81.EP626

EP627

Abstract Withdrawn

DOI: 10.1530/endoabs.81.EP627

EP628

Exposure to the endocrine disruptor cadmium alters human aortic endothelial cells homeostasis

Giuseppina Catanzaro[1], Claudia Sabato[1], Viviana Maria Bimonte[2], Zaira Spinello[1], Agnese Po[3], Zein Mersini Besharat[1], Alessandra Vacca[1], Silvia Migliaccio[2] & Elisabetta Ferretti[1]
[1]Sapienza University, Experimental Medicine, Rome, Italy; [2]Foro Italico University, Movement, Human & Health Sciences, Rome, Italy; [3]Sapienza University, Molecular Medicine, Rome, Italy

Cardiovascular diseases (CVDs) represent a complex and multifactorial issue that results from a combination of behavioural, genetic and environmental factors. Toxic metal contaminants, many of which act as endocrine disruptors (EDs), have been identified as potential risk factors for CVDs. Among EDs Cadmium (Cd), present both in cigarettes and in food, has been suggested to be cytotoxic on vascular endothelium, likely leading to blood pressure increase and vascular inflammation. We previously demonstrated that Cd exposure increased TNF-α, IL-6 and IL-8 mRNA in HUVEC endothelial cells. The aim of this study was to further evaluate and characterize the potentially detrimental effect of Cd exposure on Endothelial cells. The effect of Cd exposure on the vascular system was evaluated by using a human *in-vitro* model for vascular endothelial cells, the human Aortic Endothelial Cells (HAEC). Firstly, we evaluated HAEC morphology after 24 h exposure to increasing Cd concentrations, ranging from 1 to 10 μM. Cd induced a collapse of cytoskeleton, with a toxic effect already evident upon treatment with 1 μM. The effect on cellular morphology was accompanied by a reduction of cell proliferation and an increase in cell death. In addition, the Bax/Bcl2 ratio increased. Moreover, Cd affected the expression of pro-inflammatory cytokines, showing an increase of both IL-6 and IL-8 upon 5 and 10 μM Cd exposure, confirming our previous results obtained in HUVEC. Accordingly, a decrease of endothelial adhesion molecules, such as V-CAM and I-CAM, was observed. In conclusion, our results suggest that Cd exposure affects HAEC morphology and behaviour inducing cytotoxicity and apoptosis. In addition, already at low concentration, Cd exposure induces a pro-inflammatory state with production of pro-inflammatory cytokines and reduction of endothelial adhesion molecules, strongly suggesting that this heavy metal is able to alter endothelium homeostasis.

DOI: 10.1530/endoabs.81.EP628

EP629

Epidemiological characteristics and psychological distress of well-controlled endocrine outpatients from Crete, Greece during the COVID-19 Pandemic: preliminary results of the EPITOME study.

Panagiotis-Nikolaos Tsakalomatis[1], VASILIKI DARAKI[1], Theano Roumeliotaki[2], Grigoria Betsi[1], Maria Chrysoulaki[1], Maria Sfakiotaki[1], Eleni- Konstantina Syntzanaki[1], Rodanthi Vamvoukaki[1], Kalliopi Kontolaimaki[1], Vasiliki Venetsanaki[1], Kyriakos Nicolaou[1], Polyxeni Anomerianaki[1], George Mavrakis[1], Katerina Bouki[1], Panagiota Goulia[3] & Paraskevi Xekouki[1]
[1]University General Hospital of Heraklion, Endocrinology & Diabetes Clinic, Heraklion, Greece; [2]University of Crete, Department of Social Medicine, Heraklion, Greece; [3]Fulbourn Hospital, Cambridgeshire and Peterborough NHS Foundation, Cambridge, United Kingdom

Aim
To explore the epidemiological characteristics and symptoms of psychological distress of well-controlled endocrine patients without a diagnosis of a psychiatric disorder attending the Endocrine outpatient clinic of the University Hospital, Heraklion, Crete, Greece during the COVID-19 pandemic. **Methods**: Eighty-four patients participated by completing questionnaires about demographics, endocrine diagnosis, covid infection, preventive measures, vaccination status, source of support and lifestyle changes. Psychological distress was assessed by means of the Greek version of the DASS 21 questionnaire. Ethical approval was obtained by Institutional Review Board and all participants provided written informed consent.
Results
Participants' mean age was 50.8 years; 76.2% were female, 68.7% married and 57.8% employed. Most common endocrinopathies were thyroid diseases, diabetes mellitus and pituitary disorders. Only two patients had been infected with COVID-19 and 31% were a close contact to a COVID-19 patient. The level of adherence to COVID-19 preventive measures was 96.4%, whereas 21.7% hesitated to visit a healthcare professional due to the fear of becoming infected. Sixty-four (77.1%) had at least one dose of the COVID-19 vaccine. The majority cited family as their supportive network (84.3%) followed by friends and neighbors (16.9%) and only 2.4% the social services. Forty-one reported changes at eating habits and thirty one had gained weight; twenty-three had decreased their physical activity and thirty-one dropped hobbies due to the pandemic. Approximately one in four reported sleep difficulties. The majority did not present symptoms of stress (71.43%), anxiety (80.52%) or depression (80.3%). Patients with chronic endocrine disease reported stress symptoms less frequently. **Conclusions**: This is the first study in Crete, Greece regarding social parameters and psychological distress due to the COVID-19 pandemic in endocrine patients.

Our participants follow the recommended preventive measures and are mostly vaccinated. They would seek help from family and friends if required and do not rely on state-provided sources for support. Contrary to numerous studies indicating that depression and anxiety increased during the present pandemic, we found that our sample had low rates of moderate/severe anxiety/depression. We hypothesize that this is related to the well-controlled endocrine problems, and to protective factors such as marital status, employment, family support, as well as the vaccination status and compliance with preventive measures. This is an ongoing study with an aim to define whether different demographics and social parameters may influence levels of distress in this patient group and to develop strategies which may improve well-being during severe crises in endocrine patients.

DOI: 10.1530/endoabs.81.EP629

EP630

Comparison of perceived sufficiency of information, sources of information, worries about the pandemic and psychological distress between endocrinology patients and staff at the outpatient department of the university hospital, heraklion, crete greece: preliminary results of the EPITOME study

Vasiliki Daraki[1], Panagiotis- Nikolaos Tsakalomatis[1], Theano Roumeliotaki[2], Grigoria Betsi[1], Maria Chrysoulaki[1], Maria Sfakiotaki[1], Eleni- Konstantina Syntzanaki[1], Vasiliki Venetsanaki[1], Rodanthi Vamvoukaki[1], Kalliopi Kontolaimaki[1], Kyriakos Nicolaou[1], George Mavrakis[1], Polyxeni Anomerianaki[1], Katerina Bouki[1], Panagiota Goulia[3] & PARASKEVI XEKOUKI[1]

[1]University General Hospital of Heraklion, Endocrinology & Diabetes Clinic, Heraklion, Greece; [2]University of Crete School of Medicine, Department of Social Medicine, Heraklion, Greece; [3]Fulbourn Hospital, Cambridgeshire and Peterborough NHS Foundation, Cambridge, United Kingdom

Background
Psychological distress is elevated during pandemics such as the COVID-19 outbreak both in health care professionals and patients.
Aim
To compare worries about the COVID-19 pandemic, need and sources of information, and psychological distress between endocrinology patients and staff at an outpatient department of the University Hospital, Heraklion, Crete, Greece
Methods
One hundred and four patients and sixty members of staff completed questionnaires about demographics, need for information, sources of information, worries about the COVID-19 pandemic and the Greek version of the DASS-21 for psychological distress. Ethical approval was obtained by Institutional Review Board and all participants provided informed consent.
Results
Mean age of staff was 41.2 years and patients 50.6 years (<0.001), with predominance of women in both groups. The majority of both groups stated that they worried about the pandemic reporting a moderate degree of worry. Main worry was the risk of contagion and infection of their family, and this was more prevalent for staff ($P=0.036$). Regarding the need for information on a 5-item Likert scale (1: prefer having no more information than needed; 5: prefer as much information as possible) both groups reported moderate degrees of information needs. Regarding specific aspects of COVID-19 infection, staff was better informed about symptoms, prognosis, infection route, preventive measures (p, 0.001, 0.032, 0.001, 0.047 respectively) with no differences about information on treatment and the COVID-19 vaccine, compared to patients. Both groups preferred formal sources of information. Staff relayed mainly on information by health professionals ($P=0.006$) whilst patients showed an additional preference for informal sources ($P=0.022$). There were no differences in stress and anxiety symptoms between the two groups, which showed low rates of both; few participants displayed moderate/high symptoms of depression, and these were mostly in the staff group ($P=0.040$).
Conclusions
The current study highlights differences between endocrine patients and staff regarding their main worry about the pandemic with staff being more worried about the safety of family/relatives likely due to their higher chance of exposure. Although both groups were informed by formal sources, staff was more informed on most aspects of COVID-19, but this did not include treatment and the COVID-19 vaccine, perhaps due to the scarcity of studies. Among participants, staff reported more often moderate/severe symptoms of depression. These results are relevant when designing policies on information on pandemics and supportive measures for patients and staff in General Hospitals.

DOI: 10.1530/endoabs.81.EP630

EP631

Perception of training and job perspectives of the specialty of Endocrinology and Nutrition among final-year residents.

Joaquin de Carlos[1], Luci Zabalza[1], Ana Zugasti Murillo[1] & María Dolores Ballesteros-Pomar[2]

[1]Hospital Universitario de Navarra, Pamplona, Spain; [2]Complejo Asistencial Universitario de León, León, Spain

Introduction
Medical specialization model in Spain is carried out through specialized health training, through the residency program. Residents are a key element for the proper functioning of today's National Health System. The aim of the study is to analyze, by an anonymous survey, the opinion of three aspects among final-year residents in Endocrinology and Nutrition (E&N): self-assessment of the knowledge acquired, working prospects, care and training consequences arising from the pandemic COVID-19.
Materials and methods
Cross-sectional observational study using a voluntary and anonymous online survey, shared among final-year national interns in the last year of the E&N program, carried out between June-July 2021. The survey consisted of 20 questions. The results were analyzed with the SPSS version 25 statistical program.
Results
Fifty-one responses were obtained, 66% of the residents, most of them from the central region of the country. Fifty-nine percent of the respondents were trained in tertiary hospitals with more than 800 beds compared to 41% who were trained in centers with between 200-800 beds. Overall perception of their knowledge was 7.8 out of 10, being diabetes and thyroid the best rated sections, followed by nutrition, pituitary, adrenal and finally lipids. Most external rotations were in thyroid and nutrition areas. A total of 96.1% residents, carried out some activity associated with COVID-19, with a training deterioration of 6.9 out of 10. 88.2% have cancelled their rotations and 74.5% have extended their working schedule. The average negative emotional impact was 7.3 out of 10. Most of them carry out research work, spending time out of their working day to do so. 80.4% would like to continue in their training hospital, remaining 45.1%. 56.7% have an employment contract of less than 6 months, most of them practicing Endocrinology.
Conclusion
The perception of the knowledge acquired during the training period is a 'B'. Residents consider that the pandemic has led to a worsening of their training, generating a negative emotional impact. Employment outlook after completing the residency can be summarized as: temporality, practice of Endocrinology and hospital mobility.

DOI: 10.1530/endoabs.81.EP631

EP632

Bisphenol-A and Pentocholorophenol Sodium Levels in Patients with Acne Rosacea

Deniz Demircioglu[1], Nese Cinar[2], Suzan Demir Pektas[3], Tuba Edgunlu[4], Mustafa Unal[5] & Duygu Yazgan Aksoy[6]

[1]Acıbadem University Faculty of Medicine, Department of Dermatology, Istanbul, Turkey; [2]Mugla Sitki Kocman University Faculty of Medicine, Department of Endocrinology and Metabolism, Mugla, Turkey; [3]Mugla Sitki Kocman University Faculty of Medicine, Department of Dermatology,

Mugla, Turkey; [4]Mugla Sitki Kocman University Faculty of Medicine, Department of Medical Biology, Mugla, Turkey; [5]Istanbul Haseki State Hospital, Department of Endocrinology and Metabolism, Istanbul, Turkey; [6]Acıbadem University Faculty of Medicine, Department of Endocrinology and Metabolism, Mugla, Turkey

Objective
Rosacea is an inflammatory dermatosis. Telangiectasias, edema, erythema, and acneiform eruptions are the main symptoms. Several genetic and environmental factors have been linked to rosacea; however, the etiology of the disease is still not known. It is considered a systemic disease rather than a skin disorder. Endocrine-disrupting chemicals are substances people are exposed to through water, food, self-care products, and the environment. They interfere with normal hormonal functions and can also enter the body through the skin. Bisphenol A (BPA) and pentachlorophenol sodium (PCS) are two substances associated with different diseases. The possible association of these substances with rosacea is not known. We aimed to determine BPA and PCS levels in patients with rosacea.
Methods
We conducted a prospective study in a training hospital. Thirty-four patients with Rosacea (18F/16M; mean age 48.5 ± 11) and 34 age and sex-matched healthy controls (20 F/14 M; mean age 48.2 ± 10.2) were included. Main anthropometric measures, plasma glucose (FPG), insulin, lipids, TSH, BPA, and PCS levels were measured.
Results
Age, weight, BMI, FPG, and TSH were similar between the two groups. CRP levels were higher in patients with rosacea (9.6 ± 3.4 and 3.7 ± 1.6 for patients and healthy controls, respectively, $P < 0.001$). Serum BPA levels were 55.8 ± 14.4 and 51.9 ± 19.2, and PCS levels 63.3 ± 45.9 and 68.6 ± 40.8 for patients and healthy controls, respectively. There was no significant difference between BPA and PCS levels ($P > 0.05$).
Conclusions
CRP levels were higher with patients with rosacea compared to healthy controls; however, BPA and PCS levels were not different from healthy controls.

DOI: 10.1530/endoabs.81.EP632

EP633

Histology of the diffuse endocrine system of the lungs in ontogenesis and in pathological conditions in uzbekistan

Madina Adkhamova[1], Gulnoza Goyibova[1] & Dilfuza Karimova[2]
[1]Tashkent Medical Academy, Department of Endocrinology, Tashkent, Uzbekistan; [2]Tashkent Medical Academy, Tashkent, Uzbekistan

Background
The study of fundamental questions related to the analysis of recent advances in the field of cellular and molecular pathways involved in lung organogenesis provides a basis for understanding the pathogenesis of acute and chronic diseases of this organ. Cells of the diffuse endocrine system - apudocytes (APUD) absorb the precursors of biogenic amines introduced from the outside and subject them to decarboxylation with further formation of biogenic amines and peptide hormones. The APUD system also includes innervated clusters of endocrinocytes - neuroepithelial bodies (NETs).
Purpose
Identification in a comparative aspect of the features of the structure of the endocrine apparatus of the APUD-system of the lungs during embryogenesis, as well as in the pathology of the organ caused by inflammatory processes. Material and methods. We studied histological preparations of the lungs in human fetuses at 9-28 weeks of fetal development and full-term newborns.
Results
By the 11th week of their embryonic development, intralobular bronchi appear, the same picture is observed in fetuses of 12 and 13 weeks. Cartilaginous plates are found only in the walls of the lobar and segmental bronchi. In the lungs of fetuses of 9-10 weeks of development, endocrine cells in the epithelium of the bronchi and in the epithelial tubules are not found. Starting from 11 weeks, argyrophilic apudocytes and NET are detected in the large bronchi. In the tubular and alveolar stages of histogenesis, the number of endocrine structures increases, and it is especially significant in the distal parts of the bronchial tree. It should be noted that the branching of the bronchial tree is ahead of the development of the endocrine apparatus in it. Open-type cells are found in the proximal sections of the bronchial tree, while closed-type cells are found in the distal ones. Apudocytes and NETs are found in all children with inflammatory lung disease. Their number is much greater than in the lungs of children who died from diseases not related to the respiratory organs. Closed-type apudocytes are often found in the bronchial epithelium.
Conclusions
We found that open-type apudocytes appear in large bronchi during the development of the lungs, i.e., earlier generations of branching of the airways. Closed-type apudocytes are more characteristic of newly formed bronchial tubes. NETs during lung development appear later than apudocytes and are also more numerous in the developing small bronchi and respiratory region.

DOI: 10.1530/endoabs.81.EP633

EP634

Effect of nighttime melatonin intake on vitamin D levels

Sana Fendri[1,2], Naifar Manel[1, 2], Kamel Ichrak[3], Hammouda Omar[2, 3], Bouzid Imen[1], Turki Mouna[1, 2] & Ayadi Fatma[1,2]
[1]Habib Bourguiba Hospital, Laboratory of Biochemistry, Sfax, Tunisia; [2]Faculty of MedIcine, Research Laboratory 19 es 13, Sfax, Tunisia; [3]Higher Institute of Sport and Physical Education of Sfax, Tunisia

Introduction
Melatonin is involved in many physiological processes, including the regulation of circadian rhythms, sleep, antioxidant effect, aging, tumor growth, reproduction and bone formation. The latter function is also regulated by the metabolism of vitamin D. Our goal during this study is to detect a possible increase in vitamin D levels under the effect of exogenous melatonin.
Participants and methods
Different anthropometric parameters were collected (weight, height, body mass index, percentage of fat). The experimental protocol is carried out in a randomized clinical trial between an overnight intake (around 9 p.m.) of melatonin and double-blind placebo, once in the middle of the follicular phase and once in the middle of the luteal phase. The dose is determined at around 9 a.m. the next day, using an immuno-electro-chemiluminescence method on the Cobas 6000 analyser from Roche.
Results
Ten healthy young women between the ages of 20 and 23 were included in our study after obtaining their consent. The mean age of the participants was 21.63 ± 0.94 years. The average height of our patients was 165.72 ± 3.38 m. the average weight of our patients was 59.45 ± 3.5 kg. Vitamin D levels were significantly higher after taking melatonin (mean 13.6 ± 7.9 ng/ml) than after taking placebo (mean 12.68 ± 5.7 ng/ml) during the follicular phase ($P = 0.001$). Whereas, the increase in vitamin D with the intake of melatonin (mean of 15.8 ± 7.8 ng/ml) compared to the taking of placebo (mean of 14.6 ± 5.7 ng/ml) was not significant during the luteal phase ($P = 0.7$). In addition, there was no significant variation in vitamin D levels between the luteal phase and the follicular phase when taking placebo ($P = 0.07$) and when taking melatonin ($P = 0.25$).
Conclusion
Melatonin can regulate the metabolism of vitamin D. indeed the vitamin D receptor can act as a nuclear receptor for melatonin. Further studies are essential to better explain the relationship between melatonin and vitamin D according to menstrual cycles.

DOI: 10.1530/endoabs.81.EP634

EP635

Recurrent hypoglycemia : looking for an unsual cause

Chtioui Sara, Ijdda Sara, Rafi Sanaa, Ghizlane EL Mghari & Nawal EL Ansari
Med VI University Hospital Center, Endocrinology, Diabetology and Metabolic Diseases Department, Marrakech, Morocco

Hypoglycemia in non-diabetic patients is a rare event, and autoimmune hypoglycemia with the presence of positive anti-insulin antibodies is even rarer. We report the case of a 15 years old non diabetic female patient, she was referred to our hospital for recurrent hypoglycemia for 2 weeks before admission to hospital, these are severe hypoglycemia with impaired consciousness. The first step was to eliminate the general causes and factitious hypoglycemia. Adrenal insufficiency was also ruled out. A 72-hour fasting test was performed and the peptide C assay (<0.15 ng/ml), and Insulinemia (<1 mUi/l) were not in favor of endogenous insulin secretion. Autoimmune origin was suspected. The dosage of anti-insulin antibodies was realized with a positive result of 0.7 (Normal: 0.4). The patient was put on corticosteroid therapy with a regression of hypoglycemic episodes, pending the results of the anti-insulin antibodies after 2 months of corticosteroid therapy. The case of our patient illustrates the importance of an exhaustive exploration in the face of hypoglycemia and of thinking about the autoimmune cause, which remains rare, especially in non-diabetic patients.
Keywords Hypoglycemia-non-diabetic-autoimmune-insulin.

DOI: 10.1530/endoabs.81.EP635

EP636

Di-Butyl-Phthalate (DBP) exposure impact on human masculine reproductive hormones. A review of literature

Tiberiu Nita[1,2,3], Ariane Paoloni-Giacobino[3,4,5], Ludwig Stenz[3, 4], David Vernez[1,2,3] & Nancy Hopf[1,2,3]
[1]University of Lausanne, Faculty of Biology and Medicine, Lausanne, Switzerland; [2]Center for Primary Care and Public Health, Unisanté, Department DSTE, Epalignes, Switzerland; [3]University of Basel, Swiss Centre for Applied Human Toxicology (SCAHT), Basel, Switzerland; [4]University of Geneva, Department of Genetic Medicine and Development, Geneva, Switzerland; [5]University Hospital of Geneva, Department of Genetic Medicine, Geneva, Switzerland

Background
Phthalates are currently used in medical devices, adhesives as plasticizers. Masculine reproductive toxicity is the greatest concern associated with exposure, known as the "phthalate syndrome". The European Chemicals Agency has recognized di-butyl-phthalate (DBP, CAS 84-74-2) as an endocrine disruptor with deleterious effects on reproductive hormones, with an estimated human intake of 0.84-5.22 µg/kg/day. Effects reported include the disruption of Sertoli and Leydig cells with decreased testicular production of androgens, known as the "testicular dysgenesis syndrome". However, a quantitative relationship between DBP exposure and hormone levels is not available in the literature.
Objective
Review the scientific literature on DBP exposure measured as urinary metabolites, and corresponding reproductive hormone effects such as testosterone, in human adult men.
Methods
Four online scientific databases [PubMed, ISI Web of Science, Embase, Cochrane library] were searched in January 2022. The search criteria included English-language full text publications, human, adult men, serum testosterone total (TT) and testosterone free (fT) concentrations, urinary DBP metabolites concentrations (creatinine-adjusted values). Studies with $n>100$ participants were selected. Studies with a low score on qualitative assessment were excluded.
Results
Of the 329 search results, 11 toxicological studies met the inclusion criteria. Nine were cross-sectional studies conducted in East-Asia (4), Europe (4), North America (2), and Middle-East (1), and were conducted in the general population, occupational-exposed and fertility clinic population. The urinary DBP metabolites generally evaluated were mono-n-butyl-phthalate (MnBP) and mono-iso-butyl-phthalate (MiBP). The phthalates are often used in mixtures depending on the product specifications. Therefore, all the included studies provided urinary metabolites concentration of other phthalates. Phthalates may have a common metabolic pathway and consequently, the cumulative effect could alter the testosterone in serum but this was seldom discussed. All included studies used the same chemical analysis for quantifying urinary DBP metabolites (enzymatic hydrolysis, high-performance liquid chromatography with mass-spectrometry detection), while not all studies reported TT and fT. Preliminary results show that there is no significant correlation between urinary concentration of DBP metabolites and testosterone levels, although, several studies report a slight evidence for a reduction of TT and fT with increasing DBP exposure.
Conclusions
The review showed that the studies were incongruent and therefore, a significant correlation could not be established. However, the data suggest that adult men exposed to DBP are more likely to have altered testosterone levels. Future studies should explore possible relationships with luteinizing hormone, follicle-stimulating hormone, sex hormone binding globulin, estradiol and inhibin B in the current context.

DOI: 10.1530/endoabs.81.EP636

EP637

Vitamin D status in patients with adrenal tumors and previous COVID-19 infection

Maria - Alexandra Mohora[1], Raluca Trifanescu[1, 2], Iustin- Daniel Toma[1], Roxana Dusceac[1, 2], Cristina Capatina[1, 2], Dan Alexandru Niculescu[1, 2], Sorina Schipor[3], SUZANA VILMA VLADOIU[3] & Catalina Poiana[1,2]
[1]C.I. Parhon National Institute of Endocrinology, Pituitary and Neuro-endocrine Disorders, Bucureşti, Romania; [2]Carol Davila University of Medicine and Pharmacy, Endocrinology, Bucureşti, Romania; [3]C.I. Parhon National Institute of Endocrinology, Bucureşti, Romania

Context
The current pandemic showed a great handling of the resources and research in order to find not only a way to cure but also to prevent and improve the course of the Covid-19 infection. Optimal vitamin D (VD) levels and treatment was seen as a potential aid due, in principal, to its immunomodulatory effect. The ACE-2 receptor is the key the virus uses for entering the body, but its location is not restricted to the lungs, it's also found in the adrenal cortex. At that same level, we can find the vitamin D receptor. Romania, with its temperate climate, has a significant number of people with suboptimal levels of VD, especially during the winter season.
Objectives
To assess vitamin D status in patients with adrenal tumors who recovered from SARS-CoV-2 virus infection as compared with those without infection.
Matherials and methods
Notes of205 patients with adrenal tumors - inpatients in an Endocrine Clinic between August 2020 and August 2021 - were retrospectively reviewed. 48 patients (6M/42F) had had the COVID-19 infection - group 1, aged 57 ± 14 years, and 157 patients (30M/127F) without the infection - group 2, aged 54 ± 14 years. 25-OH-VD status, full adrenal workup and abdominal imaging were noted. Regarding tumor secretion, 82.4% were non-functioning adrenal tumors. 25-OH-VD levels were measured by electrochemiluminescence and were classified as follows: optimal 30 ng/ml, insufficiency 10-30 ng/ml, deficiency <10 ng/ml.
Results
The mean value of 25-OH-VD was 27.1 ± 7.8 ng/ml for group 1 and 25.5 ± 10 ng/ml for group 2 (P-value = ns). Regarding VD supplementation, group 1 had 41.6%(20) patients without and 58.3%(28) with treatment and group 2 had 52.8%(83) patients without and 47.2%(74) patients with treatment. In group 1, 77% (36) had VD insufficiency and 26% (12) had optimal VD status, whereas in group 2, 67.6%(106) had insufficiency or deficiency and 32.4%(51) had optimal VD status. Evaluating group 1, 30 patients had VD levels measured before and after the infection, and in the latter case the VD levels were lower for 10 patients, higher for 11 patients and remained almost the same (less than 10% modification) for 9 patients. Regarding COVID-19 risk factors, the prevalence of obesity (44% in group 1 vs 38.8% in group 2) and metabolic syndrome was similar between the 2 groups (Chi-square test = ns).
Conclusion
Patients with adrenal tumors and Covid-19 infection do not have lower levels of vitamin D compared to patients who didn't go through infection.

DOI: 10.1530/endoabs.81.EP637

EP638

Contaminación del aire ambiente y función tiroidea en adultos españoles. Un estudio de base poblacional de ámbito nacional (estudio Di@bet.es)

Viyey Kishore Doulatram Gamgaram, Sergio Valdés Hernández, Cristina Maldonado Araque, Natalia Colomo Rodríguez & Gemma Rojo Martínez
Hospital Regional Universitario de Málaga, Endocrinology and Nutrition

Objective
Recent reports have suggested that air pollution may impact thyroid function, although the evidence is still scarce and inconclusive. In this study we evaluated the association of exposure to air pollutants to thyroid function parameters in a nationwide sample representative of the adult population of Spain.
Methods
The Di@bet.es study is a national, cross-sectional, population-based survey which was conducted in 2008-2010 using a random cluster sampling of the Spanish population. The present analyses included 3846 individuals, free of thyroid disease, with negative thyroid peroxidase antibodies (TPO Abs) and TSH levels 0.1-20 mIU/l. Participants were assigned air pollution concentrations for particulate matter $<2.5\mu m$ (PM2.5) and Nitrogen Dioxide (NO2), corresponding to the health examination year, obtained by means of modeling combined with measurements taken at air quality stations (CHIMERE chemistry-transport model). TSH, FT4, FT3 and TPO Abs concentrations were analyzed using an electrochemiluminescence immunoassay (Modular Analytics E170 Roche).
Results
There was a significant association between PM2.5 concentrations and the odds of presenting lower FT4 [OR 1.30 (1.08-1.57) $P=0.006$] and FT3 levels [OR 1.34 (1.11-1.62) $P=0.002$] per each IQR increase in PM2.5 (4.86 µg/m3). The association remained after the multivariate adjustment of the data. There was no association between NO2 concentrations and thyroid hormone levels. No significant heterogeneity was seen in the results between groups of men, pre-menopausal and post-menopausal women.
Conclusions
Exposures to PM2.5 in the general population were associated with a mild thyroid dysfunction consisting of lowered levels of FT4 and FT3 without any significant changes in TSH. The nature of this association remains unknown. Additional studies are warranted to expand the data in this field.

DOI: 10.1530/endoabs.81.EP638

EP639

'Evaluation of the quality of life using patient questionnaire with autoimmune polyglandular type syndrome 2'

Gulzoda Negmatova[1] & Zamira Khalimova[2]
[1]Samarkand State Medical Institute, Department of Endocrinology, Uzbekistan; [2]Republican Specialized Scientific Practical Medical Center of Endocrinology of Public Health Ministry named by acad. Ya.Kh. Turakulov, Tashkent, Uzbekistan

The purpose of the study is to assess the quality of life of patients with autoimmune polyglandular type 2 syndrome using the questionnaire.
Material and research methods
Under our observation there were the following 2 groups of patients: 1 gr. - patients with APS with AIT (primary adrenal insufficiency and autoimmune thyroiditis) - 25 patients, 2 gr. - APS with DM 1 (type 1 diabetes mellitus type 1 - 30 patients, as well as 20 healthy persons of the appropriate age and gender. The study used generally crystal and clinical and biochemical methods of research, hormonal blood tests (TSH, free thyroxine, antibodies to TPO, cortisol), immunological studies (antibodies to thyroid gland, to the pancreas, to adrenal glands), and instrumental research methods (ECG, ultrasound of internal organs, thyroid gland, genital organs, neurophthalmologic, radiographic - MSCT of adrenal glands, statistical techniques, as well as the quality of life of patients with ADDIQOL. AddoQol consists of 30 questions with the estimate of each question in 6 points. At the same time, the patient must be selected in each question 1 answer: 'Yes' or 'no'. If the patient is gaining more than 15 points with the answer 'Yes', then this indicates a low quality of life [1].
Research results
The assessment of the quality of life (QoL) on the AddOQOL questionnaire showed that the middle score of patients 1 of the group was 18 ± 0.95, and in healthy - 2.35 ± 0.54 ($P<0.05$). The average score in patients 2 groups amounted to 19.6 ± 1.06 ($P<0.05$).
Conclusions
QoL patients in patients with APS 2 type of both groups has significantly lagging behind QoL in healthy faces.

DOI: 10.1530/endoabs.81.EP639

Pituitary and Neuroendocrinology

EP640

A method for evaluating the results of brain 18F-FDG PET/CT in the diagnosis of MRI-negative ACTH-producing pituitary adenomas.

Uliana Tsoy[1], Natalia Kuritsyna[1], Alexander Savello[2], Vladislav Cherebillo[1], Anton Ryzhkov[2], Elena Grineva[1] & Daria Ryzhkova[2]
[1]Almazov National Medical Research Center, Institute of Endocrinology, St-Petersburg, Russian Federation; [1]Almazov National Medical Research Center, Institute of Endocrinology, St-Petersburg, Russian Federation

Background
Detection of MRI-negative ACTH-producing pituitary adenomas is a challenge in the management of patients with Cushing's disease. There are some data on the ability of pituitary adenomas to accumulate 18F-fluorodeoxyglucose during the 18F-FDG positron emission tomography and computer tomography (18F-FDG PET/CT).
Aim
To study the potential of using a standardized uptake value (SUV) and a tumor – background ratio (TBR) when evaluating the results of PET/CT 18F-FDG of the brain for localization ofMRI-negative ACTH-producing pituitary adenomas.
Materials and methods
40 patients were enrolled. 32 patients had Cushing's disease, pituitary MRI scans were negative in all these patients. In all patients the pituitary source of ACTH hyperproduction was confirmed by bilateral cavernous and inferiorpetrosal sinuses sampling. Eight patients had neuroendocrine tumors with ACTH-ectopic production (NETs). Control group consisted of 19 persons without hypercortisolism. Brain 18F-fluorodeoxyglucose PET/CT was performed in all patients. Tumor –background ratio (TBR) was calculated as the ratio of the SUVmax in the pituitary gland to SUVmax in the reference zone of interest, drown above the fat tissue of the cheek. SUVmax in the pituitary gland and TBR were compared between patients with Cushing's disease and control group; patients with NETs and control group; patients with Cushing's disease and control group plus patients with NETs. The optimal threshold value of TBR for detection of MRI-negative ACTH-producing pituitary adenoma was calculated with ROC-analysis.
Results
All 32 patients with Cushing's disease patients had focal increased 18F-FDG uptake on pituitary 18F-FDG PET/CT scans. In control group and in patients with NETs there was no focus of increased accumulation of 18F-FDG. SUVmax in the pituitary gland did not differ in patients with Cushing's disease and control group ($P=0.208$); patients with Cushing's disease and patients with NETs ($P=0.63$); patients with Cushing's disease and control group plus patients with NETs ($P=0.23$). On the contrary TBR in the pituitary gland differ in patients with Cushing's disease and control group ($P=0.000$); patients with Cushing's disease and patients with NETs ($P=0.000095$); patients with Cushing's disease and control group plus patients with NETs ($P=0.000$). The optimal threshold value of TBR for detection of MRI-negative ACTH-producing pituitary adenoma calculated with ROC-analysis was 6.55. The sensitivity and specificity of the method were 90.6% and 89.5%, respectively ($p<0.001$, AUC = 0.961, 95% CI = 0.914-1.000).
Conclusion
Brain 18F-fluorodeoxyglucose PET/CT may be useful for localization of MRI-negative ACTH-producing pituitary adenomas. Application of the TBR, but not of the SUVmax is optimal for evaluating it's results.

DOI: 10.1530/endoabs.81.EP640

EP641

Patient with pregnancy and possible MEN 2b syndrome: case report

Veranika Lobashova[1,2], Elena Kuzmenkova[1], Yuliya Dydyshka[3] & Alla Shepelkevich[3]
[1]Republic Centre of Medical Rehabilitation and Balneotherapy, Endocrinologic, Minsk, Belarus; [2]Belarusian Medical Academy of Postgraduate Education, Therapy, Minsk, Belarus; [3]Belarusian State Medical University, Endocrinologic, Minsk, Belarus

Background
MEN 2b is a highly penetrant disease with an autosomal dominant pattern of inheritance. It includes medullary thyroid carcinoma, pheochromocytomas, and multiple mucosal neuromata. The common feature of all of these tumors is a

neuroectodermal origin. Although the clinical phenotype is present in all patients, individual manifestations have a variable presentation and are age dependent.
Aim.
We report a case of a patient with possible MEN 2b syndrome anв pregnancy.
A 30-year-old Caucasian woman was admitted to the cardiologic department of the hospital in October 2017 for resistant hypertension unresponsive to medical therapy. The patient had a history of hypertension for 5 years without any treatment or etiological diagnosis. On arrival indicated blood pressure was 240/120 mmHg. She denied family history of premature coronary artery disease and special personal history, such as smoking and drinking. But her mother died in young age (36 yers old) because of adrenal tumor.Contrast-enhanced computed tomography demonstrated an inhomogeneous left adrenal mass (5.5 × 4.1 cm HU +13-+88). Her plasma epinephrine and norepinephrine and levels were elevated (118 (0-65) pg/ml and 7069,5 (0-200) pg/mlm accordingly). Preoperative stabilization with alpha-adrenergic blocking agent (doxazosin) was started a month before surgery. The patient underwent laparoscopic left adrenalectomy after premedication. Histopathology confirmed adrenal pheochromocytoma with residual necrosis. The patient was diagnosed with pheochromocytoma. During the 2-year follow-up, the patient was asymptomatic, and her blood pressure remained normal without medication. Her plasma epinephrine and norepinephrine and levels normalized (15,3 (0-65)pg/ml and 114 (0-200)pg/ml). After the operation she become pregnant, there were no problems during pregnancy, her labour were in December 2018 without any complications.
She visited our center because of the second pregnancy. On examination she had several neurofibromas on her skin. She mentioned that her sister also has neurofibromatosis on her skin. Thyroid sonography demonstrated solide isooechogenic nodule 4,7*3.8 mm at the left thyroid lobe. Serum calcitonin as biochemical marker for the presence of medullar thyroid cancer was elevated - 20,4 (0-10) pg/ml. Her TSH, epinephrine and norepinephrine were normal. Just now her gestation period is 38 weeks and she is waiting for delivery. In the future, we plan to continue examination of the patient and her sister.
Conclusion
Women with MEN 2 should be screened for pheochromocytoma prior to a planned pregnancy. Family history is an important part of diagnostic algorithm of MEN 2b. Genetic tests could help to identify RET mutation.

DOI: 10.1530/endoabs.81.EP641

EP642

Circulating plasma microRNA in patients with ACTH-dependent cushing's syndrome.

Anastasia Malygina[1], Zhanna Belaya[1], Alexander Solodovnikov[2], Alexey Nikitin[3], Philipp Koshkin[4], Ivan Sitkin[1], Michael Pikunov[5], Patimat Khandaeva[1], Alexander Lutsenko[1], Diana Trukhina[1], Anastasia Lapshina[1], Andrey Grigoriev[1], Galina Melnichenko[1] & Ivan Dedov[1]
[1]The National Medical Research Centre for Endocrinology, neuroendocrinology and bone disease, Moscow, Russian Federation; [2]Ural State Medical University, Department of Preventive and Family Medicine, Moscow, Russian Federation; [3]Pulmonology Scientific Research Institute under FMBA of Russia, Moscow, Russian Federation; [4]Laboratory of Molecular Pathology, Center of Medical Genetics (Genomed), Moscow, Russian Federation; [5]National Medical Research Center of Surgery Named After A.V. Vishnevsky, Moscow, Russian Federation

Introduction
Recent studies have shown that microRNA could serve as biomarkers in various types of cancer and other diseases.
Aim
To reveal microRNA that differ in patients with Cushing's diseases (CD) and Ectopic ACTH-syndrome (EAS) to form a specific panel for differential diagnosis of ACTH-dependent Cushing's syndrome (CS).
Materials and Methods
Plasma samples from both sinuses and cubital vein were drained during inferior petrosal sinus sampling and stored at -80 C. MiRNA isolation from plasma samples was carried out by an Rneasy Plasma/Serum Kit (Qiagen, Germany) on the automatic QIAcube station. MiR expression was then analyzed by sequencing on Illumina NextSeq 500 (Illumina, USA). The libraries were prepared by the QIAseq miRNA Library Kit. Sequencing was performed on a total of 36 samples. Data analysis and interpretation was conducted on Qiagen GeneGlobe Data Analysis were Center. qRT-PCR was performed using a TaqMan Advanced miRNA cDNA Synthesis Kit (Thermo Fisher, Scientific) and TaqMan® Advanced miR Assays (Thermo Fisher Scientific), in a 96-well format on the StepOnePlus instrument (Applied Biosystems). Data analyses were performed using SDS software (version 2.3, Applied Biosystems), to obtain cycle treshold (Ct) data. We used value Ct <35 as a cutoff of detection. All samples were normalized to spike-in control, cel-miR-39-3p.
Results
Among 36 enrolled patients (mean age 47,5 years (minimum 23, maximum 69 years; M:7, F:29) 24 subjects were confirmed as CD and 12 as EAS. There were 1167 miRNA differently detected ($P<0,05$) in inferior petrosal sinus samples of patients with CD vs EAS. These miRNAs were divided into 3 groups based on the significance of the results. The first group consisted of samples with the highest levels of detected miR in both groups. 108 microRNA were included. For the verification phase 10 microRNA were chosen (miR-383-3p, miR-4290, miR-6717-5p, miR-1203, miR-1229-3p, miR-639, miR-302c-3p, miR-7g-5p, miR-145-5p, miR-16-5p) according to the discovery phase results and data from the previous pilot study. We enrolled 82 patients (mean age 44,5 years (minimum 19, maximum 70 years; M:18, F:64) for validation phase of the study. Among them 64 were confirmed as CD, 18 as EAS. RT-qPCR showed, that four microRNA differ between patients with CD and EAS: miR-383-3p ($p_{adjusted}=0,003$), miR-302c-3p ($p_{adjusted}=0,02$), miR-4290 ($p_{adjusted}=0,02$), miR-6717-5p ($p_{adjusted}=0,02$).
Conclusion
miR-383-3p, miR-302c-3p, miR-4290, miR-6717-5p differed between patients with CD and EAS in peripheral plasma samples as measured by both NGS and qRT-PCR and could form a specific panel for differential diagnosis of ACTH-dependent CS.

DOI: 10.1530/endoabs.81.EP642

EP643

Primary hyperparathyroidism response to the somatostatin analogue therapy in a patient with MEN1 syndrome: A case report

Kseniia Yakovenko[1], Karina Pogosian[1], Daria Ryzhkova[2], Lidiia Belousova[1], Tatiana Karonova[1], Elena Grineva[1] & Uliana Tsoy[1]
[1]Almazov National Medical Research Center, Endocrinology, St. Petersburg, Russian Federation; [2]Almazov National Medical Research Center, Nuclear Medicine and Theranostics, St. Petersburg, Russian Federation

Background
Management of primary hyperparathyroidism (PHPT) in Multiple Endocrine Neoplasia type 1 syndrome (MEN 1) is still a challenge. PHPT developing in MEN 1 is characterized by the involvement of all parathyroid glands. Therefore, by modern guidelines, total or subtotal removal of the parathyroid glands is recommended. But this approach often leads to the development of hypoparathyroidism, adequate correction of which is not always possible. Drug therapy of recurrent PHPT in MEN 1 patients may be the alternative to radical surgery. We present a clinical case of MEN 1 patient in whom somatostatin analogue therapy resulted in normalization of serum calcium level.
Clinical case
40 years old Caucasian woman, with a history of insulinoma, that was operated on at the age of 10 and prolactin-secreting pituitary macroadenoma diagnosed at the age 19. In 2015 the patient was tested for PHPT, iPTH level was 28 pmol/l (1.3-9.3), serum Ca^{++} level - 1.47 mmol/l (1.13 – 1.29), CT scans revealed two lesions suspicious for parathyroid adenomas. Subtotal parathyroidectomy of both right and left lower parathyroids glands was performed. Postoperative iPTH was 5.2 pmol/l. All removed lesions were confirmed to be parathyroid adenomas by the pathology examination. Genetic testing was done and variant in MEN1 gene was found. In 2020 PHPT recurrence was confirmed (iPTH 200.10 pg/ml (15.0 – 68.3)), serum Ca^{++} level 1.57 mmol/l (1.11 – 1.29), serum total Ca 2.78 mmol/l (2.15 – 2.65)). 68Ga-DOTA-TATE PET/CT was carried out, it revealed three lesions in the pancreas head and body which intensively accumulated radiopharmaceutical, also 68Ga-DOTA-TATE positive foci was found in the projection of the left upper parathyroid. Subsequently endosonography was performed; it showed multiple lesions in pancreas and submucosal lesions in duodenum. Fine needle aspiration biopsy of pancreatic and duodenal formations confirmed neuroendocrine tumors in all of them. Preoperative short-acting somatostatin analogue (Octreotide) was started. Subtotal pancreatectomy, 2/3 stomach resection, duodenectomy were performed. After surgery octreotide therapy was continued. After 6 weeks of octreotide therapy calcium and parathyroid hormone levels were assessed. Decrease of iPTH and calcium levels was found: iPTH from 172,5 to 122 pg/ml (15.0 – 68.3), serum total Ca from 2,73 to 2.59 mmol/l (2.15 – 2.65).

Conclusion
Our clinical case demonstrated the ability of octreotide to reduce iPTH and normalize calcium levels in a patient with MEN 1 syndrome. It is necessary to further study the potential of somatostatin analogues in the treatment of recurrent PHPT in MEN 1 syndrome.

DOI: 10.1530/endoabs.81.EP643

EP644

Dynamics copeptin and apelin in patients before and after transnasal adenomectomy and their relationship with the development of post-operative hyponatremia

Khava Fargieva, Nino Katamadze, Larisa Dzeranova, Ekaterina Pigarova, Elena Przhiyalkovskaya, Andrey Grigoriev & Natalia Mokrysheva
Endocrinology Research Centre, Moscow, Russian Federation

Introduction
Transnasal adenomectomy is the main treatment for various pituitary adenomas. The hypothalamic-pituitary region is the site of synthesis and secretion of several hormones that have a direct effect on sodium-water metabolism, which leads to its frequent violation with the development of central diabetes insipidus and severe transient hyponatremia, the latter of which is the second most important cause of rehospitalization in the postoperative period. Currently, the causes and factors predisposing to the development of this complication have not been identified.
Objective
To study the perioperative dynamics of apelin and copeptin neuropeptides after transnasal transsphenoidal adenomectomy for pituitary adenomas.
Materials and methods
The study included 22 patients who underwent transnasal adenomectomy for pituitary adenoma (inactive pituitary adenoma - 8 patients, acromegaly - 8 patients, Cushing's disease - 6 patients, 6 men and 16 women, median age 52 years [Q25 39; Q75 62]), 10 of whom developed hyponatremia (group 1) with a median serum sodium of 125 mmol/l and 12 did not have any fluid and electrolyte disturbances (group 2). All patients were tested for serum Na, plasma apelin 12 (ELISA, Phoenix) and copeptin (ELISA, Phoenix) at 24 hours before surgery, 24 hours, days 2-3, 5 and 7 after surgery.
Results
The debut of hyponatremia was observed in the period 5-7 days after the operation. In both groups, there was a change in the level of copeptin with a decrease on days 2–3 after surgery and a further increase in group 1 and a decrease in group 2 by day 5 after surgery and returning to baseline values on day 7 after surgery. The level of apelin had different dynamics in the groups: in group 1, it decreased on the first day with a further increase with a maximum on day 5 and a return to the original values on day 7; in group 2, no statistically significant changes were recorded.
Conclusions
Transnasal adenomectomy is the cause of severe hyponatremia in the genesis of which, apparently, the hypothalamic neuropeptides copeptin and apelin play the leading role. The secretion dynamics of these neuropeptides changes reciprocally in groups with and without the development of hyponatremia, which makes them potential hormonal markers of this severe complication.

DOI: 10.1530/endoabs.81.EP644

EP645

Hyponatremia, central diabetes insipidus after transnasal adenomectomy and its' risk factors

Darya Mikhaylova[1], Larisa Dzeranova[2], Olga Yu. Rebrova[3], Ekaterina Pigarova[2], Ludmila Rozhinskaya[2], Andrey Grigoriev[4], Oksana Ivashenko[4] & Vilen Azizyan[4]
[1]Moscow Regional Research and Clinical Institute, Neuroendocrine Unit, Department of Endocrinology, Moscow, Russian Federation; [2]Endocrinology Research Centre, Neuroendocrinology, Moscow, Russian Federation; [3]Endocrinology Research Centre, Education, Moscow, Russian Federation; [4]Endocrinology Research Centre, Neurosurgery, Moscow, Russian Federation

Objectives
To assess the frequencies of hyponatremia and central diabetes insipidus (CDI) after transnasal adenomectomy and to identify its risk factors.

Patients and methods
The study included 152 patients aged 18 to 65 years (median [Q1; Q3] 40 [31; 52]) who underwent endoscopic endonasal transsphenoidal surgery due to Cushing's disease, acromegaly, prolactinoma, non-functioning pituitary adenoma, thyreotropinoma or Nelson's syndrome at Endocrinology Research Centre in 2010-2011 years. All patients underwent clinical and laboratory examinations and were discharged on 10-14 days after surgery.
Results
Severe hyponatremia (116 mmol/l) developed in 2 patient (1.3%), moderate (127 mmol/l) in 1 patient (0.7%) on the 1^{st}-7^{th} day after surgery and in all cases it was reversed by fluid restriction. Mild transient hyponatremia (131-134 mmol/l) occurred in 8 patients (5.3%). Persistent CDI (pCDI) has developed in 34 patients (22.4%) with 3 cases of three-phase CDI (including 2 cases of three-phase CDI with mild hyponatremia), transient CDI (tCDI) occured in 25 (16.4%), 82 patients did not have any disturbances (53.9%) by discharge. Postoperative pCI and tDI were promoted by Cushing's disease (odds ratio (OR) 2.5, 95% CI (1.1-5.6) for pDI, 3.6 (1.4-9.2) for tDI), whereas acromegaly decreased the risk (OR 0.3 (0.1-0.6) for pDI, 0.3 (0.1-0.8) for tDI)). Secondary adrenal insufficiency (OR 2.6 (1.2-5.9) for pDI, 3.1 (1.3-7.6) for tDI), microadenoma (OR 4.1 (1.6-10.6) for pDI, 5.2 (1.9-14.6) for tDI), MRI tumor's volume $<0{,}75$ cm^3 (OR 4.8 (1.8-12.6) for pDI, 7.5 (2.1-26.8) for tDI) and surgery pituitary injury (OR 4.1 (1.6-10.6) for pDI, 5.2 (1.9-14.6) for tDI) provoked pDI and tDI. Postoperative DI was also more common at trend level in patients with adrenocorticotropic hormone levels of $<$ 16,5 pg/ml and cortisol level of <228 nmol/l and pDI was more often associated with secondary hypothyroidism at trend level as well.
Conclusions
The proportion of hyponatremia was 7.3%, persistent postoperative CDI – 22.4%, and that of the transient form 16.4% by discharge. Cushing's disease, secondary adrenal insufficiency, microadenoma, MRI tumor's volume $<0{,}75$ cm3 and surgery pituitary injury increase the odds of postoperative CDI, whereas acromegaly does decrease these odds.

DOI: 10.1530/endoabs.81.EP645

EP646

A clinical case of hypogonadism and anosmia associated with a new mutation of the KAL1/ANOS1 gene: a preliminary report

Michela Del Prete[1], Gianleone Di Sacco[1], Marco Bonomi[2, 3], Federico Vignati[4], Fabrizio Muratori[1] & Luca Persani[3,4]
[1]Ospedale Sant'Anna, Endocrinology and Diabetology, San Fermo della Battaglia, Italy; [2]Italian Auxological Institute San Luca Hospital, Medical Biotechnologies and Translational Medicine, Milano, Italy; [3]University of Milan, Medical Biotechnologies and Translational Medicine, Milano, Italy; [4]Italian Auxological Institute San Luca Hospital, Endocrine and Metabolic Diseases, Milano, Italy

Introduction
Kallmann syndrome (KS) is a genetic condition characterized by the association of anosmia or hyposmia and GnRH deficiency resulting in congenital hypogonadotropic hypogonadism (CHH). Different genes can be implicated in KS, and the most frequent allelic variant occurs in the KAL1/ANOS1 gene in the X-linked form. Differential diagnosis is often made with other rare genetic diseases as CHARGE syndrome (CS) that includes hypogonadism, hyposmia and several organ defects including eyes and heart defects. Here we report a clinical case of a patient with a clinical diagnosis of KS and in which a new genetic gene variant was found.
Methods
Patient history was collected through questionnaires and physical examination at our outpatient clinic. Blood sample for genetic evaluation of the patient was collected after obtaining informed consents. Gene variants were amplified and verified by Sanger direct sequencing after the next generation sequencing (NGS) of related genes.
Results
A 48-year-old male patient was referred to our endocrinology service for evaluation of hypogonadism. The medical history of patient started when he was 17-year-old. At that time patient was diagnosed with hypogonadism and anosmia wherefore placed on testosterone replacement therapy. No genetic tests had been conducted until our visit on suspicion of KS. Patient had no other further suspected signs or symptoms of genetic disease or CS. NGS sequencing revealed the presence of two different gene allelic variants: a heterozygous variant in the region 8 q12.2 of the CHD gene (p.L2806V: c.84716C$>$G) and a hemizygous X-linked variant in the Xp22.31 region of the KAL1/ANOS1 gene (p.R46H: c.137G$>$A). This latest is a newly identified variant and has never been described so far. Laboratory examination confirmed hypogonadotropic hypogonadism without other pituitary hormonal alterations. Magnetic resonance imaging of the

olfactory bulb and of the pituitary gland and the smell test have been requested and are ongoing.
Conclusion
Both KAL1/ANOS1 and CHD7 genes are known to be important causal gene in the development of KS. Differential diagnosis between KS and CS should be considered in patients with anosmia and hypogonadism. Until now p.R46H variant in KAL1/ANOS1 gene has never been reported, while p.L2806V variant was described in the literature to be associated with benign forms of CS with CHH/KS. A possible oligogenic form of KS might be considered in this specific case.
Keywords Kallmann syndrome; KAL1/ANOS1 mutations; CHD7 mutations; CHARGE syndrome; congenital hypogonadotropic hypogonadism; anosmia.

DOI: 10.1530/endoabs.81.EP646

EP647

Sellar plasmacytoma revealing a multiple myeloma.
Samia Hamoudi, Safia Achir & Safia Mimouni
CPMC, Service d'Endocrinologie et Maladies d'Endocrinologie, Alger, Algeria

Introduction
The sellar plasmacytoma, an exceptional localization that can be solitary or associated with a multiple myeloma. We report the case of a sellar mass wrongly diagnosed as an invasive non-functional pituitary adenoma, the diagnosis was rectified postoperatively by the anatomopathological study.
Case description
A 44 year old female patient, with history of cholecystectomy and megaloblastic anemia, was referred to our center for management of a sellar mass initillay diagnosed as a pituitary adenoma. The patient had galactorrhea for 3 years and than she developped severe hedeache with worsening visual impairement. The physical examination revealed bilateral blindness, with galactorrhea, without neurological abnormalities. Magnetic resonance imaging (MRI) of the brain revealed an Iso intense mass in T1 and T2 sequences with intra and supra sellar development strongly enhanced after injection of gadolinium. The tumor compressed the optic chiasma and the right optic nerve in its intracranial portion, invading the cavernous cavity bilaterally (KNOSP 3), measuring **44X36X37 mm** suggesting an invasive macroadenoma; however the endocrine assessment did not show any abnormalities. She underwent an emergency transphenoidal surgery. Immunophenotypic analysis of tissues showed that all tumor cells were positive for CD1389 and confirmed the diagnosis of plasmacytoma. The hematological examination revealed a medullar plasmacytosis of 32% without blood desemination in favor of a multiple myeloma. She underwent radiation therapy centered on the sella turcica, followed by chemotherapy. There was a slight regression of the osteolytic tumor process, which currently measures 38.5 X 32.6 X 27.5 mm.
Conclusion
Plasmacytomas of the skull base revealing multiple myeloma represent a rare entity. However, solitary or multiple, plasmacytoma should be considered in the differential diagnosis of any invasive lesion of the sphenoidal sinus. The clinical presentation is aspecific, histological certainty must be obtained.

DOI: 10.1530/endoabs.81.EP647

EP648

Medical treatment of active acromegaly - the results from the Croatian Acromegaly Registry
Lana Sambula[1], Mirsala Solak[2], Ivana Kraljevic[2], Hrvoje Popovac[2], Tanja Skoric Polovina[2], Karin Zibar Tomšić[2], Tina Dusek[2], Annemarie Balasko[2] & Darko Kastelan[2]
[1]General Hospital Koprivnica, Department of Internal Medicine, Koprivnica, Croatia; [2]University Hospital Centre Zagreb, Department of Endocrinology, Zagreb, Croatia

Background
The aim of this study was to evaluate the outcomes of medical treatment in patients with active acromegaly.
Material and Methods
We performed a retrospective analysis of 163 patients (101 female, age at diagnosis 47.2 ± 13.4 years) treated between 1990 and 2020., of which 53 were on medical treatment (32.5%). Remission rate after pituitary surgery was 66.5% (n = 105/158; 5 patients refused surgery). Patients who did not achieve remission and with relapse (n = 2) underwent another surgery (n = 18/60, 30%) and/or radiotherapy (n = 33/60, 55%) and/or medical treatment (n = 53/60, 88.3%). One patient refused further treatment after failed first pituitary surgery. The duration of follow-up was 115.8 ± 304.4 months.
Results
Out of 53 patients on medical treatment, during follow-up monotherapy was used in 34 (64.2%) and combination therapy in 19 (35.8%) patients. Remission (IGF-1 < 1.2 ULN) was achieved in 51 patients (96.2%); in 21/53 (39.6%) with first generation somatostatin analogue (SSA-1) monotherapy, in 10/53 (18.9%) with dopamine agonist (DA) monotherapy, in one (1.9%) with pegvisomant monotherapy, in 13/53 (24.4%) with combination of SSA-1 and DA, in three (5.7%) with combination of SSA-1, DA and pegvisomant, in two (3.8%) patients with combination of SSA-2, DA and pegvisomant and in one (1.9%) after adding temozolomide on top of SSA-1 and DA. Two patients currently have active disease, both on SSA-1 monotherapy, of whom one is non-adherent to the tratment.
Conclusion
Our results indicate that medical treatment, when combined appropriately, can lead to biochemical remission in almost all patients with acromegaly.

DOI: 10.1530/endoabs.81.EP648

EP649

Lipid accumulation product (LAP) as surrogate marker of fatty liver in patients with Cushing's disease (CD)
Dragana Miljic[1,2], Sandra Pekic Djurdjevic[1, 2], Mirjana Doknic[1, 2], Marko Stojanovic[1, 2], Marina Nikolic Djurovic[1, 2], Zvezdana Jemuovic[1], Sara Radovic[2], Nevena Radić[2] & Milan Petakov[1,2]
[1]Clinic for Endocrinology, Diabetes and Diseases of Metabolism, University Clinical Centre of Serbia, Belgrade, Serbia; [2]University of Belgrade - Faculty of Medicine, Belgrade, Serbia

Introduction
The most common etiology of endogenous Cushing's syndrome (CS) is Cushing's disease (CD). Patients with CS also represent a model of patients with metabolic syndrome (MetS) with associated increased cardiovascular morbidity and mortality. Insulin resistance and obesity, two major characteristics of CS, lead to the accumulation of triglycerides within hepatocytes and formation of fatty liver in these patients.
Aim
To evaluate the prevalence of metabolic syndrome and fatty liver and the importance of using lipid accumulation product (LAP) and fatty liver index (FLI) in patients with CD.
Material and methods
We conducted a cross-sectional study analyzing electronic medical histories of 52 patients (41 women, 11 men) diagnosed with CD (33 microadenomas and 19 macroadenomas) treated from 2009 to 2019. Mean age 50.5 ± 13.5 years and body mass index (BMI) 29.3 ± 5.8 kg/m^2.
Results
MetS defined by NCEP ATP III was present in 63.5% (n = 33) of patients with CD. Ultrasound findings of fatty liver in a cohort of our patients with CD were present in 40.4% (n = 21) patients, while only 11.5% (n = 6) had elevated transaminases**.** Patients with CD and MetS were significantly older from patients with CD alone (52.6 ± 13.2 vs. 44.3 ± 12.8 years). Obesity was present in 41.3% while diabetes and glucose intolerance were present in 60% of patients. Prevalence of obesity was even higher in patients with diabetes (72.2% vs. 27.8%; P = 0.007). Obese patients had significantly higher values of LAP (174.7 ± 79.4 vs. 54.4 ± 24.3 P < 0.05) and FLI (29.3 ± 29.5 vs. 1.5 ± 1, P < 0.05). Patients with CD and ultrasonographic features of fatty liver had statistically significant higher values of LAP than those with CD alone (142.6 ± 9.6 vs 61.1 ± 21.2, P = 0.045), while their FLI values were not statistically different. Arterial hypertension was observed in as many as 82.4% of patients. In 96% of patients, some form of dyslipidemia was present.
Conclusion
Cushing's disease is characterized by an unfavorable metabolic profile and grouping of cardiovascular risk factors in the large percentage of patients. Fatty lever extends this unfavorable metabolic phenotype. LAP but not FLI is a good surrogate marker of fatty liver in CD.

DOI: 10.1530/endoabs.81.EP649

EP650

Hypopituitarism in patients with pituitary macroadenomas - the prevalence and prognostic factors

Yulya Krivosheeva & Irena Ilovayskaya
Moscow Regional Research and Clinical Institute (MONIKI), Neuroendocrinology, Moscow, Russian Federation

Hypopituitarism due to pituitary lesions may have unclear clinical manifestations, and for its diagnosis it is necessary to conduct a hormonal examination. There are clinical recommendations to conduct a hormonal investigation in all cases of pituitary tumors > 6 mm that seems to be uncertain.
The objective to evaluate the frequency of hypopituitarism in patients with pituitary macroadenomas with different hormonal activity and to identify its possible prognostic factors.
The materials and methods
We have analyzed medical records of 293 newly diagnosed patients with pituitary macroadenomas before any treatment: 121 non-functioning adenomas (NFAs), 59 prolactinomas, 113 somatotropinomas. Median patients' age was 59 [50;64.5] y.o., 32 [27;48.5] y.o. and 53 [41;60] y.o., accordingly.
The results
The hypopituitarism was diagnosed in 59/148 (39.9%) NFAs, in 18/66 (27.3%) prolactinomas and 19/136 (14%) somatotropinomas ($p<0.001$). The proportion of men with hypopituitarism was higher in NFAs but not in prolactinomas and somatotropinomas. The relative risk (RR) of hypopituitarism in male patients with NFAs was 1.575 (95% confidence interval (CI) 1.212–2.047, $P=0.001$). MR-signs of chiasm compression, as well as the presence of chiasmal syndrome, were significantly more common in patients with hypopituitarism compared to patients without hypopituitarism in all subgroups. The RR of hypopituitarism in patients with MR-signs of chiasm compression was for NFAs 2.10 (95% CI 1.50 – 2.95, $p=0.003$), for prolactinomas 1.667 (95% CI 1.29 – 2.18 $p=0.005$), for somatotropinomas 1.45 (95% CI 1.56 – 2.48, $p=0.001$). The RR of hypopituitarism in patients with chiasmal syndrome was for NFAs 1.66 (95% CI 1.26 – 2.18, $p=0.009$), for prolactinomas 2.08 (95% CI 1.60 – 2.69, $p=0.001$) , for somatotropinomas 1.97 (95% CI 1.56 – 2.48, $p=0.005$). The vertical size and volume of tumor were significantly larger in patients with than without hypopituitarism. Vertical tumor size over 22.5 mm (area under the ROC curve (AUC-ROC) 0.7209, sensitivity 55.91% and specificity 73.44%, $P<0.001$) and tumor volume over 4472 mm3 (AUC ROC 0.7066, sensitivity 62.77% and specificity 70.16%, $P<0.001$) were statistically significant cut-off points for the presence of hypopituitarism.
The conclusions
Hypopituitarism should be excluded in patients with pituitary macroadenomas in the presence of the following factors: in non-functioning adenomas – male sex; regardless of hormonal activity – signs of chiasm compression, chiasmal syndrome, vertical tumor size more than 22.5 mm, tumor volume more than 4472 mm3.

DOI: 10.1530/endoabs.81.EP650

EP651

Unusual evolution of a non-functionning pituitary adenoma

Yosra Hasni[1, 2], Marwa El Arem[1], Hamza Elfekih[1,2], wiem saafi[1], Abdelhafidh Slimane[3], Amel Maaroufi[1, 2], Maha Kacem[1, 2], Molka Chadli Chaieb[1, 2] & Koussay Ach[1,2]
[1]Farhat-Hached University Hospital, Endocrinology-Diabetology Department, Sousse, Tunisia; [2]Faculty of Medicine Ibn El Jazzar, University of Sousse, Sousse, Tunisia; [3]National Institute of Neurology, Department of Neurosurgery, Tunis, Tunisia

Introduction
Pituitary neuroendocrine tumors (PitNET) represent 15.5% of primary brain tumors and they can be clinically functioning or non-functioning. Although they are mostly benign, PitNET may be invasive in 30-45% of cases and aggressive in at least 15%. Here, we report the case of a patient who presented a multiple and rapid recurrence of a non-functional pituitary macroadenoma.
Observation
A 42-year-old man was admitted initially for headaches, monocular blindness and Knosp grade 3A macrodenoma on MRI. Biochemial analysis didn't reveal hormones deficiencies nor hypersecretions. He underwent a transphenoidal resection with a visual improvement. Histologic diagnosis was a null cell adenoma with Ki67 index = 4% and a positive p53. Based on the new classification of PitNET, it was proliferative and invasive tumor, classsified garde 2b. Six months later, he deveolpped a tumor regrowth with visual impairment (diplopia), for which he underwent a partiel resection and an adjuvant radiotherapy was planned. Before starting the radiotherapy, he was readmitted 6 months later for a complete ptosis of the right eye and an increase in size of his non-functionning pituitary macroadenoma.
Discussion
This case showed that invasive and proliferative non-functionning pituitary adenomas can have an unpredictable rapid recurence and an agressive behaviour than usual. Null cell adenoma are known to be more aggressive than the other types of tumors with a mean time to recurrence of 15.9 months. In our case, the time to recurrence was 6 months only between the first and second surgeries. Selecting the high risk of recurrence tumors is essential to avoid their impacts and to improve the quality of life of patients.

DOI: 10.1530/endoabs.81.EP651

EP652

Isolated ACTH deficiency with unusual clinical presentation and normal morning cortisol levels

Hassan Ibrahim, Natalie Fox, Heba Bashir & Ali Rathore
Southend University Hospital, Mid and South Essex NHS Foundation Trust, Diabetes & Endocrinology Department-Carlingford Building, Southend-on-Sea, United Kingdom

A 74-year-old male presented to hospital following an episode of brief loss of consciousness and several hours of post ictal confusion. There was no witnessed seizure activity, tongue biting, or incontinence. His past medical history included SCC right scalp, TIA and primary hypothyroidism. He had been commenced on Cemiplimab (immunotherapy) for metastatic SCC seven months before. On assessment, he appeared well and general examination including neurological examination was normal. However, he was found to have a postural blood pressure drop of 40 mmHg. ECG and Blood tests were unremarkable, except his random cortisol was 163 nmol/l. Repeat 9 am cortisol was 183 nmol/l. Hydrocortisone was commenced as primary adrenal insufficiency could not be ruled out. A differential diagnosis of ictal syncope was also considered but later ruled out after normal MRI and EEG. Subsequently, Synacthen test showed baseline cortisol of 155 nmol/l, rising to 449 nmol/l at 30 minutes and 521 nmol/l at 60 minutes. ACTH was 16 ng/l. He was advised to stop hydrocortisone as primary adrenal insufficiency was ruled out. However, within a few days of stopping hydrocortisone, he felt symptomatic again with dizziness and pre-syncope, and was readmitted to hospital. Oral Hydrocortisone, at a dose of 20 mg daily, was restarted and his symptoms settled. A glucagon stimulation test was performed to investigate possible secondary adrenal insufficiency. Surprising, his morning cortisol came back as <11 nmol/l and remained undetectable (<11 nmol/l) throughout the test, whilst growth hormone levels peaked to 19.6 mg/l confirming severe ACTH deficiency. FSH, LH, testosterone, prolactin and TFTs were all normal. MRI pituitary showed no abnormality. He was treated as isolated ACTH deficiency, secondary to Cemiplimab. He remains well on hydrocortisone replacement. Secondary adrenal insufficiency due to Isolated ACTH deficiency is being increasingly reported to be associated with immune checkpoint inhibitors including Cemiplimab. In our case, clinical presentation was unusual as postural hypotension and syncope are not common with secondary adrenal insufficiency due to preservation of renin-aldosterone axis. Initial investigations were misleading with relatively preserved morning cortisol and good response to Synacthen. However, Cortisol levels became undetectable subsequently with no response to glucagon stimulation confirming diagnosis of severe ACTH deficiency. This case highlights that ACTH deficiency can present with postural syncope and normal morning cortisol levels in the early stages. High index of suspicion and repeated investigations may be required to confirm diagnosis.

DOI: 10.1530/endoabs.81.EP652

EP653

The impact of Sheehan Syndrome on bone mineral density

Ameni Salah, Amel Maaroufi, Rihab Ajili, Ghada Saad, Yosra Hasni & Koussay Ach
University Hospital Center Farhat Hached, Endocrinology Department, Sousse, Tunisia

Introduction
Sheehan syndrome (SS), or postpartum pituitary necrosis, is a complete or dissociated adeno-pituitary insufficiency due to hypovolemia secondary to excessive blood loss during or after delivery. Although few studies have investigated osteoporosis in isolated hormone deficiencies, the relationship between SS and osteoporosis has not been investigated in large series of SS. In this study, we aimed to evaluate bone mineral density (BMD) in patients with SS.
Patients and methods
This is a descriptive cross-sectional study, involving 65 patients. It was carried out in the Endocrinology-Diabetology department of University Hospital Farhat Hached in Sousse, Tunisia, over a period of nine months, from July 2019 to March 2020. Patients were evaluated by Dual Energy X-ray absorptiometry to determine bone mineral density (BMD), T-score and Z-score.
Results
The mean age at diagnosis of SS was 48.2 $\pm$ 12.4 years. The incidence of SS in our study was 2.8 cases/year. A causal hemorrhagic delivery was found in all of our patients. Thyrotropic and corticotropic insufficiency were present in 86.2% of our patients, followed by gonadotropic and lactotroph insufficiency in 72.3% and 38.5% of patients, respectively. Somatotropic insufficiency was explored by a dynamic test in only 8 patients, concluding with somatotropic deficiency in 10.8% of cases. Hormone replacement therapy was initiated in all patients based on the affected anterior pituitary axis. In no case has the somatotropic sector been substituted in our series. Bone densitometry was performed in 21 patients, on average 5 years after the diagnosis of SS. Bone mineralization disorders were found in 18 patients: 10 patients had osteoporosis and 8 patients had osteopenia. The lumbar spine was more frequently involved than the femoral neck. Two patients had femoral neck fractures associated with low energy falls, on average 33 years after the diagnosis of SS. In univariate analysis, bone mineral loss was correlated with age, body mass index, vitamin D level, duration of SS and estrogen progesterone Hormone replacement. However, in multivariate analysis no factor was significantly correlated with an elevated risk of bone mineral loss.
Discussion-Conclusion
Anterior pituitary insufficiency, especially in sex and growth hormones, as well as an overdose of thyroid hormones and glucocorticoids could increase bone mineral loss. In fact, bone loss is increased in SS compared to other causes of anterior pituitary insufficiency since patients with SS had an earlier disease onset and more severe hormonal deficits.

DOI: 10.1530/endoabs.81.EP653

EP654

Drug-induced galactorrhea and gynecomastia: a case report

Erika Jurkutė[1], Tomas Masilionis[1], Aistė Kondrotienė[1,2], Birutė Žilaitienė[1,2] & Rasa Verkauskienė[1,2]
[1]Lithuanian University of Health Sciences, Kaunas, Lithuania; [2]Institute of Endocrinology, Medical Academy, Lithuanian University of Health Sciences, Kaunas, Lithuania

Introduction
Finding the cause of gynecomastia and galactorrhea can be challenging, hence one of the most important cornerstones is detailed case history. Hereby we present gynecomastia and galactorrhea case, caused by drug abuse.
Case
A 24-year-old male, 3 years suffering from gynecomastia and galactorrhea, came for an endocrinologist consultation in 2020. As known from documentation laboratory blood results, lungs X-ray and abdominal ultrasound did not reveal any pathological changes. Chest ultrasound confirmed gynecomastia without any lymph nodes changes, although repeated prolactin concentration (165,26 mU/l) stayed in the normal range (89-365 mU/l). Unfortunately, due to the pandemic of Covid-19, further investigation stopped. The patient was referred for the consultation of an endocrinologist in 2021 summer since heavy galactorrhea and gynecomastia remained. The patient denied any diseases, medication use, allergies, family history of endocrine diseases. Objective examination showed normal body mass (BMI 24,9 kg/m^2), heavy whitish secretion from both nipples, normal volume testes (20 ml). Laboratory blood tests were done in July 2021- moderate hyperprolactinemia was observed (419,44 mU/l). The patient was referred for the head MRI, no pathological findings were identified in the hypothalamus-pituitary region. The case was discussed in the multidisciplinary meeting and it was suggested to abstain from the medical treatment, to repeat testicular and abdominal ultrasound, lungs Xray for ruling out an active oncology process, to perform a cytological examination of secretion, to review the history of the case including possible drug abuse. While planning further investigations during the next consultation, the patient unwillingly confirmed regular cocaine abuse and discontinued further testing.
Conclusion
after taking cocaine, the levels of prolactin in the blood fall to baseline. However, hyperprolactinemia develops within 4 days of dosing (in the absence of repeated administration) [1]. These prolactin fluctuations, as well as unwillingness to reveal drug abuse, makes gynecomastia and galactorrhea causes identification challenging in drug users.
1. Walsh S.L., Stoops W.W. Et al. 2009. Repeated Dosing with Oral Cocaine in Humans: Assessment of Direct Effects, Withdrawal and Pharmacokinetics. *Exp. Clin. Psychopharmacol.*

DOI: 10.1530/endoabs.81.EP654

EP655

Somatostatin analogues in the treatment of a patient with acromegaly - possible positive effects on concomitant epilepsy (a clinical case)

Sergey Seferyan, Polina Zakharova & Irena Ilovayskaya
Moscow Regional Research and Clinical Institute (MONIKI), Neuroendocrinology, Moscow, Russian Federation

Somatostatin may act as a neurotransmitter in the neural network. Ìts associated with a possible long-term effect on calcium channels and, as a result, on the membrane potential of the cell. Bradycardia due to somatostatin analogues' use could be a clinical demonstration of such effect. We would like to present a clinical case of a female patient with acromegaly and possible positive effect of octreotide treatment on concomitant epilepsy. From 2000 (age 40) a woman noted swelling of the face, a slow increase in the size of the hands and feet, hyperhidrosis, but she did not pay much attention to these signs. In 2011 (age 51) she noted episodes of loss of consciousness and convulsive seizures that why she referred for medical help. Endocrinologists recognized clinical signs of acromegaly. According to brain MRI pituitary macroadenoma (4.5x3.0x6.0 cm, V 38.7 cm3) with latero-suprasellar extension and the frontal lobe of the right hemisphere invasion was revealed. IGF-1 levels were 829 ng/ml (56-261) so active acromegaly was diagnosed, epilepsy was considered as secondary condition due to giant adenoma. Debulking surgery with consequent radiosurgery (Novalis) of the residual tumor was performed. Then she received octreotide prolonged release 30 mg monthly and achieved biochemical control. At the same time with acromegaly treatment, she started anticonvulsant therapy with valproic acid (1200 mg daily) and convulsive symptoms disappeared. Till February 2021 (age 61) she was stable, and octreotide was withdrawn, IGF-1 without treatment 118-159 ng/ml (43-220). Since April 2021 she noticed convulsive syndrome again despite the continuous use of valproic acid. Neurologist recommended to continue valproic acid at the same dose, however, convulsive symptoms occurred. In this case, we suggested that treatment with somatostatin analogues was associated with absence of convulsive symptoms in acromegaly patient with lesion-induced epilepsy. We cannot exclude that withdraw of possible positive effect of somatostatin analogues on ion channels disorders resulted in epilepsy relapse, which requires further study of additional therapeutic properties of drugs in this group.

DOI: 10.1530/endoabs.81.EP655

EP656

Delayed diagnosis of pituitary stalk interruption syndrome in a 26-years-old patient

Yosra Abderrahim, Boubaker Fadia, Hana Charfi, Arige Abid, Houcem Mrabet, Zantour Baha, Najoua Lassoued, Alaya Wafa & Sfar Mohamed Habib
University Hospital Tahar Sfar Mahdia, Endocrinology-Diabetology and Internal Medicine Department, Mahdia, Tunisia

Introduction
Pituitary stalk interruption syndrome (PSIS) is a rare congenital pituitary defect with an estimated incidence of 0.5 per 100,00 births. This syndrome has

heterogeneous clinical presentations with varying degrees of pituitary hormones deficiencies. PSIS is commonly diagnosed during neonatal period and infancy. However, when symptoms are not evident or overlooked, the diagnosis could be delayed exposing the patient to acute, such as acute adrenal insufficiency, and chronic complications.
Case report
We report a case of a 26 year-old male patient who was referred to our endocrinology department with complaints of short stature and impuberism. The patient had a history of prematurity, poor statural growth, learning and attention difficulties resulting in an early school dropout. On physical examination, the patient's weight and height were 47 kg and 140 cm respectively, both under the 5th percentile. He had a micropenis and a reduced testicular volume with absence of pilosity (Tanner stage 1). A blood test assessing pituitary hormones was performed showing an anterior hypopituitarism with undetectable testosterone level. Magnetic resonance imaging exhibited the diagnostic triad of PSIS associating hypoplasia of the anterior pituitary gland, absence of the posterior pituitary and a thin and interrupted pituitary stalk. Further investigations revealed metabolic and bone complications manifesting in Hypercholesterolemia (Total cholesterol = 8 mmol/l) and a pre-diabetic status (HbA1c= 6%). DEXA scan showed a femoral neck osteopenia and a spinal osteoporosis. The patient started immediately hormonal replacement therapy with a close clinical and biological follow-up.
Conclusion
Growth retardation is the most common presentation of PSIS. Hence the importance of early detection and investigation of short stature as any delay in diagnosis may lead to severe complications and heavy psychosocial consequences.

DOI: 10.1530/endoabs.81.EP656

EP657

Pathomorphological markers of somatotroph neuroendocrine tumors predicting the treatment outcome in acromegaly

Agnieszka Tomasik[1], Maria Stelmachowska-Banaś[2], Maria Maksymowicz[3], Izabella Czajka-Oraniec[2], Dorota Raczkiewicz[4], Grzegorz Zieliński[5], Jacek Kunicki[6] & Wojciech Zgliczyński[2]
[1]Centre of Postgraduate Medical Education, Department of Endocrinology, Warsaw, Poland; [2]Centre of Postgraduate Medical Education, Department of Endocrinology, Poland; [3]Maria Sklodowska-Curie National Research Institute of Oncology, Department of Cancer Pathomorphology, Warsaw, Poland; [4]School of Public Health, Centre of Postgraduate Medical Education, Department of Medical Statistics, Warsaw, Poland; [5]Military Institute of Medicine, Department of Neurosurgery, Warsaw, Poland; [6]Maria Sklodowska-Curie National Research Institute of Oncology, Department of Neurosurgery, Warsaw, Poland

Background
Transsphenoidal adenomectomy of GH-secreting pituitary tumour is a first-line treatment of acromegaly. Pharmacological treatment is recommended if surgery did not lead to disease remission. Pathological assessment of postoperative tissue provides clinicians with valuable information on the disease course.
Aim
The aim of this study was to assess whether clinical, imaging, and pathological characteristics can predict surgical remission and response to first-generation somatostatin analogs (SRLs) and pasireotide LAR in acromegaly patients.
Patients and methods
A retrospective analysis of a study cohort of 120 patients with acromegaly, treated in one endocrinology centre was performed. Data on demographics, hormonal and imaging results, pathological evaluation (immunostaining for pituitary hormones, Ki-67 index and granulation pattern) and treatment outcome was extracted from the Polish Acromegaly Registry and analyzed.
Results
Patients who achieved surgical remission were older at diagnosis (50 *vs.* 37 years on average, $P<0.001$), had lower fasting GH, IGF-1 and PRL concentrations at diagnosis (4.68 *vs.* 18.9μg/l on average, $P<0.001$; 2.99 *vs.* 3.53xULN on average, $P=0.004$, 11.1 *vs.* 22.4 ng/ml on average, $P=0.015$, respectively) and had smaller tumours (12 *vs.* 24 mm on average, $P<0.001$) which were less invasive than in patients with active acromegaly after surgery. The pathology results showed that patients with surgical remission more often had densely granulated tumours (73.17% *vs.* 40.00%, $P=0.001$) with positive staining for α-subunit (58.33% *vs.* 35.48%, $P=0.021$) and lower Ki-67 index (87.50% *vs.* 65.57% with Ki-67 index $<1\%$, $P=0.002$) compared to patients without surgical remission. Patients, who responded well to first-generation SRLs, presented less common extrasellar expansion and compression of the optic chiasm at diagnosis of acromegaly (58.62% *vs.* 90.00%, $P=0.006$ and 13.79% *vs.* 56.67%, $P=0.001$, respectively) compared to patients with poor response to SRLs. They also had more common densely granulated tumours (62.96% *vs.* 14.29%, $P<0.001$). However, no significant differences between patients with good and poor response to pasireotide LAR were found. In multivariate logistic regression analysis, independent predictors of post-surgical remission were normoprolactinaemia at diagnosis (OR=5.87, $P=0.023$), densely granulated tumour in electron microscopy (OR=5.92, $P=0.012$) and lower fasting GH concentration at diagnosis (OR=0.88, $P=0.001$).
Conclusions
Patients with densely granulated somatotroph tumours are more likely to achieve surgical remission and to respond well to first-generation SRLs. Positive staining for α-subunit and lower Ki-67 index increase the likelihood of surgical remission in acromegaly. The pathological assessment of tumour tissue is an important part of acromegaly patient's evaluation providing valuable information on tumour's characteristics. Together with clinical and imaging parameters it can help to predict the treatment outcome.

DOI: 10.1530/endoabs.81.EP657

EP658

Two cases: hemorrhagic rathke cleft cysts mimicking a hemorrhagic adenoma

Hatice Sebile Dökmetaş[1], Ayberk Bayramgil[2], Meriç Dökmetaş[2], Fatih Kılıçlı[1], Güneş Dorukhan Çavuşoğlu[2], Kü bra Karaipek[2] & Ayşe Gül YILDIRIM KIZILKAYA[2]
[1]Medipol Mega University Hospital, Endocrinology, Istanbul, Turkey; [2]Medipol Mega University Hospital, Internal Medicine, Istanbul, Turkey

Introduction
Rathke Cleft Cysts(RCCs) are benign cysts arising from the remnants of Rathke's pouch. The most common symptoms are visual field disorders, headache, and pituitary dysfunction.
Case 1
A 26-year-old male was admitted with headache that started 4 days ago. Cranial MRI revealed an appearance mimicking a hemorrhagic adenoma in pituitary. Pituitary hormones were found as normally. Pituitary MRI showed a 12x10x10 mm hemorrhagic RCCs located in the midline. The patient's headache disappeared spontaneously within 3 days without the use of any medication. One month and six months later, MRI showed a progressive shrinkage of hemorrhagic RCCs diameters as 4.5x5x7.5 mm and 3 mm, respectively. In the pituitary MRI taken at the last follow-up 15 months later, it was observed that sequelae remained as a millimetric-thick slit-shaped microcyst in the central gland.
Case 2
A 24-year-old female was admitted with a complaint of headache that started one month ago. The patient, who had a throbbing headache on the right side of her head, was relieved with analgesics. Pituitary MRI revealed a hemorrhagic RCCs with diffusely expanding pituitary gland with a size of 18x13x8 mm and leveling inside. The patient's pituitary hormones were checked and no pathological values were found. In the control pituitary MRI one month later, the size of the hemorrhagic RCCs decreased to 8x13x8 mm.
Conclusion
Patients with hemorrhagic RCCs whose symptoms decreased during close follow-ups and who did not have hormonal disorders were not operated on. The sizes of the masses of the patients who did not develop any complaints or hormonal disorders during their follow-ups decreased.
Key words: Hemorrhagic Rathke Cleft Cysts; Hemorrhagic Adenoma

DOI: 10.1530/endoabs.81.EP658

EP659

Central precocious puberty on pituitary adenoma : about a case report

Kaoutar Rifai, Kamel Farah, Hind Iraqi & Mohamed Hassan El Gharbi
Ibn Sina University Hospital, Endocrinology and Metabolic Diseases, Rabat, Morocco

Introduction
Central precocious puberty (CPP) is a frequent reason for consultation in pediatrics. It is defined as the development of sexual characteristics before the age

of 8 years in girls and 9 years in boys. Pediatric pituitary adenomas are rare. We report the case of a patient who presented with central precocious puberty on pituitary adenoma.
Observation
This is a patient aged 7 years and 6 months, without any particular history, having consulted initially for a premature thelarche. Her history of the disease goes back to the age of 7 years by the development of mammary glands, appearance of pubic and axillary hair without metrorrhagia, with an acceleration of the statural growth rate. Moreover, she did not report any pituitary tumor syndrome, and she had a significant psychological impact. The clinical examination found: a weight: 38 kg (+3DS), a height: 1,42 m (+3DS), BMI: 18,8 kg/m^2, blood pressure: 120/60 mmhg, estimation of the pubertal stage: S3P3 and a dry vulva. The rest of the clinical examination was unremarkable. Pelvic ultrasound objectives a thin and median vacuity line, ovarian length $\geq$ 25 mm, body to neck ratio $>$1. Estradiol level :20 pg/ml. Bone age is 9 and ½ years (advanced by 2 years/chronological age). For etiological orientation : Inhibin B : 85 pg/ml, LH : 2.6 IU/l, FSH :6 IU/l, LHRH TEST : peak LH : 50 IU /l, LH/FSH ratio : 6. The diagnosis of central precocious puberty is confirmed. Hypothalamic-pituitary MRI shows a pituitary adenoma of 10*9 mm far from the optic chiasm. The fundus and the visual field did not show any abnormalities. The evaluation of the various endocrine axes is without particularity. Therapeutically, she was treated with GnRh agonists with a good clinical and biological evolution.
Discussion and conclusion
Central precocious puberty is frequent, the search for a tumoral etiology remains a priority. Pediatric pituitary adenomas are rare, representing 3% of all pediatric intracranial tumors and 5% of all pituitary adenomas. They are mainly functional tumors, more frequently secreting prolactin, ACTH, and growth hormone, while gonadotropin hypersecretion is very rare. 4 cases of PPC on pituitary adenoma have been reported in the literature: 2 cases secreting FSH alone and 2 cases secreting FSH and TSH. Treatment with GnRH analogues is indicated in the case of clinically, biologically and radiologically progressive PP, with an impact on adult height, and on the psychological level.

DOI: 10.1530/endoabs.81.EP659

EP660

Automated data extraction of structured clinical correspondence with SNOMED coding to assess regional epidemiology of common pituitary conditions

Shao Hao Alan Yap[1], Alex Graveling[2], Prakash Abraham[2] & Sam Philip[2]
[1]University of Aberdeen, Medical Student, Aberdeen, United Kingdom; [2]JJR Macleod Centre for Diabetes & Endocrinology (David Anderson Building), Aberdeen Royal Infirmary, Diabetes & Endocrinology, Aberdeen, United Kingdom

Introduction
Pituitary disorders are associated with increased mortality and morbidity. Data on the prevalence of pituitary disorders is scarce. Formal routine coding of diagnoses in outpatient endocrine practice lags behind medical coding of inpatients. Standardised coding could improve our understanding of disease burden and highlight areas of increasing need within our services.
Objective
Automatically extract and assign SNOMED codes for endocrine diagnoses from structured outpatient correspondence. The coded information was used to ascertain the prevalence of pituitary disorders in patients attending endocrine outpatient clinics at Aberdeen Royal Infirmary, Aberdeen, Scotland.
Method
Retrospective study conducted in a tertiary outpatient endocrine clinic. Patients from postcodes within 2 regional areas of NHS Grampian were included (Aberdeen City and Aberdeenshire), who attended clinics between 1st January 2018 to 31st December 2019. Based on the mid population estimates from the National Records of Scotland, the total study population was 489,880 inhabitants. After each clinical consultation, which may be face to face or remote, a structured letter was created, containing a detailed problem list. Structured correspondence was introduced to provide more uniform output from clinic appointments and ensure key information was captured (despite clinics being conducted by several different healthcare professionals). An automated script was developed to extract each problem statement and update a database. Unique problem list entries were manually coded using the 'disorder' concepts from SNOMED CT (UK edition).
Results
A total of 1870 patients attended the outpatient services (1251 of them were female with a male to female ratio of 1:2); age ranged from 16-96 years. 464 (21.2%) had pituitary disorders. Pituitary disorders have a prevalence of 94.7 per 100,000 inhabitants, with a mean age of 51yrs (SD $\pm$ 18) and male to female ratio at 1: 1.5. The most common diagnosis was pituitary adenoma with a prevalence rate of 65.3 per 100,000 inhabitants. The prevalence per 100,000 for the subcategories were functionless pituitary adenoma (22), acromegaly (7.1) and pituitary-dependent Cushing's disease (3.1). The prevalence is consistent with previous studies.
Conclusion
Automated text parsing of structured endocrine correspondence allowed the creation of a database of endocrine problems. SNOMED coding enabled us to create a common endocrine reference set. Standardised coding helped assess the prevalence of pituitary disorders in this population. A similar automated approach to allow medical coding of routine medical correspondence could help improve understanding of the epidemiology of conditions managed predominately in outpatient settings, as well as facilitate quality improvement projects.

DOI: 10.1530/endoabs.81.EP660

EP661

Acromegaly-related cardiovascular morbidity In Tunisian Patients: Prevalence and clinical peculiarities

Faten Haj Kacem Akid[2], Wafa Belabed[2], Mohamed Abdellahi Ahmed[2], Mouna Elleuch[2], Dhoha Ben Salah[2], Fatma Mnif[2], Nabila Mejdoub[2] & Mohamed Abid[2]
[1]Hedi Chaker University Hospital, Endocrinology Department, Sfax, Tunisia; [2]Hedi Chaker University Hospital, Endocrinology Department, Sfax, Tunisia

Background and Aims
Cardiometabolic comorbidity is a well-established complication related to GH hypersecretion. Several studies have highlighted an increased cardiovascular risk in this population. The objective of the current work was to investigate the cardiovascular complications in Tunisian patients diagnosed with acromegaly.
Patients and Method
We conducted a retrospective study that included all patients diagnosed with acromegaly who have been followed up, from 1997 to 2021, at the Endocrinology Department of Hedi Chaker University Hospital, Sfax, Tunisia. The review of medical charts provided a detailed cardiovascular evaluation in the investigated population.
Results
Our sample included 29 with a mean age at diagnosis of 45.8 $\pm$ 12.4 years old (extremes: 23-72 years) and slight male predominance (52.0%). The overall prevalence of arterial hypertension in the studied population was 20.7% with a mean duration of the evolution of 9.3 years (extremes: 2– 20 years). Hypertension was newly diagnosed in 6.9% of patients. Arrhythmia and cardiac conduction disorders were observed in 10.3%. The cardiac ultrasound assessment revealed a concentric left ventricular hypertrophy in 15.4% of patients. Severe complicated hypertrophic cardiomyopathy with left heart insufficiency was reported in 3.4%. Aortic valvulopathy was found in 3.4% of cases. Ischemic heart disease affected 6.9% of patients.
Conclusion
Cardiovascular complications represent the leading cause of mortality in patients with acromegaly [1]. A various spectrum of cardiovascular manifestations can occur due to GH exaggerated secretion. Hypertension, ischemic heart disease, and arrhythmia are the most common ones. Other acromegaly-specific cardiac conditions can be found such as acromegalic cardiomyopathy [2]. The GH and IGF-1 excess affects the heart morphology and may impair its performances leading to insidious alterations of heart tissue and functions, independently of additional cardiovascular factors. The optimal surgical and medical management of acromegaly is associated with an improvement of cardiovascular risk in this population [3].
References
1. Lombardi, Gaetano, et al. 'Acromegaly and the cardiovascular system.' Neuroendocrinology 83.3-4 (2006): 211-217.
2. Pivonello, Rosario, et al. 'Complications of acromegaly: cardiovascular, respiratory and metabolic comorbidities.' Pituitary 20.1 (2017): 46-62.
3. Mosca, Susanna, et al. 'Cardiovascular involvement in patients affected by acromegaly: an appraisal.' International journal of cardiology 167.5 (2013): 1712-1718.

DOI: 10.1530/endoabs.81.EP661

EP662

The frequency of water and electrolyte disorders after transnasal surgery for adenomas of the hypothalamic-pituitary region: what does active control of blood sodium level give?

Khava Fargieva, Daria Mikhailova, Oksana Ivashenko, Vilen Azizyan, Andrey Grigoriev, Arkadiy Sergeev, Elena Przhiyalkovskaya, Pigarova Ekaterina, Larisa Dzeranova & Natalya Mokrysheva
Endocrinology Research Centre, Moscow, Russian Federation

Introduction
Water-electrolyte disorders are serious complications after transnasal adenomectomy for formations of the hypothalamic-pituitary region. The purpose of this work was to evaluate the incidence of postoperative hyponatremia in the tactics of active control of sodium levels in the blood.
Materials and methods
The study included the results of a dynamic study of blood sodium levels in 53 patients (mean age 46.6 years [min 19; max 68]) with pituitary adenomas (GH-secreting - 31 patients, ACTH-secreting - 14 patients, hormonally inactive - 6 patients, TSH-secreting - 1 patient), who underwent endoscopic transnasal transsphenoidal adenomectomy. Sodium control was carried out initially before surgery, after 12-24 hours, on days 2-3, 4-5 and 6-7 after surgery. Comparison of the frequency of hyponatremia was carried out with data on the lack of alertness about the possibility of developing postoperative hyponatremia and the lack of blood sodium control in 2008 (0.7%), the absence of alertness, but periodic monitoring of blood sodium but without mandatory monitoring of blood sodium levels in 2017 (7.2%).
Results
Initially, before surgery, only one patient with a TSH-secreting pituitary tumor had a decrease in the sodium concentration in the blood to 135 mmol/l (reference values 136-145 mmol/l) - 1/53 (1.8%). During the first 12-24 hours and on days 2-3 after surgery, hyponatremia of 135 mmol/l was also detected in 1 case in different patients with ACTH-secreting pituitary adenomas (1.8%), as well as 1 case of low sodium blood to 130 mmol/l in the period of 2-3 days after the operation, which was of a long-term nature and a tendency to reduce the level of sodium in the blood to 125 mmol/l. On days 4-5, a total of 5 hyponatremias (4 newly emerged), 3 of which were of moderate severity 129-125 mmol/l (7.5%), were detected, on days 6-7, 12 hyponatremias were recorded (8 newly emerged), of of which 4 were of moderate severity, and 8 of mild severity (22.6%). The overall incidence of postoperative hyponatremia was 28.3%.
Conclusions
Transient hyponatremia of the early postoperative period up to the 3rd day after surgery does not appear to be clinically significant. An increase in the frequency and severity of hyponatremia was noted from the 4th post-operative intervention, which necessitates mandatory monitoring of blood sodium levels. The approach of active monitoring of the blood sodium level allowed to increase the detection of hyponatremia by 3.9-32.6 times

DOI: 10.1530/endoabs.81.EP662

EP663

Hypothalamic syndrome secondary to systemic sarcoidosis

José Vicente Gil Boix, Guillermo Serra Soler, Mercedes Noval Font, Javier Bodoque Cubas, Meritxell Viñes Raczkowski, Alicia Sanmartín Sánchez, Santiago Tofé Povedano, Elena Mena Ribas, Mercedes Codina Marcet, Josefina Olivares Alcolea, Francisca Caimari Palou, Vicente Pereg Macazaga & Iñaki ArgüElles Iménez
Hospital Universitari Son Espases, Endocrinology and Nutrition, Palma, Spain

Introduction
Sarcoidosis is a rare systemic disease where clusters of immune cells form granulomas in various organs of the body. Its prevalence ranges from 1-40 per 100,000 people in Europe. Neurological involvement of the disease occurs in 5-10% of cases, with the hypothalamus-pituitary gland being one of the most commonly affected structures.
Clinical Case
A 36-year-old male with a history of hypertension, obesity, asthma and OSAS. He went to the emergency department due to symptoms of 4 months of evolution of asthenia, hypersomnia, compulsive food intake with a weight gain of 30 kg and behavioral disorders, being admitted to the Internal Medicine department. Physical examination revealed a weight of 157 kg, height 177 cm (BMI 50.1) and white striae on the abdomen. Cardiopulmonary auscultation was normal. Neurologically, there was evidence of decreased strength and painful stiffness on extension in the upper limbs.
Cranial CT scan showed two intracranial lesions, at hypothalamic and right parietal level, with associated perilesional oedema. These lesions were confirmed by MRI, suggesting an inflammatory-granulomatous aetiology. Fine-needle aspiration with Endo Bronchial Ultra Sound of a mediastinal lymph node revealed non-necrotising granulomatous lymphadenitis and a diagnosis of systemic neurosarcoidosis was made. Treatment with corticosteroids, rituximab and mycophenolate mofetil was started. After discharge, he was admitted to the intensive care unit a few days later due to disturbance of consciousness consciousness secondary to hypernatraemia. Ionogram showed a serum sodium of 172 mEq/l with a plasma osmolality of 380 mOs/Kg and a urinary osmolality of 843 mOsm/kg. The endocrinology department, after ruling out diabetes insipidus and assessing the hormone analysis, diagnosed it of hypothalamic syndrome secondary to neurosarcoidosis, presenting with hypernatraemia due to hypodipsia/adipsia, morbid obesity, type 2 diabetes mellitus, hypogonadotropic hypogonadism and hyperprolactinaemia. At discharge, treatment for diabetes was started with metformin and weekly dulaglutide, hormone replacement therapy was started with testosterone gel and a controlled water intake of 2.5-3 litres per day was indicated, depending on physical activity and the season of the year.
Conclusions
- Hypothalamic syndrome as a consequence of neurosarcoidosis can affect a number of vital endocrine and non-endocrine functions that are difficult to control.
- Hypothalamic adipsic hypernatremia can present with severe symptoms and these patients should be educated in controlled fluid intake.

DOI: 10.1530/endoabs.81.EP663

EP664

Peak cortisol level on synacthen stimulation test in cushing's disease

Razan Ali Rashid, Christopher S Boot, Andy James & Yaasir Mamoojee
The Newcastle upon Tyne Hospitals, Endocrinology and Metabolic medicine, Newcastle upon Tyne, United Kingdom

Background
Diagnostic work-up for Cushing 's syndrome (CS) can be challenging, with variable performance characteristics on screening tests. We were recently referred a young female patient with Cushing's disease (CD) due to a microadenoma. She presented with a seizure and initial biochemical work-up included a Synacthen stimulation test (SST). Her peak cortisol rose to over 1,000 nmol/l. Exaggerated response during SST is expected in hyperestrogenic states due to elevation in cortisol-binding globulin concentrations, for e.g. pregnancy and those taking estrogen-containing pills. However, overstimulation of the adrenal cortex by increased ACTH, as in ACTH-driven CS, is physiologically expected to result in hypertrophy of the zona fasciculata and therefore produce a heightened cortisol response during SST.
Aim
We retrospectively compared the difference in peak cortisol concentrations, after 250 µg tetracosactide administration during SST, in patients with active CD and those without CS but intact steroid axis.
Methods
In our unit, all patients with CD undergoing Transphenoidal Sugery (TSS) are started on steroid replacement post-operatively. SST is performed, after a standard steroid weaning, at 6-8 weeks post-operatively and if normal, standard biochemical work-up for steroid excess takes place again. We included all patients who were not in biochemical remission after TSS. Our comparator cohort includes all patients with a normal SST result after pituitary surgery for non-Cushing tumours. Roche I and Roche II Cortisol assays were used, with a normal SST response defined as peak serum cortisol level of >550 nmol/l or >420 nmol/l, respectively. Conversion of peak cortisol level from Roche I to Roche II equivalent concentration was done using validated regression equation. Mann-Whitney U test and Fisher's exact test were used for statistical analysis for continuous and categorical variables respectively. Results are expressed as mean ($\pm$SD).
Results
13 patients with active CD and 210 patients with normal SST results were included in our CD and control cohort. Mean peak cortisol in our CD cohort was higher at 1020 ($\pm$305) nmol/l compared to 677 ($\pm$144) nmol/l ($P<0.01$). 62% of SSTs in the CD cohort had a peak cortisol of >850 nmol/l compared to 9% in the control cohort ($P<0.01$).
Conclusion
Patients with active CD demonstrate a higher than average cortisol response during SST. Clinicians should keep a high index of suspicion for ACTH-driven

CS in patients with an exaggerated cortisol response on SST, especially in the context of initial biochemical work-up for pituitary incidentalomas.

DOI: 10.1530/endoabs.81.EP664

EP665

Giant prolactinomas: a descriptive study and prognostic analysis

Mouna Elleuch, Hamdi Frikha, Loukil Fatma, Dhoha Ben Salah, Maalej Souhir, Mouna Mnif, Fatma Mnif, Nadia Charfi, NABILA REKIK MAJDOUB, Faten Haj Kacem Akid & Mohamed Abid
Hedi Chaker University Hospital, Department of Endocrinology, Sfax, Tunisia

Introduction
Giant prolactinomas (GP), defined as prolactinomas ≥4 cm in maximum dimension, are uncommon, with reported prevalence of 2 to 3% of all prolactinomas.
Aim
The aim of this study is to describe clinical and paraclinical characteristics of GP and to identify predictors of therapeutic response.
Matherials and methods
A retrospective, single-center, descriptive study including 18 patients with GP followed at the endocrinology department of Hedi Chaker University Hospital of Sfax, Tunisia.
Results
Mean age was 42.9 ±16.9 years. Patients were predominantly male (77.8%). Mean tumor size was 50.4 ±9.3 mm with a maximum of 70 mm. Prolactinemia at diagnosis was 10569.1 ±19667 ng/ml on average [56-81940]. Clinically, main symptoms included signs of intracranial hypertension (78%) and visual field defects (72.2%). Galactorrhea was reported in 25% of patients only. Pituitary insufficiency included thyrotropic, corticotroph and gonadotropic axes in 33%, 11% and 50% of cases respectively. Sixteen patients were treated with dopamin agonists (bromocriptin 75% and cabergolin 25%), 3 of them showed resistance to medical treatment. Surgery was indicated in 7 cases during follow-up: optic chiasm compression (4 cases) and resistance to medical treatment (3 cases). Mean prolactinemia at 1 year of follow-up was 726.3 ±1315.2 ng/ml. A strong correlation was found between initial prolactinemia and six-month decrease of prolactin level ($r=0.68$; $P=0.04$). However, therapeutic response did not correlate with age or initial tumor size. There was no reported case of complete remission.
Conclusion
GP is a rare form of prolactinomas. It mainly affects men and its symptoms are due to mass-effect. GP respond generally well to dopamin agonists. Initial prolactinemia could be a good marker of therapeutic response.

DOI: 10.1530/endoabs.81.EP665

EP666

Pharmacokinetic profile of cabergoline in patients with dopamine agonist resistant prolactinomas: a pilot study

Aleksandra Shutova[1], Natalia Fedorova[1], Svetlana Vorotnikova[1], Vitalii Ioutsi[1], Juriy Panov[2], Ekaterina Pigarova[1], Larisa Dzeranova[1] & Ekaterina Troshina[2]
[1]Federal state Budgetary Institution 'National Medical Research Centre of Endocrinology' Ministry of Health of the Russian Federation, Department of neuroendocrinology, Moscow, Russian Federation; [2]Federal State Budgetary Institution 'National Medical Research Centre of Endocrinology' Ministry of Health of the Russian Federation, Moscow, Russian Federation

Introduction
Approximately 20% of patients with prolactinomas do not respond satisfactory (resistant) even to high dose dopamine agonist treatment. Worth noticing that there are no clear prognostic signs of treatment's resistance as well as its etiology is a subject of discussion.
Aim
The aim of our study was to assessabsorption and metabolism of cabergoline in patients with dopamine agonist-resistant prolactinomas.
Materials and methods
In patients ($n=4$) with resistant prolactinomas (no normalization of PRL, no menses with max tolerated dose of cabergoline more than 3 mg a week) and one with normal effect of the drug we conducted a pharmacokinetic test: 1) cabergoline was preliminary withdrawn 4 days before the test; 2) at 9:00 the blood was taken before and 30-, 60-, 90-, 120-minutes and 4 hours after taking the cabergoline in a fixed doze of 0.5 mg. The concentration of cabergoline substance in the serum was measured using LC-MS/MS.
Results
It is shown that the serum cabergoline concentration curve in 3 patients with resistance to treatment doesn't represent expected pharmacokinetic peaks (the growth rate less than + 1-50%). The pharmacokinetic curve of 1 resistant patient represented a cabergoline concentration peak at 30 min point (the growth rate +175%) with subsequent decline to baseline levels. The serum cabergoline concentration curve of drug-sensitive patient is characterized by an already significant baseline concentration that becomes progressively higher reaching an outstanding peak (the growth rate +112%) at the end of the test period.
Conclusion
Our pilot results show that the patients with dopamine-resistant prolactinomas may have a defect in forming (absorption or metabolic abnormalities) an adequate blood concentrations of the drug. Understanding the underlying mechanisms will allow us to develop personalized treatment strategy.

DOI: 10.1530/endoabs.81.EP666

EP667

Male pituitary-gonadal axis function in obstructive sleep apnoea syndrome: the effect of continuous positive airway pressure

Richard Leigh[1,2], Siobhá n Hamon[3], Michael McWeeney[4], Aonghus O'Loughlin[5] & Paula O'Shea[5]
[1]Galway Clinic, Biochemistry Laboratory, Galway, Ireland; [2]Trinity College Dublin, Dublin, Ireland; [3]Ryan Institute, National University of Ireland, Galway, Galway, Ireland; [4]Galway Clinic, Galway, Ireland; [5]University Hospital Galway, Ireland

Background
Obstructive sleep apnoea syndrome (OSAS) is common; disproportionately affecting the overweight and obese. Continuous positive airway pressure (CPAP) is the first-line treatment for moderate to severe OSAS. Clinical equipoise exists as to whether CPAP treatment directly affects pituitary-gonadal hormone synthesis.
Study Aim
This study aimed to determine the effect of CPAP treatment on gonadotropins, prolactin, sex-hormone binding-globulin (SHBG), total testosterone (TT) and calculated free testosterone (cFT) in newly diagnosed male OSAS patients. 2018 European Health Research Compliance. Ethical approval was sought from the Bon Secours Health System Clinical Ethics Committee (CEC) and granted on the 08/03/2019. All participants in the research gave informed consent, obtained in accordance with guidelines provided by the CEC, Trinity College Dublin and the Royal College of Surgeons Ireland.
Methods
OSAS was diagnosed via gold standard in-house polysomnography studies. Participants provided venous blood samples before and twice after (first night CPAP, n = 25 and 3 months CPAP, n = 13) commencing CPAP treatment. At each time-point, concentrations of TT, SHBG, prolactin and gonadotropins were measured. In total, 53 males with a diagnosis of OSAS confirmed by polysomnography were prospectively enrolled to this study.
Results
Hypogonadism in the cohort was low ($n=2$). Hyperprolactinaemia was prevalent ($n=25$). TT and cFT were significantly negatively correlated with obesity. cFT was correlated with OSAS severity, but not TT. Significant reductions were observed in TT (pre 16.6 nmol/l, post 13.5 nmol/l, $P=0.003$), cFT (pre 332 pmol/l, post 250 pmol/l, $P=0.001$) and prolactin (pre 360 mIU/l, post 225 mIU/l, $P=0.006$) after 3-months of CPAP ($n=13$). No significant change was observed in other pituitary hormones or SHBG.
Conclusions
The prevalence of hypogonadism is low in this cohort. CPAP treatment reduced testosterone and prolactin in eugonadal males with OSAS. The benefits of CPAP treatment for OSAS may be independent to change in serum testosterone levels. Hypogonadal OSAS patients should be managed via strategies other than CPAP alone.

DOI: 10.1530/endoabs.81.EP667

EP668

A multicenter retrospective study on a large cohort of patients with primary empty sella: hormonal and neuroradiological features over a long follow-up

Giulia Carosi[1,2], Alessandro Brunetti[3, 4], Alessandra Mangone[1, 5], Roberto Baldelli[6], Alberto Tresoldi[7], Giulia Del Sindaco[1, 5], Elisabetta Lavezzi[4], Elisa Sala[1], Roberta Mungari[1], Letizia Maria Fatti[8], Elena Galazzi[8], Emanuele Ferrante[1], Rita Indirli[1, 5], Emilia Biamonte[4], Maura Arosio[1, 5], Renato Cozzi[9], Andrea Gerardo Antonio Lania[3,4], Gherardo Mazziotti[3, 4] & Giovanna Mantovani[1,5]

[1]Fondazione IRCCS Cà Granda Ospedale Maggiore Policlinico, Endocrinology Unit, Milan, Italy; [2]Sapienza University of Rome, Department of Experimental Medicine, Rome, Italy; [3]Humanitas University, Department of Biomedical Sciences, Pieve Emanuele, Italy; [4]IRCCS Humanitas Research Hospital, Endocrinologia, Diabetologia e Andrologia Medica, Rozzano, Italy; [5]University of Milan, Department of Clinical Sciences and Community Health, Milan, Italy; [6]A.O. San Camillo Forlanini, Endocrinology Unit, Department of Oncology and Medical Specialities, Rome, Italy; [7]Humanitas Gavazzeni, Endocrinologia, Bergamo, Italy; [8]Istituto Auxologico Italiano IRCCS, Division of Endocrine and Metabolic Diseases, Milan, Italy; [9]Niguarda Hospital, Division of Endocrinology, Milan, Italy

Background

primary empty sella (ES) represents a frequent finding (up to 35% of the general population). According to the literature, the prevalence of hypopituitarism in ES ranges between 19-52%. Data on the natural history of ES over a long time, especially in incidental ES, are still lacking and the management can be challenging.

Objective

our primary aim was to assess in a large cohort of patients with ES the prevalence and determinants of hypopituitarism. Our secondary aim was to explore the hormonal and neuroradiological evolution after at least 6-months of follow-up.

Design and methods

retrospective and multicenter study based on medical records of all patients with ES attending four Pituitary Units between 1984-2020. The availability of the neuroimaing and hormonal assessment at diagnosis represented the inclusion criteria. Data collected at diagnosis and at the last available follow-up were analysed.

Results

402 patients (63% females, mean age 51.5 ± 15.5 years) were enrolled. Dynamic evaluations of pituitary function were available in 326 (81%). Longitudinal data were available in 166/402 with a median follow-up of 58 months.

Diagnosis

ES was incidentally discovered in 72% patients whereas in 28% it was diagnosed because of a suspected endocrinopathy (hypopituitarism or hyperprolactinemia). ES was partial in 66.4%, total in 13.4%, and not defined in 20.2%. Traumatic brain injury (TBI) was reported in 23% cases evaluated for this issue. In the overall group, at least one pituitary hormonal deficiency was present in 40.5% (hypogonadism = 20.4%, hypoadrenalism = 14.7%, GHD = 14.7%, hypothyroidism = 10.2%, DI = 1.5%; multiple deficiencies = 11%) and hyperprolactinemia in 6.5%. Hypopituitarism resulted significantly associated with male sex ($P = 0.03$), symptoms/signs suggestive of pituitary disease ($P < 0.001$), and TBI ($P = 0.004$), without significant associations with age, BMI, number of pregnancies and entity of ES. Interestingly, hypopituitarism was present in 29.1% patients with incidental ES (hypoadrenalism = 13.5%, GHD = 12.5%, hypogonadism = 8.7%, hypothyroidism = 2.8%, DI = 1.7%).

Follow-up

at the last evaluation, 5/166 (3%) patients, displayed new hormonal deficiencies and 6.1% showed a neuroradiological progression from partial to total ES. Most patients with hormonal deterioration were already hypopituitaric at diagnosis (80%). The development of new deficiencies was only associated with the increasing grade of ES ($P = 0.004$).

Conclusions

we described one of the largest cohort of patients with primary ES. Patients with ES need to be carefully evaluated at diagnosis, even if ES is incidentally discovered. We suggest completing the assessment with dynamic tests (screening for GHD and adrenal insufficiency). Hypopituitarism is frequent (40%) but a deterioration in pituitary function seems uncommon (3%).

DOI: 10.1530/endoabs.81.EP668

EP669

Predictors of surgical outcome and early criteria of remission in acromegaly

Ludmila Astafyeva[1], Alexsey Shkarubo[1, 2], Ibrahim Sameh R.A.[2], Inna Badmaeva[1], Yuliya Sidneva[1], Julia Strunina[1], Maxim Kutin[1], Dmitrii Fomicev[1], Oleg Sharipov[1], Dmitrii Andreev[1], Ilya Chernov[1] & Pavel Kalinin[1]

[1]N.N. Burdenko National Medical Research Center of Neurosurgery, Moscow, Russian Federation; [2]Peoples' Friendship University of Russia, Russian Federation

Objective

To analyze the remission factors of surgical treatment of acromegaly

Methods

A retrospective study involving 227 patients with acromegaly: 143 (63%) women and 84 (37%) men were operated via trassphenoidal endoscopic approach for pituitary adenoma removal between the periods of 2018-2021. The average age was 45 years [36.00, 56.00]. 118 patients had 6 months follow-up period (3-40 months). The IGF-1 index used for the evaluation, which was calculated using the formula: IGF-1 index = IGF-1 patient (ng/ml) /upper reference interval IGF-1 for this age (ng/ml). The remission for acromegaly was considered as decrease of the IGF-1 index less than 1.0 not later than 3 months following surgery. Intrasellar adenomas were observed in 99 (44%) cases, 128 (56%) tumors had different directions of extrasellar growth (suprasellar in 81, infrasellar in 28 and laterosellar in 64 cases). The tumor size were classified into microadenomas – 20 (8,8%) ($\leq$10 mm in diameter), small and medium (10-35 mm)-164(72,2%), large (36-59 mm)-38(16,7%), giant ($\geq$60 mm)-5(2,0%).

Results

Remission after the surgical procedure was achieved in 65 (55%) of 118 cases with a long follow-up period. The average [IQR] age of patients in the group with remission - 46 years [37,56], and those without remission - 39.00 [31, 50] years ($P = 0.044$). Median [IQR] GH before surgery in the group with remission was 10,77 ng/ml [5.84, 21.23], without remission – 28,00 [9.02, 65.75] ($P = 0.001$). Following the removal of microadenomas or macroadenomas of smaller and medium sizes, remission was achieved in 8(88,9%) and 50(58,8%) cases respectively, during the removal of tumors of large and giant sizes remission was achieved only in 7(29,2%) cases ($P = 0,004$). Considering the intrasellar localization of the tumor, remission was achieved at 36(75%) cases, whereas with adenoma with extrasellar growth in 29(41,4%) cases ($P = 0,001$). The risk of surgical treatment of acromegaly was low: postoperative transient diabetes insipidus was noted in 16,7% of cases, hyponatremia - in 4,8%, rhinorrhea - in 1,3%, meningitis - in 0,88%, epistaxis in one (0,4%) and visual impairment in one (0,4%) case. There were no deaths.

Conclusion

Significantly predictors affecting the remission of acromegaly were recorded in average aged, the absence of visual disturbances, low GH level before surgery, the presence of microadenoma or small and medium-sized pituitary macroadenoma, the absence of extrasellar tumor growth, a decrease in GH $<$2,06 ng/ml and IGF-1 index $<$1,9 in the early postoperative period, the absence of residual tumor tissue after surgery.

DOI: 10.1530/endoabs.81.EP669

EP670

Xantho-granulomatous hypophysitis: analysis of clinical, biochemical, radiological and etiological characteristics

Dragana Miljic[1,2], Sandra Pekic Djurdjevic[1, 2], Mirjana Doknic[1, 2], Marko Stojanovic[1, 2], Marina Nikolic Djurovic[1, 2], Zvezdana Jemuovic[1], Toplica Milojevic[3], Mihailo Milicevic[2, 3], Emilija Manojlovic Gacic[2, 4], Jovan Jovanovic[2], Sanja Medenica[5] & Milan Petakov[1,2]

[1]Clinic for Endocrinology, Diabetes and Diseases of Metabolism, University Clinical Center Belgrade, Belgrade, Serbia; [2]School of Medicine, University of Belgrade, Belgrade, Serbia; [3]Clinic of Neurosurgery, University Clinical Center Belgrade, Belgrade, Serbia; [4]Institute of Pathology, University Clinical Center Belgrade, Belgrade, Serbia; [5]Department of Endocrinology, Internal Medicine Clinic, Clinical Center of Montenegro, School of Medicine, University of Montenegro, Podgorica, Montenegro

Introduction

Xanthomatous hypophysitis (XH) is characterized by inflammatory infiltration of the pituitary gland in which lipid laden macrophages predominate. It can be primary (3% of all primary hypophysitis) and secondary arising in the setting of other lesions: craniopharyngioma, Rathke's cleft cyst (*RCC*), adenomas (with subclinical apoplexy). It is more common in women and younger people. The clinical presentation is similar to pituitary tumors and may present with headaches, visual disturbances, hypopituitarism, and diabetes insipidus.

Aim

The aim of this study was to analyze a cohort of patients in whom the existence of xantho-granulomatous hypophysitis (XGH) was confirmed pathohistologically

(PH): their clinical, biochemical, radiological, etiological and pathohistological characteristics.
Material and methods
The study analyzed retrospectively collected data from electronic medical histories of patients with PH finding of XGH or XH diagnosed from 2015. to 2020. All patients were hospitalized at the Clinic for Endocrinology, Diabetes and Diseases of Metabolism, and the Clinic of Neurosurgery, University Clinical Center of Serbia.
Results
Cohort included three pediatric and nine adult patients, with an average age of 14.6 $\pm$ 4.7 and 54.9 $\pm$ 14.4 years (8 male and 4 female). Panhypopituitarism was diagnosed in 5 patients, exclusively men. Compression symptoms were present: headache in 8 patients (66%) and neuro-ophthalmic disorders in 4 patients (33%). Pituitary tumor, as a secondary cause, was found in 5 patients, three women and two men. One patient had a xanthomatous form of hypophysitis, others XGH. Cystic form were present in 3 (25%) patients, and solid in the remaining 9 (75%) patients. Primary, isolated forms were found in five cases (41%) while secondary ones were associated with RCC (2 patients, 16%) and pituitary tumors (5 patients, 41%).
Conclusion
In conclusion, we presented and analyzed a group of 12 patients with a rare form of XGH that differs from previously published studies in terms of sex dimorphism, lower prevalence of xanthomatous form and predominance of solid comparing to cystic forms on magnetic resonance imaging findings. Primary forms were, as expected, less frequent than secondary ones.

DOI: 10.1530/endoabs.81.EP670

EP671

The many faces of Granulomatosis with Polyangitis(GPA) presenting with Diabetes Inspidus, visual disturbances, epistaxis and haematuria

Gideon Mlawa[1], Noha Meneissy[2], Shrini Patel[2], Muhammad Saleem[2], Zahid Khan[2], Saiful Islam[2], Rachel Gunnell[2], Hassan Rehmani[3], Barney Low[3] & Mahamud Bashir[2]
[1]Queen's Hospital, Diabetes and Endocrinology/Acute Medicine, London, United Kingdom; [2]Queen's Hospital, London, United Kingdom; [3]Queen's Hospital, Acute Medicine, London, United Kingdom

Introduction
Granulomatosis with polyangiitis (GPA) is an anti-neutrophil cytoplasmic antibody (ANCA)-associated systemic vasculitis of both small and medium-sized vessels. Pituitary involvement in GPA is uncommon and few cases have been previously reported. Isolated pituitary involvement in GPA is rare and 96% of cases are associated with other organ involvement. GPA commonly affects the upper respiratory tract (93%), lungs (73%) and kidneys (67%).
Case
A 46-year-old male was admitted for investigation of vision changes. He had a 2–3-month history of blurred vision, headaches (retro-orbital discomfort), left eye redness, arthralgia, and epistaxis. His visual acuity was 6/60 with a central scotoma. A pituitary MRI revealed a likely inflammatory mass, involving the hypothalamus and infundibulum, suggestive of hypophysitis. Whilst an inpatient, he was diagnosed with diabetes insipidus and hypopituitarism. His blood test showed FSH 1.0 iu/l, LH $<$0.2 iu/l, Testosterone $<$0.4 nmol/l, TSH 0.03 mu/l, FT4 7.4 pmol/l, Prolactin 83 miU/l, random Cortisol 323 nmol/l and a normal short Synacthen test. An ear, nose, and throat opinion was sought due to the recurrent epistaxis. A nasal biopsy was taken with histology diagnostic of GPA. This was backed by positive ANCA and an elevated ESR (79 mm/hr). He was treated with high-dose steroids and cyclophosphamide. This rapidly and remarkably relieved his symptoms. His visual acuity, central scotoma, and red eye improved. His ESR normalised and a repeat pituitary MRI revealed substantial resolution of the mass. He was commenced on hormonal replacement (thyroxine and testosterone).
Discussion
GPA is a multi-system disorder characterised by necrotising granulomatous small-vessel vasculitis. GPA mainly affects a combination of the ear, nose, and throat. However, it may also affect the joints, skin, eyes, and other organs. GPA occurs in equal proportions between men and women. Although, in the few previously reported cases with pituitary involvement, there were more female patients. The time of pituitary symptom onset in 13(56%) of previous reported cases occurred between 2 months and 15 years after receiving a diagnosis of GPA. The prevalence of central nervous system involvement ranges from 15% to 54%. The most common neurological manifestation is peripheral neuropathy due to small vessel vasculitis (10-28%).
Conclusion
GPA is a rare cause of pituitary failure and should be considered in the differential diagnosis of hypophysitis. Multisystemic presenting symptoms, such as those demonstrated in this case, should alert clinicians to the possibility of pituitary involvement. This is likely to be as part of a multisystemic disease process since isolated pituitary involvement is rare.

DOI: 10.1530/endoabs.81.EP671

EP672

Service evaluation of endocrine and surgical outcomes post-pituitary surgery for non-functioning pituitary macroadenomas (NFPAs) in a subset of patients

Rosemary Ikegwu[1,2], Nijaguna Mathad[2, 3], Jonathan Hempenstall[2, 3], Alicja Knysak[2, 3] & Ma'en Al-Mrayat[1,2]
[1]University of Southampton, Faculty of Medicine, Southampton, United Kingdom; [2]Southampton General Hospital, Department of Endocrinology and Metabolism, Southampton, United Kingdom; [3]Wessex Neurological Centre, Southampton, United Kingdom

Background
Non-functioning pituitary adenomas (NFPAs) are the most common pituitary macroadenomas with a prevalence of 7-22 per 100,000 population. As they are non-secretory, they tend to present late with visual disturbances, headaches or hormonal deficiencies. Surgery is the main treatment for NFPAs, particularly endoscopic transsphenoidal surgery which can be associated with surgical and endocrine complications.
Aims
To compare pre- and post-operative endocrine outcomes and surgical complications and benchmark the findings with similar published cohorts
Methods
The clinical and laboratory records of 71 NFPA patients who underwent endoscopic pituitary surgery between 2017-2018 at Southampton General Hospital/UK were reviewed to note their pre-and post-operative endocrine and surgical outcomes. This included assessing of thyroid, adrenal, growth hormone and gonadotrophin axes, clinical hormone deficiencies and post-surgical complications. The data was tabulated for each individual patient and statistically analysed using SPSS for both quantitative and descriptive parameters.
Results
In our cohort, there was little increase in the proportion of patients with hypocortisolism and hypogonadism post-operatively compared with pre-operatively increasing from 31.0% (22/71) to 38.0% (27/71) and from 19.7% (14/71) to 21.1% (15/71) respectively. There was no post-operative increase in the 31% (22/71) of patients with hypothyroidism pre-operatively.11.3% (8/71) of the patients developed diabetes insipidus post-operatively. The most common surgical complication was intra-operative CSF leak affecting 19.7% (14/71) of the patients with 1.4% (1/71) of the cohort having post-operative CSF leaks. Post-surgically, epistaxis affected 7.0% (5/71), deterioration of vision affected 5.6% (4/71). The Wilcoxon Signed Rank Test demonstrated the increase on the number of hormone deficiencies per patient post-operatively was not statistically significant ($P=0.751$). Only 44 patients had their post-operative visual status recorded, 56.8% (25/44) of these had improved vision post-op, 34.1% (15/44) remained stable while 9.1% (4/44) worsened.
Conclusion
Visual status is mostly improved by transsphenoidal surgery. Additionally, endocrine function is only slightly worse following pituitary surgery. Our cohort's endocrine and surgical outcomes are comparable to the findings in previously published studies.

DOI: 10.1530/endoabs.81.EP672

EP673

Growth hormone (GH) replacement therapy (GHRT) in patients with adult GH deficiency (AGHD) aged $\geq$60 years: data from NordiNet® IOS and the ANSWER Program

Matthias M. Weber[1], Murray B. Gordon[2], Charlotte Höybye[3], Anne H. Olsen[4], Nicky Kelepouris[5], Navid Nedjatian[6] & Beverly M.K. Biller[7]
[1]University Hospital, Universitätsmedizin Mainz, der Johannes Gutenberg-Universität, Unit of Endocrinology, Medical Department, Mainz, Germany;

[2]Allegheny General Hospital, Allegheny Neuroendocrinology Center, Division of Endocrinology, Pittsburgh, United States; [3]Karolinska University Hospital and Karolinska Institute, Department of Endocrinology and Department of Molecular Medicine and Surgery, Stockholm, Sweden; [4]Novo Nordisk A/S, Epidemiology, Søborg, Denmark; [5]Novo Nordisk Inc, US Medical Affairs – Rare Endocrine Disorders, Plainsboro, United States; [6]Novo Nordisk Health Care AG, Global Medical Affairs – Rare Endocrine Disorders, Zurich, Switzerland; [7]Massachusetts General Hospital, Neuroendocrine Unit, Boston, United States

Introduction
There are limited data on the effectiveness and safety of GHRT in older patients with AGHD. We compared real-world GHRT outcomes in older (aged ≥60 years) vs middle-aged (35–<60 years) adults.
Methods
NordiNet® IOS (NCT00960128) and ANSWER (NCT01009905) were non-interventional studies investigating long-term effectiveness and safety of GHRT with Norditropin® (somatropin, Novo Nordisk). Safety was assessed in the full analysis set (FAS) from both studies (non-GH-naïve patients included). The effectiveness analysis set (EAS) was from NordiNet® IOS only (GH-naïve patients; ANSWER-EAS included patients previously treated for ≤6 months). Serious adverse reactions (SARs) and non-serious adverse reactions (NSARs) with a suspected causal relationship to GHRT, and serious adverse events (SAEs) not considered related to GHRT, are presented as incidence rates per 1000 patient-years and as incidence rate ratios (IRRs) for older vs middle-aged adults.
Results
Baseline characteristics are shown (table). Mean GH exposure was greater in women than men, and in middle-aged than older women (FAS); it increased slightly over time in all groups. Baseline IGF-I SDS was slightly higher in older vs middle-aged women, but not men (EAS). Mean IGF-I SDS increased from below 0 to values ≤1.24 with GHRT. Mean changes in BMI (EAS) and HbA_{1c} (EAS and FAS) were small and similar between age groups in both sexes. No statistically significant differences were observed between older and middle-aged adults regarding incidence rates for NSARs (5.66 vs 5.38; IRR [mean, 95%CI] 1.051 [0.604;1.831]) and SARs (1.00 vs 2.52; IRR 0.396 [0.119;1.324]). As expected, SAE incidence rate (considered unrelated to GHRT) was higher in the older group (16.64 vs 9.04, IRR 1.840 [1.291;2.622]). Similarly, the IRRs of patients ≥75 years ($n=59$) vs the middle-aged group were only significant for SAEs (23.09 vs 9.04; IRR 2.553 [1.113;5.855]).
Conclusion
These data suggest similar clinical outcomes with GHRT in patients with AGHD aged ≥60 compared with 35–<60 years without additional risk of adverse drug reactions in older patients. Baseline characteristics (mean [SD] except for sex).

Table 1

	EAS		FAS	
	35–<60 years ($n=545$)	**≥60 years ($n=214$)**	**35–<60 years ($n=1696$)**	**≥60 years ($n=652$)**
Female, %	45.9	39.3	52.4	43.3
Age, years	48.51 (6.98)	67.16 (4.89)	48.43 (7.05)	67.09 (5.13)
GH dose, mg/day	0.24 (0.16)	0.20 (0.10)	0.32 (0.24)	0.26 (0.18)
IGF-I SDS	−0.94 (1.40)	−0.82 (1.36)	−0.58 (1.53)	−0.27 (1.54)
BMI, kg/m^2	29.29 (6.09)	28.95 (4.58)	30.50 (7.26)	29.42 (5.39)
Duration of follow-up, years	5.37 (4.28)	5.28 (3.92)	5.19 (4.50)	4.65 (3.86)

DOI: 10.1530/endoabs.81.EP673

EP674

Cushing's disease and health-related quality of life: a cure for all dimensions?

Diana Borges Duarte[1], Francisca Puga[1], Isabel Ribeiro[2] & Cláudia Amaral[1]
[1]Centro Hospitalar e Universitário do Porto, Department of Endocrinology, Diabetes and Metabolism, Porto, Portugal; [2]Centro Hospitalar e Universitário do Porto, Department of Neurosurgery, Porto, Portugal
-Diana Borges Duarte and Francisca Puga are joint first authors and contributed equally

Background
As therapeutic options improve for Cushing's disease (CD), most patients can now achieve control or cure of hypercortisolism. However, persistent complaints are often reported. Evaluation of health-related quality of life (HR-QoL) can highlight impairments beyond the stricter clinical aspects. Our aim was to evaluate HR-QoL with a specific focus on mental and emotional health subscales and to compare reported outcomes between patients with cure and persistent hypercortisolism under medical treatment.
Methods
Consecutive CD patients diagnosed between 2006 and 2020, with a minimum follow-up of 1 year, were invited, between June and August 2021, to complete a QoL evaluation. *CushingQoL* questionnaire was employed to assess disease-related quality of life. When analysing specific subscales on the questionnaire, the scores are based on Likert scales with five response categories (1-5 point-scale): the lower the score, the greater impact on HR-QoL. Clinical, anatomopathological and demographic data were retrieved from clinical records.
Results
Thirty-seven patients (86.5% females) agreed to complete the QoL assessment. Mean age at diagnosis was 42.2 ± 14.7 years and median time of onset of hypercortisolism symptoms was 2.0 (interquartile range 1.0-3.0) years. At the time of QoL evaluation, mean age was 48.0 ± 15.4 years and the median follow-up time was 4.1 (2.5-7.7) years. Concerning CD clinical status, 51.4% ($n=19$) were considered cured and 48.6% ($n=18$) had persistent CD (all patients were on medical therapy: n=6 on cabergoline monotherapy, n=4 on ketoconazole monotherapy, n= 3 on metyrapone monotherapy, the remainder in combination therapy). Median *CushingQoL* score was significantly higher in cured CD patients [68.8 (43.8-77.1) % in cured CD patients vs 35.4 (16.7-42.7) % in persistent CD patients, $P=0.002$]. Concerning the specific *CushingQoL* subscales, Mental Health [3.0 (2.0-3.0) points in cured CD patients vs 3.0 (2.0-3.0) points in persistent CD patients, $P=0.73$] and Emotional Health [3.0 (3.0-4.0) points in cured CD patients vs 3.0 (2.0-4.3) points in persistent CD patients, $P=0.98$] scores did not differ from the persistent hypercortisolism status.
Conclusion
In our cohort, clinical cure of CD was associated with higher health-related QoL score. However, equal scores on Mental and Emotional Health subscales were found. Either the impairment of these specific QoL domains persist beyond long-term control of hypercortisolism or medical treatment is associated with a surgical cure-comparable improvement of these domains while not achieving equal QoL scores on *CushingQoL*.

DOI: 10.1530/endoabs.81.EP674

EP675

Association between acromegaly and papillary thyroid cancer: A case series

Andreea Anne-Marie Stefan[1], Dumitriu Roxana Ioana[1, 2], Burcea Iulia-Florentina[1,2], Trifănescu Raluca[1,2], Dan Alexandru Niculescu[1, 2] & Catalina Poiana[1,2]
[1]C.I. Parhon National Institute of Endocrinology, Departament of Pituitary and Neuroendocrine Disorders, Bucureşti, Romania; [2]Carol Davila University of Medicine and Pharmacy, Bucureşti, Romania

Background
Acromegaly is a rare disorder caused by hypersecretion of growth-hormone (GH) and insulin-like growth factor (IGF-1), the underlying lesion being most frequently a pituitary adenoma. This disease is associated with a higher risk of malignancy. We describe the clinical and biochemical particularities in a series of patients with acromegaly and papillary thyroid carcinoma (PTC).
Case study
Out of 311 acromegalic patients, five cases that associated subsequent PTC were included, resulting in a prevalence of 1.6%. Acromegaly diagnosis was sustained by clinical characteristics, hormonal assays and imaging data. The median age at diagnosis was 42 years with only female patients. One patient had GH and prolactin co-secretion. Transsphenoidal intervention was performed, with postoperative tumor remnant in all cases requiring subsequent medical treatment. Two patients also underwent Gamma knife radiosurgery. Following multimodal treatment, one patient was cured and four had controlled disease. Thyroid cancer was diagnosed at a median of 7.5 years after the diagnosis of acromegaly. All

cases presented with the papillary variant. At the time of the cancer diagnosis, 2 out of 5 patients had controlled acromegaly. All five underwent total thyroidectomy and three of them received radioactive iodine. The histopathological analysis revealed four papillary thyroid microcarcinomas (PTMC). One patient had a focus of sclerosing subtype of PTC of over 10 mm, lymph node metastases, and extrathyroidal extension – this patient had co-secretion of prolactin and was the only case with poor oncological outcome. The other patients were cured.

Conclusions

Several studies indicate that a prolonged excess of IGF-1 levels has proliferative and anti-apoptotic effects on follicular thyroid cells, with a prevalence of thyroid cancer in acromegaly of 1.2-10.6% [1]. In our series, all patients were diagnosed with PTC after prolonged and persistent high levels of IGF-1 due to uncontrolled disease. Furthermore, prolactin has a potential tumorigenic role on thyroid follicles [2], the patient with GH and prolactin co-secretion being the one with an aggressive evolution of the PTC. Four patients had PTMC which is acknowledged as a very-low risk neoplasm. In conclusion, although at this point thyroid malignancies are not considered more aggressive in acromegalic patients, periodic thyroid examination is useful in identifying complications in earlier stages.

References

[1] M. Heidarpour et al, "Acromegaly and papillary thyroid carcinoma: A case series," J Res Med Sci, vol. 24, p. 81, 2019.

[2] A. A. Tam et al, "Differentiated thyroid cancer in patients with prolactinoma," Turk J Med Sci, p. 6.

DOI: 10.1530/endoabs.81.EP675

EP676

Idiopathic isolated adrenocorticotropic hormone deficiency

Paraskevi Komzia, Apostolos Gogakos, Fanny Kalograni, Georgios Tsoutsas, Marina Kita & Zoi Efstathiadou

'Hippokration' General Hospital of Thessaloniki, Endocrinology, Thessaloniki, Greece

Introduction

Idiopathic Isolated Adrenocorticotropic hormone (ACTH) deficiency (IIAD) is a rare cause of secondary adrenal insufficiency. It can present with a variety of clinical symptoms, mainly chronic fatigue and euvolemic hyponatraemia, and may coexist with autoimmune disease, most commonly Hashimoto's thyroiditis. Radiographically, an empty sella turcica image can be seen. We present 3 cases of isolated ACTH deficiency.

Case 1

A 47-year-old woman was referred for investigation of adrenal insufficiency due to low morning cortisol levels in a laboratory test performed in the context of investigation of hypertension. Hormone lab tests showed morning Cortisol $<$ 1μg/dl, ACTH 6.8 pg/ml (NL 7-64). The rest of pituitary axes were intact. Tetracosactrin (250μg) stimulation test showed a maximum cortisol response of 8.56μg/dl. Pituitary on imaging was normal. The patient was set on hydrocortisone replacement therapy while continuing to receive her antihypertensive treatment.

Case 2

A 45-year-old man, with no previous history, had an episode of confusion during febrile diarrheal syndrome. During his hospitalization he also presented episodes of hypoglycemia. The initial hormonal test showed very low basal serum cortisol levels (morning $<$0.2μg/dl) and ACTH (1 pg/ml), while in the glucagon test there was no cortisol response (maximum value $=$ 0.2μg/dl). The rest of hypothalamic-pituitary axes were intact. Pituitary imaging test was negative. At the same time, the patient was also diagnosed with autoimmune primary hypothyroidism and treated with thyroxine one week after the initiation of hydrocortisone replacement.

Case 3

A 74-year-old man with hyperthyroidism due to Graves' disease treated with methimazole was hospitalized for fever and hyponatremia (Na $=$ 124). The hormonal tests revealed low levels of cortisol (morning $<$0.7μg/dl) and ACTH (4 pg/ml), as well as thyrotoxicosis [TSH 0.017, FT4 1.74 (FT 0.80-1.28 mg/dl)]. Corticosteroid deficiency was confirmed by a subsequent stimulation test with 250μg tetracosactrin (maximum cortisol response 5.56μg/dl) and a glucagon test (maximum cortisol response 1μg/dl). The rest of pituitary axes were intact and pituitary MRI showed no anatomical damage. The patient was treated with hydrocortisone.

Conclusion

- The diagnosis of IIAD is often missed and becomes apparent after a triggering event such as fever or thyrotoxicosis.
- The presence of hyponatraemia or hypoglycaemia should raise the suspicion of adrenocortical insufficiency
- The etiology of IIAD remains unclear, although the coexistence of autoimmune thyroid disease is common.

DOI: 10.1530/endoabs.81.EP676

EP677

Role of new peptide biomarkers in metabolic profiling of adult growth hormone deficiency patients: preliminary data on neudesin and its relationship with LEAP-2

Edoardo Vergani[1], Carmine Bruno[1], Cesare Gavotti[1], Alessandro Oliva[1], Diego Currò[2] & Antonio Mancini[1]

[1]Fondazione Policlinico Universitario A. Gemelli IRCCS, Catholic University of the Sacred Heart, Department of Medicine and Translational Surgery, Rome, Italy; [2]Catholic University of the Sacred Heart, Department of Safety and Bioethics, Section of Pharmacology, Rome, Italy

Patients affected by adult growth hormone deficiency (aGHD) show worse metabolic profile, with insulin-resistance, increased total cholesterol, LDL, triglycerides, reduced HDL, and higher risk of developing type 2 diabetes mellitus and cardiovascular complications. Adult GHD and metabolic syndrome (MetS) are closely related to each other, since they share the previous depicted clinical features, while obese MetS patients display lower IGF-1 levels due to a functional reduction of GH secretion. Neudesin is a newly discovered peptide mainly secreted in brain and adipose tissue, under evaluation for its possible activity as negative regulator of energy expenditure, as it decreases food intake in mice models. Liver expressed antimicrobial peptide (LEAP)-2 is involved in ghrelin physiological regulation as it acts as a competitive antagonist with slow dissociation from the GSH receptor-1a, blunting the magnitude of ghrelin activities. We have already demonstrated higher LEAP-2 levels and significantly lower ghrelin/lEAP-2 ratio in aGHD. To better characterize the metabolic profile of aGHD patients we performed an observational cross-sectional study testing the hypothesis that neudesin may be affected in this clinical setting. Given the role in energy balance of the two peptides, we also evaluated any eventual relationship between neudesin, LEAP-2 and metabolic and anthropometric parameters. 39 patients were included in the study. Group A: 18 aGHD patients, 7 females and 11 males. Mean $\pm$ SEM age of the group was 59.7 $\pm$ 2.7 years, while BMI was 30.2 $\pm$ 2.2 kg/m^2. Group B: 21 healthy controls (13 females and 8 males). Mean $\pm$ SEM age of the group was 47.1 $\pm$ 2.5 years, while BMI was 24.5 $\pm$ 0.9 kg/m^2. They were evaluated for glucose and insulin, HOMA and QUICKI index, total/lDL/HDL cholesterol, triglycerides, uric acid and IGF-1. Neudesin, LEAP-2 and ghrelin were measured by ELISA, according to manufacturers' protocols. As expected, aGHD patients showed higher HOMA index, triglycerides and lower HDL than controls. Neudesin is significantly higher in aGHD than controls (2.83 $\pm$ 0.37 vs 1.55 $\pm$ 0.12 ng/ml). We confirmed significantly lower ghrelin levels and significantly higher LEAP-2 (5.19 $\pm$ 0.42 vs 3.69 $\pm$ 0.49 nM) in aGHD, leading to lower ghrelin/lEAP-2 ratio. A significant and strong direct correlation between neudesin and LEAP-2 was found both in aGHD ($r^2 = 0.76$) and in all the analyzed population. While LEAP-2 directly correlated significantly with BMI, neudesin did not. These results, although preliminary, may suggest a possible adaptation to a worse metabolic scenario in aGHD. The presence of two distinct pathways related to food intake and the relative scarce knowledge on neudesin suggest future developments in this field.

DOI: 10.1530/endoabs.81.EP677

EP678

Incipient adrenal crisis following ChAdOx1 SARS-CoV-2 vaccination in a patient with undiagnosed isolated adrenocorticotropic hormone deficiency

Yotsapon Thewjitcharoen, Natthakan Saiwaew, Hussamon Prasartkaew, Soontaree Nakasatien & Thep Himathongkam

Theptarin Hospital, Diabetes and Thyroid Center, BANGKOK, Thailand

Background

Isolated adrenocorticotropic hormone (ACTH) deficiency is a rare entity defined by secondary adrenal insufficiency and normal secretion of all other pituitary hormones. Delays in adrenal insufficiency (AI) diagnosis frequently encounter

among older patients because of non-specific symptoms. The occurrences of actual or incipient adrenal crises following coronavirus disease 2019 (COVID-19) vaccine administration are increasingly reported over the last year after vaccine rollout program. Here, we present an interesting case of incipient adrenal crisis following ChAdOx1 SARS-CoV-2 vaccination in a patient with undiagnosed isolated ACTH deficiency.
Clinical case
A 73-year-old Thai woman with underlying uncontrolled type 2 diabetes mellitus and unclear etiology of AI presented with a 2-week history of general malaise, dizziness, nausea, and weight loss of 4 kilograms following the first dose of AstraZeneca (ChAdOx1 SARS-CoV-2) vaccination. She had a past history of AI diagnosed at age of 52 from the previous hospital and had taken prednisolone 2.5 mg per day thereafter. Patient denied history of postpartum hemorrhage and was able to lactate after pregnancy and never had serious traumatic head injury. She also denied the use of other exogenous glucocorticoids and other medications except her current prescribed oral prednisolone. When seen in our hospital 2 weeks after immunization, physical examination and vital signs were unremarkable. Re-evalutation of AI after prednisolone discontinuation for 3 days was performed with the standard 250-microgram ACTH stimulation test. The diagnosis of secondary AI was confirmed. Brain MRI showed normal pituitary gland and evaluation of other anterior pituitary hormones revealed normal results. Isolated ACTH deficiency was diagnosed and the patient had been instructed to increase the dose of prednisolone to 15 mg per day. Insulin treatment was also up-titrated to tightly control glycemic control. Her symptoms considerably improved over a week and backed to the usual weight over a few months. With increasing the dose of prednisolone on the day of vaccination, the patient was uneventful following the second dose of AstraZeneca vaccination.
Conclusions
Late-onset isolated ACTH deficiency is a rare entity but has emerged as a cause of AI. Healthcare professionals should be vigilant about the possible diagnosis or worsening of AI especially in elderly patients who receive COVID-19 vaccine administration. Ongoing educations of sick day management should be emphasized in all AI patients.

DOI: 10.1530/endoabs.81.EP678

EP679

ACTH-GH pituitary adenoma in an adolescent: a Case Report

Sahar Abidi, Grira Wafa, Nadia Khessairi, Ibtissem Oueslati, Meriem Yazidi, Fatma Chaker & Melika Chihaoui
RABTA Hospital – Endocrinology Department, Tunis, Tunisia

Plurihormonal pituitary adenomas represent 10-15% of all functioning pituitary adenomas. Functioning ACTH-GH pituitary adenomas constitute an extremely rare entity. Most patients present a clinically manifested acromegaly and subclinical Cushing's disease. We present the case of a 14 years old female who referred to the endocrinology department for inaugural diabetic ketosis. She had a six-month history of amenorrhea and headaches. On examination, she had facial dysmporphia suggestive of acromegaly. Weight was 93 kg, height was 1.77 m . The body mass index was 29,3 kg/m^2. Blood pressure was normal; she had purple abdominal stretch marks. Polysomnography revealed a mild sleep apnea. The hormonal assessment confirmed acromegaly by a nadir of GH of 39 mUI/l in glucose tolerance test. A none suppressive cortisol secretion of 8.9 mg/dl and a high ACTH of 29.14 ng/l. Thyrotropic and lactotropic axis were normal, The gonadotropic axis was deficient. MRI showed a macroadenoma of 18*14*20 mm that extends into the cavernous sinus and compresses the optic chiasm. The patient received basal-bolus insulin therapy. She underwent transsphenoidal surgery. Postoperatively presented with clinical and biochemical adrenal insufficiency and had a transient insipidus diabetes. The MRI documented an empty sella. At a one-year follow-up she was clinically well with no clinical or radiological evidence of pituitary tumor recurrence. She remained on replacement hydrocortisone and necessitated low doses of insulin for her diabetes. ACTH-GH plurihormonal pituitary adenomas are a rare entity. This is a case that illustrates an ACTH-GH pituitary adenoma revealed by diabetic ketosis in an adolescent.

DOI: 10.1530/endoabs.81.EP679

EP680

Pituitary adenoma associated with intracavernous meningioma: Case report

Aicha Lachkhem[1], Abdelkader Yahi[2], Haffaf Lounes[1], Benabdelatif Katia[1], Ahcen Staifi[3], Hakim Derradji[4], Elmountassir Ourrad[5] & Ould Kablia Samia[1]
[1]Central Army Hospital, Endocrinology, Algeria; [2]Central Army Hospital, Endocrinology, Algiers, Algeria; [3]Central Hospital Army, Ophtalmology, Algeria; [4]Central Hospital Army, Neurosurgery, Algeria; [5]Central Army Hospital, Radiology, Algeria

Introduction
Pituitary adenoma and meningioma are the most benign tumors in the central nervous system (meningioma 35,9%, pituitary tumor: 15,5%). Pituitary adenoma associated with meningioma without a history of radiotherapy is extremely rare.
Case
A 70 years old man operated for post-traumatic subdural hematoma in whom the brain MRI (magnetic resonance imaging) had also shown a macroadenoma, completed with an MRI of the sellar region which were confirmed in the coronal section in T1 weighted image, an iso-intense adenoma taking up gadolinium poorly measuring 16 x 8,5 mm. This adenoma is associated with a right intra-cavernous lesion measuring 11,8 x 8,8 mm presenting intimate contact with the intravenous portion of the internal carotid artery, iso-intense in T1 weighted images and hyper-intense in T2 weighted images which is intensely and homogenously enhanced after injection of gadolinium salts, corresponding to meningioma. Hormonal work-up revealed a serum prolactin level of 1300 ng/ml and a central hypothyroidism. The patient was then started on dopamine agonist (cabergoline 03 mg/week). The response to treatment was excellent, on his MRI follow-up one year after, the adenoma has disappread leaving an arachnoidocele while the meningioma has remained stable. The patient is being followed by Endocrinolgy and Neurosurgery.
Conclusion
The association of meningiomas and pituitary tumors is very rare. If patients who have under- gone previous radiation therapy are excluded from consideration, the presence of these two types of tumors in the same patient becomes even rarer. To our knowledge, the association of an intracavernous meningioma and a prolactinoma in a patient without previous radiation therapy had never been reported.

DOI: 10.1530/endoabs.81.EP680

EP681

Severe hyponatremia after coronary angiogram - the link between ischemic cardiac disease and hypopituitarism

Cristina Ene[1], Angelica Nour-Dinca[2], Dorin Bica[3] & Mihaly Enyedi[4]
[1,2]'Dr Victor Babes' Foundation, Endocrinology, Bucharest, Romania; [2]'Dr Victor Babes' Foundation, Cardiology, Bucharest, Romania; [3]Neurohope, Neurosurgery, Bucharest, Romania; [4]'Dr Victor Babes' Foundation, Radiology, Bucharest, Romania

Background
Hyponatremia in not uncommon in elderly. Common causes include medication, heart, kidney and liver diseases, digestive loses, syndrome of inappropriate anti-diuretic hormone. Hormonal imbalances are sometimes overlooked. Sudden onset after a recently invasive procedure could challenge the diagnostic.
Methods
We present a case report of a severe hyponatremia diagnosed after a coronary angiogram. It is a rare case of hypopituitarism secondary to a pituitary macroadenoma.
Case reports
The patient is a 69 years old man that presented in December 2019 in cardiology department for a coronary angiogram. 48 h after angiography the patient was admitted in ICU for severe hyponatremia and rhabdomyolysis – interpreted at the time as side effect to the contrast agent. At that moment he had normal TSH (T4 or T3 were not analysed) and SIADH was infirmed. The adrenal insufficiency was not rule out. Progressively, in the next 6 month the patient presented asthenic syndrome and significant weight loss, which is why he came to our clinic for second opinion. He had a cardiological check-up and an endocrinological exam. The biological evaluation reveals mild hyponatremia, still elevated creatine kinase and also mild anemia. The hormonal profile established the panhypopituitarism and we started substitutive treatment, with rapidly normalisation of biological disturbance. The MRI exam revealed a pituitary macroadenoma, with of the optic chiasm compression, confirmed by visual field.

The patient needed to repeat coronary angiogram for unstable angina and revealed multiple coronary stenosis and 3 active stents were fitted. This time the procedure was performed after Cortisone dose supplementation, without electrolyte imbalance. Considering double antiplatelet therapy after coronary stenting and cardiac risk, the surgical treatment of macroadenoma was scheduled after 6 months, with closely ophthalmologic follow. Transsphenoidal hypophysectomy was successfully performed, and immunohistochemistry diagnosed a non-functional adenoma.
Conclusion
Hormonal imbalance should be suspected in a sudden-onset of life-threatening hyponatremia. Hypopituitarism is a rare cause of hyponatremia and in this case was overlooked, TSH value being normal, without initial testing of T4 and cortisol value. The acute illness and the iodine agent used for angiography revealed long-term hypocortisolemia. A noncardiac surgery could be very challenging in a recently stented patient, due to the risk of bleeding secondary to antiplatelet therapy and treatment discontinuation may lead to perioperative thrombotic cardiac events. In this case the multidisciplinary team was essential for ensuring an excellent outcome.

DOI: 10.1530/endoabs.81.EP681

EP682

A 29 year old woman with aggressive acromegaly as a single manifestation of multiple endocrine neoplasia type 1

María Dolores Moure[1,†,1], Gregorio Catalán[2], Iñigo Pomposo[2], Miren Badiola[1], Iker Miret[1], Luis Castaño[3] & Sonia Gaztambide[1]
[1]Cruces University Hospital, Endocrinology and Nutrition, Bilbao, Spain; [2]Cruces University Hospital, Neurosurgery, Bilbao, Spain; [3]Biocruces, Bilbao, Spain

Introduction
Parathyroid tumors are the most common (90%) and usually the first manifestation feature of *MEN1* syndrome. The occurrence of anterior pituitary tumors in *MEN1* syndrome may range between 10% and 60%. Pituitary involvement includes the initial manifestation of *MEN1* syndrome in 10% to 25% of individuals and usually show more aggressive behavior; 20% secrete prolactin, fewer than 10% secrete GH, 5% secrete ACTH, and the remainder appear to be nonfunctioning.
Objective
Description of a 29-year-old female diagnosed of aggressive acromegaly as single manifestation of MEN1 syndrome.
Case
The patient was referred to endocrinology due to oligomenorrea. Elevated prolactin 69 (3-30 ng/ml) and IGF1 854 ng/ml (117-329) were detected. GH after oral glucose tolerance test (OGTT) (12 ng/ml) confirmed the acromegaly. Magnetic resonance showed a 7.5 x 6 x 8 mm adenoma without cavernous sinus invasion. Transsphenoidal surgery was performed. Histopathological exam described an atypical adenoma with Ki 9% and GH positivity. After surgery, the patient became pregnant and the evaluation of the disease was carried out after delivery. A 3 mm tumor rest was observed. IGF 1 levels 399 ng/ml (71-234) and GH after OGTT (1.2 ng/ml) indicated persistent acromegaly. In a second intervention the rest can not be removed and Octreotide Lar (20 mg/month) was initiated. Despite the increase in medical therapy, IGF 1 remained elevated and the patient was referred to Radiation oncology. *MEN 1* (c.512G > A;p.Arg171Gln) and *SDHD* (c149A>G; p.His50Arg) heterozygous mutations were detected. Calcium metabolism exam and radiological screening were normal. Fathers patient carried the same mutation in both genes (*MEN 1 and SDHD*). He referred a single episode of nephritic colic and myocardial infarction at the age of 38. Calcio and PTH were normal. Radiological image showed a 1 cm nonfunctioning pancreatic mass. No other first-degree relatives showed mutations.
Conclusions
An aggressive acromegaly could be the first manifestation of a MEN1 syndrome.

DOI: 10.1530/endoabs.81.EP682

EP683

Pituitary Coma? Discordant pituitary biochemistry after consumption of a commercially available 'Sleep Activator'.

Benjamin Phillips & Mohit Kumar
Wrightington, Wigan & Leigh NHS Foundation Trust, Department of Endocrinology and Diabetes Mellitus, Wigan, United Kingdom

We present a case of discordant pituitary biochemistry which resolved after discontinuing a commercially available combination vitamin supplement. A 35 year-old man presented following an episode of headache and dizziness, preceding collapse and possible seizure activity. Investigations revealed deranged pituitary function: TSH 0.02 mU/l (0.35-5.50), fT4 3.6 pmol/l (10.0-20.0), 9 am cortisol 18 nmol/l (200-500), testosterone >52 nmol/l (8.4-28.7), FSH <0.3 U/l (1.0-18.0), LH <0.1 U/l (2.0-9.0), oestradiol 611 pmol/l (0-146), prolactin 452 mU/l (45-375) IGF-1 207 ng/ml (71.0-234.0). He reported weight gain, low mood, sweats, and reduced libido. 7 months prior he had sustained a head injury from a concrete block. He was commenced on hydrocortisone and levothyroxine. MRI found normal pituitary gland and surrounding structures. On further questioning at follow-up he admitted taking a combined nutritional supplement called 'Kodiak Coma'. Based on clinical suspicion that the supplement was contributing to the derangement in pituitary function tests the patient was asked to stop taking it. Subsequent pituitary function tests returned to normal, with normal short synacthen test (0 min 249, 30 min 659 nmol/l). He was able to discontinue hydrocortisone and remained well. He continued to take levothyroxine replacement for primary hypothyroidism. None of the listed ingredients in 'Kodiak Coma' are known to affect pituitary function or related hormonal axes and the discordant biochemical picture did not correlate to this patient's clinical presentation. Rather we hypothesise that a component or components of the supplement caused assay interference. Biotin is commonly included in nutritional supplement preparations; it is well known to interfere with certain assays of thyroid function, and rarely has been reported to interfere with other pituitary hormone assays. However, a different pattern of interference would have been expected if biotin was the culprit. The manufacturer of Kodiak Coma was contacted for information about its ingredients, but no reply was forthcoming. Nutritional supplements are often marketed towards individuals with no underlying deficiency, illness, or disease. Such products are readily available in high street shops and online. However, it is well documented that active ingredients in products of this kind can lead to negative health outcomes, either by drug interaction, by unintended effect upon clinical investigations, or by a direct effect to cause disease. This patient was subjected to a 4-day hospital admission, medical therapy, and several months of clinical and biochemical follow-up as a result. This case illustrates the unintended risks of nutritional supplements and highlights a potential cause for discordant pituitary biochemistry.

DOI: 10.1530/endoabs.81.EP683

EP684

Two case: hemorrhagic rathke cleft cysts mimicking a hemorrhagic adenoma

H. Sebile Dokmetas[1], Ayberk Bayramgil[2], Meriç Dökmetaş[2], Fatih Kılıçlı[1], Güneş Dorukhan Çavuşoğlu[2], Kü bra Karaipek[2] & Ayşe Gül Yildirim Kizilkaya[2]
[1]Medipol Mega University Hospital, Endocrinology; [2]Medipol Mega University Hospital, Internal Medicine, İstanbul, Turkey

Introduction
Rathke Cleft Cysts(RCCs) are benign cysts arising from the remnants of Rathke's pouch. The most common symptoms are visual field disorders, headache, and pituitary dysfunction.
Case 1
A 26-year-old male was admitted with headache that started 4 days ago. Cranial MRI revealed an appearance mimicking a hemorrhagic adenoma in pituitary. Pituitary hormones were found as normally. Pituitary MRI showed a 12 x 10 x 10 mm hemorrhagic RCCs located in the midline. The patient's headache disappeared spontaneously within 3 days without the use of any medication. One month and six months later, MRI showed a progressive shrinkage of hemorrhagic RCCs diameters as 4.5 x 5 x 7.5 mm and 3 mm, respectively. In the pituitary MRI taken at the last follow-up 15 months later, it was observed that sequelae remained as a millimetric-thick slit-shaped microcyst in the central gland.

Case 2
A 24-year-old female was admitted with a complaint of headache that started one month ago. The patient, who had a throbbing headache on the right side of her head, was relieved with analgesics. Pituitary MRI revealed a hemorrhagic RCCs with diffusely expanding pituitary gland with a size of 18 x 13 x 8 mm and leveling inside. The patient's pituitary hormones were checked and no pathological values were found. In the control pituitary MRI one month later, the size of the hemorrhagic RCCs decreased to 8 x 13 x 8 mm.
Conclusion
Patients with hemorrhagic RCCs whose symptoms decreased during close follow-ups and who did not have hormonal disorders were not operated on. The sizes of the masses of the patients who did not develop any complaints or hormonal disorders during their follow-ups decreased.
Key words: Hemorrhagic Rathke Cleft Cysts; Hemorrhagic Adenoma

DOI: 10.1530/endoabs.81.EP684

EP685

Ectopic Neurohypophysis
Hatice Sebile Dökmetaş[1], Güneş Dorukhan Çavuşoğlu[2], Meriç Dökmetaş[2], Fatih Kılıçlı[1], Ayberk Bayramgil[2] & Kübra Karaipek[2]
[1]Medipol Mega University Hospital, Endocrinology, Istanbul, Turkey; [2]Medipol Mega University Hospital, Internal Medicine, Istanbul, Turkey

Introduction
Ectopic neurohypophysis is a congenital abnormality related to faulty embryogenesis resulting in incomplete caudal extension of the infundibulum**.** It may present itself with symptoms of growth hormone deficiency or panhypopituitarism and patients require replacement treatment for panhypopituitarism.
Case Presentation
Our female patient was shorter (138 cm) than her peers and did not menstruate at the age of 19 when she first applied to our hospital with this complaint. Her tests were found to be compatible with panhypopituitarism. Her bone age was found to be 15. On pelvic USG, uterus and ovaries were hypoplasic/atrophic. Breast development: Tanner 1-2. Pituitary MRI revealed total loss of stalk and ectopic neurohypophysis. With the diagnosis of pituitary insufficiency, she took prednisone, levothyroxine and growth hormone for 5 years. Oral contraceptive was not started and final height increase was awaited. Her height increased from 138 cm to 165 cm. Oral contraceptive was added later. After two years, breast development and menstrual order were established and significant improvement was seen in bone mineral density.
Conclusion
Ectopic neurohypophysis might show itself with hypopituitarism like in our patient. Replacement of missing hormones is generally required. If the bone age is lower than the chronological age, it was possible to achieve sufficient height growth with GH treatment before starting oral contraceptives.
Key words: Ectopic neurohypophysis, panhypopituitarism, Replacement treatment

DOI: 10.1530/endoabs.81.EP685

EP686

Case report: pituitary macroadenoma with thyroid stimulating hormone (TSH) and growth hormone (GH) co-secretion
Chin Voon Tong, Yen Nee Low, Eng Hui Ooi & Azliana binti Alias
Melaka Hospital, Medicine, BANDAR MELAKA, Malaysia

Introduction
The prevalence of pituitary adenoma is estimated to be 17% and about half secrete a distinct hormone. Prolactin secretion is the commonest, followed by GH or adrenocorticotropic hormone (ACTH). TSH producing pituitary adenoma is rare and occurs in less than 1% of pituitary adenomas. We report a challenging case of a 30-year-old man who presented with TSH and GH secreting pituitary macroadenoma with mass effect.
Case Report
A 30-year-old man presented with typical symptoms of thyrotoxicosis (palpitation, tremor and weight loss of 20 kg) over four months associated with headache. There were no symptoms suggestive of GH excess or hypogonadism. On examination, he was normotensive. He had a small goitre and fine tremor. He was started on Carbimazole and propranolol by his primary care doctor and referred to the Endocrine Clinic for discordant thyroid function. His Free Thyroxine (Free T4) was elevated at 69.6 pmol/l (11.5-22.7) with a normal TSH of 4.06 mIU/l (0.55-4.78). This was confirmed with sample sent to a second laboratory. A high alpha subunit of 12 ng/ml ($\leq$0.5) and absent TSH response to Thyrotropin Releasing Hormone (TRH) stimulation test support the diagnosis of TSH secreting tumour. Other anterior hormones were assessed and showed elevated Insulin Growth Factor -1 (IGF-1) of 401.8 ng/ml (74-258) and prolactin, 1167.6 mIU/l (45-375). Oral glucose tolerance test confirmed GH excess. Testosterone level was 2.5 nmol/l (5.72-026.14) with Follicle stimulating (FSH) 7.3 IU/l (1.4-18.1) and Luteinizing Hormone (LH) 3.6 IU/l (1.5-9.3). ACTH level was 1.8 pmol/l (1.8-13.9) and there was appropriate adrenal response to tetracosactrin test. Magnetic Resonance Imaging (MRI) showed a sellar-suprasellar mass measuring 3.8 x 3.3 x 3.5 cm which displaced the optic chiasm and compressed it antero-superiorly. Pituitary stalk was not visualized. Therefore, the elevated prolactin was attributed to stalk effect. Visual field assessment showed bitemporal hemianopia. In preparation for surgery, he was given Carbimazole, Propanolol and Lugol's iodine. Pre surgery Free T4 was 20.98 pmol/l, TSH 21.04 mIU/l and GH 4.29 ng/ml ($<$2.47). He underwent Endoscopic Transsphenoidal Surgery with tumour excision successfully. Free T4 post-surgery was 20.66 pmol/l with normalization of TSH at 2.2 mIU/l and GH at 1.26 ng/ml. Preliminary histopathology examination revealed features of pituitary adenoma.
Conclusion
We present here, a rare case of pituitary macroadenoma with TSH and GH co-secretion. This case illustrates the importance of careful evaluation of discordant thyroid function test and the following pre-surgery management of such cases.

DOI: 10.1530/endoabs.81.EP686

EP687

Primary Empty Sella Syndrome revealed by a growth retardation : about 14 cases
Khadra Faraoun & Mohammedi Fatiha
Oran University Hospital, Endocrinology, Oran, Algeria

Background
Empty sella turcica (EST) is characterized by the passage of cerebrospinal fluid (CSF) into the sella turcica through the sellar diaphragm. The aim of our work is to study the clinical and hormonal characteristics of patients with EST discovered due to height delay.
Patients and methods
Descriptive study on 14 patient files. Data studied : history, anthropometry, endocrine deficits and associated pathologies.
Results/Discussion
6 boys, 8 girls; average age at first consultation: 8.2 years (range: 2 and 15 years); main reason for consultation: height delay (HD). No cases of fetal distress, neonatal hypoglycemia, peri natal trauma, pituitary surgery or radiotherapy. 5 cases of intrauterine growth retardation, 1 case of mental retardation, 5 cases of celiac disease, 2 cases of autoimmune hypothyroidism. HD on average at -3.8 SD (range: -6 and -2 SD), average weight deficit at -2.8 SD (range: -4.5 and - 2 SD); 1 case of total anterior pituitary insufficiency, 6 cases of dissociated anterior pituitary insufficiency; Partial GH deficiency in 4 cases and complete in 10 cases. 2 cases of partially empty sella turcica and 12 cases of EST. 10 children substituted for the different deficits. One child referred for Neurosurgery for hydrocephalus. There is a delay in the diagnosis of stature delay. Primary EST does not preferentially affect one sex, the congenital origin is most likely. Lifelong monitoring is necessary in order to detect possible endocrine, neurological and ophthalmological complications.

DOI: 10.1530/endoabs.81.EP687

EP688

Rupture of the pituitary stalk : clinical, para-clinical and evolutionary aspects of 9 patients followed in the Endocrinology department, Oran University Hospital.
Khadra Faraoun[1] & Mohammedi Fatiha[2]
[1]Oran University Hospital, Endocrinology, Oran, Algeria

Background
The non-traumatic pituitary stalk interruption syndrome described after the advent of MRI is a congenital pituitary abnormality, often responsible for

pituitary insufficiency revealed during the neonatal period. We note 9 cases of late diagnostic during the exploration of growth retardation.
Patients and methods
Descriptive cross-sectional study on files of 9 patients, 5 boys and 4 girls with an average age of 10.5 years (range 3 and 18 years). The diagnosis was made by MRI, the deficit in GH was sought by 2 stimulation tests: insulin hypoglycemia and glucagon test.
Results
Circumstances of discovery : growth retardation including one case with primary amenorrhea. All patients had a severe delay in height of -4DS to -2DS. All 5 boys had a micropenis. On MRI: 4 cases of pituitary stem interruption with ectopia of the post pituitary and pituitary hypoplasia, 3 cases with ectopia of the post pituitary, 1 case with hypoplasia and 1 case of pituitary stem interruption only. Familial history : 3 cases of consanguinity, 2 cases of hydrocephalus and cleft palate and 1 case of trisomy 21 in the siblings. Personal history : 1 case of fetal distress, 3 cases of celiac disease, 1 case of congenital primary hypothyroidism, 1 case of mental retardation. The somatotropic deficit is complete in all patients, gonadal deficit in all patients of puberty, 5 cases of thyrotropic deficit, 3 corticotropic deficits, the latter 2 appearing 1 to 6 years after the diagnosis of the somatotropic deficit. The outcome was favorable with a significant gain in height in children replaced early by growth hormone, the current height delay is at -2DS. The other deficits were replaced as and when they appeared.
Discussion
The presence of midline abnormality in the family and association with malformation syndromes reinforces the genetic origin. Growth retardation may indicate pituitary stem disruption syndrome; this form of late revelation should no longer be underestimated.

DOI: 10.1530/endoabs.81.EP688

EP689

Hypopituitarism caused by intravascular large B cell lymphoma (IVLBCL)

Natia Vashakmadze[1,2]
[1]Israeli-Georgian Medical Research Centre 'Helthycore', Department of Endocrinology, Tbilisi, Georgia; [2]David Tvildiani Medical University, Department of Biochemistry and Molecular Biology, Tbilisi, Georgia

Intravascular Large B-Cell lymphoma (IVLBCL) is an extremely rare type of non-Hodgkin lymphoma involving the growth of lymphoma cells within the vessel lumen without lymphadenopathy. As disease has various modes of presentation and is exceptionally rare, IVLBCL is often diagnosed postmortem. Herein, we report a case of IVLBCL with hypopituitarism, an extremely rare complication, that was successfully treated with chemotherapy. 60 years old woman noticed redness of the abdomen, fatigue, and fever. As she was diagnosed with recurrent erysipelas in the past, it was considered as recurrence of the known infection. Despite antibiotics, disease progressed, redness involved whole abdomen and thighs, fever worsened and swelling of the face and limbs as well as tingling and numbness of the lower extremities, difficulty to walk and acute kidney failure has developed. It was clear that patient did not have an ordinary infection but something else. During next few weeks patient developed severe anasarca (+20 liter), general fatigue, telangiectasis of the trunk, severe polyneuropathy, weight loss and marked panniculitis, she was unable to eat or move independently, mental changes were also notable. As all the possible causes (infections, systemic diseases, etc) were excluded, deep skin biopsy was performed from the abdominal part of the body and IVLBCL was diagnosed. IVLBCL can cause damage of virtually any organ, including endocrine glands, as patient had severe fatigue, anasarca, weight loss and mental changes, pituitary function was carefully evaluated. She was found to have hypopituitarism with central hypothyroidism, central hypogonadism, central adrenal insufficiency, and hyperprolactinemia. IGF-1 was not measured due to technical issues. Brain MRI with contrast showed no tumor or mass in the seller region. It was unclear hypopituitarism was due to intravascular spread of the lymphoma cells in hypophysial portal system and microvascular damage of the pituitary cells, or due to disease severity per se, that is sometimes accompanied with idiopathic hypopituitarism. Patient was started on replacement of hydrocortisone first and only after that levothyroxine was added to treatment regimen. Whole body CT/MRI showed no MTS or lymphadenopathy at all. Chemotherapy with R-CHOP scheme was started with dramatic improvement of patient's clinical and laboratory parameters. Hypopituitarism was resolved after 3 months. After 8 course of chemotherapy patient progressed with new skin nodules all over the body, however before starting the second line Chemotherapy, patient started to go into spontaneous remission, nodules disappeared without any treatment at all and she is in remission until now.

DOI: 10.1530/endoabs.81.EP689

EP690

Complete remision of nelsońs syndrome with cabergoline treatment

Nerea Egaña Zunzunegui, Cristina Elias Ortega, Inmaculada Venegas Nebreda, Ane Amilibia Achucarro, Ismene Bilbao Garay, Maite Aramburu Calafell, Cristina García Delgado & Alfredo Yoldi Arrieta Donostia Unibertsitate Ospitalea, Donostia, Spain

Introduction
Nelsońs Syndrome is defined as the presence of an enlarging pituitary tumor associated with elevated fasting plasma ACTH levels and hyperpigmentation in patients submitted to bilateral adrenalectomy for the treatment of Cushińgs disease.
Case Report
We present a case of a 48 y/o woman who in 2015, was diagnosed of Cushing's disease and underwent transsphenoidal adenomectomy but remission was not achieved, so the patient was then treated with ketoconazole. However, after a 2-month period bilateral adrenalectomy was performed due to persistent hypercortisolism, and the development of severe hepatitis and simultaneously she was referred to radiotherapy. Subsequently, few months after adrenalectomy, the patient developed Nelson's syndrome with intense skin hyperpigmentation, headaches, and elevated ACTH levels (> 1000 pg/ml). The magnetic resonance imaging demonstrated slight increase in size of adenoma. The patient was initially treated with cabergoline (1 mg/week) observing only a short and transient decline of ACTH so the dose was adjusted. After increasing dose of cabergoline (2 mg/week) ACTH levels decreased and the headaches and hyperpigmentation improved significantly. Four years later, plasma ACTH levels were normalized (33 pg/ml) and MRI showed the disappearance of the pituitary adenoma. In order to investigate on the direct effect played by cabergoline treatment on the remission of Nelson's syndrome, the treatment was withdrawn. ACTH levels are normalized (50 pg/ml) since nowadays.
Discussion
This case demonstrated that cabergoline treatment is able to induce the remission of Nelson's syndrome and may be a valid therapeutic alternative in this syndrome. The peculiar expression pattern of D2 receptors in some non functional and corticotroph tumors could explain the favorable clinical response to cabergoline in the setting.

DOI: 10.1530/endoabs.81.EP690

EP691

Genomic and epigenomic aspects of Aspirin antitumoral effect in pituitary adenoma

Borbála Szabó[1], Lilla Krokker[1], Katalin Mészáros[2], Éva Saskői[3], Krisztina Németh[4], Pál Szabó[4], Nikolette Szücs[5], Sándor Czirják[6], Attila Patócs[2] & Henriett Butz[1,2,3]
[1]Semmelweis University, Budapest, Hungary, Department of Laboratory Medicine,, Budapest, Hungary; [2]Hungarian Academy of Sciences - Semmelweis University, Hereditary Tumours Research Group, Budapest, Hungary; [3]National Institute of Oncology, Department of Molecular Genetics, Budapest, Hungary; [4]Research Centre for Natural Sciences, Hungarian Academy of Sciences, MS Metabolomics Laboratory, Budapest, Hungary; [5]Faculty of Medicine, Semmelweis University, Department of Endocrinology, Internal Medicine and Oncology, Budapest, Hungary; [6]National Institute of Clinical Neurosciences, Budapest, Hungary

Background
In our previous works the interdependence of DNA demethylation with proliferation and differentiation of pituitary neuroendocrine tumours (PitNET) and the inhibitory effect of Aspirin on pituitary cell proliferation were demonstrated. Although the role of Aspirin in epigenetic regulation was

described in other malignancies, its correlation with pituitary tumorigenesis is currently unknown.
Our objective
was to investigate the genomic and epigenomic effects of Aspirin in PitNET.
Materials and Methods
DNA methylome by HPLC-MS/MS, and whole transcriptome profile were evaluated by next-generation sequencing in RC4-B/C and GH3 pituitary cell lines upon Aspirin treatment. Effects of Aspirin and demethylation agent, decitabine were further tested *in vitro* by RT-qPCR, western blot and functional (proliferation, viability, migration, luciferase promoter reporter) assays. DNA methylome was also correlated with *PTTG1* expression in 41 human PitNET samples. Gene and protein expression data of 77 PitNET with 35 control samples were obtained from Gene Expression Omnibus and literature mining.
Results
Aspirin induced global DNA demethylation and consequential transcriptome changes *in vitro* including decreased global histone expression. Overexpression of *Tet* enzymes and their cofactor *Uhrf2* was identified behind the increase of 5-hydroxymethylcytosine (5 hmC). Transcription factor regulatory relationships assessed by gene set enrichment analysis showed that Aspirin increased p53 and decreased E2f1 activities. The increased p53 activity was due to its acetylation at the K382 residue. Among p53 controlled genes, *Pttg1* was also identified as downregulated upon Aspirin treatment. Aspirin reduced the expression of *Pttg1* together with its interacting partners by inhibiting *Pttg1* promoter activity. 5 hmC positively correlated with *Tet1-3* and *Tp53* expression, and negatively correlated with *Pttg1* expression that was also reinforced by the effect of decitabine on *Pttg1* expression. Both transcriptome data and *in vitro* assays proved that Aspirin inhibited the cell viability, cell proliferation and migration. Additionally, high overlap (20.15%) was found between Aspirin regulated genes and dysregulated genes in PitNET tissue samples. The 757 common genes were implicated mostly in cell proliferation, cell cycle – including p53 activity and function –, while cellular migration and genome stability were also detected.
Conclusion
We described a regulatory network where Aspirin regulated global demethylation, *Tp53* activity and *Pttg1* expression in pituitary cells along with decreased cell proliferation and migration. These data may suggest the potential beneficial effect of Aspirin in PitNET.
Funding
NKFI FK135065; Bolyai Research Fellowship of the Hungarian Academy of Sciences; TKP2021-EGA-44

DOI: 10.1530/endoabs.81.EP691

EP692

Soluble alpha klotho in blood is a new and highly stable biomarker

Junia Ribeiro de Oliveira Longo Schweizer, Michael Haenelt, Katharina Schilbach, Sylvere Störmann, Jochen Schopohl & Martin Bidlingmaier
LMU Klinikum; Med. Klinik und Poliklinik IV/Endokrinologie, Munich, Germany

Background
Soluble alpha klotho (sαKL) is a circulating protein that has been linked to the growth hormone (GH) axis. We previously showed its association to disease activity in patients with acromegaly, with considerable robustness towards biological confounders. However, there is scarce data in literature regarding the analytical performance of the assay, and pre-analytical stability of sαKL in blood samples.
Objective
We aimed to evaluate analytical performance and pre-analytical stability of sαKL in blood samples, following the guidelines from the Clinical & Laboratory Standards Institute.
Methods
SαKL concentrations were measured by an ELISA (Immuno-Biological Laboratories, Hamburg, Germany). We compared different incubation times (1 h vs. overnight), analyzed precision by 10 repeated measurements within a plate and linearity by serial dilutions (no dilution, 1:2, 1:4, 1:8 and 1:16). We also tested stability of sαKL under different storage conditions: 1) room temperature before (whole blood, 1, 24, 48 or 120 h) or after centrifugation (serum, 15 min, 24, 48 or 72 h); 2) freeze/thaw cycles (0-4 cycles); 3) long-term storage at -20°C (baseline compared to 20 and 31 months). Finally, we compared sαKL concentrations in serum and EDTA samples collected in parallel from the same individuals ($n=18$).
Results
Short incubation times were associated with a significant drift of concentrations obtained over the plate (>25%), an effect not seen after extending the first incubation to overnight (<5%). sαKL measurements by this assay presented with low intra- and inter-assay coefficients of variation (%CV) (<10% for both). Dilution linearity was good at concentrations below 3,000 pg/ml (recovery rate (RR) (%mean (range)): 96 (92-107). Measured sαKL concentrations were not significantly affected by storage for up to 120 hours at room temperature (CV (%mean (range)) (whole blood, before centrifugation: 2.9 (1.5-5.1) or serum, after centrifugation: 8.9 (1.8-18.9)), or by up to 4 freeze/thaw cycles (CV: 4.9 (1.4-10.1), RR: 99.1 (87.3-105.8)). Serum sαKL also exhibits excellent long-term storage stability for more than 2 years at -20°C (CV: 8.6 (2.7-17.5), RR: 89.1 (76.5-111.7)). Furthermore, sαKL concentrations (pg/ml) (median (interquartile range) in serum did not differ from those seen in EDTA (404.4 (341.8-462.6) vs. 428.6 (384.8-514.8), $P=0.27$).
Conclusion
After extending incubation times to overnight, the sαKL assay exhibits good performance characteristics. We suggest to dilute samples at least 1:4, especially in patients with GH excess. sαKL is a biomarker with considerable preanalytical stability at different storage conditions. This facilitates its use as a GH responsive biomarker in studies and clinical practice.

DOI: 10.1530/endoabs.81.EP692

EP693

Influence of Desmopressin treatment in patients undergoing surgery for cushing's disease

Paloma Moreno-Moreno, Ángel Rebollo-Román, Soraya León-Idougourram, Carlos Manuel Alzá s Teomiro & María Ángeles Gálvez-Moreno
Reina Sofia University Hospital, Endocrinology and Nutrition, Córdoba, Spain

Objective
ACTH-secreting pituitary tumors (ACTHomas) express vasopressin (AVP) receptors. AVP receptors are also present in other types of cancer, exerting different effects on tumor growth depending on the receptor subtype. AVP type 1 receptors (V1a and V1b) are associated with stimulation of cell proliferation, AVP receptor type 2 (V2r) is associated with antiproliferative effects. Desmopressin (DAVP) is a synthetic analog of AVP that acts as a selective agonist for V2r, which has shown antitumor properties in models of breast and colorectal cancer. In addition, DAVP stimulation the release of ACTH in ACTHomas. Remission of Cushing's disease (CD) in the postoperative vary between 55-85%, recurrence of up to 25%. Objective: describe the influence of DAVP treatment in patients undergoing surgery for cushing's disease (CD) who develop insipidus diabetes (ID).
Patients and methods
Retrospective analysis of patients who underwent as transsphenoidal surgery (TSS) for CD. Statistical analysis: t-student for comparison of means and Chi squared for comparison of proportions.
Results
60 patients with CD treated with TSS. Age 41,72 ± 14,85 years. Women: 88.3%. Remission 75%. Postsurgical complications: 20% (3 meningitis, 9 transient DI). Of the patients in remission, 15.6% had transient ID. 26.7% had recurrence of CD. Of patients who presented transient ID: 28,57% had recurrence of CD vs 71,42% ($P=0,901$).

Table 1

	Transient ID	No transient ID	p
Age (years)	32.43 ± 8.97	42.50 ± 15.60	0.11
Tumor size (mm)	8.24 ± 11.33	9.53 ± 7.37	0.71
Postsurgical basal cortisol (μg/dl)	8.59 ± 10.64	6.46 ± 4.91	0.64
Midnight salivary cortisol (μg/dl)	0.13 ± 0.10	0.23 ± 0.15	0.31
24-hour urinary cortisol (μg/24 h)	62.45 ± 111.28	64.07 ± 74.98	0.95
Postsurgical ACTH (pg/ml)	42.28 ± 55.95	15.81 ± 16.37	0.35

Conclusions
Transient ID is the most frequent complication in the postoperative period of CD. Patients with ID presented higher postsurgical ACTH and postsurgical basal cortisol levels without being statistically significant. CD recurrence does not differ from patients who did not present ID. Treatment with DAVP does not associated with increased risk of recurrence CD.

DOI: 10.1530/endoabs.81.EP693

EP694

Evaluation of the effectiveness of patients with acromegaly treatment (according to the moscow register)

Mikhail Antsiferov, Tatiana Alekseeva, Evgenii Pronin, Olga Ionova, Elena Goldman, Ekaterina Orlova & Karina Matosyan
Endocrinological Dispensary, Moscow Health Care Department, Moscow, Russian Federation

The aim
To determine the prognostic parameters affecting the course of acromegaly (A.) and the effectiveness of drug therapy (MT).
Matherials and methods
779 patients of A. [218 men (28%)] aged 60 (48/69) years, [Me(25%/75%)] were included in the Moscow register. The prevalence of A. in Moscow is 61.6; the incidence is 4.0 cases/million inhabitants. The treatment algorithm included surgical aid (495 patients), primary (I) or secondary (II) MT (584) and radiation treatment (115). Radical adenomectomy was performed in 31% of patients. 69% of patients with pituitary macroadenomas were prescribed II MT. The effectiveness of treatment was assessed by the dynamics of the GH, IGF-1, IGF-1 index (IGF-1/ULN).
Results
An inverse correlation was revealed between the age of diagnosis, the content of GH, IGF-1 and the volume of the pituitary tumor [(r=-0.24; -0.13; -0.41, respectively, (P<0.001)], which indicates a more active course of the disease with its early manifestation. I MT was received by 295 (69 m), II MT – 289 (106 m) patients. Somatostatin analogs of the first-generation (SA1) (lanreotide and octreotide) and cabergoline were used. A retrospective analysis of the effectiveness of MT was carried out between non-selective and selective groups. The selective groups for I and II MT included patients (72 and 50 patients) with a decrease in the level of IGF-1 of more than 70% of the baseline level after 3 months of taking SA1. Control A. at I/II MT in nonselective groups was achieved in 48 and 58% of cases, whereas in selective groups in 72 and 80% of patients [IGF-1 index was 0.9(0.4) and 0.8(0.3), respectively, P<0.001]. The duration of effective MT in selective groups with I MT was 49 (49) vs. 29 (29), with II MT – 53 (48) vs. 30 (37) months (P=0.0001). In both I and II MT, a moderate correlation was found between a decrease in the level of IGF-1 after 3 months of treatment, levels of IGF-1 after 12 months of treatment and at the last visit, as well as the duration of disease control [r=-0.57 (-0.51); r=-0.61 (-0.43); r=-0.58 (-0.4); r=0.52 (0.43), respectively, (P<0.001)].
Conclusion
1. Independent signs associated with the effectiveness of SA1 are: the level of IGF-1 after 3 months of treatment, the initial value of the IGF-1 index and the age of diagnosis. 2. Predictors of low sensitivity to SA1 treatment are: young age of diagnosis; male gender; large size of adenoma; the value of the IGF-1 index > 2.7.

DOI: 10.1530/endoabs.81.EP694

EP695

Epidemiological description of 20 years of experience in the management of insulinomas in a third level hospital

Alejandra Maricel Rivas Montenegro[1], Roberto José Añ ez Ramos[1], Sergio Santos Belinchon[2], Laura González Fernández[1], Diego Muñ oz Moreno[1], Elisa Fernández Fernández[1], Marcel Sambo Salas[1], Juan Carlos Percovich Hualpa[1], Olga González Albarrán[1] & Rogelio García Centeno[1]
[1]Hospital Gregorio Marañón, Endocrinología y Nutrición, Madrid, Spain; [2]Hospital Gregorio Marañón, Medicina Interna, Madrid, Spain

Introduction
Insulinoma, despite its low incidence of 0.4%, it is the most common functioning pancreatic neuroendocrine tumor. Most are benign, solitary and sporadic. Around 10% can be malignant and 5-10% are part of MEN-1. On certain occasions, the differential diagnosis is difficult when there is a history of Diabetes Mellitus (DM). Our objective was to describe clinical-epidemiological data and its diagnostic-therapeutic management.
Materials and Methods
Retrospective study that used electronic records of 21 patients with a diagnosis of insulinoma confirmed by pathological anatomy treated at our Hospital from 2000-2020. Qualitative variables were described in frequencies. Shapiro-Wilk test was used to determine the normality of the variables. Data were represented according to median and interquartile range(p25-p75).
Results
76.2% were women. The median age was 57 years(50-74). A median prior to diagnosis was 12 months(5-24). Of note, 3 patients had a previous history of DM2 and 16.7% had MEN-1. Within the laboratory parameters at diagnosis: basal insulin 18 mui/ml(11-37.9), basal C-peptide 1.61 ng/dl(1.1-2.3) and basal glucose 47 mg/dl(37-63). The most used functional test was the 72-hour fasting test; positive in all cases and in the first 24 hours(75%) and the rest in 24-48 hours (25%). Regarding non-invasive preoperative localization studies: the most application and with the best rate of correct localization was computed tomography (TC) (88.9% and 93.8% respectively), followed by magnetic resonance (RM) (42.9%) and abdominal ultrasound(19%). With a registered median size of 1.50 cm(1.3-2.1). The most frequent invasive preoperative localization study was ultrasound endoscopy(9.5%) and the most used intraoperative study was ultrasound(28.6%), which identified the tumor in all the patients. The treatment of choice was surgery in 90.4%; the majority surgical method was open approach(60%). The most frequent surgical complication was pancreatic fistula(17.6%). Four cases(20%) of malignant insulinomas were reported, all were multicentric and metastatic, predominant localization was liver. In relation to the pathological anatomy report, most were unicentric, most prevalence positive immunohistochemical markers were synaptophysin, chromogranin A and insulin. Ki67% had a median of 2%(1.5-5). The most common location was head and body(50%). Cure rates of 94.11% in benign cases and 25% in malignant cases were reported. No recurrences were recorded.
Conclusions
Insulinoma is a rare pancreatic tumor. CT or MRI are preferred non-invasive localization tests. The choice of treatment is pancreas-preserving surgery with a high cure rate. However, its morbidity and mortality increases when it is a malignant insulinoma.

DOI: 10.1530/endoabs.81.EP695

EP696

AQP2 gene mutation C.450T>A in a Tunisian family

Fatma Mnif[1], Hana Charfi[1], Fatma Abdelhédi[2], Malek Bouassida[2], Faten Haj Kacem Akid[1], Dhoha Ben Salah[1], Mouna Mnif[1], Nadia Charfi[1], NABILA REKIK MAJDOUB[1], Mouna Elleuch[1], Hassen Kammoun[2] & Mohamed Abid[1]
[1]Hedi Cheker University Hospital, Endocrinology, Tunisia; [2]Hedi Cheker University Hospital, Genetics, Tunisia

Introduction
The nephrogenic diabetes insipidus (DI) is an entity to be known. It is essential to know its etiologies and especially its therapeutic modalities which are different from those of the central DI. The familial nature of the disease should suggest a genetic origin. In our paper, we are presenting the case of a Tunisian family with genetic nephrogenic DI.
Case reports
Our family had a history of neglected polyuro-polydipsic syndrome (PPS), delayed growth, deafness, death at an early age and urinary malformations. Our first patient was a 35 years old female. She had a personal history of delayed growth and chronic renal failure. She was suffering from PPS for several years but neglected. A biological workup ruled out simple causes of DI and the water restriction test confirmed its nephrogenic origin. The patient was put on indomethacin with improvement of her symptoms. Her brother, 25-year-old, with a history of deafness and delayed growth, developed a post-traumatic polyuro-polydipsic syndrome evoking the diagnosis of central DI but refuted by the non-improvement of the symptoms after ddVAP. It was the use of the medical records of the sister already known to be a nephrogenic DI carrier that allowed us to correct the diagnosis of central DI. This allowed us to combine indomethacin and thiazide diuretics with improvement of the symptoms. Radiological exploration of the hypothalamic-pituitary region was without abnormality and pituitary hormonal exploration showed hyper gonadotropic hypogonadism and hyperprolactinemia at 39.55 ng/ml. A CT scan with urinary tract revealed a bilateral

dilatation of the pyelo-caliceal cavities with no detectable obstruction and a neurologic bladder. The genetic study of the AQP2 and AVPR2 genes was carried out by PCR-sequencing for our patients as well as some relatives. This analysis showed the presence of a homozygous missense mutation in exon 2 of the AQP2 gene in our female patient and in another affected sibling. It is a substitution of a thymine (T) by an adenine (A) at positon 450 of the cDNA: C.450T > A. This mutation was present in the heterozygous state in the mother.
Conclusion
Currently, the use of molecular biology facilitates the management of familial DI with genetic counselling and early detection of the different anomalies before their clinical exacerbation. In our case, the study of this family will incite us to do genetic counseling in its different members and to follow them closely to detect other affected members in time.

DOI: 10.1530/endoabs.81.EP696

EP697

Endocrine dysfunction secondary to pituitary tuberculoma: a case report

Fatma Mnif, Hana Charfi, Dhoha Ben Salah, Faten Haj Kacem Akid, Nadia Charfi, Nabila Rekik Majdoub, Mouna Mnif, Mouna Elleuch & Mohamed Abid
Hedi Cheker University Hospital, Endocrinology, Tunisia

Introduction
Tuberculosis is an infectious disease that involves any organ. However, the primary pituitary tuberculosis is an extremely rare disease. Intracranial tuberculomas account for 0,15-5% of intracranial space-occupying lesions, of which pituitary as the primary site, and easily misdiagnosed as pituitary adenoma. In this setting, the late diagnosis can result in permanent endocrine dysfunction. We hereby report the case of a patient with pituitary tuberculoma discovered following the onset of diabetes insipidus.
Case report
The patient was a 36-year-old woman. She presented with polyuro-polydipsic syndrome (PPS) associated with holocranial headaches and secondary amenorrhea. Hormonal exploration identified corticotropic insufficiency with hyperprolactinemia. Central DI was retained in view of the hypothalamo-pituitary MRI aspect showing the disappearance of the spontaneous T1 hypersignal and the presence of a thickening of the pituitary stem. The tubercular origin of this thickening was oriented by the presence of a history of erythema nodosum with a positive intradermal reaction to tuberculin. It was confirmed by the presence of Mycobacterium Tuberculosis in the sputum, urine and bronchial fluid. Anti-tubercular drugs were combined with hormone replacement therapy: Hydrocortisone at a dose of 20 mg/d, ddVAP at a dose of 0.3 ml/d and dopamine agonist at a dose of 5 mg/d. After 3 months of treatment, the patient showed a clear improvement of her symptoms with a weight gain of 8 kg, disappearance of headaches, PPS and galactorrhea. But she still had amenorrhea despite normoprolactinemia (PRL < 0.4 ng/ml) with a normal LH level at 3.5 mUI/ml and an elevated FSH level at 11.6 mUI/ml. MRI control after 8 months of anti-tuberculosis treatment also showed a clear improvement with a fine pituitary stalk taking contrast correctly and a normal looking pituitary gland. The total duration of treatment was extended to 24 months. At the last MRI check-up after 24 months of treatment, the tubercular pituitary abscess had completely disappeared and clinically, the patient no longer had PPS or galactorrhea. However, the amenorrhea persisted, with a negative progestin test. The diagnosis of a physiological menopause was retained in view of an explosive gonadotropin response under LHRH.
Conclusion
The non-specific radiological findings challenge the diagnosis of primary pituitary tuberculomas. However, a high clinical suspicion, especially in endemic regions, can minimize unnecessary invasive procedures and surgical interventions. The early clinical suspicion and prompt use of anti-tubercular drugs help to prevent irreversible endocrine dysfunction.

DOI: 10.1530/endoabs.81.EP697

EP698

Age and puberty based IGF-1 normative data in healthy children from North India.

Bhanu Malhotra[1], Kv Ravi Teja[1], Sanjay Bhadada[1], Ashu Rastogi[1], Anil Bhansali[1], Naresh Sachdeva[1], Ranjana Walker Minz[1], Rama Walia[1], Mahesh Prakash[1], Arun Kumar Aggarwal[1], Gajinder Dewan[2], Liza Das[1], Philip Monaghan[3], Peter Trainer[3], Marta Korbonits[4], Raman Kumar Marwaha[5] & Pinaki Dutta[1]
[1]PGIMER, Endocrinology, Chandigarh, India; [2]GMSH-16, Chandigarh, India; [3]Christie NHS Foundation Trust, Manchester, United Kingdom; [4]William Harvey Research Institute at Barts and the London School of Medicine, Queen Mary University of London, Endocrinology, London, United Kingdom; [5]SEHEAC, New Delhi, India

Context
Serum IGF-1 levels are of paramount importance for diagnosis and management of growth related disorders. The reference range of IGF- 1 should be ethnicity and Tanner specific. Indian data on the same is scarce and there is a need to develop the same.
Objective
To develop age, sex and Tanner based normative reference range of serum IGF-1 level for Indian children and correlate the same with peri-pubertal hormonal parameters.
Setting and participants
After excluding children with short stature, anemia, chronic systemic illnesses, underlying endocrinopathies and celiac disease; 1929 children (916 girls, 1013 boys) were eligible for participation out of 2191 children screened. They were stratified as per chronological age and pubertal stage (Marshall and Tanner).
Outcome measures
Serum IGF-1 was measured by in house electrochemiluminescence immunoassay by Roche Diagnostics (cobas e 801) Mannheim, Germany; at PGIMER, Chandigarh. External validation of assay was done by robust immunodiagnostics method (iSYS) at Manchester, UK. Normative reference range and correlation were obtained based on Roche method.
Result
Serum IGF-1 levels peaked at chronological age of 13 years (median 50thcentile 397.38 ng/ml) [Greulich Pyle BA 14 years(389 ng/ml)] in girls and at 15 years in boys (327 ng/ml) [BA 16 years (370 ng/ml)], followed by a decline to nadir at 18 years in both. Girls had an early peaking of IGF-1 as compared to boys. The median IGF-1 levels in girls increased from Tanner stage 1 to stage 4, with peak value of 345 ng/ml at stage 4 and declining sharply thereafter. For boys, levels increased from Tanner stage 1 to stage 3, peaked at 308 ng/ml at stage 3, after which the levels were stable and fluctuated around the peak from stage 3 to 5. IGF-1 also correlated significantly with hormonal parameters of puberty (girls: LH (r =0.52), estradiol (r=0.40), DHEAS (r = 0.44); boys: LH (r= 0.57), testosterone (r=0.56), DHEAS (r=0.47); with LH showing the best correlation. This early peaking of IGF- 1 levels in the present study vis-a vis Caucasians (14-16 years) has also been reported in other studies from Asia (11-13 years).
Conclusion
Along with chronological age, Tanner based reference range will further improve the diagnostic utility of IGF-1 normative data in school going children.

DOI: 10.1530/endoabs.81.EP698

EP699

Pituitary adenomas characteristics in patients with multiple endocrine neoplasia type 1, its phenocopies and sporadic acromegaly

Diana Trukhina[1], Elizaveta Mamedova[1], Anastasia Lapshina[1], Alexey Nikitin[2], Philipp Koshkin[3], Vilen Azizyan[1], Andrey Grigoriev[1], Zhanna Belaya[1] & Galina Melnichenko[1]
[1]Endocrinology Research Centre, Russian Federation; [2]Pulmonology Scientific Research Institute under FMBA of Russia, Russian Federation; [3]Center of Medical Genetics 'Genomed', Russian Federation

Multiple endocrine neoplasia type 1(MEN1) is a hereditary condition caused by mutations in the *MEN1* gene, which encodes menin protein. The syndrome predisposes to the development of tumors in both endocrine and non-endocrine systems. In patients with MEN1, pituitary adenomas (PA) occur in approximately 40% of all cases. If patient has MEN1 phenotype with no mutations in *MEN1* gene, the condition is regarded as a phenocopy. The reason of several endocrine MEN1-associated tumors combination in these patients remains unknown. Knowing menin expression in groups and if there are any somatic mutations in

PA can provide insight into the oncogenesis of PA. Formalin-fixed paraffin-embedded PA tissues were obtained after transnasal transsphenoidal adenomectomy(TTA). We have used following immunohistochemistry (IHC) markers: Pit-1;T-box;CAM5.2; EK-alpha; GH, ACTH, PRL, TSH, FSH, LH, menin(ab-Menin-ChIP Grade, Abcam, UK). *MEN1* mutations were assessed either by Sanger sequencing or by NGS(NextSeq550, Illumina, USA). Automated bioinformatic analysis was carried out to search for somatic mutations(annotation with SnpEff, ANNOVAR, AlamutBatch). A total of 47 samples were included in the study; *MEN1* gene somatic mutations were determined in 30 samples. Menin expression was assessed in 47 PAs: 11 genetically confirmed MEN1(gMEN1), 13 phenocopies of MEN1(phMEN1) — a combination of acromegaly and primary hyperparathyroidism, 23 – sporadic acromegaly(SAm). The distribution of PA according to the type of secretion in the gMEN group was: 5-ACTH, 1-PRL, 4-adenomas with mixed secretion (2-GH + PRL; 1-TSH + PRL; 1-ACTH + PRL) 1-silent gonadotroph adenoma. All 13 samples phMEN1 and 23 samples SAm were secreting GH. The median age at the time of TTA in gMEN1 was 33 years[16;47], in phMEN1 — 59[56;64], in SAm — 57[52;62]. The groups were similar in terms of sex($P > 0.05$). The results of menin staining (negative staining/positive cytoplasmic staining/positive nuclear staining): gMEN1-5/6/0; phMEN1-0/12/1; SAm-2/14/7. The phMEN1 showed significantly greater cytoplasmic expression of menin than gMEN1 ($P = 0.011$). The gMEN1 differed from SAm: nuclear staining was not detected in any case ($P = 0.011$). There were no statistically significant differences between the phMEN1 and SAm groups ($P = 0.141$). Although there were no differences, in phMEN1 only one case showed weak menin nuclear expression, while in SAm 7 cases had nuclear expression. No somatic mutations of *MEN1* gene in phMEN1 and SAm groups were identified. Menin expression is generally preserved in PA in phMEN1 and SAm groups, though with different pattern of nuclear and cytoplasmic expression, while its expression varies in PA in MEN1. No detection of somatic mutations in phMEN1 and SAm groups leads to investigate other responsible genes or epigenetic causes of different menin expression.

DOI: 10.1530/endoabs.81.EP699

EP700

A Delphi panel of Italian endocrinologists to define the unmet needs on the current management of Cushing's Syndrome

Rosario Pivonello[1], Scaroni Carla[2], Barbara Polistena[3], Antonio Migliore[3] & Andrea Giustina[4]
[1]Università Federico II di Napoli, Dipartimento di Medicina Clinica e Chirurgica, Naples, Italy; [2]Università degli Studi di Padova, Dipartimento di Medicina Clinica U.O.C. Endocrinologia, Padova, Italy; [3]C.R.E.A. Sanità - Centro per la Ricerca Economica Applicata in Sanità, Rome, Italy; [4]San Raffaele Vita-Salute University and IRCCS Hospital, Institute of Endocrine and Metabolic Sciences, Milan, Italy

Introduction
Cushing's Syndrome (CS) requires an accurate diagnosis, patient-tailored treatments and long-term management. To define the unmet needs of patients with CS, a consensus among a panel of Italian endocrinologists was promoted. The panel involved 57 specialists with expertise in CS management.
Methods
The endocrinologists were identified by convenience sampling. The survey was built around a set of statements formulated after literature review and discussion with an experts' advisory board. A total of 24 statements were finally included in the survey. The Delphi method was used to reach consensus on the statements using scores on a 1-to-9 scale (with 1 indicating disagreement with the statement and 9 indicating full agreement). A 70% threshold was set to define consensus, meaning that strong agreement was believed reached if at least 70% of participants had assigned scores in the range 1-3 or 7-9, respectively.
Results
Twenty-three endocrinologists (40% of the sample) working in 10 Italian regions took part into the survey. Among them, 52% reported to follow between 5 and 10 Cushing patients per year, 22% between 10 and 20 patients, 17% more than 20 patients, and 9% less than 5 patients. The Delphi process was concluded in 2 rounds. Agreement was reached on 18 of the 24 proposed statements (75%). The statements for which consensus was not reached ($n = 6$; 25%) were mainly related to the definition of a standard pharmacological therapy for CS, the response time to the available pharmacological therapies, the achievement of a complete control of the clinical condition, the evidence base needed for CS pharmacological therapies, and the satisfaction with the safety and effectiveness profiles of the current pharmacological therapies. Some statements in particular accounted for extremely high level of agreement (values over 90%) and they were related to the need of a constant and periodic follow-up of the patients, given the possibility of mid-long term relapse; to the relevance of the escape, which can have a strong impact on the overall management of the condition; to the need to promote the development of management pathways which are specific for CS; to the need that a newer pharmacological option, with improved safety and effectiveness profile, could radically change the current management of the CS.
Conclusions
The survey revealed that the experts involved perceive some relevant unmet needs in the management of CS, mainly related to the lack of a pharmacological treatment with more favourable safety and effectiveness profile.

DOI: 10.1530/endoabs.81.EP700

EP701

Age at the diagnosis or age at the onset of symptoms- which should be taken into consideration in patients with early-onset acromegaly- pilot study

Magdalena Godlewska, Anna Bogusławska, Łukasz Kluczyński, Ewelina Rzepka, Alicja Hubalewska-Dydejczyk & Aleksandra Gilis-Januszewska
Jagiellonian University Medical College, Department of Endocrinology, Kraków, Poland

Introduction
The group of young adults with acromegaly, despite initial reports about their aggressive course of disease, has not been thoroughly characterized.
Aim
Our aim was to investigate the differences between the patients with early-onset acromegaly and with onset in older age.
Material and methods
Consecutive patients diagnosed with acromegaly between 01.2014 and 12.2021 were included in this retrospective study, approved by the local Bioethics Committee. Firstly, the arbitrary division (Group A: with patients ≤ 30 and Group B: with patients > 30 y.o. upon diagnosis) was used. Secondly, retrospective estimation of age upon symptoms onset divided the patients into Group C and D (≤ 30 and > 30 y.o. at the onset, respectively). We statistically compared Groups A and B and subsequently Groups C and D in terms of clinical, biochemical and radiological parameters, using IBM SPSS Statistics, ver. 27.
Results
Out of 72 consecutive patients with acromegaly, 64 were included in the study. Group A consisted of 11 patients, 54.5% males, Group B had 53 patients, 41.5% males. Retrospective estimation of the age at diagnosis was available in 50 patients: there were 18 patients in Group C (44.4% males) and 32 patients in group D (34.4% males). There were no statistically significant differences between group A and B as well as between C and D in terms of: gender, median diagnostic delay, frequency of accidental diagnosis, hypopituitarism, hyperprolactinemia and, radiologically, occurrence of macroadenomas, median maximal tumor diameter, pituitary apoplexy, cavernous sinus invasion, compression of the optic chiasm. Median growth hormone (GH) nadir concentration was higher in Group A than in Group B: 38.4 uIU/ml(24.1; IQR 65.7) vs. 20.8 uIU/ml(10.45; IQR 34.5), respectively ($P = 0.046$). GH was higher in Group C(37.7 uIU/ml, IQR 67.2) than in Group D(15.3 uIU/ml, IQR 27.7) ($P = 0.046$). No differences in IGF-1 concentration related to upper normal limit were discovered between the groups in both steps of the analysis. Biochemical control was after surgery was similarly frequent in groups A and B; and groups C and D.
Conclusions
In our study, patients with early-onset acromegaly did not statistically differ from typical-onset patients, even when considering two division criteria: arbitrary and based on the estimated symptoms onset. Our main limitation is the small number of patients enrolled, even though all of the newly diagnosed patients in a tertiary endocrinology center over 8 years were included. Further, prospective studies are needed to identify and assess the differences between age groups of acromegaly patients.

DOI: 10.1530/endoabs.81.EP701

EP702

Giant pituitary adenomas in children and adolescents: clinical presentation, management and long-term outcome

Giuseppe Giuffrida[1], salvatore giovinazzo[1], Ylenia Alessi[2], Marta Ragonese[1], Oana Ruxandra Cotta[2], Filippo Flavio Angileri[3], Francesco Ferraù[1,2] & Salvatore Cannavò[1,2]
[1]Department of Human Pathology "G. Barresi", University of Messina, Italy; [2]Endocrine Unit, University Hospital "G. Martino", Messina, Italy; [3]Department of Biomedical and Dental Sciences, and Morpho-Functional Imaging, University of Messina, Italy

Background
Pituitary adenomas in children/adolescents represent around 3% of all intracranial neoplasms. They are more frequently hormone-secreting lesions, usually diagnosed in early childhood and late adolescence. Female gender is generally prevalent, because of most evident symptoms (i.e., irregular periods, galactorrhea, etc.). Giant pituitary adenomas (GA) very rarely occur in pediatric age, posing frequent challenges in their management.
Patients and methods
We retrospectively evaluated the records of 7 teenager patients (5 males, median age 16.7 $\pm$ 1.6 yrs) with GA, referred to the Endocrine Unit of the University Hospital of Messina (Italy) from 1990 to 2020. All patients underwent biochemical, clinical and neuroradiological workup. The median follow-up was 16.1 $\pm$ 9.9 years.
Results
GAs were clinically characterized as follows: five functioning PAs (4 PRL-secreting, 1 ACTH-secreting) and two non-functioning pituitary adenomas (NFPAs). Median pituitary tumor diameter was 43 $\pm$ 2.2 mm. Genetic analysis revealed only 1 carrier of MEN1 mutation (a patient with PRL-secreting tumor), while no changes of AIP gene were detected. At diagnosis, main presenting symptoms were headache (n.5), visual disturbances (n.4), menstrual irregularities (n.2), and growth delay (n.1). In terms of pituitary function, 1 patient presented with panhypopituitarism, 2 with multiple pituitary deficits. One patient with NFPA was lost to follow-up, of the remaining 6 patients: 3 (1 PRL, 1 ACTH, 1 NFPA) were referred to first-line surgery by endoscopic trans-nose-sphenoidal approach, 3 PRL-omas were treated with medical therapy (cabergoline) exclusively or prior to surgery. After first-line treatment, stable remission (no tumor remnant and/or no hormone hypersecretion) was observed in 3 subjects, progression (growing tumor remnant and/or persistent hormonal hypersecretion) in 3 cases. In these last cases, second-line treatment was radiotherapy. At last follow-up visit: 5 patients were in remission while 1 patient with PRL secreting tumor was still under effective cabergoline treatment; 2 patients had panhypopituitarism, 3 single/multiple pituitary deficits, while pituitary function was preserved in one subject. GH deficiency (GHD), isolated as well in association with other deficits, was the most frequent pituitary hormone deficit (n.5/7 patients). During follow-up, the following comorbidities were diagnosed: metabolic syndrome (n.3), osteoporosis (n.2), second tumors (n.1).
Conclusions
Giant pituitary adenomas management in children/adolescents is challenging and require a multidisciplinary approach.

DOI: 10.1530/endoabs.81.EP702

EP703

The clinical implication of macroprolactinemia detection using PEG 6000 in a group of women of childbearing-age with hyperprolactinemia in sub-Saharan Africa: experience of a tertiary hospital

Anne Ongmeb Boli[1], Mendane Ekobena Francine[2], Etoa Etoga Martine[1,2], Charly FEUTSEU[3], Mbono Samba Esther Aristide[1,2], Falmata Amazia[4], Djahmeni Éric Noël[1], Ndi Manga Arnaud[1], Katte Jean Claude[1], Dehayem Mesmin[1,2], Ama Moor Vicky Jocelyne[5] & Sobngwi Eugène[1,2]
[1]Yaounde Central Hospital, National Obesity Centre, Endocrinology and Metabolic Disease Unit, Yaoundé, Cameroon; [2]University of Yaoundé 1, Faculty of Medicine and Biomedical Sciences, Department of Internal Medicine and Specialities, Yaoundé, Cameroon; [3]University of Yaoundé 1, Biotechnology Centre, Yaoundé, Cameroon; [4]University of Yaoundé 1, Faculty of Medicine and Biomedical Sciences, Doctoral School of life, Health and Environnemental Sciences, Yaoundé, Cameroon; [5]University of Yaoundé 1, Faculty of Medicine and Biomedical Sciences, Department of Biochemistry, Yaoundé, Cameroon

Introduction
Macroprolactin (MacroPRL), a variant of human prolactin may interfere with hormonal assay and falsely increase serum prolactin levels. Therefore, failure to identify macroprolactinemia can lead to inappropriate investigations and treatment in women who are already susceptible to anxiety and stress. We aimed to identify macroprolactinemia among women of childbearing age with hyperprolactinemia.
Materials and methods
We conducted a cross-sectional study at the endocrine unit of one of the tertiary hospitals in Cameroon. Study participants were recruited from both endocrine and gynecological outpatient consultations services. They were women of child-bearing age (18 to 49 years) consulting for signs and symptoms of gonadal dysfunction or hyperprolactinemia (PRL $>$25 ng/ml). Total prolactin was measured using a Human direct ELISA method. Polyethylene glycol 6000 (PEG 6000) precipitation was used to detect macroprolactinemia.
Results
We enrolled 33 women with a mean age of 31 $\pm$ 7 years (range 21-48). Twenty-seven (81.8%) participants were symptomatic with the majority 23/27 (69.7%) reporting galactorrhea and 21 (63.4%) women reported having an irregular menstrual cycle. The median pre-precipitation prolactinemia reduced significantly after PEG precipitation from 61.2 (IQR: 33.2-115.9) ng/ml to 33.8 (IQR: 17.9-70.5) ng/ml, $P < 0.001$. After PEG precipitation, 5 participants had a serum prolactin recovery rate below 60%, and therefore a prevalence of macroprolactinemia at 15.2%. Four (80%) women with macroprolactinemia presented with symptoms, and there was no association between macroprolactinemia and symptoms of hyperprolactinemia among these participants.
Conclusion
Macroprolactinemia was detected in 5/33 (15.2%) of the study population. There was no association between macroprolactinemia and symptoms of hyperprolactinemia. Oligomenorrhoea, amenorrhoea, and galactorrhea were present in the majority of patients with macroprolactinemia hence routine screening for macroprolactinemia is recommended or advised in order to reduce the use of dopamine agonist treatment and imaging.
Keywords: Prolactin, Macroprolactin, PEG, Prolactin recovery rate, hyperprolactinemia

DOI: 10.1530/endoabs.81.EP703

EP704

Cessation of GH secretion in acromegaly without medical or surgical intervetion; Covid-postponed surgery was escaped

Annamária Erdei[1], Eszter Dániel[1], Annamaria Gazdag[1], Mihá ly Griger[2], Edit B Nagy[3] & Endre V Nagy[1]
[1]Division of Endocrinology, Department of Internal Medicine, Debrecen, Hungary; [2]Department of Internal Medicine, Debrecen, Hungary; [3]Division of Radiology and Imaging Science, Department of Medical Imaging, Debrecen, Hungary

Introduction
Acromegaly is usually caused by pituitary macroadenoma producing excess growth hormone. Treatment options include surgery to remove the tumor, medications, and radiation therapy.
Case report
A 39-year-old woman has been referred to the endocrine clinic with suspected acromegaly in December 2019. Surgery for benign ovarian cyst, endometriosis, amenorrhoea, unsuccessful in vitro fertilisations were present in her medical history. She complained about thickening of fingers, facial bloating, dry skin and vision impairment. Laboratory examinations proved acromegaly, central hypothyroidism, hypogonadism and mild hyperprolactinaemia. ACTH and cortisol levels were in the normal range. Sella MR showed pituitary macroadenoma in size 17 x 12 x 14 mm. There was no abnormal finding detected by ophthalmological examination. After the diagnosis was established, levothyroxine was started and pituitary surgery was scheduled for March of 2020. Restrictions due to the coronavirus pandemic prevented the operation; this was postponed to an uncertain date in the future. We decided to start long-acting somatostatin analogue treatment. Before treatment could be started, something unexpected happened. In April 2020, severe headache, nausea, vomiting, weakness, hypotension occurred. Urgent MR showed substantial decrease in the size of the macroadenoma and haemorrhage in the tumor. Laboratory findings confirmed hypadrenia and decrease in growth hormone and insulin-like growth factor 1 levels. On follow-up, hypopituitarism was treated effectively with hormone replacement therapy. Growth hormone and insulin-like growth factor 1 levels were further reduced, the size of the pituitary adenoma decreased below 1 cm on repeated MR, the clinical features of acromegaly disappeared and no special treatment for acromegaly was required.
Conclusions
Pituitary apoplexy is a rare condition, occurs in 2-12 % in pituitary adenomas and in 0.05-4.8% in acromegaly. Typical symptoms are headache, vomiting, visual

disturbances. Pituitary apoplexy might cause remission in acromegaly as seen in the case presented here.

DOI: 10.1530/endoabs.81.EP704

EP705

When we count Ki67 in a gonadotropinoma- matters- case report

Mariana Costache Outas
Coltea Clinical Hospital, Endocrinology, Bucharest, Romania

We report the case of a 49 y.o male with an incidental sphenoidal-sellar tumour discovered during a cerebral CT scan during the workup of a medium to severe SARS COV 2 infection. The cerebral MRI describes an invasive tumour located in the sellar region and sphenoidal sinus – extended around the right optic nerve and into both cavernous sinuses. An emergency biopsy from the sphenoidal extension of the tumour revealed a neuroendocrine tumour. The reported diagnostic was olfactory neuroblastoma grade I Hyams (positive stains for synaptophysin, NSE, Ki67 index of 8%). The patient was referred to a mixt expertise surgical team (ENT- neurosurgery). He undergoes removal of the sphenoidal- sellar tumour – 5 weeks from the diagnostic. His first endocrine evaluation was following surgery due to the development of central hypocortisolism, and replacement therapy was started. He undergoes radiotherapy for residual tumour two months after surgery. The initial anatomopathological report from the surgical sample described an olfactory neuroblastoma grade I Hyams (Ki67 index 1%). Reconsideration of immunohistochemistry from the tumour sample stains positive for SF1, GATA3, LH and FSH with a Ki67 index of 1%, and a diagnostic of invasive gonadotropinoma was concluded. We assume the systemic inflammatory status during SAR COV2 infection is responsible for the difference in the Ki67 index counted five weeks apart from the biopsy sample and the tumour sample during surgery.

DOI: 10.1530/endoabs.81.EP705

EP706

The septo-optic dysplasia associated with adipsic hypernatremia

Mouna Mezoued[1], Habouchi Amine[2], Bessaid Khadidja[1] & Malha Azzouz[1]
[1]Bologhine Hospital, Endocrinology, Alger, Algeria; [2]Mustapha Hospital, Radiology, Alger, Algeria

Introduction
SOD is a rare congenital anomaly, with an incidence of 1 in 10 000 live births, the adipsic hypernatremia is a rare osmoregulation Disorder observed in SOD.
Case report
We report a case of a 28 months infant, the eldest of a sibling group of 2 children, referred by the pediatrician for exploration of a staturo-ponderal delay. At clinical examination we found a harmonious staturo-ponderal delay and a median line anomaly of development as a single central incisor, ogival palate and a convergent squint. GH deficiency was confirmed in laboratory. Cerebral MRI showed a pituitary stem interruption syndrome with pituitary hypoplasia, an absence of the pituitary stem, an ectopic pituitary gland with infundibular location and an agenesis of the septum pellucidum. At 8 years she presented an important headache associated with vomiting asoociated to a hypernatremia at 185 meq/l, having required rehydration. The diagnostic of adipsic hypernatremia was retained due to the absence of thirst (adipsia) a very high osmolality and a normal urine osmolality concluding to a normal production of AVP. The management is based on the obligation of a daily intake (1,5-2 l/day) of water, an adjustements of these intakes in case of climatic variations or acute illness and regular serum sodium monitoring

DOI: 10.1530/endoabs.81.EP706

EP707

Hyperprolactinemia and connective tissue diseases: which significance of such exceptional association?

Arij Ezzouhour Yahyaoui, Asma Kefi, Khaoula Ben Abdelghani, Mounira El Euch, Syrine Sassi, Sami Turki & Ezzeddine Abderrahim
Charles Nicolle, Tunis, Tunisia

Introduction
Dermatomyositis is a chronic, idiopathic inflammatory myopathy that can overlap with rheumatoid arthritis. The immunostimulatory effect of prolactin is suggested by many authors. Herein we report an original association of hyperprolactinemia with a scarce condition: dermatomyositis-rheumatoid arthritis overlap in a young woman.
Case description
A 26-year-old woman with no significant medical history was referred to our department to investigate deterioration of physical condition with myalgia. She was apyrectic and had clinical features of dermatomyositis including Gottron's papules, heliotrope rash, proximal nail fold erythema, symmetric weakness affecting predominantly the proximal muscles of the legs and arms. Serum creatinin kinase was elevated at 395 UI/l and lactate deshydrogenase levels were at 546 UI/l. The muscle biopsy and the electromyogram confirmed dermatomyositis diagnosis. Respiratory function tests and CT chest were normal. There were no symptoms of infection. Given possible association with neoplasms, exhaustive investigation was performed and showed no underlying neoplastic disease. Since the patient had polyarthralgia and a biological inflammatory syndrome, we suspected the presence of another connective tissue disease. An overlap of dermatomyositis and rheumatoid arthritis was diagnosed as the patient presented symmetric swelling of small joints, morning stiffness, and a boutonniere deformity in the 4th and 5th right fingers. Rheumatoid factor was at 80 UI/l and anti-CCP levels were at 15. Menstrual irregularities were reported, therefore hormone tests were performed. They highlighted a hyperprolactinemia at 1136 UI/l and normal levels of FSH, LH and estrogen. Gynecological examination and pelvic sonography showed no abnormalities. The patient was commenced on prednisone 50 mg/day (1 mg/kg), with satisfying clinical and biological evolution. No prolactin inhibitors were prescribed. Prolactin levels were normalized in follow-up and menstrual cycles of our patient became more regular. Pituitary MRI was not performed as the patient lost to follow up.
Conclusion
The effect of hormones on the immune system has been widely described. Many research reported hyperprolactinemia in patients with autoimmune diseases; it might promote the development of autoimmune diseases, leading some authors to suggest some role of dopamine agonists in the therapy of those diseases. More large-scale studies are needed to establish the exact relationship between hyperprolactinemia and autoimmune diseases and effeciency of dopamine agonists in such conditions.

DOI: 10.1530/endoabs.81.EP707

EP708

A Rare Case of Isolated ACTH deficiency, Possible cause: long-term use of opioid analgesics for severe Migraine management/Opioid-induced adrenal insufficiency (OIAI) (?)

Nino Zavrashvili[1], Ketevan Chanturishvili[1,2], Ketevan Gvazava[1], Natia Margvelashvili[1] & Natia Shonia[1]
[1]Tbilisi Institute of Medicine, Endocrinology, Tbilisi, Georgia; [2]David Tvildiani Medical University, Endocrinology, Tbilisi, Georgia

Context
Hypothalamic-pituitary-adrenal axis (HPA) may be disrupted by drugs, including opioids. Opioids are widely used for treatment of acute and chronic pain, but they also carry a wide range of adverse effects. Opioid receptors are present in the pituitary gland and hypothalamus and chronic use of opioids may lead to adrenal insufficiency because of central suppression of the hypothalamic-pituitary-adrenal axis (HPA).
Case Presentation
We report a 26-year-old female with a history of severe Migraines and autoimmune primary hypothyroidism who presented with decreased energy, weakness, fatigue, myalgia, arthralgia, nausea, vomiting, diarrhea and urinary frequency. She is checking blood pressure, which is little higher than 130/90 mmHg. Since 2013 the patient had 5 hospitalizations (twice in Germany) in connection with status migranosus. To manage her symptoms during hospitalizations multiple medications would be tried for pain without any success. The patient describes that fentanyl, propofol, morphine and tramadol

would have to be ultimately used. Given the patient's symptoms Cortisol deficiency was suspected. Cortisol was measured and was found to be very low, repeated several times. ACTH at the same time was very low suggestive of secondary adrenal insufficiency. To investigate the reason for secondary adrenal insufficiency, patient had MRI of pituitary gland which was normal, revealing no pituitary tumors or pituitary stalk lesions/other lesions. Additional pituitary hormonal workup was performed. Overall, the biochemical picture was consistent with idiopathic ACTH deficiency. Hydrocortisone therapy was initiated 30 mg QD, lead to significant improvement of symptoms. Hyperglycemia and secondary hyperaldosteronism was incidentally found during workup for above symptoms. Hemoglobin A1c was above normal ranges-5.9 %, but GAD antibodies and C-peptide were not indicative of autoimmune type 1 diabetes. Blood pressure measurements were high and aldosterone and renin plasma activity was elevated. Patient continuous levothyroxine supplementation therapy. However, after 3 years of hydrocortisone therapy patient suddenly started gaining weight and developed Cushing's symptoms so we performed trial with slow down titration of hydrocortisone which lead to improvement of symptoms. We checked morning cortisol and ACTH which were normal. For migraines she is using NSAID'S and is aware of overuse headaches and is trying to be mindful of that.
Conclusion
We should bear in mind the possibility of adrenocorticotropic hormone deficiency even when patients with history pain syndromes and opioid use.

DOI: 10.1530/endoabs.81.EP708

EP709

A rare association of Neurofibromatosis type 2 and hypopituitarism

Lina Ghram, Radhouen Gharbi, Sawsen Essayeh, Hajer KANDARA, Manel Jemel & Ines KAMMOUN
Institut De Nutrition, Tunis, Tunisia

Introduction
Neurofibromatosis type 2 (NF2) is an autosomal dominant genetic disorder that cause a growth of noncancerous tumors in the nervous system, it associates cranial schwannomas, meningiomas, and skin and ophthalmologic lesions. It is a rare condition and its association with an intrasellar arachnoidocele has not been reported yet. We report the case of a patient who presents a NF2 associated with hypopituitarism related to an intrasellar arachnoidocele.
Case presentation
It was a 37-year-old, patient referred for symptoms of hypopituitarism. She reported galactorrhea, menses return, constipation, weight loss, asthenia and frequent hypoglycaemia. On physical examination, she presented café-au-lait spots, dry skin with neurofibromas, body hair loss and hypoactive deep tendon reflexes. Biologically, cortisol and FT4 levels were very low at <2 ng/ml (reference : 50 - 180 ng/ml) and 1.38 pmol/l (reference: 9-22 pmol/l) respectively. TSH was 5.86 uUI/ml (reference: 0.27-4.2). The patient received hydrocortisone and L-thyroxine. A hypothalamic-pituitary MRI showed complete atrophy of the pituitary parenchyma with intrasellar arachnoidocele, a meningioma of the foramen magnum and an acoustic neurinoma. The association of a unilateral acoustic neuroma and café au lait spots with skin neurofibromas and a meningioma led to the diagnosis of NF2.
Conclusion
NF2 can cause fluid buildup in the brain, but its association with intra sellar arachnoidocele and hypopituitarism has never been reported .
The prognosis of the disease is reserved and its management requires a multidisciplinary team.

DOI: 10.1530/endoabs.81.EP709

EP710

Langerhans cell histiocytosis revealed by an isolated central diabetes insipidus in an adult

Halladja Chaima, Safia Achir, Zina Belheddad & SAFIA MIMOUNI
CPMC Centre Pierre Et Marie-Curie, Endocrinology and metabolic diseases department, Algiers, Algeria

Introduction
Langerhans cell histiocytosis (LCH) is a systemic disorder characterized by clonal proliferation of immature dendritic cells observed mainly in children. The affection of the sellar region in adults with central diabetes insipidus as the first manifestation of the disease is extremely rare creating a problem of etiological diagnosis especially when central diabetes insipidus (CDI) is apparently isolated.
Case description
A 21-year-old man was referred for evaluation of recent polyuria and polydipsia with a history of headache for the past 03 years. Initial biochemistry and hormonal evaluation were normal. Magnetic resonance imaging(MRI) of the brain showed a loss of spontaneous T1 hyperintensity of the posterior pituitary, a globular anterior hypophysis and a thickened *pituitary stalk measured at 07 mm, filling the opto-chiasmatic cistern and exerting a mass effect on the optic chiasma In addition,* the patient had a type II Chiari malformation with intramedullary cyst and a malformation of the colobomatous eyeballs. Notably, The MRI showed a non-expansive osteolytic lesion of the frontal *bone*. Additional investigations were performed in order to establish etiological diagnosis but were non contributory. A bone biopsy of the frontal bone was then performed, and the pathologic examination concluded to LCH diagnosis. Desmopressin therapy was therefore initiated. The patient was referred to the hematology department where he received chemotherapy (vinblastine, Etoposide) with corticosteroid therapy
During follow-up: the patient developed GH deficiency, TSH deficiency, and FSH and LH deficiencies, corticotropic axis has not been evaluated because the patient was on corticosteroid therapy. There was no reduction of desmopressin doses. The frontal lesion was not present on the follow-up MRI. On the other hand, it showed a new lesion in the left frontal sinus suggesting an osteoma; a CT scan remains necessary for a better evaluation of the bony structures
Conclusion
In this patient LCH was revealed by central diabetes insipidus as the first manifestation, associated with solitary bone lesion. Treatment included desmopressin replacement and chemotherapy. During follow-up, the patient developed a panhypopituitarism with no improvement in diabetes insipidus with the appearance of a second bone lesion in the left frontal sinus

DOI: 10.1530/endoabs.81.EP710

EP711

Pituitary adenoma in the young adult

Lamiae Zarraa, Abdellaoui Wahiba, Imane Assarrar, Siham ROUF & Hanane Latrech
Laboratory of Epidemiology, Clinical Research and Public Health, Faculty of Medicine and Pharmacy Mohammed Premier University Oujda, Endocrinology-Diabetology and Nutrition Department CHU MOHAMED VI, Oujda, Morocco

Introduction & Background
Pituitary adenomas represent 10-25% of all intracranial tumors. Their incidence is higher between the ages of 40-60 years and less frequent in young adults. The objective of this work was to evaluate the prevalence as well as the clinical and etiological profile of pituitary adenomas in young adults.
Key words : pituitary adenoma- yount adult.
Material and methods
Retrospective descriptive study of 21 patients followed-up for pituitary adenoma whose age was less than 30 years. Data were collected from medical records and analyzed by SPSS-V21 software.
Results
Pituitary adenoma in young adults under the age of 30 represented 23% of all cases of pituitary adenoma in our series ($n=21/91$). The mean age at diagnosis was 24 ± 4.9 years with a clear female predominance (61.9%). The clinical presentation was dominated by pituitary secretion syndrome in 66% of cases ($n=15$) followed by pituitary tumor syndrome in 23.8% of cases ($n=5$). Hypothalamohypophyseal MRI showed a pituitary macroadenoma in 71.1% of cases, 72% of which had an extrasellar extension associated with invasiveness in 4 patients (19% of cases), and a pituitary microadenoma was noted in 38.9% of cases. Corticotropic adenomas were reported in 42.8%, followed by prolactin adenomas in 33.3% and somatotropic adenomas in 14.3% of cases. A non-secreting pituitary adenoma was reported in only one patient, i.e. 4.7% of our series. The evaluation of the anteropituitary insufficiency showed a gonadotropic insufficiency in 28% of the cases, 30% of which was secondary to hyperprolactinemia, followed by thyroid and corticotropic insufficiency in 14.3% of the cases respectively and somatotropic insufficiency in one patient.57% of the patients benefited from a surgical treatment with the necessity of a surgical revision in only one patient presenting with a non-secreting pituitary macroadenoma invading the optic chiasma.

Discussion-Conclusion
Pituitary adenomas of the young adult is an uncommon clinical entity of pituitary adenomas. The results of our study are consistent with those of the literature which show a lower prevalence of adenomas in young adults. Mostly, they present as secreting adenomas such as the results found in our series where the most prevalent type was corticotropic adenoma.
Reference
1 Aflorei ED, Korbonits M (2014) Epidemiology and etiopathogenesis of pituitary adenomas. J Neuro-Oncol. https://doi.org/10.1007/s11060-013-1354-5. **2** Ezzat S, Asa SL, Couldwell WT, et al. The prevalence of pituitary adenomas: A systematic review. Cancer 2004;101:613–9

DOI: 10.1530/endoabs.81.EP711

EP712

Evolution from recurrent cushing's disease to pituitary carcinoma

Miruna Anisia[1], Teodora Dumitru[1], Alexandra Stoica[1, 2], Maria Christina Ungureanu[1, 2], Cristina Preda[1,2], Daniel Rotariu[2, 3] & Letitia Leustean[1,2]
[1]'Sf.Spiridon' Clinical Emergency Hospital, Endocrinology, Iasi, Romania; [2]"Gr. T. Popa" University of Medicine and Pharmacy, Iasi, Romania; [3]"Prof. Dr. Nicolae Oblu" Emergency Clinical Hospital, Neurosurgery, Iasi, Romania

Introduction
ACTH-secreting pituitary adenomas occasionally present as aggressive pituitary tumors (APT), with invasion of surrounding structures, rapid growth, resistance to conventional therapies and multiple recurrences. In rare cases they can progress to pituitary carcinomas (PC) in several years, diagnosis being made upon the documentation of systemic or central nervous system (CNS) metastatic spread. Among pituitary carcinomas, the most common malignant subtypes are lactotroph and corticotroph carcinomas.
Case report
We present the case of a 66 years-old female diagnosed with an invasive ACTH-secreting pituitary macroadenoma in 2015. She underwent transsphenoidal surgery followed by Gamma-knife radiation due to recurrent disease. Pasireotide was initiated but discontinued after only two months due to serious side effects, including corticotroph insufficiency. After 2 years of remission, hypercortisolism reappeared but in the absence of approachable residual tumor Cabergoline treatment was initiated, to which she responded well, developing adrenal insufficiency. One year later, considering the increase in tumor size, the second course of Gamma-knife radiosurgery was performed with no efficacy, and in 2020 she underwent transcranial adenomectomy. The immunohistochemistry revealed high agressiveness of the tumor - Ki67 5% and mitotic index was greater than 10 mitoses per 10HPF. The last MRI showed a 9 mm tumor at the vermis and the immunohistopathology report described a pituitary carcinoma metastasis (ACTH intense positive, p53 expression in 40% of the cells and Ki67 5%). External radiotherapy was performed; Temozolomide therapy was contraindicated due to poor clinical condition of the patient. She ultimately died just 2 months following the diagnosis of carcinoma.
Conclusion
The evolution of APTs may have periods of radiological and hormonal quiescence. Morbidity and mortality are increased, even in the absence of progression to PC, especially in functioning corticotroph APTs, where they exacerbate in relation to cortisol excess. So far, no pathological marker has been shown yet to reliably predict pituitary tumor behavior. Early diagnosis would offer the chance for prompt intensive treatment in an attempt to reduce overall morbidity and possible progression to carcinomas.
Keywords: pituitary carcinoma, Cushing's disease;

DOI: 10.1530/endoabs.81.EP712

EP713

Bronchial carcinoma as debut in MEN-1 Syndrome

Alicia Justel Enriquez, Carolina Knott Torcal, Sara Jimé nez Blanco, Victor Navas Moreno & Mónica Marazuela
Universitary Hospital La Princesa, Endocrinology and Nutrition Department, Madrid, Spain

Background
Neuroendocrine tumors present in the MEN-1 syndrome are usually located in pancreatic islets and more than 10% appear de novo, affecting any age group. The debut of a carcinoid tumor is rare, with a prevalence of 2% of bronchial carcinoid tumors.
Materials and methods
We present the case of a 49-year-old woman referred from the Oncology clinic for the assessment of thyroid incidentalomas found in a follow-up CT scan of multifocal bronchial carcinoid tumor (typical carcinoid tumorlet), operated in 2015 with persistently increased chromogranin A (CrgA). Pathology results showed a non-infiltrating, low-grade neuroendocrine neoplasm (carcinoid tumor), within the surgical margins, and < 2 mitoses/mm^2. (2 in the mediastinal face of the left lobe and another in the right lobe)
Results
Thyroid ultrasound showed a multinodular goiter with a dominant 28-mm nodule classified as Bethesda category II. Laboratory tests revealed a pituitary profile, thyroid hormones, catecholamines, 5-HIA, and CEA within normal ranges, elevated ChromograninA levels and undetectable calcitonin. Increased levels of calcium and phosphorus are displayed in table 1. Octeoscan, bone densitometry and calciuria were requested, which didn't show any abnormalities. Parathyroid scintigraphy was performed due to elevated calcaemia >1 gr/dl, with possible adenoma in the upper pole of the right thyroid lobe. Patient was referred for surgery in February 2020, although it was delayed due to the pandemic until June 2021. A total thyroidectomy and a parathyroidectomy were performed, and a parathyroid adenoma was found. Afterwards, the patient temporarily presented phosphocalcic metabolism values within a normal range, followed by a subsequent increase (Table 1). MEN-1 genetic study was requested. A pathogenic variant in the MEN-1 sequence was detected: c.1252G$>$A, *P* (Asp418Asn) in Heterozygosis (rs104894264).
Discussion
Following the suspicion of MEN-1, even in patients with an atypical condition, a genetic study should be requested early, prior to the indication of parathyroidectomy. This is due to the possible implication in the surgical technique, given the great recurrence of hyperparathyroidism in these cases and to avoid the appearance of early complications derived from it.

DOI: 10.1530/endoabs.81.EP713

EP714

Block and replacement therapy of a patient with Cushing's disease and aggressive complications: a case report

Denisa-Isabella Tănasie[1], Găloiu Simona Andreea[1,2], Andra Caragheorgheopol[2], Cristina Corneci[2], Nicoleta Baloseanu[2] & Catalina Poiana[1,2]
[1]University of Medicine and Pharmacy 'Carol Davila' Bucharest, Romania; [2]National Institute of Endocrinology CI Parhon

Introduction
We describe a patient with Cushing's disease caused by a pituitary macroadenoma treated by double transsphenoidal surgery, stereotactic radiosurgery and steroidogenesis inhibitors and also the challenging management of a

Table 1

	17/09/2018	29/01/2019	11/06/2019	16/09/2019	13/02/2020	16/04/2021	25/06/2021 (Surgery 14/06/2021)	29/07/2021	08/2021	02/12/2021
CrgA (ng/ml)	542	258	260	148	106	192				443
PTH (pg/ml)	86.9		166	156.4	124	142	56	54	74.6	87.3
Vit D (ng/ml)	13.88		10.09	20.9	52.79	59.56		68	61.8	46
Ca (mg/dl)	12		11.3	10	11.3	11	9.9	9.7	9.7	10.1
P (mg/dl)	2.8		2.8	2.6	2.1	3	3	2.3	2.7	2.7

patient with multiple comorbidities, including chronic leg ulcers, which are related to increased morbidity and health costs.
Case report
In October 2019, a 67-year-old patient presented with intense headache, left temporal visual impairment and pituitary macroadenoma (3.4 cm). He was diagnosed with Cushing's disease (serum cortisol = 17.55 mcg/dl after 2 mg/day x48h Dexamethasone, ACTH = 197 pg/ml), optic chiasm syndrome and thyrotropin and gonadotropin insufficiency. The patient had significant comorbidities: secondary hypertension and diabetes, episodes of tachyarrhythmia and femoral artery stenosis. After transsphenoidal surgery, despite 3 months remission of hypercortisolism (basal serum cortisol = 0.14 mcg/dl), a 2.1 cm remnant progressive tumor along with biochimical hypercortisolism-serum cortisol = 14 mg/dl after 1 mg Dexamethasone, led to a 6 months dopamine agonist treatment. In 2020, progressive chronic ulceration appeared in the lower limbs. Despite the January 2021 second transsphenoidal operation, in June 2021, the hypercortisolism worsened: severe hypokaliemia (2.5 mmol/l despite potassium replacement), uncontrolled diabetes (HbA1c = 11%), BP = 220 mmHg despite triple therapy, so a steroidogenesis inhibitor and glucocorticoid receptor blocker therapy were initiated. Afterwards, right opthalmoplegia and severe headaches appeared. Pituitary apoplexy and stroke were ruled out by MRI showing a tumoral remnant, invasive in both cavernous sinuses. The treatment was continued only with Metyrapone 500 mg/day. In August 2021, the patient developed adrenal insufficiency while using Metyrapone (BP = 110/70 mmHg, serum glucose = 69 mg/dl, serum cortisol = 1.57 mcg/dl), so Prednisone 5 mg/day was prescribed, thus receiving block and replace regimen. The patient was treated with gamma knife radiosurgery in September 2021. Afterwards, the infected leg ulcers with Grame negative bacteriae forced him to become wheelchair-bound, requiring repeated hospital admissions, with two episodes of acute renal injury. In January 2022, laboratory tests found persistent hypercortisolism (serum cortisol = 20 mcg/ml after 1 mg Dexamethasone without any treatment). Block and replace regimen was restarted. The cardiovascular examination established the need for bilateral thigh amputation, for now, only one having being performed.
Conclusions
This case highlights how the multiple and aggressive complications of Cushing's disease can significantly affect the quality of a patient's life. The chronic leg ulcers, the risks of hospitalisation and the drug toxicity eventually led to amputation. Furthermore, achieving eucortisolism is a constant challenge in the management of recurrent Cushing's disease. Consequently, rigorous and repeated long-term follow-up evaluations of this condition are mandatory.

DOI: 10.1530/endoabs.81.EP714

EP715

Growth hormone leading to faster recovery in pure motor Guillain-Barre syndrome: report of the first off-label use in one patient

Felix Amereller[1], Schopohl Jochen[1], Störmann Sylvère[1], Bidlingmaier Martin[1], Rieckmann Peter[2] & Gulde Philipp[2]
[1]LMU Klinikum, Medizinische Klinik und Poliklinik IV, Munich, Germany; [2]Medical Park Loipl, Center for clinical Neuroplasticity, Bischofswiesen, Germany

Background
Although the prognosis inGuillain-Barré syndrome (GBS) is generally good, the protracted and sometimes incomplete recovery is a heavy burden for patients. Animal studies suggest that treatment with growth hormone (GH) could stimulate myelin repair and thus accelerate functional recovery in acute polyneuropathy. We report on the first use of GH in GBS.
Objective
To monitor safety and tolerability as well as to evaluate the effect of off-label GH therapy during recovery from GBS in one patient.
Patient and methods
A 28-year old male with flaccid tetraparesis caused by pure motor GBS was treated with GH (1 mg/day) for 10 weeks. Muscle strength was measured regularly before, during and after the treatment (total time span 330 d). Strength gain was used as the main parameter of efficacy. A polynomial regression was calculated for strength measurements prior to treatment, and a second one for strength measurements during GH treatment. Using these functions, alterations in strength gain were examined. α was set to 0.05. Effect-sizes are given in R^2 and Glass' Δ. Pearson cross-correlation was computed for IGF-1 and relative strength gains.
Results
No side effects of GH treatment were observed. Serum IGF-1 increased from 177 ng/ml at baseline (50^{th} percentile of age- and sex-adjusted reference interval) to a mean value of 342 ng/ml during GH treatment ($>97.5^{th}$ percentile). Prior to GH administration, body mass ($R^2 = 0.85$, $P < 0.01$) and relative strength ($R^2 = 0.99$, $P < 0.01$) were significantly associated with time, representing the natural course of recovery. During GH treatment, the slope of strength gain was increased ($R^2 = 0.95$, $P = 0.025$). There were three significant alterations of strength gains: both inpatient stays at a neurorehabilitation facility and the GH application (Glass' $\Delta_{Rehab1} = -1.50$, $P < 0.01$, Glass' $\Delta_{Rehab2} = 0.57$, $P < 0.04$, Glass' $\Delta_{GH} = 1.08$, $P < 0.01$). Alterations of strength gain correlated with IGF-1 serum levels ($R^2 = 0.36$, $P = 0.09$). Body mass gain was not increased during GH treatment.
Conclusion
In this single case, GH treatment seemingly led to an acceleration of strength recovery in GBS. Controlled studies should be discussed in order to establish GH as a therapeutic approach in GBS recovery.

DOI: 10.1530/endoabs.81.EP715

EP716

Pituitary Hyperplasia secondary to Severe Primary Hypothyroidism

Harriet Esdaile, Majid Alameri, Abdulla Alnuaimi, Niamh Martin & Karim Meeran
Charing Cross Hospital, Department of Diabetes and Endocrinology, London, United Kingdom

Introduction
Thyrotroph pituitary hyperplasia in context of severe primary hypothyroidism is rare and usually occurs due to loss of thyroxine feedback inhibition and overproduction of thyrotropin-releasing hormone, leading to pituitary gland enlargement. Pituitary hyperplasia caused by primary hypothyroidism responds well to thyroid hormone replacement therapy and rarely requires surgical intervention.
Case presentation
A 42-year-old female with background history of type 2 diabetes, hypothyroidism, transient ischaemic attack (TIA) glaucoma and epilepsy presented initially with light-headedness. Systemic examination was unremarkable. Biochemical assessment revealed severe primary hypothyroidism with TSH of 442 milliunit/l (NR 0.30- 4.20 milliunit/l), free T4 5.2 pmol/l (NR 9-23 pmol/l) and mild hyperprolactinaemia. Magnetic resonance imaging (MRI) revealed a large pituitary macroadenoma with extension into the suprasellar compartment, without compression of the optic chiasm. The patient required escalating doses of levothyroxine, maximally 300 mg daily due to variable compliance (levothyroxine absorption test normal). Imaging was repeated when the patient's TSH had fallen to 0.37 milliunit/l. The repeat MRI pituitary showed marked reduction in the size of the pituitary enlargement, making the diagnosis of thyrotroph pituitary hyperplasia.
Conclusion
Pituitary hyperplasia caused by primary hypothyroidism usually has a good response to thyroid hormone replacement therapy. Surgical intervention is not usually required.

DOI: 10.1530/endoabs.81.EP716

EP717

An aggressive macroprolactinoma in young boy about a case.

Charlene Ludwine Bifoume Ndong, Fatima Zahra El Jaafari, Sana Rafi, Ghizlane El Mghari & Nawal El Ansari
Chu Mohammed VI, Marrakech, Marrakech, Morocco

Introduction
Pituitary adenomas are a rare condition in children and young people. The prolactinoma represents the most frequent of them. We report a case of an atypically evolution of aggressive macroprolactinoma in young patient.
Case
It's about a boy of 14 years old with previous history of headache from 5 years without visual disturbance. He was admitted for intracranial hypertension syndrome. In clinical examination no dysmorphic syndrome, a growth retardation

and a bilateral gynecomastia. MRI showed a macroadenoma with lateral extension to the cavernous sinuses with envelopment of carotid arteries. The hormonal test showed a hyperprolactinemia of 470 ng/ml with a secondary gonadal, corticotropic and thyrotropic deficiency. Partial transsphenoidal adenomectomy was performed and the histological assessment confirmed a macroprolactinoma with upper Ki67 at 7%. Cabergoline was started at 1 mg/week to 2 mg/week. The evolution done by the progressive normalization of blood prolactin and reduction of the size of the residual tumor.

Discussion

Pituitary adenomas in young people are frequently hormonally active. These patients typically presented with endocrine symptoms related to their adenoma type, in our case he presented gynecomastia and tumoral syndrome. Prolactinoma is a more common one.

The radiological caracteristics and the Hight Ki67 proliferation index gave an idea of aggressive tumor. Taking in account the young age it can be part of AIP mutation or another type of genetic predisposition syndrome. These two conditions tend to predict recurrence and resistance to conventional therapy. The good evolution by dopaminergic agonist was atypical. Long-term follow-up will make it possible to report on the recurrence or otherwise of the process.

Conclusion

The management of pituitary adenoma in young patients must take in account the progress on histopathology and molecular fields. The specific medical treatment of prolactinoma may be try as part of complex management.

Reference

1 Öngürü Ö, Düz B, Şimşek H, Günal A, Gönül E. Pituitary macroadenomas (> 3 cm) in young adulthood: Pathologic and proliferative characteristics. Neurol Neurochir Pol. 2015;49(4):212-6.

2 Cuny T, Chanson P. Adénomes hypophysaires agressifs et résistants au traitement Aggressive and resistant-to-treatment pituitary tumors. Ann Endocrinol (Paris). 2013 Oct;74 Suppl 1:S3-12.

DOI: 10.1530/endoabs.81.EP717

EP718

Abstract Withdrawn

DOI: 10.1530/endoabs.81.EP718

EP719

FSH- secreting pituitary microadenoma and ovarian hyperstimulation

Marian Andrei[1], Luminita Nicoleta Cima[1, 2], Mihaela Tarna[1], Marina Iliescu[1] & Fica Simona[1,2]

[1]Elias University Emergency Hospital, Endocrinology Department, Bucharest, Romania; [2]Carol Davila University of Medicine and Pharmacy, Bucharest, Romania

Introduction

The prevalence of functioning gonadotropinoma is difficult to assess since most of reports are case reports. Gonadotropinomas rarely lead to a noticeable clinical syndrome. They usually produce symptoms associated with mass effect such as headaches, visual field impairment and hormonal deficiencies.

Case report

We present the case of a 38 years old women diagnosed in 2017 with microprolactinoma. She had elevated prolactin level (108 ng/ml) and a small pituitary adenoma with 9/8 mm in diameter. She was treated with dopamine agonist for 3 weeks after the diagnosis, treatment stopped afterwards due to side effects. In follow-up examinations prolactin level normalized with no treatment, IRM exam revealed 2 pituitary microadenomas (4/3/6 mm and 3.7/2.5/3.5 mm respectively) and she developed bilateral ovarian cysts. She underwent surgical intervention and the cysts were evacuated, but after 1 month, at next follow-up the cysts reappeared. In our department she presented with headache, amenorrhea and recurrent bilateral ovarian cysts. Serum prolactin was normal but she had a high serum estradiol level (963.2 pg/ml) with a FSH and LH of 2.01 mUI/ml and 2.36 mUI/ml respectively. This was enough to raise the suspicion of a functional gonadotropinoma, unfortunately we could not measure serum gonadotropin hormone alpha-subunit to confirm the diagnosis.

Conclusion

The patient initially presented with a prolactin producing pituitary microadenoma and later developed a second pituitary adenoma. The elevated estradiol level and recurrent bilateral ovarian cysts raised the suspicion of a functional gonadotropinoma. The patient needs further evaluation to confirm the diagnosis.

DOI: 10.1530/endoabs.81.EP719

EP720

Clinical and laboratory features and management of pituitary apoplexy: Case series

Özge Özer, Medine Nur Kebapci, Aysen Akalın, Belgin Efe & Goknur Yorulmaz

Eskisehir Osmangazi University, Department of Endocrinology and Metabolism, Eskisehir, Turkey

Introduction

Pituitary apoplexy (PA) is a clinical emergency resulting from acute ischemia or bleeding of the pituitary gland. Complaints of patients are usuallay headache and vision problems. We tried to discuss the reasons for presentation, pituitary imaging and hormones of patients.

Patients and Methods

10 patients (5 men and 5 women), median age 53 years at diagnosis were retrospectively reviewed. FSH, LH, estradiol/testosterone, GH, IGF1, TSH, FT4, cortisol, ACTH, PRL were measured. Pituitary MRI were performed.

Results

When we look at the reasons for the patients' admission; headache, nausea and vision problems in 4 patients; weakness, fatigue, nausea in 3 patients; confusion in 1 patient; abdominal pain in 1 patient;polyuria, polydipsia, weight loss in 1 patient. Only one patient had a previous history of pituitary adenoma. Panhypopituitarism was present in all patients. One patient had diabetes insipidus too. Macrodenoma was detected in 6 patients (median tumor diameter 31.8 mm). 4 patients were referred to the operation. The pathology result of all of them was seen as nonfunctioning pituitary adenoma(NFA). In one other patient, the mass involved the pituitary and hypothalamus. The operation was not considered due to the general condition of that patient. This patient died in the follow-up. Another operated patient died despite post-operative replacement therapy. The other patient with PA had been operated for NFA about a month ago. The management of this patient was performed with medical therapy. One of the 4 patients with pituitary apoplexy detected on MRI presented at the 24th week of pregnancy with severe headache that did not go away with analgesics. Her treatment was with medical therapy. No complications were observed in the follow-up and she was discharged. Another patient developed PA while receiving radiotherapy for acromegaly. The other one of these 4 patients had complaint with fatigue. The other patient developed PA after coronary bypass procedure. It was thought that this might cause lost a lot of blood during the bypass procedure. Empty sella developed in the follow-up of these patients. Management of these patients was performed with hormone replacement therapies.

Conclusion

Although PA often presents with headache, there are also different forms of presentation. Patients should always be evaluated from this point of view. PA is a condition that can develop very quickly. It can have very serious consequences. In our case series, it was observed that two patients died. Treatment consists of sellar decompression with steroid replacement and, in severe cases, transsphenoidal surgery

DOI: 10.1530/endoabs.81.EP720

EP721

A case of pituitary hyperplasia in a patient with neurofibromatosis type 1.

Faten Cherchir, Ibtissem Oueslati, Meriem Yazidi & Melika Chihaoui

La Rabta University Hospital, Department of Endocrinology, Tunis, Tunisia

Introduction

Neurofibromatosis type 1 (NF1) is an autosomal dominant disorder with diverse manifestations. Patients with NF1 are particularly prone to developing tumors of the central nervous system (CNS) and endocrine disorders. Herein we report a case of pituitary hyperplasia in a woman with NF1.

Observation
A 55-year-old woman was referred to our department for the exploration of recurrent hypoglycemia. Her past medical history included NF1, asthma treated with inhaled glucocorticoids, and ischemic stroke. On physical examination she had a body weight of 46 Kg, a body height of 1m40, corresponding to a body mass index of 23.5 kg/m^2 blood pressure of 120/80 mmHg, a heart rate of 90 bpm, a normal thyroid gland, multiple cutaneous neurofibromas, mainly in the chest and abdomen, café-au-lait spots, and thoracic scoliosis. No dysmorphic syndrome was observed. Biological investigations revealed a morning cortisol level of 11 ng/ml (nr: 40-200), an ACTH level of 4.9 pg/ml (nr: 10-48), a TSH level of 0.68 mUI/l, a FT4 level of 1.13 ng/dl, a prolactin level of 25 ng/ml, a FSH level of 68.7U/l, and a LH level of 18.5 U/l. The diagnosis of isolated corticotroph deficiency was established. A steroid-induced adrenal insufficiency was evoked. The first pituitary magnetic resonance imaging (MRI) scan showed an enlarged sella measuring 7.8 mm in height with superior convexity and homogeneous contrast enhancement. No focal lesion was detected. The patient was treated with hydrocortisone. A follow-up pituitary MRI scan performed at seven months showed the same aspect.
Conclusion
NF1 is a tumor predisposition syndrome, frequently associated with CNS tumors, especially optic gliomas. Few cases of pituitary adenomas have also been reported. To the best of our knowledge, this is the first report of pituitary hyperplasia with no evidence of prolactin and GH hypersecretion diagnosed in the context of NF1. The mechanisms inducing pituitary abnormalities remain misunderstood.

DOI: 10.1530/endoabs.81.EP721

EP722

Assessment of the thyroid status in acromegaly patients
Bahar Gokce Sezgin Yuksel[1], Goknur Yorulmaz[2], Ahmet Toygar Kalkan[2], Medine Nur Kebapci[2], Aysen Akalin[2] & Belgin Efe[2]
[1]Eskişehir Osmangazi University, Internal Medicine, Eskisehir, Turkey; [2]Eskişehir Osmangazi University, Endocrinology, Eskisehir, Turkey

Acromegaly is a rare disease associated with hypersecretion of growth hormone due to adenoma of somatotroph cells in the pituitary gland, with elevated morbidity and mortality. Acromegaly and thyroid diseases show high co-occurrence. In our study; we aimed to determine the relationship between disease activity at the time of admission and after treatment with the presence of goiter, presence of nodules, and possible accompanying thyroid malignancy in 119 patients with acromegaly that we followed in our clinic. Material Method: Patients age, gender, body mass index, age at diagnosis, pituitary adenoma size, thyroid gland volume, thyroid nodule dimensions, GH (Growth hormone), IGF-1 (Insulin-like growth factor-1) values, thyroid function tests, fasting glucose, insulin, HbA1c, thyroid autoantibody levels, frequency of thyroid malignancy, whether or not pituitary insufficiency developed after pituitary surgery and medical treatments were recorded.
Results
58% ($n=69$) of the patients had at least one thyroid nodule. MNG (Multinodular goiter) was present in 47.9% ($n=57$) of the patients. Patients dominant nodule mean size with thyroid ultrasonography was 13.6 ± 9.8 mm. In the follow-up of the patients, thyroid malignancy was detected in 4.2% ($n=5$) of the patients. Histopathology was compatible with papillary thyroid carcinoma in all of these patients. A statistically significant correlation was observed between last admission IGF-1 levels and insulin resistance ($P=0.019$). In addition, a positive correlation was found between HbA1c levels and thyroid nodule size in our study ($P=0.025$). It was observed that 26.1% of the operated patients developed hypopituitarism. Postoperatively, 59.1% of the patients were treated with a long-acting somatostatin analog, 27.3% with cabergoline, and only 1 patient with pegvisomant.
Conclusion
Nodular thyroid disease is a common condition in patients with acromegaly. For this reason, clinicians should pay attention to the thyroid examination in the physical examination of patients with acromegaly.

DOI: 10.1530/endoabs.81.EP722

EP723

Digestive complications of acromegaly : about 40 cases
Ajili Rihab[1], Salah Ameni[2], Hasni Yosra[2], Zantour Baha[1], Sfar Habib[1] & Ach Koussay[2]
[1]University Hospital Tahar Sfar Mahdia, Endocrinology, Mahdia, Tunisia; [2]University Hospital Farhat Hached Sousse, Endocrinology, Sousse, Tunisia

Introduction
Acromegaly is a rare hormonal condition that results from an excess amount of growth hormone (GH) in the body. A variety of complications have been reported in patients with acromegaly including cardiovascular diseases, diabetes mellitus or respiratory disorders. In addition, Acromegaly is associated with gastrointestinal complications. The aim of this study was to evaluate gastrointestinal complications and their impact on the quality of life among patients suffered from acromegaly.
Methods
We conducted a cross-sectional study including patients admitted for acromegaly in the endocrinology departments of Sousse and Mahdia (Tunisia), over a period of 20 years. The QOL was assessed with ACROQOL questionnaire.
Results
A total of 40 patients were included with a mean age of 38.9 years [13-77]. The sex ratio (M/F) was 0.74. The mean IGF1 level was 937 ng/ml [367-1700]. Anterior pituitary insufficiency was present in 32.5% of cases. The most common functional gastrointestinal symptom was constipation (32%). Among our patients, abdominal ultrasound performed in 20 patients showed splenomegaly and hepatomegaly in 2 cases each. Colonoscopy realized in 9 cases showed dolichocolon in 4 cases and colonic polyps in 2 cases. In our population, acromegaly complicated by dolico-colon was associated with impaired QOL, especially for socio-relational life ($P=0.04$).
Discussion and conclusion
Upper and lower functional gastrointestinal tract disorders are significantly more prevalent in patients with acromegaly. Gastrointestinal complications make the QOL altered. Furthermore, poorer QOL may in part be attributable to the increased prevalence of abdominal symptoms.

DOI: 10.1530/endoabs.81.EP723

EP724

Short-term and long-term surgical remission of acromegaly in a tertiary medical center
Alexander Lutsenko, Zhanna Belaya, Elena Przhiyalkovskaya, Liudmila Rozhinskaya, Andrey Grigoriev, Vilen Azizyan & Galina Melnichenko
Endocrinology Research Centre, Moscow, Russian Federation

Background
Surgical outcomes in patients with acromegaly are highly dependent on a surgeon's level of expertise, as the majority of patients present with macroadenomas at diagnosis.
Aim
To assess remission rates in patients with acromegaly admitted to a tertiary medical center.
Materials and methods
We included patients admitted to the neuroendocrinology and bone disease department with no previous radiation therapy or current medical therapy with SSA or pegvisomant. Suppression of GH levels less than 1.0 ng/ml was a criterion for short-term remission. Normalization of IGF-1 levels according to an age-specific reference range was a long-term remission criterion.
Results
44 patients were included in the study: gender (32.8% m, 68.2% f), median age 47.0 [34.0;55.0], IGF-1 744.75 ng/ml [548.83;889.85], GH 9.5 ng/ml [4.94;17.07], tumor volume 832 mm3 [419,25;2532,38]. Microadenomas were identified in 8 patients (18.2%), 36 patients had macroadenomas at diagnosis (81.8%). Early postoperative remission was achieved in 35 patients (79.5%). For microadenomas the remission rate was 87.5% ($n=7$) and for macroadenomas it was 77.7% ($n=28$). Surprisingly, we did not observe differences between patients with and without early remission in age, tumor volume, histological variants and SSTR2, SSTR5 expression – this could be explained by the small sample size. Patients who achieved short-term remission had higher IGF-1 and basal GH levels: IGF-1 935,60 ng/ml [649.60;1186.00] vs 737.60 ng/ml [532.10;876.20], $P=0.047$, GH 36.40 ng/ml [9.61;63.30] vs 8.90 ng/ml [3.74;15.20]. Patients with no remission after surgery were prescribed with SSA. All patients were followed-up, median 19.0 months [12.5;29.0]. Long-term remission was achieved in 61.4% (27 patients), 9

patients had no remission (20.5%), 2 patients had recurrence (4.5%), 6 patients were lost to follow-up (13.6%). In line with short-term remission, patients with long-term remission had lower basal GH 8,9 ng/ml [3,76;11,9] vs 28,0 ng/ml [6,75;47,2], $P=0.006$ and IGF-1 674,80 ng/ml [482,5;876,2] vs 771,0 ng/ml [649,6;992,0], $P=0.030$. We assessed the predictive value of basal GH for long-term remission: AUC 0.811 (95%CI:0.649; 0.973). A cut-off value of 15.55 ng/ml yielded the following results: sensitivity 70.0% (34.8%;93.3%) specificity 85.7% (67.3%;96.0%), accuracy 81.6% (65.7%;92.3%), positive predictive value 63.6% (39.3%;82.5%), negative predictive value 88.9% (75.4%;95.4%). This model demonstrates poor PPV, however, good NPV shows the potential predictive use.
Conclusion
Our study demonstrates short-term and long-term remission rates comparable with literature-reported rates for experienced pituitary centers. Basal GH shows potential for prediction of long-term remission of acromegaly in the Russian population, however cohorts should be substantially increased for more accurate results.

DOI: 10.1530/endoabs.81.EP724

EP725

Decreased quality of life in adult patients with sheehan syndrome

Ameni Salah, Amel Maaroufi, Rihab Ajili, Ghada Saad, Yosra Hasni & Koussay Ach
University Hospital Center Farhat Hached, Endocrinology Department, Sousse, Tunisia

Introduction
Sheehan Syndrome (SS) is the oldest known cause of non-tumor acquired anterior pituitary insufficiency in women. The incidence of SS would probably have decreased in recent decades in developed countries thanks to the development of obstetric care. However, it still remains a public health problem in developing countries. In addition, it constitutes a chronic disabling pathology and is strongly linked to an alteration of the quality of life. In this study we aimed to evaluate the impact on quality of life of SS.
Patients and methods
This is a descriptive cross-sectional study. It was carried out in the Endocrinology department of the University Hospital Farhat Hached, Sousse, Tunisia, over a period of nine months, from July 2019 to March 2020. The assessment of quality of life was based on the specific questionnaire "Quality of Life Assessment of Growth Hormone Deficiency in Adults (QoL-AGHDA)". It is composed of 25 items. The answer choice of the 25 "yes/no" items is scored 1/0. The total score is calculated as the sum of the item scores, ranging from 0 to 25, with a higher score indicating a lower quality of life.
Results
Sixty five patients were included to the study. The mean age at diagnosis of SS was 48.2 $\pm$ 12.4 years. Thyrotropic and corticotropic insufficiency were present in 86.2% of our patients, followed by gonadotropic and lactotroph insufficiency in 72.3% and 38.5% of patients, respectively. Somatotropic insufficiency was explored by a dynamic test in only 8 patients, concluding with somatotropic deficiency in 10.8% of cases. Quality of life was assessed in 15 patients, with a mean QoL-AGHDA quality of life questionnaire score of 12.8 $\pm$ 5.5. Eight patients had a total score of the QoL-AGHDA questionnaire greater than or equal to 11. Seven patients, including three with a total QoL-AGHDA quality of life score of more than 18, were followed for an anxiety-depressive disorder. A 66-year-old patient presented cognitive disorders such as memory and concentration disorders after 26 years of evolution of SS. We did not note any significant correlation between the quality of life score and the SS dependent factors (duration of the SS, the existence or not of corticotropic or gonadotropic insufficiency, the dose of hydrocortisone...).
Discussion-Conclusion
SS is a chronic disease strongly associated with impaired quality of life, mainly due to GH deficiency and glucocorticoid overdose.

DOI: 10.1530/endoabs.81.EP725

EP726

Predictive factors of biological remission in patients with prolactinoma treated with dopamine agonists

Mouna Elleuch, Hamdi Frikha, Loukil Fatma, Dhoha Ben Salah, Matiem Souissi, Fatma Mnif, Mouna Mnif, Nadia Charfi, Nabila Rekik Majdoub, Faten Haj Kacem Akid & Mohamed Abid
Hedi Chaker University Hospital, Department of Endocrinology, Sfax, Tunisia

Introduction and aim
Dopamine agonists (DA) are prescribed as first-line treatment for prolactinomas and are generally effective and well tolerated. However, the degree and quickness of therapeutic response is variable among patients. The aim of this work is to study the predictive factors of biological remission in patients with prolactinoma treated with DA.
Methods
A single-center, retrospective and analytical study of patients with prolactinoma followed in the endocrinology department of Hedi Chaker University Hospital of Sfax, Tunisia between 2000 and 2020. Biological remission was defined as prolactinemia <25 ng/ml.
Results
We enrolled 69 patients. Patients were predominantly female (69%), aged 38.1 $\pm$ 14.5 years at diagnosis. One third of patients were obese. Mean initial prolactinemia was 2790.4 $\pm$10780 ng/ml. Adenomas were classified as follows: 24 microprolactinomas, 29 macroprolacinomas and 16 giant prolactinomas. Bromocriptine was prescribed in 46 cases while the remaining were treated with cabergoline. Biological remission was obtained in 24 patients at 6 months of treatment (34.8%) and reached 65.2% at 12 months. Univariate analysis shoewed that the use of cabergoline was significantly associated with remission at 6 months and 12 months ($P<0.001$). The effect of age reached statistical significance at 12 months ($P=0.05$). Using multivariate analysis, factors associated with remission at 6 months were cabergoline use only ($P=0.04$, OR$=6$) while those that significantly influenced remission at 12 months were cabergoline use ($P=0.005$, OR$=11$) and tumor size at diagnosis ($P=0.028$, OR$=1.2$, IC[1.02;1.35]). In this series sex and BMI were not significant markers of remission both in univariate and multivariate models.
Conclusion
Cabergoline has proven to be a safe and effective treatment for prolactinomas. Cost and affordability remain major barriers in developing countries.

DOI: 10.1530/endoabs.81.EP726

EP727

Challenging management of giant prolactinomas in men: from efficient small dose of cabergoline to SSA, neurosurgery and Temozolomide

Aleksandra Gilis-Januszewska, Anna Bogusławska, Magdalena Godlewska, Łukasz Kluczyński & Alicja Hubalewska-Dydejczyk
Chair and Department of Endocrinology, Jagiellonian University, Medical College, Cracow, Poland

Giant prolactinomas are very rare and constitute 2-3% of all lactotroph PitNETs with male preponderance. We present a case series of five male patients with giant prolactinomas with various clinical presentation.
Case 1
A 66-year-old male hospitalized due to left peripheral facial palsy. In computer tomography (CT) pituitary mass (41 x 43 x 64 mm) invading cavernous/sphenoid sinuses/carotid arteries/optic chiasm was visualized. Bitemporal hemianopia/-headaches/decreased libido were observed. Prolactin level was 22083 uIU/ml (N: 86-324 uIU/ml). Cabergoline up to 1 mg/week was implemented. After 3 months, regression of pituitary tumor by 14 mm and normal range prolactin level were observed. Milder headaches and improvement of visual field were reported.
Case 2
A 62-year-old male presented with life-threatening panhypopituitarism/diabetes insipidus at the age of 52. In MRI pituitary tumor 36 x 62 x 35 mm with extrasellar extension/optic chiasm compression/invading third ventricle was found. Prolactin level was 223549 uIU/ml. Despite dopamine agonist treatment (bromocriptine 22.5 mg/day and cabergoline 1.5 mg/week) progression of pituitary tumor/high prolactin level were observed. In 2016 patient did not consent to neurosurgery. Short-acting somatostatin analogues was introduced. In 2019, significant visual filed deterioration was observed- patient consent to craniotomy. Histopathology revealed lactotroph-PitNET with Ki67>3%. After 6 months, tumor progression was noted. Patient was disqualified from radiotherapy. Temozolomide (200 mg/m^2 per 5 days every 28 days) was introduced. After 9 cycles, regression of pituitary tumor was observed and decrease of prolactin level by 2600%.
Case 3
A 56-year-old male was hospitalized due to syncope. In CT pituitary tumor 40 x 30 mm was diagnosed with bitemporal hemianopsia. Prolactin level was 10446 uIU/ml. Cabergoline(1 mg/week) was implemented. After 3 months, regression of pituitary tumor (21 x 26 x 19 mm)/normal prolactin level/improvement of vision were noted.
Case 4

A 23-year-old male presented with severe headaches and visual impairment at the age of 21. In MRI pituitary mass 52 x 52 x 41 mm with extrasellar extension was found. Prolactin level was 21522uIU/ml. Insufficiency of thyroid and gonadal axis was diagnosed. Cabergoline was implemented (4 mg/week) with regression of the tumor (25 x 13 x 23 mm), decrease of prolactin level (8400uIU/ml) and complete remission of headaches. Cabergoline was decreased to 2 mg/week.
Case 5
A 67-year-old male diagnosed with a pituitary tumor (65 x 35 x 40 mm) at the age of 50 years. Due to hyperprolactinemia, cabergoline was implemented (7 mg/week). After few weeks, pituitary apoplexy occurred. Patient underwent emergency neurosurgery. Insufficiency of thyroid, adrenal and gonadal-axis appeared. MRI over next 20 years demonstrated stable residual tumor(22 x 28 x 11 mm). Patient is now treated with 0.25 mg of cabergoline/week. The management of giant prolactionomas in men is challenging. Studies on prognostic factors of the efficient treatment in prolactinomas are needed.

DOI: 10.1530/endoabs.81.EP727

EP728

The incidence of hyperprolactinemia in patients with breast cancer.

Zamira Khalimova[1] & Aliya Gumarova[2]
[1]Republican Scpecialized Scientific Medical Center of Endocrinology, Neuroendocrinology, Tashkent, Uzbekistan; [2]Republican Scpecialized Scientific Medical Center of Endocrinology Neuroendocrinology, Neuroendocrinology, Tashkent, Uzbekistan

Objectives
To study the relationship between hyperprolactinemia and various forms of breast cancer in women of fertile age.
Methods and materials
The study included 100 breast cancer patients, aged 25 to 43 years (mean age 34.5 $\pm$ 1.4 years). The patients were divided into 2 groups: Group I 33 patients with hyperprolactinemia, which corresponded to 33%. Group II 67 patients with breast cancer without hyperprolactinemia, which corresponded to 67%. Clinical (examination of somatic, endocrine and mammological status), hormonal, immunohistochemical, histological, and instrumental studies (ultrasound of the mammary glands, MRI of the brain with a pituitary gland, mammography) were used in the work. The studies were carried out in patients on outpatient and inpatient treatment.in 3 (9.0%) tubular carcinoma, in 2 (6%) medullary cancer, and in 1 case (3%) colloid and papillary breast cancer. In group II, in 67 patients, the distribution of the corresponding forms of breast cancer occurred in 19.4%, 16.4%, 7.5%, 10.4%, 7.5%, 6%, respectively. And also in 25 patients there were other forms of breast cancer (apocrine cancer, cystic hypersecretory carcinoma, adenoid cystic cancer. In 3 (9.0%) tubularcarcinoma, in 2 (6%) medullarycancer, andin 1 case (3%) colloidandpapillarybreastcancer. In group II, in 67 patients, the distribution of the corresponding forms of breast cancer occurred in 19.4%, 16.4%, 7.5%, 10.4%, 7.5%, 6%, respectively. And also in 25 patients there were other forms of breast cancer (apocrine cancer, cystic hypersecretory carcinoma, adenoid cystic cancer.
Conclusion
1. The association of hyperprolactinemia due to formations of the pituitary gland is the main problem that deserves methods of their diagnosis and management.
2. Hyperprolactinemia may increase the incidence of such forms of breast cancer as ductal and lobular breast cancer *in situ* (63.4% vs 19.4%) and tubular carcinoma (9% vs 7.5%) in patients with breast cancer and normoprolactinemia.

DOI: 10.1530/endoabs.81.EP728

EP729

Case report: a challenging gastrinoma in a patient with renal cell carcinoma

Alina Ioana Paduraru[1], Iulia Florentina Burcea[1, 2] & Catalina Poiana[1,2]
[1]C.I. Parhon National Institute of Endocrinology, Bucureşti, Romania; [2]Carol Davila University of Medicine and Pharmacy, Bucureşti, Romania

Introduction
Gastrinomas are rare neuroendocrine tumours (NETs) that arise from enterochromaffin-like cells and produce gastrin. Most are discovered in the duodenum and pancreas. The clear cell type of renal cell carcinoma (RCC) is known for the expression of gastrin-releasing peptide receptor (GRP-R) and some studies have shown GRP can stimulate tumor cell proliferation and neoangiogenesis. Therefore, we present a case with metachronous development of renal cell carcinoma and gastrinoma.
Case presentation
A 55-year-old obese, hypertensive female patient with a history of renal cell carcinoma (histopathology: Grawitz tumour grade 2) treated with surgery, radiotherapy and interferon at the age of 36 years old, presents with the suspicion of a neuroendorine tumour. SPECT/CT scan identified a possibly neuroendocrine tumour localised in the ileum and the blood tests revealed a gastrin level of 30 times x upper limit of normal (ULN) and chromogranin A 2.11 times x ULN. All other neuroendocrine markers were in the normal range. Treatment with Octreotide LAR 30 mg/28 days was initiated and gastrin level dropped to 5 x ULN. One year later, another SPECT/CT scan revealed radiotracer accumulation in the gastric antral region and first part of duodenum, associated with increased gastrin level (10 x ULN), which led to the increase of Octreotide LAR to 40 mg/28 days and after 2 months, the gastrin level dropped to 2.4 x ULN. Imaging evaluation showed no metastases. Abdominal surgery was performed, but the primary lesion could not be identified during laparotomy. In the meantime, the patient suffered a severe form of COVID-19 infection with 80% of the lungs being affected. The patient stopped treatment for gastrinoma for almost 2 months and gastrin raised again to 7 x ULN. Morever, the pacient was diagnosed with type 2 diabetes and started treatment with Metformin. Currently, gastrin level is 2.8 x ULN, with mild cholestasis syndrome and normochromic normocytic anemia.
Conclusion
Despite the high gastrin levels, the patient has no metastatatic lesions. One particularity of this case is that even though surgery is thought to be the only curative treatment, the surgical intervention could not find any gastrointestinal tumour. Another particular aspect is the unusual association between RCC and gastrinoma, considering that GRP and its receptor can play an important role in carcinogenesis, this being a future path for novel targeted therapy.
Keywords. gastrinoma, neuroendocrine tumours, carcinoid syndrome, renal cell carcinoma

DOI: 10.1530/endoabs.81.EP729

EP730

Hypogonatropic hypogonadism with craniopharyngioma in adults before and after surgery.

Irina Klockova, Ludmila Astafieva, Pavel Kalinin, Maksim Kutin & Aleksandr Konovalov
Burdenko Neurosurgical Institute, Neyroonkologiya, Moscow, Russian Federation

Craniopharyngiomas (CF) - a benign tumor of the embryologic origin. The surgical method of treatment is the basic.
Objective
to estimate incidence of hypogonatropic hypogonadism before and after surgical treatment of CF at different topographical variations, and after the preservation of the pituitary stalk.
Methods
The research involved 79 patients older than 18 years (41 women and 38 men) with a mean age - 40 [17; 69] with a verified diagnosis of CF. All patients were operated, in 12 cases the pituitary stalk was saved. Before and 7 days, 3 and 6 months after the surgery all patients were examined by means of hormonal blood tests (LH, FSH, estradiol, testosterone, TSH, free T4, cortisol, prolactin, IGF-1). By localizing tumor patients were divided into 3 groups: 1 – intra-suprasellar (9), 2 – at location of the pituitary stalk (48), 3 –intra-ventricular (22).
Results
hypogonatropic hypogonadism was confirmed. In group 1 : before the surgery - 9 (100%). 3 patients have subtotal ablation. After the surgery the nature of disturbance has not changed. In group 2: hypogonatropic hypogonadism before the surgery - 38 (80%). In 12 cases the pituitary stalk was saved. After the surgery – 46 (96 %). Two women with saved the pituitary stalk had high levels of gonadotropins, respectively postmenopausal period. In group 3: hypogonatropic hypogonadism – 19 (86%, after the surgery - 17 (90 %). Reproductive function recovered in two patients (one woman has a natural pregnancy).
Conclusion
The high incidence of hypogonatropic hypogonadism is caused by the localization of the CF. Preservation of the pituitary stalk does not lead to restoration of the pituitary-gonadal axis in 83 % of cases. Non-radical ablation of ventricular CF can maintain fertility.

DOI: 10.1530/endoabs.81.EP730

EP731

Antioxidant and protective effect of estradiol in liver functions of aged female rats

Pardeep Kumar & Najma Baquer
Jawaharlal Nehru University, Life Sciences, New Delhi, India

Background
The objective of this study was to observe the changes in activity of antioxidant enzymes, hepatic glucose homeostasis, lipogenic enzymes and lipid metabolism, serum lipid profile and liver function occurring in livers of female rats of 3, 12 and 24 months age groups, and to see whether these changes are restored to 3 months control levels rats after exogenous administration of steroid hormone estrogens (17-β-estradiol, E2).
Methods
The aged rats (12 and 24 months old) ($n=$ 8 for each group) were given subcutaneous injection of 17 beta estradiol (0.1 mg/g body weight) daily for one month. After 30 days of hormone treatment, experimental animals of all the groups were sacrificed and livers were isolated for further study. A detailed study was carried on non-enzymatic glutathione (GSH) and enzymatic antioxidants [superoxide dismutase (SOD), glutathione peroxidase (GPX) and catalase (CAT)], hepatic glucose homeostasis, lipogenic enzymes, lipid metabolism, serum aspartate aminotransferase (GOT), alanine aminotransferase (GPT), alkaline phosphatase (ALP), gamma-glutamyl transferase (GGT), phosphatase alkalin (PAL) as well as bilirubin level.
Results
The results obtained in the present work revealed that normal aging was associated with significant decrease in the activities of antioxidant enzymes, serum expression and an increase in hepatic glucose homeostasis, lipogenic enzymes and lipid profile and GGT, PAL, GOT, GPT, ALP as well as bilirubin level increased significantly in livers of aging female rats. Our data showed that exogenous administration of E2 brought these changes to near normalcy in aging female rats.
Conclusions
The present study showed that E2 treatment reversed the changes to normal levels. E2 treatment may be beneficial in preventing some of the age related changes in the liver by increasing antioxidant defences and decrease oxidative stress. E2 plays important role in the progression of chronic hepatic diseases.

DOI: 10.1530/endoabs.81.EP731

EP732

Rare case of cushing with papillary thyroid cancer

Marwa Fathy[1,2], Farouk Hassan[2, 3] & Randa Salam[1,2]
[1]Faculty of Medicine-Cairo University, Internal Medicine-Endocrinology Unit, Cairo, Egypt; [2]Cairo University, Clinical Endocrinology, Faculty of Medicine, Cairo, Egypt; [3]Faculty of Medicine-Cairo University, Interventional Radiology, Cairo, Egypt

Introduction
Papillary thyroid carcinoma is the most common type of thyroid cancer (70-80% of all thyroid cancer). It is a differentiated type of carcinoma, it affects women between 30-60 years old, 3 times more often than males. Clinical outcome in patients with differentiated thyroid carcinoma is often favorable. Glucocorticoids (GC) play major role in the physiologic stress response. However chronic exposure to glucocorticoids as seen in Cushing's disease (CD) has detrimental effects on multiple systems: cardiovascular, metabolic, immune, psychological. CD, caused by a pituitary adrenocorticotropic hormone (ACTH)-secreting tumor, is probably underestimated at 1.2-.2.4 per million per year and it affects mostly women). Association of Cushing's disease and papillary thyroid carcinoma is very rare and it appears that ACTH secretion is insufficient to cause typical cushingoid feature
Case report
36 year old female, known to be hypertensive 4 years ago on BB, diuretics and ACEI. In 3/2018, she underwent thyroidectomy and was pathologically proved to have follicular variant of low grade papillary carcinoma. Thyroidectomy was followed by radioactive iodine ended at 2019 and she is on regular follow up with department of Radiotherapy and Nuclear Medicine, she is maintained on Thyroxine 300 mcg/day. Over the last 4 months, she noticed weight gain especially in upper chest and abdomen. She also noticed swelling of both hands and feet associated with generalized weakness.
Examination
Bp: 110/70, Pulse: 90/min, w: 95 kg, Height: 1.57 m. BMI: 38 kg/m^2. Acanthosis Nigerians, Fat accumulation has a central distribution (face, trunk, abdomen more than extremities).
Investigations
Urinary free cortisol (UFC) was (530.6 µg/24 h, N: 20.9- 292.3µg/24 h), Cortisol (am): 19.6 Mg/dl(6.2- 19.4), Low dose dexamethasone suppression test revealed autonomous hypercortisolemia, suggesting cushing disease. MRI of the pituitary revealed a microadenoma of 5 mm on the left side, IPSS on LF side ACTH 517.5 pg. At this point the patient was diagnosed with CD and referred for trans sphenoidal pituitary surgery that removed the tumor. After operation ACTH <10 pg, BMI droped to 32 kg/m^2, regular cycles she stopped antihypertensive medication
Conclusion
Association between papillary thyroid carcinoma and Cushing's disease is very rare and so far there is no known genetic mutation to link the two neoplastic conditions, and no clear relationship between neoplastic thyroid and hypercortisolemia has been established in the current endocrine literature

DOI: 10.1530/endoabs.81.EP732

EP733

Analysis of the causes and frequency of discrepancies between GH and IGF-1 levels in patients with acromegaly based on the polish register of acromegaly patients

Magdalena Ostrowska, Agnieszka Tomasik, Wojciech Zgliczyński & Piotr Glinicki
Centre of Postgraduate Medical Education, Department of Endocrinology, Warsaw, Poland

Introduction
Acromegaly is a rare disease of the pituitary gland. Both GH and IGF-1 levels are of key importance for monitoring of treatment effects in patients with acromegaly. In some patients, divergent results of measurements of these hormones are observed.
Purpose
The purpose of the study was to estimate frequency of GH and IGF-1 inconsistencies in the population of patients with acromegaly included in the Polish Register of Acromegaly Patients, and to investigate whether selected biochemical parameters can predict the possibility of GH/IGF-1 incompatibility.
Material and methods
143 patients with acromegaly were included in the analysis.
- G1 ($n=43$) GH <1 µg/l and IGF-1 within the reference range for sex and age,
- G2 ($n=51$) GH $>$ 1 µg/l and IGF-1 above the reference range for sex and age,
- G3 ($n=15$) GH $>$ 1 µg/ml and IGF-1 within the reference values for sex and age,
- G4 ($n=34$) GH <1 µg/ml and IGF-1 above the reference range.

Results
The discrepancy of results of GH and IGF-1 hormonal tests in the studied population was found in 49 patients (34%). There were no statistical differences between the study groups in terms of age, disease duration, time since surgery, GH and IGF-1 levels at diagnosis, fasting glucose and HBA1C. Based on unidimensional logistic regression models, it was found that the GH/IGF-1 discrepancy was significantly associated with GH level at the time of diagnosis of acromegaly (OR $=$ 0.98 CI95 [0.96; 0.99], $P=$ 0.039) and with creatinine level (OR $=$ 10.94 CI95 [1.75; 82.77], $P=$ 0.014). The multivariate regression model showed that parameters studied: surgery, IGF-1 concentration at diagnosis, and creatinine levels, turned out to be the best combination of factors predicting the possibility of GH/IGF-1 incompatibility. The surgery to remove the pituitary adenoma and increasing concentration of creatinine increased the possibility of discrepancy (OR $=$ 15.45 CI95 [2.24; 358.92], $P=$ 0.023 and OR $=$ 15.71 CI95 [1.87; 160.48], $P=$ 0.014, respectively), while the increase in IGF-1 concentration at diagnosis reduced the possibility of GH/IGF-1 discrepancy (OR $=$ 0.998 CI95 [0.997; 0.999], $P=$ 0.008).
Conclusions
1. On the basis of obtained results, the discrepancy between GH and IGF-1 hormonal determinations among the studied patients was 34%. 2. An increase in IGF-1 concentration at the time of diagnosis decreased the possibility of GH/IGF-

1 discrepancy, while adenoma resection and the observed increase in creatinine level increased the risk of GH/IGF-1 discrepancy.

DOI: 10.1530/endoabs.81.EP733

EP734

Metabolic and inflammatory parameters for baseline characterization and treatment outcome of prolactinoma patients

Susanna Hofbauer[1,2], Matthias Ernst[1, 2], Laura Horka[1, 2], Samuel Seidenberg[1, 2], Lucas Regli[2, 3], Carlo Serra[2, 3], Felix Beuschlein[1, 2] & Zoran Erlic[1,2]
[1]University Hospital Zurich, Endocrinology, Diabetology and Clinical Nutrition, Zurich, Switzerland; [2]University of Zurich, Zurich, Switzerland; [3]University Hospital Zurich, Neurosurgery, Clinical Neuroscience Center, Zurich, Switzerland

Background
Prolactinomas (PRL) are pituitary adenomas mainly characterized by hyperprolactinemia. In addition to the endocrine effects of prolactin, metabolic alterations have been described in PRL patients. Changes in inflammatory parameters have recently been identified in pituitary adenoma patients. Since both, metabolic (MM) and inflammatory markers (IM) showed promising results in characterization/prognosis of tumor patients, it is tempting to speculate whether those might be useful also in PRL patients.
Patients, methods, results
In this retrospective analysis of medically treated PRL, 23 patients with microprolactinoma (56% women, mean age 34.5) and 30 patients with macroprolactinoma (37% women, mean age 40.7) were included. No difference between micro- and macroprolactinoma patients were evident regarding age, sex, and rate of obesity, hypertension and prediabetes/diabetes mellitus. At baseline, macroprolactinoma patients presented with higher heart rate (HR) ($P=0.005$) and higher likelihood of thyrotropic- ($P=0.007$) and gonadotropic-insufficiency ($P=0.006$). We found a significant correlation between prolactin and BMI (rs=0.364; $P=0.007$) as well as PRL-size with HbA1c (rs=0.413; $P=0.032$), BMI (rs=0.316; $P=0.021$) and HR (rs=0.284; $P=0.050$). Considering prolactin or PRL-size separately in a multivariate analysis with BMI, HbA1c and HR a significant positive association persisted between prolactin and HbA1c ($P=0.009$), whilst HR and BMI were positively associated with each other and independent from prolactin or PRL-size. HbA1c had also a negative correlation with testosterone (rs=-0.478; $P=0.038$), which was not persistent after including prolactin in the multivariate analysis. No correlation could be identified at baseline between prolactin/PRL-size with the studied IM (Glasgow Prognostic Score, Neutrophil-Platelet-Score, Neutrophile-to-Lymphocyte-Ratio [NLR], Platelet-to-Lymphozyte-Ratio [PLR], Prognostic Nutrition Index, Systemic Immune Inflammation Index) and other studied MM (LDL- and HDL-cholesterol, triglyceride, blood pressure [BP]). An association between NLR and fT4 (rs=0.329; $P=0.038$) as well as LDL (rs=-0.617; $P=0.014$) was identified, which did not persist in a multivariate analysis considering both variables together and PRL-size. A correlation between fT4 and PLR (rs=0.351; $P=0.026$) could not be confirmed in the multivariate analyses with prolactin level and PRL-size, separately. In 47 patients complete follow-up data (median follow-up time 17 months, interval 2–141 months) were available. Cabergoline dosage required to achieve normoprolactinemia correlated with baseline LDL (rs=0.493, $P=0.052$), systolic (rs=0.341; $P=0.024$) and diastolic (rs=0.324; $P=0.032$) BP as well as baseline testosterone (rs=-0.447; $P=0.019$). Tumor shrinkage correlated with LDL at baseline (rs=0.570; $P=0.033$). Only systolic and diastolic BP remained predictive for Cabergoline dosage required to achieve normoprolactinemia in the regression analysis.
Conclusion
Metabolic but not inflammatory markers might be related with initial presentation and outcome in PRL.

DOI: 10.1530/endoabs.81.EP734

EP735

Endocrine treatment of anabolic-androgenic steroid induced hypogonadism in males: A pilot study

Hans Christian Bordado Henriksen[1,2], Anders Palmstrøm Jørgensen[3], Astrid Bjørnebekk[4], Sudan Prasad Neupane[4] & Ingrid A. Havnes[5,6]
[1]Anabolic Androgenic Steroid Research Group, Section for Clinical Addiction Research, Division of Mental Health and Addiction, Oslo University Hospital, Oslo, Norway; [2]Institute of Clinical Medicine, University of Oslo, Oslo, Norway; [3]Section of Specialized Endocrinology, Department of Endocrinology, Oslo University Hospital, Oslo, Norway; [4]National Centre for Suicide Research and Prevention, Institute of Clinical Medicine, University of Oslo, Oslo, Norway; [5]Division of Mental Health and Addiction, Oslo University Hospital, Oslo, Norway; [6]Adult Psychiatry Unit, Institute of Clinical Medicine, University of Oslo, Oslo, Norway

Background and aims
Non-prescribed use of anabolic-androgenic steroids (AAS) is associated with a wide range of health risks including AAS-induced hypogonadism (ASIH) caused by negative feedback suppression on the hypothalamic-pituitary-gonadal (HPG) axis. Testicular function might be reduced for months up to years after AAS-cessation, increasing the risk of developing fatigue, decreased libido, erectile dysfunction, infertility, sleep disorder, depression and anxiety. There is no consensus on whether endocrine therapy should be used in the treatment of ASIH. In our study, a group of AAS-dependent men will receive endocrine therapy consisting of clomiphene citrate, a selective oestrogen receptor modulator. According to the theory, clomiphene citrate might stimulate endogenous testosterone production by blocking the negative feedback mechanism on the HPG-axis. The primary aim is to explore whether use of clomiphene citrate is safe and effective for AAS-withdrawal. The secondary aims are to detect health risks during ongoing AAS use and assess whether physical and mental health risks are reversed 12 months after cessation.
Methods
This one-site open off-label longitudinal pilot study at Oslo University Hospital in Norway will include 25-30 AAS-dependent men referred to outpatient addiction treatment with a desire to end AAS use permanently. The intervention group will be given endocrine therapy consisting of clomiphene citrate for 16 weeks including exogenous testosterone replacement for the first four weeks following AAS-cessation to ensure that the testosterone level is within normal range before reaching a HPG response. They will be compared to male participants in an already ongoing study of men who end AAS use temporarily without endocrine treatment. Participants from both studies will self-report withdrawal symptoms and other health measures every 2 weeks for 6 months and have visits at inclusion and after 6 months. The intervention group will be monitored using within-subjects repeated measures design on physical and mental health before, during 16 weeks of intervention, and at follow-up 6 and 12 months after AAS-cessation. Physical health parameters are obtained via clinical examinations, investigation of cardiovascular status, blood and fat tissue sampling, dual-energy x-ray absorptiometry (DXA), testicular ultrasound and semen analysis.
Results
Study inclusion started in December 2021. The study protocol and preliminary results will be presented at the conference.
Conclusion
This pilot is the first intervention study to test safety and efficacy of off-label use of clomiphene citrate among withdrawing AAS-dependent men. If this therapeutic approach works, full-fledged clinical trials need to be conducted.

DOI: 10.1530/endoabs.81.EP735

EP736

MRI intensity and pituitary volume predict adult-onset growth hormone deficiency in patients with obesity and overweight: a new potential tool guiding subsequent diagnostic testing

Davide Masi[1], Renata Risi[1], Angela Balena[1], Alessandra Caputi[1], Maria Elena Spoltore[1], Rebecca Rossetti[1], Mikiko Watanabe[1], Rossella Tozzi[2], Elena Gangitano[1], Mariaignazia Curreli[1], Stefania Mariani[1], Andrea Lenzi[1], Lucio Gnessi[1] & Carla Lubrano[1]
[1]Sapienza University of Rome, Department of Experimental Medicine, Section of Medical Pathophysiology, Food Science and Endocrinology, Roma, Italy; [2]Sapienza University of Rome, Department of Molecular Medicine, Roma, Italy

Background
Reduced growth hormone (GH) secretory capacity is common in patients with obesity and metabolic derangements. The prevalence of GH deficiency (GHD) in this population is difficult to establish. Magnetic Resonance Imaging (MRI) pituitary findings may reflect specific endocrine alterations, as for GHD which is associated with lower pituitary height and volume (PV).
Purpose
Our aim was to identify the pituitary morphological alterations predicting GHD in subjects with obesity or overweight.
Methods
We conducted a retrospective evaluation of 152 patients undergoing pituitary-MRI and a dynamic test (GHRH + arginine) for suspected adult-onset GHD admitted to our institution from 2015 to 2022. Clinical history and anthropometric parameters were collected. Mean and standard deviation (SD) of pituitary signal intensity was quantified (Horos, Nimble Co, Annapolis, MD USA). Gray matter signal intensity was used as a normalizer. PV was calculated by adopting the ellipsoid formula.
Results
Of 152 patients, 126 had obesity (BMI: 39 ± 6 Kg/m^2) and 26 were overweight (BMI: 28 ± 1 Kg/m^2). An inverse correlation between BMI and PV was observed ($r = -.2844$, $P < 0.0001$). Of note, after normalization with grey matter intensity, T2-weighted-scan derived pituitary intensity and PV showed an inverse correlation ($r = -.2761$, $P = 0.008$). As far as GH secretory capacity is concerned, we found a direct correlation between the area under the curve of the dynamic test and pituitary volume (PV) ($r = .41488$, $P < 0.0001$). Finally, a receiver operating characteristic curve allowed to identify a PV < 75.8 ml and a pituitary height < 3.7 mm as predictors of GHD with a sensitivity of 86.1% and 72.2% and a specificity of 63.6% and 64.5%, respectively.
Conclusion
Our work demonstrates that patients with obesity exhibit a GH-IGF1 axis impairment associated with a reduced PV. Furthermore, we found an inverse correlation between PV, pituitary intensity and GH secretion capacity. The increase in pituitary intensity may reflect the presence of an inflammatory infiltrate possibly leading to pituitary damage and subsequent shrinkage, although this hypothesis needs to be confirmed with *ad hoc* studies. When subjects suffering from overweight/obesity undergo a head MRI for other reasons, those not reaching the identified cut off values of PV and pituitary coronal height predicting GHD in our cohort, might benefit from undergoing dynamic testing in order to assess for eventual GHD.
Key Words: obesity, pituitary volume, Growth Hormone Deficiency

DOI: 10.1530/endoabs.81.EP736

EP737

Pituitary autoimmunity and hormonal changes in patients with severe obesity

Carla Carbone[1,2], Graziella Botta[2], Paolo Cirillo[3], Miriam Longo[1, 3], Raffaela Carotenuto[1, 3], Daniela Forestiere[1, 3], Salvatore Tolone[4], Ludovico Docimo[4], Maria Ida Maiorino[1, 3], Giuseppe Bellastella[1, 3] & Katherine Esposito[1,3]
[1]University of Campania 'Luigi Vanvitelli', Division of Endocrinology and Metabolic Diseases, Naples, Italy; [2]University of Campania 'Luigi Vanvitelli', Department of Experimental Medicine; [3]University of Campania 'Luigi Vanvitelli', Department of Advanced Medical and Surgical Sciences, Naples, Italy; [4]University of Campania 'Luigi Vanvitelli', Division of General, Mininvasive and Bariatric Surgery, Naples, Italy

Background and aim
Obesity is associated with a dysregulation of the immune system which can result in a predisposition to the development of autoimmune diseases. The aim of this cross-sectional study was to evaluate anti-pituitary antibodies (APA) in severe obese patients, in order to identify a possible role of the immune system in obesity and to correlate these antibodies with pituitary hormone changes found in obese patients.
Matherials and methods
36 obese patients from the Bariatric Surgery Unit and 50 non-obese subjects as control group were recruited. Weight, body mass index, blood pressure, heart rate, glycemic and lipid profile and insulinemia were measured in all subjects participating in the study. Basal levels of pituitary hormones (FSH, LH, TSH, GH, ACTH) and peripheral glands hormones (cortisol, testosterone, estradiol, free T4, free T3, IGF-1) were evaluated in all patients. APA were evaluated by indirect immunofluorescence method on cryostatized sections of the pituitary gland of a young baboon.
Results
10 patients (28%) resulted APA positive while no APA positive subject was found in the control group. Therefore, the obese patients were divided into two groups, based on the presence or absence of APA (APA +, APA-); we compared the clinical characteristics and we found a significant lower cortisol level in obese APA + subjects than in obese APA- subjects ($P = 0.045$). The anti-pituitary antibodies titer was inversely correlated with cortisol and growth hormone (GH) levels.
Conclusion
we found a higher prevalence of APA in obese patients than in control group and this result is in line with studies that suggested a higher risk and prevalence of autoimmune diseases in obese patients.
References
1. Tsigalou C, Vallianou N, Dalamaga M. Autoantibody Production in Obesity: Is There Evidence for a Link Between Obesity and Autoimmunity?. *CurrObes Rep*. 2020;9(3):245-254.
2. Versini M, Jeandel PY, Rosenthal E, Shoenfeld Y. Obesity in autoimmune diseases: not a passive bystander. *Autoimmun Rev*. 2014;13(9):981-1000.
3. Bellastella G, Maiorino MI, Longo M, et al. Impact of Pituitary Autoimmunity and Genetic Disorders on Growth Hormone Deficiency in Children and Adults. *Int J Mol Sci*. 2020;21(4):1392. Published 2020 Feb 19.

DOI: 10.1530/endoabs.81.EP737

EP738

Visual impairment in the empty sella syndrome

Mnif Fatma, Asma Zargni, Kawthar El Arbi, Faten Haj Kacem Akid, Dhoha Ben Salah, Nadia Charfi, Mouna Mnif, Nabila Rekik Majdoub, Mouna Elleuch & Mohamed Abid
Hedi Chaker Hospital, Diabetology and Endocrinology Department, Sfax, Tunisia

Introduction
Empty sella syndrome (ESS) is a rare condition in which the sella turcica is partially or completely filled with cerebrospinal fluid. It can be primary or secondary. Ophthalmologic involvement is rare in primary empty sella Syndrome. It is described in only 1.6 to 16% of cases.
Patients and methods
We report a retrospective study of 46 cases of ESS collected in the endocrinology department over the period from 1991 to 2020. The clinical and biochemical profile of ESS patients were analyzed.
Results
We included 46 patients, with a mean age of 50.4 years (with extremes from 21 to 81 years), with a female predominance (75%). The average parity was 9.5 children per woman. The circumstances of discovery were dominated by headaches (66.67%). Obesity was noted in 19.45% of cases. The hormonal assessment showed a corticotropic deficiency (53.6%), a thyrotropic deficiency (36.11%), a gonadotropic deficiency (22.8%) and diabetes insipidus in 2 patients. Hyperprolactinemia was noted in 13.88% of cases. Visual impairment was noted in 30.56% of cases (11 patients). two patients had diplopia. A decline in visual acuity was present in 2 cases. Visual blur was described in 7 cases. Hormone deficiency replacement was prescribed. The evolution was marked by the persistence of visual disorders in 8 patients.
Discussion
ESS is a benign pathology provided that antehypophyseal insufficiency is detected. We underline the interest of a systematic ophthalmologic examination in patients with ESS in order to detect visual disorders which can be serious and threaten the visual prognosis.

DOI: 10.1530/endoabs.81.EP738

EP739

Giant pituitary adenomas: about 15 cases

Lamiae Zarraa, Soumiya Berrabeh, Imane Assarrar, Siham ROUF & Hanane Latrech
Endocrinology-Diabetology and Nutrition Department CHU MOHAMED VI, Laboratory of Epidemiology, Clinical Research and Public Health, Faculty of Medicine and Pharmacy Mohammed Premier University Oujda, Oujda, Morocco;

Key Words : Giant – pituitary adenoma

Introduction & Background

Giant pituitary adenomas are uncommon tumors defined by a tumor diameter ≥ 4 cm. Their prevalence estimated at 6-10% of all pituitary adenomas, whose clinical characteristics and prognosis are not well known. The purpose of this work was to evaluate the prevalence as well as the clinical and evolutionary characteristics of giant pituitary adenomas in our series.

Material and methods

Retrospective descriptive study including 15 patients followed-up for giant pituitary adenoma which tumor diameter was greater than or equal to 4 cm. Data were collected from medical records and analyzed by SPSS-V21 software.

Results

Giant pituitary adenomas represent 16.6% of our series of pituitary adenomas ($n=15/90$) with a mean age of 44.8 ± 16.5 years (extremes of age of 22 and 69 years), with a clear male predominance and a sex ratio of 4. The clinical presentation was dominated by a decrease in visual acuity associated with headaches in 73.3% of cases, associated with cranial nerve damage (III, VI) in 20% and pituitary apoplexy in 13.3% followed by acrogigantism in one case. The hypothalamohypophyseal MRI showed a giant pituitary macroadenoma with a mean diameter of 5.34 cm (with extremes of 4 and 8.2 cm) and a mean volume of 47.9 $\pm$45.5 cm 3. Invasion of the cavernous sinus was observed in 46.6% of the cases and reaching the contact of the internal carotid artery in 40% of the cases, with invasion of the chiasma and optic pathways in 93%. It was a pituitary prolactin adenoma in the most of cases (53,3%) cases followed by non functional pituitary adenoma. Twenty-four percent of the patients benefited from transphenoidal surgical treatment with an indication for revision surgery in 46% of cases. 13.4% of the cases benefited from radiotherapy as a complement to pituitary surgery and 60% were put on dopaminergic analogues and 13.3% on somatostatin analogue. The Ki67 of the operated patients was 4% in one patient with somatotropic adenoma, 2% in one case with prolactin adenoma and 1% in 4 cases.

Discussion-Conclusion

Giant pituitary adenomas, although uncommon, represent a challenge in clinical endocrinology because their prognosis is uncertain requiring multidisciplinary management in diagnosis, therapeutic management and long-term follow-up.

DOI: 10.1530/endoabs.81.EP739

EP740

The changing features of a corticotroph PITNET: from silent to Cushing's disease - case report

Radu Andrei Emilescu[1], Iulia Florentina Burcea[1, 2], Roxana Ioana Dumitriu[1, 2], Valeria Nicoleta Năstase[1], Gheorghe Vasile Ciubotaru[3], Liga Gabriela Tătăranu[2,3] & Cătalina Poiană[1,2]

[1]C. I. Parhon National Institute of Endocrinology, Department of Pituitary and Neuroendocrine Disorders, Bucharest, Romania; [2]Carol Davila University of Medicine and Pharmacy, Bucharest, Romania; [3]Emergency Hospital Bagdasar-Arseni, III, Bucharest, Romania

Introduction

The spectrum of corticotroph cell pituitary adenomas is very wide, silent corticotroph adenomas (SCAs) being a rare subtype with positive immunohistochemistry for adrenocorticotropic hormone (ACTH), without causing Cushing's disease. SCAs may exhibit a more aggressive behavior, and the changing of the clinical phenotype towards Cushing's disease is described.

Case report

We present the case of a 74 years old, ex-smoker, hypertensive, male patient who was admitted to our clinic after sudden unilateral hearing loss, with no signs of hypercortisolism. Magnetic resonance imaging (MRI) of the pituitary showed a large mass of 14.3/15/12.3 mm. There was no opto-chiasmatic involvement and the hormonal profile revealed normal pituitary function with normal serum cortisol, suppressed after a 2 mg x 2 days dexamethasone suppression test (LDDST). The patient underwent transsphenoidal pituitary surgery. Postoperatively he did not have any pituitary deficiencies. Subsequently, 7 years after surgery, the patient is readmitted to our department, with central obesity, hypertension, dyslipidemia, and low bone mass. The hormonal profile showed an elevated ACTH (148.9 pg/ml), with elevated 8.00 a.m. serum cortisol, unsuppressed after a LDDST (14.74 µg/dl). Brain imaging showed a pituitary tumor of 17.9/18.8 mm with suprasellar extension, associated with bilateral adrenal hyperplasia on abdominal computed tomography (CT). Morphological and retroactive immunohistochemical (IHC) analysis of the pituitary tumor revealed strong positive staining for ACTH and weak immunostaining for TPIT; Ki-67 labelling index had a value of $>3\%$. After neurosurgical evaluation found reintervention to be unfeasible, gamma knife radiosurgery was performed and therapy with dopaminergic agonists was initiated. The morning serum cortisol normalized, but remained unsuppressed after LDDST 2 years after radiosurgery, with ACTH values in regression under cabergoline 4 mg/week.

Conclusion

Bidirectional transformation of the clinical phenotype between Cushing's disease and SCA is described, the time interval varying from 1 to 7 years. The silent phenotype is related to TPIT, the dysfunction of its expression being an early change in differentiation of this tumor type. SCAs are more biologically aggressive tumors than NFAs, therefore, close neuroimaging and clinical follow-up are mandatory. Also, patients with SCAs who present with postoperative residual disease should be considered for early adjuvant radiosurgery or long acting pasireotide.

References

Strickland et al (2021). Silent corticotroph pituitary adenomas: clinical characteristics, long-term outcomes, and management of disease recurrence, Journal of Neurosurgery, 135(6), 1706-1713.

Righi A et al. The changing faces of corticotroph cell adenomas: the role of prohormone convertase 1/3. Endocrine 2017; 56:286–97.

DOI: 10.1530/endoabs.81.EP740

EP741

Growth hormone deficiency due to a rare central nervous system tumor

Simona Gabriela Duta[1], Sebastian Pavel[2], Sergiu Stoica[2] & Simona Fica[1,3]

[1]Elias Emergency University Hospital, Endocrinology Department, Bucureşti, Romania; [2]Monza Metropolitan Hospital, Neurosurgery Department, Bucureşti, Romania; [3]Carol Davila University of Medicine and Pharmacy, Bucureşti, Romania

Introduction

Short stature is a common reason for pediatric endocrine evaluation and it can have a variety of causes, including constitutional, genetic short stature, dysmorphic syndromes, chronic illnesses and also endocrine disorders. Growth hormone deficiency accounts for 8% of the cases and it can be isolated or associated with other pituitary hormones deficiencies, congenital or acquired, such as in central nervous system tumors.

Case report

A 15-year-old female patient presented to our department for growth deficit and primary amenorrhea. The mother reports normal psychomotor development and no significant medical history. The clinical examination revealed an underweight patient (percentile under 1%) with short stature (- 3.38 SD) and a prepubertal Tanner stage. A complete hormonal assay showed low GH and IGF-1 levels, with no GH response at the clonidine stimulation test. FSH, LF, estradiol and prolactin levels were also low. Cerebral MRI showed a solid, lobulated suprasellar mass of 2.8/2.7/4 cm, with well-defined outline and microcalcifications, hyperintense T2 signal and hypointense T1 signal, predominantly located in the third ventricle, in close contact with the circle of Willis. Tumoral markers and a lumbar spine punction were recommended to rule out a germ-cell tumor. The patient was referred to a neurosurgeon and underwent surgery with complete resection of the tumor, and histopathology and immunohistochemistry evaluation supporting the diagnosis of rosette-forming glioneuronal tumor. Postoperatively, the patient developed diabetes insipidus and central adrenal and thyroid insufficiency, with favorable evolution and recovery under substitution treatment.

Conclusions

Rosette-forming glioneuronal tumor is a very rare tumor, with about 100 cases reported in literature. It is a grade I neoplasm, with indolent evolution and a low recurrence rate following total resection. In our case, it presented with hormonal disturbances due to its size and unusual location. A multidisciplinary approach from an experienced team is absolutely necessary for an appropriate diagnosis, an effective treatment and long-term follow-up for this type of cases.

DOI: 10.1530/endoabs.81.EP741

EP742

Hypophysitis and reversible hypopituitarism developed after COVID-19 infection - a clinical case report.

Natalia Gorbova, Liudmila Rozhinskaya, Viktoria Vladimirova & Zhanna Belaya

The National Medical Research Centre for Endocrinology, Neuroendocrinology and Bone Disease Department, Russian Federation

Aim
To present a clinical case of reversible hypopituitarism due to hypophysitis developed after COVID-19 infection.
Materials and methods
A patient with residual clinical manifestations of hypopituitarism underwent clinical evaluation at the time of symptoms of hypopituitarism and in follow-up. Morning serum cortisol (171-536 nmol/l) was measured by electrochemiluminescence immunoassay. Morning ACTH (7.2-63.3 pg/ml), prolactin (66-436 mU/l), TSH (0.25-3.5 mIU/l), fT4 (9-19 pmol/l) and fT3 (2.6-5.7 pmol/l) were measured by chemiluminescence immunoassay. General Electric 3T MRI scanner was used to do an MRI of the brain with standard contrast. Data were analyzed throughout the course of the disease.
Results
A 35-year-old female developed clinical symptoms of hypopituitarism two months after recovery from a confirmed COVID-19 infection. Laboratory investigation confirmed hypocorticism, hypothyroidism, hypogonadism and the patient was prescribed appropriate hormonal therapy in January 2021. Four months later the symptoms were alleviated (April 2021) and there were signs of recovery shown by imaging and hormonal profile (hormonal treatment was stopped for evaluation): morning serum cortisol 227 nmol/l, morning ACTH 33.96 pg/ml, prolactin 68.3 mU/l, TSH 2.626 mIU/l, fT4 10.75 pmol/l, fT3 3.96 pmol/l. Thyroid hormone was discontinued, but hypogonadism and hypocorticism persisted with estradiol - 51.48 pmol/l, 24 h urine cortisol levels - 41.8 nmol/day. Secondary adrenal insufficiency was confirmed during a test with insulin hypoglycemia (serum glucose reached 0.7 mmol/l), the maximum release of cortisol was 410.8 nmol /l. MRI results showed that the signs of hypophysitis were alleviated in comparison with MRI from January 2021. Full recovery of pituitary axis was reported in October 2021, with recovery of normal menstrual cycle. Furthermore, hormonal profile was likewise normal: morning serum cortisol 14,7 µg/dl (6,2-19,4), ACTH 33,2 pg/ml, T4 0,88 ng/dl (0,8-2,1), TSH 2.17 mIU/l.
Conclusions
This report provides evidence of delayed damage to the pituitary gland after infection with the COVID-19, with recovery of its function and structure. To date, the mechanisms of such an impact are not entirely clear; further collection of data on such cases and analysis is required.

DOI: 10.1530/endoabs.81.EP742

EP743

Pituitary apoplexy and Staphylococcus infection in a previously undiagnosed macroadenoma

Iulia Alexandra Pirga
Filantropia Hospital, Endocrinology, Craiova, Romania

Background
Pituitary apoplexy is a rare clinical syndrome, caused by hemorrhagic or ischemic necrosis of the pituitary gland. It is often associated with an existing pituitary adenoma, especially nonfunctioning tumors. Pituitary apoplexy may mimic the clinical findings of an infectious meningoencephalitis.
Case report
A 57-year-old man was admitted to the emergency department following sudden onset of severe headaches, fever, chills, and signs of meningeal syndrome, associated with unilateral ptosis, mydriasis and diplopia. His medical history included arterial hypertension, diabetes mellitus and epilepsy. Blood test revealed a high CRP at 403 mg/l with a white blood count of 11600/mm3. A lumbar puncture was performed, revealing a hyperleukocytosis with a polymorphonuclear predominance at 87%, proteinorachy of 0.93 g/dl, without glycorachy, raising the suspicion of meningitis. The MRI scan demonstrated a 24 x 20 x 27 mm pituitary mass, extending upwards into the suprasellar cistern and compressing the optic chiasm, images consistent with haemorrhage into a pre-existing pituitary macroadenoma. The patient underwent transsphenoidal surgery. Histopathology examination confirmed the diagnosis of pituitary adenoma with apoplexy and inflammation, and microbiologic examination was positive for Staphylococcus Aureus and Staphylococcus Capitis. The post-surgery endocrine workup showed a deficiency of the thyrotropic and gonadotropic axes, a partial deficiency of the corticotrope axis and a moderate increase in prolactin level.
Conclusion
We hypothesize that either there was an underlying inflammatory pathology due to Staphylococcus infection that contributed to the development of pituitary apoplexy, or the presence of necrosis and haemorrhage at that level represented the departure point for the infection. Surgical intervention should urgently be performed when there is a compression of the optic chiasm.
Key words: pituitary apoplexy, infection, macroadenoma

DOI: 10.1530/endoabs.81.EP743

EP744

Vanishing Pituitary tumour in a postpartum patient - a diagnostic dilemma

Noha Meneissy[1, 2], Moustafa Hosni[2, 3], Belayet Hossain[4], Barney Low[3], Janessa Bell[3], Writaja Halder[3], Debbie Falconer[3], Shrini Patel[3], Muhammad Saleem[3], Saiful Islam[3], Musarat Hussain[3], Jessica Howes[3], Hassan Rehmani[3], Gideon Mlawa[3,5] & Catherine Qin[1]
[1]Queen's Hospital, London, United Kingdom; [2]Queen's Hospital, Acute Medicine, London, United Kingdom; [3]Barking, Havering and Redbridge University Hospital NHS Trust (BHRUT), Acute Medicine, London, United Kingdom; [4]Barking, Havering and Redbridge University Hospital NHS Trust (BHRUT), Diabetes and Endocrinology, London, United Kingdom; [5]Queens Hospital, Diabetes and Endocrinology/Acute Medicine, London, United Kingdom;

Introduction
Resolution of pituitary tumour without surgical intervention is rare. The mechanism of spontaneous resolution of pituitary adenoma is unclear but may be explained by either pituitary apoplexy or hypophysitis responding to steroids. Bray BP, et al(2021) reported the case of vanishing pituitary mass due pituitary apoplexy. Park SM, et al (2014) reported 22 cases of pituitary mass due hypophysititis which improved mostly with medical therapy.
Case
29-year-old lady presented to hospital in January 2014 with vomiting, abdomen pain, headaches and profound hyponatraemia of 112. She had undectable LH < 0.2), FSH(1), SST normal, Prolactin 407. IGF-1 normal. She was treated with iv fluids. She had MRI pituitary which showed homogenous enhancing pituary macroadenoma measuring (1.0 x 1.5 x 1.8 cm). She was 1 year postpartum. Second baby was born 2012 and stopped breast feeding in 10/2013 and her periods were regular She was seen initially by neurosurgeons for surgical intervention. She was started on hydrocortisone 10 mg then reduced to 5 mg twice a day then stopped in July 2014 as 9 am cortisol was normal at 300. She required no hormonal replacement therapy. Repeat MRI after10 months reported as normal appearance of pituitary gland and surgery was not required.
Discussion
Pitutary adenomas can be divided into functioning and non-functioning. The causes of non-functioning tumours include neoplastic, inflammatory and vascular. Non-functioning pituitary macroadenoma are usually managed surgically if patients are symptomatic unless contra-indicated. Spontaneous resolution of pituitary tumours is rare. The mechanism of spontantoeus resolution of pituitary adenoma is unclear but may be explained by either pituitary apoplexy or hypophysitis responding to steroids. Patient with pituitary apoplexy may present with headaches, vomiting and visual distrubances. The time of onset of spontaneous regression of pituitary adenoma following pituitary apoplexy is unclear, some cases were previously reported to be as early as 1 week. Hypophysitis as an inflammatory process which may response to steroids. It can be postulated that giving steroids facilitates regression of pituitary adenoma. Is unclear whether the patient being on steroid contributed to spontaneous regression of pituitary tumour or not.
Conclusion
Spontaneous regression of pituitary adenoma is uncommon and possible causes discussed above should be considered. Is unclear whether patients with spontaneous pituitary adenoma are at risk of recurrence and they need for long term follow up. The case raises a question of how long can non function pituitary adenoma can be monitored before when to intervening surgically in non functioning pituitary adenomas.

DOI: 10.1530/endoabs.81.EP744

EP745

Cardio-metabolic and articular complications of somatotropic adenomas in a single-center study

Khadra Faraoun & Mohammedi Fatiha
Oran University Hospital, Endocrinology, Oran, Algeria

Introduction/Objective
Chronic exposure to hypersomatotropism exposes to multiple co-morbidities, rarely reversible, which can worsen both functional and vital prognosis and impair quality of life. The aim of our work is to list the different complications of acromegaly at the time of diagnosis.
Patients and methods
Descriptive cross-sectional study concerning 81 patients with somatotropic adenomas followed in the Endocrinology department of the Oran University Hospital.
Results
Sex ratio M/F at 1.4, pituitary macroadenomas are involved in 81% of cases, the mean age at diagnosis at 40.2 $\pm$ 15.5 years, the mean consultation time at 23.8 $\pm$ 31.3 months, the mean BMI at 26.4 $\pm$ 4.9 kg/m^2. At diagnosis, we identified hypertension in 41% of cases with a mean duration of 4.5 $\pm$ 5.9 years, congestive valvular heart disease with or without arrhythmia in 31% of cases, sleep apnnea syndrome (SAS) in 50% of cases explored ($n=$ 20), diabetes mellitus in 35% of cases with a mean duration of 5.2 $\pm$ 6.5 years, intolerance to carbohydrates in 15.3% of cases with a mean duration of 2.0 $\pm$ 3.1 years, dyslipidemia in 28%, axial arthropathy in 39% of cases including 3 Erdheim spondylosis and carpal tunnel syndrome in 40% of cases.
Discussion
Our results are similar to those in the literature which vary from 18-60% for hypertension, from 19 to 56% for diabetes mellitus and carbohydrate intolerance, from 33 to 47% for dyslipidemia and from 20 to 80% for SAS; They reflect the need for early diagnosis of acromegaly and for hormonal control to improve prognosis.

DOI: 10.1530/endoabs.81.EP745

EP746

Hormonal profile of pituitary adenomas

Khadra Faraoun & Mohammedi Fatiha
Oran University Hospital, Endocrinology, Oran, Algeria

Background
Pituitary adenomas (PA) or endocrine pituitary tumors are the most common pituitary tumors. Our goal is to assess their hormonal profile.
Patients and methods
Our study is observational, multicenter, with prospective and retrospective data collection. Data entry and analysis was performed by CDC (USA) EPI Info version 6, SPSS20, Statistica10, Medcalc12.
Results
Concerning the hormonal profile of the 475 PA collected, 77.5% were secreting against 22.5% not or apparently non-secreting. Macroadenomas were predominant (66.5%, *P* 0.001). Prolactin was elevated in 62.7%. It was either a functional or disconnected hyperprolactinemia, or of tumor origin. The mean prolactinemia was significantly ($P=0.006$) higher in men: 578.2 Vs 189.1 ng/ml. Hypopituitarism ($\geq$2 axes) calculated as for macroadenomas was noted in 35%. Gonadal deficit, functional in microlesions and organic and/or functional in macroadenomas, was the most common (56.5%) compared to the other deficits. Impaired gonadal function is followed by the thyrotropic deficit noted in 32%. Corticotropic and somatotropic deficits come last, 27% and 6.5%, respectively. Somatotropic function was not systematically explored in our retrospective study. Multiple deficits affecting more than 3 axes were noted in 17.0%. Post-pituitary function impairment was present in 4.7%.
Conclusion
Our results can of course be explained by the frequency of macrolysis but also by the delay in the diagnosis of these tumors.
Key words: pituitary adenomas, hormonal profile, hyperprolactinemia, pituitary deficits.

DOI: 10.1530/endoabs.81.EP746

EP747

Delayed Diagnosis of Cushing's Disease Manifested in Adolescence

Irina A. Vaychulis
South-Ural State Medical University, Internal Medicine Department, Chelyabinsk, Russian Federation

Diagnosis of Cushing's syndrome (CS) can be challenging, particularly in mild cases or in cyclic disease, because of the variable, non-specific clinical manifestations and the overlap with more common medical problems. Female patient was referred to our clinic in Dec 2015, at the age of 18 years, presented with headaches, arterial hypertension (AH), excessive body hair growth, irregular menstrual periods, sleep disturbances and mood fluctuations. She smoked, but denied use of alcohol or any drugs. Menarche occured at 10 years of age and her menstrual cycle (MC) was regular. At the age of 14 years she had noticed excessive body hair growth, alopecia, weight gain (15 kg), purple striae and menstrual irregularities. At examination in pediatric clinic AH, normal morning cortisol, TSH, prolactin, electrolites, elevated testosterone and DHEA-s levels were detected. Her brain's MRI and CT of adrenal glands were unremarkable. US showed multifollicular ovaries. She was followed by pediatricians with the diagnosis of PCOS, obesity. Oral contraceptives were not effective to control her MC and were discontinued. In 2015 she lost weight (15-20 kg) with striae discoloration and her MC was temporarily restored without specific treatment. In a few months the described symptoms had returned and she was referred to endocrinologist. At examination in Dec 2015 plethoric rounded face, hyperstenic constitution, normal BMI (23 kg/m^2), hirsutism (lower abdomen, hips, lumbal area), acne, pale striae, AH were found. 24-h urine free cortisol within the normal range, slightly elevated testosterone, androstendione and ACTH (48 ng/ml, ULN 46) levels, normal TSH, prolactin, OGTT, electrolytes and liver function tests were revealed. Further investigation demonstrated ACTH at the upper border of normal range (46 ng/ml), but inadequate suppression of plasma cortisol (350 nmol/l) and ACTH (44 ng/ml) after overnight 1-mg DST. At the same time 6 x 3 mm microadenoma on pituitary MRI had been detected. The diagnosis of ACTH-dependent endogenous hypercortisolism - Cushing's disease (CD) was established and confirmed by subsequent deterioration of laboratory parameters accompanied by weight regain. Symptoms of hypercortisolism have completely disappeared after repeated transsphenoidal adenomectomy in 2016-2017. This case demonstrates the delayed diagnosis of CD with first clinical presentation at the age of 14 years, resembling PCOS. Fluctuating signs of cortisol excess and inconsistent laboratory results raise suspicion about cyclic CD. As no single diagnostic test is 100% accurate in the diagnosis of CS/CD, repeated monitoring is needed. Education of pediatricians and gynecologists to maintain awareness about CS/CD is required.

DOI: 10.1530/endoabs.81.EP747

EP748

Clinical, paraclinical and genetic features of diabetes insipidus

Fatma Mnif[1], Hana Charfi[1], Fatma Abdelhédi[2], Malek Bouassida[2], Mouna Elleuch[1], Dhoha Ben Salah[1], Mouna Mnif[1], Nabila Rekik Majdoub[1], Nadia Charfi[1], Faten Haj Kacem Akid[1], Hassen Kammoun[2] & Mohamed Abid[1]
[1]Hedi Cheker University Hospital, Endocrinology, Tunisia; [2]Hedi Cheker University Hospital, Genetics, Tunisia

Introduction
Diabetes insipidus (DI) is a rare pathology. The advent of hypothalamic-pituitary MRI has made it possible to make a positive diagnosis by avoiding the water restriction test (WRT). The etiological diagnosis is still a challenge in view of the diversity of diseases involved, which influences the therapeutic management and prognosis.
Work Objectives
The objectives of our work were to describe the clinical, paraclinical and genetic features of DI.

Patients and Methods
We conducted a retrospective and descriptive study of all cases of DI collected in the endocrinology department of Hèdi Chaker University Hospital, Sfax Tunisia during a 21-year period (2000-2021).
Results
We collected 44 patients, with a mean age of 53.2±16.05 years and a sex ratio M/F of 0.7. The most frequent reason for consultation was SPUPD in 70.5% of cases. The severity of SPUPD was variable: polyuria > 5l/24 h in 75% and polydipsia > 10l/24 h in 38%. There were no adverse effects of SPUPD described in our study. The positive diagnosis was made by WRT in 13 patients, and bases on hypothalamic-pituitary MRI in the other cases: an abnormal spontaneous T1 hyper signal was present in 70.4% of patients. Three patients had a nephrogenic DI, one of which was drug-induced (lithium intoxication) and the other two of genetic origin (AQP2 mutations). CDI was identified in 41 patients, 2 of whom had partial diabetes and 5 had transient diabetes. The most frequent etiologies were: post neurosurgical interventions (24.4%), pituitary tumors (17%) and lymphocytic hypophysitis (14.6%). An idiopathic origin was present in 12.2% of cases. Minirin treatment was initiated in all patients suffering from CDI with a clear clinical improvement. For NDI, an association with indomethacin or thiazide diuretic was necessary.
Conclusions
At the end of this work, we insist on the necessity of a better knowledge of this pathology, allowing an early diagnosis and a management, only guaranteeing a better prognosis.

DOI: 10.1530/endoabs.81.EP748

EP749

Hypopituitarism revealing small cell pulmonary carcinoma: an original case report

Asma Tekaya, Asma Kefi, Khaoula Ben Abdelghani, Cyrine Sassi, Sami Turki, Mounira El Euch & Ezzedine Abderrahim
Charles Nicolle Hospital, Department of Internal Medicine A, Tunis, Tunisia

Background
Anterior pituitary insufficiency or anterior hypopituitarism is a defect in the secretion of one or more of the pituitary hormones (ACTH, TSH, FSH and LH, GHand prolactin). It is a rare condition. A variety of diseases may be the cause, the most common being adenoma. In rare cases, it can be a clinical presentation of metastatic disease. Herein, we describe a case of a pituitary metastasis revealing a lung carcinoma in a 61-year old man.
Case report
A 61-year old man, with a history of heavy smoking and type 2 diabetes, was admitted with deterioration of general state. He reported constipation, anorexia, weight loss and decreased libido for 2 years and has stopped taking his insulin for 2 months because of hypoglycemic episodes. Examination showed psychomotor retardation, blood pressure (BP)at 106/62 mmHg, heart rate at 62 bpm, normal blood glucose and BMI of 32 kg/m^2. Ganglionic node palpation revealed several cervical, axillary and inguinal adenopathies. Laboratory tests found hyponatremia, lymphocytosis and elevated inflammatory markers. Colonoscopy was normal. Endocrine investigations revealed central hypothyroidism (TSH: 0.107 microUI/ml, FT4: 0.63 ng/dl) and hypocorticism (cortisol: 35 nmol/l), low testosteronemia at 0.081 ng/ml and hyperprolactinemia at 862 mUI/l. The patient was therefore started on hormonal replacement therapy (hydrocortisone and levothyroxine). Cerebral MRI found 4 metastases: right frontal, left parietal, sellar and suprasellar mass lesions isointense on precontrast T1 weighted, hyperintense T2 weighted and demonstrated predominately rim enhancement on FLAIR. Body scan was concordant with the diagnosis of pulmonary neoplasm with multiple secondary lesions (lymph node, bone, adrenal, cerebral, hepatic, pleural and peritoneal metastases), therefore classified T4N3M1c. Cervical ganglions biopsy confirmed the diagnosis of small cell pulmonary carcinoma. The patient was started on radiotherapy and was addressed to a specialized oncology center for follow up.
Discussion
Our report depicts an original and challenging diagnosis approach of small cell lung carcinoma revealed by pituitary metastasis with hypopituitarism. Pituitary metastases are uncommon. They represent 0.14 to 3.6% of all intracranial metastasis, and are rarely symptomatic (1% to 6%). In scarce cases, pituitary metastasis is the first manifestation of the cancer. Breast and lung cancer are the most frequent cause of pituitary metastasis. The association of infundibular metastasis and elevated serum prolactin has been reported.
Conclusion
Pituitary metastases may be the initial presentation of neoplasms or may occur during therapy. Physicians must be cautious, and must suspect the diagnosis when confronted with any sign that may suggest pituitary damage (hypothyroidism, adrenal insufficiency, etc.)

DOI: 10.1530/endoabs.81.EP749

EP750

Neurosarcoidosis and pituitary metastasis of a small cell carcinoma: an unusual association

Fatma Mnif, Hana Charfi, Mouna Elleuch, Dhoha Ben Salah, Nadia Charfi, Mouna Mnif, Nabila Rekik Majdoub, Faten Haj Kacem Akid & Mohamed Abid
Hedi Cheker University Hospital, Endocrinology, Tunisia

Introduction
Pituitary stalk thickening (PST) is often identified on magnetic resonance imaging (MRI), either incidentally or during diagnostic workup of hypopituitarism. Currently, there is no unified standard for the definition of PST. As a reference, a pituitary stalk with width over 3 mm has been used as the diagnostic criterion for PST in recent years. The disease spectrum of PST is quite diverse and can be grouped into three broad categories: neoplastic, inflammatory and congenital diseases. Here, we report a rare case of PST secondary to Neurosarcoidosis and pituitary metastasis of a small cell carcinoma.
Case report
We report the case of a 49 years old man with no personal medical history. The diagnosis of neuro-sarcoidosis was suspected in view of the presence of pituitary tumor syndrome, central diabetes insipidus, hypopituitarism and the presence of nodular thickening of the stalk at hypothalamic-pituitary MRI. Biological explorations had shown an increase in 1-25 OH vitamin D, a decrease in 25 OH vitamin D and a slight increase in the tumor marker NSE estimated at 42 ng/l. Chest X-ray and thoracic-abdominal CT scan were in favor of pulmonary, hepatic and adrenal involvement. Labial biopsy and bone scan were negative. To confirm the diagnosis, bronchial biopsies were performed 3 times under fibroscopic control but returned negative. Then they were redone under CT scan to conclude to a small cell lung carcinoma, but the liver biopsy was in favor of a sarcoidosis. The patient was put on replacement therapy (ddAVP at a dose of 0.1 ml*2/d, hydrocortisone at a dose of 30 mg/d and L-thyroxine at a progressive dose up to 100µg/d) with clinical and radiological monitoring. The thoracic CT scan showed an aggravation of the lesions, an increase in the tumor mass and a small pleural involvement. The diagnosis retained was that of a pituitary metastasis of a small cell carcinoma associated with sarcoidosis. Given the deterioration of the general condition and the worsening of the radiological lesions, the patient was referred to the carcinologists for vinblastine and prednisone16 - cisplatin chemotherapy. He received 3 courses of chemotherapy with a good clinical and biological evolution. Since then, the patient was regularly followed up in carcinology.

DOI: 10.1530/endoabs.81.EP750

EP751

Immunohistochemichal expression of ephrin receptor (EPH)-A4, -A5, -B2 and -B5 in pituitary lesions

Eirini Papadimitriou[1], Georgios Kyriakopoulos[2], Konstantinos Barkas[3], Ioannis Gkalonakis[3], Panagiota Pantoula[4], Stamatios Theocharis[5], Gregory Kaltsas[1] & Krystallenia Alexandraki[1]
[1]National and Kapodistrian University of Athens, Endocrine Unit, 1st Department of Propaedeutic Medicine, Athens, Greece; [2]Evangelismos General Hospital, Department of Pathology, Athina, Greece; [3]General Hospital of Nikea, Neurosurgery Department, Nikea, Greece; [4]General Hospital of Nikea, Department of Pathology, Nikea, Greece; [5]National and Kapodistrian University of Athens, First Department of Pathology, Athens, Greece

Introduction
Ephrin receptors (EPHs) compose the largest known subfamily of receptors tyrosine kinases and are bound and interact with EPHs-interacting proteins (Ephrins). They have a role in tumor growth, invasion, angiogenesis and metastasis of several neoplasms. Aim of the study was to investigate the expression of EPH-A4, -A5, -B2 and -B5 in pituitary lesions.
Material and Methods
Our study group consisted of 18 patients (9 males with median age 54 and females with median age 59) with pituitary lesions (7 somatotropic and 2 corticotropic adenomas, 8 non-functioning macro-adenomas and 1 resistant prolactionoma) .Formalin fixed-paraffin embedded (FFPE) tissue sections from the lesions were assessed immunohistochemically for EPH-A4, -A5, -B2 and -B5 expression. Positivity is defined when $>4\%$ of pituitary cells have positive staining, after observation of at least 1000 cells. An immunoreactive score (IRS) was created according to the sum of percentage of EPH-A4, -A5, -B2 and -B5 positivity (0/negative staining: 0–4% of pituitary cells positive; 1: 5–30% of pituitary cells positive; 2: 31-60% of pituitary cells positive; 3: 61–100% of pituitary cells positive) and the intensity of staining (0: negative staining, 1: mild staining; 2: intermediate staining; 3: intense staining). A case was characterized to present low, medium or high EPH expression if the total score was 0-2, 3-4 and 5-6, respectively. The H-score is determined by adding the results of multiplication of the percentage of cells with staining intensity ordinal value (scored from 0 for "no signal" to 3 for "strong signal") with 300 possible values.
Results
Cytoplasmic and nuclear for EPH-A4 and cytoplasmic for EPH-A5, -B2 and -B4 pattern of immunostaining was noted. Positivity for EPH-A4 was seen in 17/18 (94%) of the specimens (17/18 with cytoplasmic and 13/18 with nuclear pattern). All corticotropic and somatotropic adenomas found positive for EPH-A4 with both patterns. Positivity for EPH-A5 and EPH-β2 was seen in 4/18 (22%) specimens and for EPH-β4 in 1/18 (5.5%), all non-functioning adenomas with cytoplasmic pattern. EPH-A4 IRS was mild for 4, intermediate for 6 and intense for 3 cases. H-score for EPH-A4 expression ranging from 30-255, whereas for EPH-A5,-B2 and -B4 was lower (10-65).
Conclusion
Our data indicate for the first time the increased expression of mainly EPH-A4 and to a lesser extent of EPH-A5, -B2 and -B4 in pituitary lesions. Their involvement in the pathophysiology of pituitary lesions requires further investigation to clarify their role and their possible potential prognostic value.

DOI: 10.1530/endoabs.81.EP751

EP752

Clinical presentation of non-functioning pituitary tumors: the experience at a tertiary care hospital in Portugal

Maria Inês Alexandre[1], Ana Gomes[1, 2], Ema Lacerda Nobre[1, 2], Pedro Marques[1, 2] & Maria Joao Bugalho[1, 2]
[1]Hospital Santa Maria, Endocrinology, Diabetes and Metabolism Department, Lisboa, Portugal; [2]Faculty of Medicine, University of Lisbon, Lisboa, Portugal

Introduction
Clinically non-functioning pituitary tumors (NFPTs) lack clinical or biochemical evidence of pituitary hormone excess. Their clinical presentation is heterogeneous, including mass effect-related symptoms and/or hypopituitarism, or even no symptoms in incidentally-detected NFPTs. We aimed to evaluate the clinical presentation spectrum of NFPTs in a cohort of patients managed at our hospital.
Methods
Clinical, demographic, biochemical and imaging data from 227 patients was retrieved and retrospectively analyzed using SPSS®.
Results
Our cohort included 115 women (50.7%) and the median age of the study population was 58 ± 15 years. Most patients had NFPT-related symptoms at presentation (75.3%), predominantly visual disturbances (56.8%) and headache (35.7%). In contrast, 56 patients (24.7%) had an incidental diagnosis on neuroimaging performed for other reasons, largely trauma (21.4%). Patients with incidentally-discovered NFPTs were significantly older than those with clinically-presenting NFPTs (62.8 ± 14.2 vs 54.8 ± 14.7; $P=0.001$). Regarding the entire group of patients, at diagnosis, the majority had one or more pituitary hormone deficiencies (55.9%), which occurred more frequently in men than women (66.1 vs 46.1%; $P<0.001$), in older patients and in patients with larger tumors ($P<0.001$). Of the 227 NFPTs, 210 (92.5%) were macroadenomas, and 180 (79.3%) had extrasellar extension. The mean diameter at diagnosis was 2.41 ± 1.15 cm. Clinically-presenting patients had larger tumors (2.60 vs 1.97 cm; $P=0.006$). A total of 140 patients (61.7%) underwent surgery, 75.7% of these within the first 12 months since the NFPT diagnosis. The subgroup of incidentally-discovered NFPTs required less often an operation than the clinically-presenting counterparts (41.1 vs 68.4%; $P<0.001$).
Conclusion
Our NFPT cohort included patients who mostly presented with large tumors associated with compressive symptoms and hormonal deficiencies. However, a quarter of cases were incidentally-discovered NFPTs, typically found in older patients, and despite their smaller size still more than one third needed surgery.

DOI: 10.1530/endoabs.81.EP752

EP753

Acromegaly: a rare disease with multiple, complex complications

Andra Cristiana Istrate, Letitia Leustean, Maria- Christina Ungureanu, Laura Teodoriu, Stefana Bilha, Alexandru Florescu & Cristina Preda
'Grigore T. Popa' University of Medicine and Pharmacy of Iaşi, Department of Endocrinology, Iaşi, Romania

Introduction
Acromegaly is a rare, challenging disease that if not appropriately treated can lead to numerous complications. Some of the most frequent complications are cardiovascular (hypertension, secondary cardiomyopathy, arrhythmias, valvulopathies, heart failure) and metabolic (secondary diabetes, various alterations of the lipid metabolisms).
Aim
The aim is to asses the impact of long-term acromegaly on the cardiovascular system and glucide and lipid metabolisms.
Patients and method
In this retrospective study the records of 107 patients with previously diagnosed acromegaly, who have been assessed at least once in our tertiary referral centre (Department of Endocrinology, University Hospital "Sfântul Spiridon", Iaşi) over a period of 6 years have been reviewed.
Results
Out of the 107 patients with mean age 51.96 ± 12.14 years, 34 (31.78%) were male and 73 (68.22%) were female. From the total of 107 patients 93 (86.92%) had cardio-metabolic complications. Out of the assessed cardiovascular comorbidities, hypertension was present in 46 patients (42.99%), rhythm disorders were found in 8 patients (20%), cardiomyopathy in 5 patients (12.5%), valvulopathies in 3 cases (7.5%), 6 cases of heart failure (15%), chronic venous insufficiency in 2 patients (5%), cardiac ischemic events were found in 11 patients (27.5%), 2 cases of stroke (5%) and 3 cases (7.5%) of other cardiovascular diseases were also noted. Alterations of the glucide metabolism were determined in 36 patients (33.64%): type 2 diabetes mellitus was found in 21 cases (58.33%), impaired fasting glucose in 6 cases (16.67%) and impared glucose tolerance in 9 patients (25%). Dyslipidemia was found in 44 patients (41.12%), while an increased body mass index was determined in 46 patients (57.01%).
Conclusions
The design of the present research has offered a chance for thorough investigation of cardiovascular and metabolic alterations in acromegaly patients, thus revealing a significant number of complications. Although acromegaly is an orphan disease, the multi-organ severe complications rise complex issues in relation with the diagnosis and treatment approach. This aspect could justify the use of a personalised multi-modal treatment for each patient.
Key words: acromegaly, cardiovascular disease, metabolic complications

DOI: 10.1530/endoabs.81.EP753

EP754

Early diagnostic tools in milder forms of central hypothyroidism in patients harbouring a pituitary adenoma: cross-sectional study on 142 patients from a single tertiary center

Elena Galazzi[1], Federico Nicoli[1], Silvia Carrara[1], Chiara Milan[2], Letizia Maria Fatti[1], Mirella Moro[1] & Luca Persani[2]
[1]Istituto Auxologico Italinao, San Luca Hospital, Endocrine and Metabolic Diseases Unit, Milano, Italy; [2]University of Milan, Department of Medical Biotechnology and Traslational Medicine (BIOMETRA), Italy

Introduction
Milder forms of central hypothyroidism (CeH) are still challenging to diagnose due to absence of gold standards, wide variability of fT4 values and aspecificity of symptoms. We aimed to find diagnostic clues at diagnosis (pituitary lesion dimensions, other hormonal deficit) and during long-term follow-up, guiding the clinician to a precocious diagnosis of CeH.
Study
142 patients harbouring a pituitary adenoma with complete pituitary assessment at diagnosis (hormonal/imaging) were studied between 2000 and 2020. Median age was 47.5 years (SD 16.5). Lesions were 45% microadenomas (55% macroadenomas)., 62% were functioning and 30% incidentalomas. At diagnosis, 67% of patients with CeH suffered from at least another hormonal deficit, especially gonadotropins failure (OR 6.9, $P=$ 0.0001) and corticotrope failure (OR 7.6, $P=$ 0.001). No correlation was found between CeH and having a functional adenoma ($P=$ NS). Radiological measures were available in 102/142 patients. Patients with CeH at diagnosis had bigger adenomas ($P=0.054$). Given a maximum adenoma diameter $>$ 12 mm, the probability of carrying CeH was statistically significant (OR 3.53, $P=$ 0.03, sensitivity 68.7%, specificity 61.6%). Mean follow-up was 7.64 years (2-53-9.73) and follow-up data were available for 69 patients, with at least one evaluation of paired TSH and fT4 per year. Only 4/69 developed overt CeH defined by inappropriately normal or low TSH with fT4 values beyond the lower limit of normal. In those patients mean fT4 variability (defined by the difference between the median value of fT4 and the lowest fT4 value detected over follow-up) was -18% (SD $\pm$ 10) and median TSH index (TSH_i) was $+1.7$ (IQR 0.36-2.18) with a mean decrease of -47% (SD $\pm$ 50). Among the other 65/69 patients with a normal thyrotrope reserve, mean ft4 variability was -2% (SD $\pm$ 9) displaying a -2 SD as low as -20% and mean TSH_i was $+2.51$ (SD $\pm$ 0.522) with a median decrease of – 7% (IQR -16; -3) displaying a 2.5° percentile as low as -38%. The difference in intra-individual ft4 variations and TSH_i decrease was statistically different in these two cohorts ($P=0.04$, $P=0.048$ respectively).
Conclusions
In patients carrying pituitary adenomas, the presence of mild CeH could we inferred at diagnosis if adenoma diameter is $>$ 12 mm and gonadotropin or corticotrope deficiency coexist. During follow-up, if intra-individual variation of fT4 from baseline exceed -20% and TSH index decreases by more than -38%, the development of CeH could be suspected.

DOI: 10.1530/endoabs.81.EP754

EP755

Pituitary adenomas and pregnancy: descriptive observational study

Miriam Veleno, Sara Menotti, Antonella Giampietro, Sabrina Chiloiro, Alfredo Pontecorvi, Laura De Marinis & Antonio Bianchi
Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Università Cattolica del Sacro Cuore, Pituitary Unit, division of Endocrinology and Diabetes, Rome, Italy

Introduction
Pregnancy results in a significant change in pituitary gland size and function. Due to this physiological adaptation, management of pituitary adenomas during pregnancy represents a particularly complex challenge. Aim of this study was to focus on a single referral institution experience with special attention to this subgroup of patients: pregnant woman affected by pituitary adenoma.
Materials and methods
This is a descriptive observational study, all patients with macroadenoma and who had at least one pregnancy were included. We studied 10 women who got pregnant during their endocrinological follow-up. They were divided as follows: 4 GH and PRL secreting tumors, 2 Cushing diseases, 2 acromegaly, 1 PRL secreting tumor and 1 non functioning macroadenoma. In order to describe the outcome of the adenoma during pregnancy, we considered the previous surgical and medical therapy, hormonal serum levels, imaging data and medical therapy during and after pregnancy. We also analyzed the obstetrical outcomes of their pregnancies.
Results
The median age of the patients was 35. They all had a previous transphenoidal surgery of the pitutitary adenoma. The two patients affected by Cushing disease also had bilateral surrenectomy, due to lack of disease control and due to hyposurrenalism undergone therapy with hydrocortisone. After surgery, because of residual disease, a patient affected by GH and PRL secreting tumors, one affected by acromegaly and the patient affected by non functioning macroadenoma were treated with somatostatin analogs and the other one affected by acromegaly started dopamine agonists. When the patients showed desire for pregnancy, medical therapy was discontinued evaluating hormonal tests and MR imaging. The residual disease at MRI was stable during and after pregnancy and did not affect the optic chiasma, without visual field alterations or reduced vision. Obstetrical outcomes showed no malformation, one twin pregnancy, two caesarean-sections. The patients already undergoing medical treatment before pregnancy, restarted it after pregnancy.
Conclusions
Studies on pituitary adenoma management during pregnancy are limited. In our study, no complication was reported in patients with or without residual tumour on the preconception MRI, regardless of the initial size and of the discontinuation of medical therapy. Patients did not need any kind of therapy during pregnancy and did not show any symptomatic progression of adenomas, without ophthalmological abnormalities or apoplexy. Because of the potential risk that these conditions represents for the mother and the fetus, it is essential to keep patients under close follow-up and treat them quickly and successfully.

DOI: 10.1530/endoabs.81.EP755

EP756

Clinical & Epidemiological characteristics of patients undergoing pituitary-related surgeries in a tertiary care centre in Sri Lanka

Piyumi Wijewickrama[1,2], Sathyajith Ambawatte[1, 3], Manilka Sumanatilleke[1], Chaminda Garusinghe[1], Sanjeewa Garusinghe[1], Deepal Attanayake[1], H.K. de. S Kularatne[1], Wadanambi Saman[1] & Noel P Somasundaram[1]
[1]NHSL, Colombo, Sri Lanka; [2]University College Hospital, United Kingdom; [3]St George's Hospital, United Kingdom

Introduction
For clinically relevant sellar masses, early identification and effective endocrine & surgical management is the key. National Hospital of Sri Lanka (NHSL), which is the largest tertiary care centre in Sri Lanka, manages a wide variety of patients with sellar/supra-sellar pathologies, regularly conducting pituitary related surgeries. The aim of the current study was to determine epidemiological and clinical characteristics as well as immediate post-operative course of the patients undergoing pituitary surgeries.
Methods
Prospective, cross-sectional study of demographics, clinical & biochemical characteristics & post-operative course of all adult patients (above 15 years) undergoing pituitary related surgeries in NHSL over 18 months from February 2019.
Results
During this period, 139 persons underwent pituitary related surgeries, with a mean age of 44 years (+/- 15) and a female to male ratio of 3:2. 25% had re-operations while the rest were first surgeries. The majority (68.3%) presented with pressure symptoms while 10.1% & 20.1% presented with hypopituitarism & hormone hypersecretion respectively. Sixty-seven (48.2%) were on pre-operative Levothyroxine, with 12 of them having long standing primary hypothyroidism. Forty-seven (33.8%) patients were on pre-operative long term hydrocortisone replacement. Pituitary adenoma in 111 (79.9%), craniopharyngioma in 22 (15.8%), and supra-sellar meningioma in 6 (4.3%) were observed. MRI of sellar masses demonstrated cavernous sinus invasion in 49 (35.3%), while 80 (57.6%) had optic chiasm compression. Out of pituitary adenomas, the majority 81 (72%) had non-functioning adenoma, 20 (18%) had Acromegaly, 9 (8.1%) had Cushing's and 1 patient with resistant prolactinoma underwent surgery. The majority, 108 (77.7%) were trans-sphenoidal surgeries, while 31 (22.3%) underwent craniotomy. Post-operative complications observed were CSF rhinorrhoea in 25 (18%), bleeding in 8 (5.8%), progressive deterioration of vision in 21(15%) and ischemic stroke in 2 persons. No significant difference was

observed with the type and attempt of surgery with these complications. Fifty-two developed post-operative transient or permanent cranial Diabetes Insipidus while 12 (8.6%) had Syndrome-of-inappropriate-ADH secretion. 137 (99%) were discharged on hydrocortisone. Post-operative Levothyroxine was required in 74(53%) with a significant difference in the re-operation group compared to first surgery ($P=0.02$).
Conclusion
This study identifies baseline characteristics of patients undergoing pituitary-related surgeries in a south Asian developing country, along with immediate post-operative complications. These findings have a national & a regional relevance in improving patient care. This will also have a global relevance due to the rising ethnic diversity all over the world.

DOI: 10.1530/endoabs.81.EP756

EP757

Fluid and sodium disorders in patients undergoing pituitary related surgeries in a tertiary care centre in Sri Lanka, with associations and risk factors; a prospective, observational study

Piyumi Wijewickrama[1,2], Sathyajith Ambawatte[1, 3], Manilka Sumanatilleke[1], Chaminda Garusinghe[1], Kasun Kamaladasa[1] & Noel P Somasundaram[1]
[1]NHSL, Colombo, Sri Lanka; [2]University College Hospital, United Kingdom; [3]St George's Hospital, United Kingdom

Introduction
Fluid and sodium disorders are a relatively frequent occurrence after sellar/supra-sellar surgeries. National Hospital of Sri Lanka (NHSL) is the main tertiary care centre in Sri Lanka, conducting regular pituitary surgeries.
Methods
A prospective cross-sectional study was conducted in all adults (above 15-years) undergoing pituitary-related surgeries in NHSL over 18 months from September 2019. The relationship between demographic factors, clinical, biochemical & tumour characteristics, diagnosis and indication for surgery, type and attempt of surgery with the post-operative fluid and sodium outcomes [syndrome-of-inappropriate-anti-diuretic-hormone (SIADH), polyuria, Cranial Diabetes Insipidus (CDI)] were analysed.
Results
There were 139 patients with a mean age of 44 years (+/- 15), 60% females, undergoing Trans-sphenoidal-surgery(TSS) or craniotomy for varying indications related to sellar/supra-sellar pathologies. Mean baseline pre-operative sodium was 138.9 (+/-3.2). Post-operatively, 76(54.6%) developed polyuria (>3l/24-h) with peak median urine output on day 2. Out of them, 52 (68.5%) were diagnosed with CDI (80.7% having only transient CDI) and the rest had transient polyuria without confirmed Cranial-Diabetes-Insipidus (TPWCDI). Out of all polyuric patients, 71 received at least a single dose of Desmopressin at some point. Twenty-eight (20.1%) developed post-operative hyponatremia (sodium<135), with only 12(8.6%) having confirmed SIADH. All SIADH patients were managed with fluid restriction, with only 2 requiring hypertonic saline. Five demonstrated triple phase response. Patients undergoing re-operation had a significant association with confirmed CDI & TPWCDI, compared to first surgery ($P<0.0001$ & $P=0.03$ respectively). However, none developed SIADH. Risk of CDI was higher in patients with a tumour size of >2 cm (OR-1.37;95%CI-1.08-1.726; $P=0.018$). Craniopharyngioma demonstrated a higher risk of post-operative CDI compared to other diagnoses (OR-6.8;95%CI 2.7-17;$P<0.0001$). Acromegaly patients had a higher risk of post-operative TPWCDI (OR-1.46; 95%CI 1.04-2.06; $P<0.0001$) and none developed CDI. Post-operative SIADH was more likely in patients undergoing craniotomy, than TSS ($P=0.001$). Patients with tumour size>3 cm (OR1.6; 95%CI 1.2-2;$P<0.0001$), and craniopharyngioma (OR 2.9; 95%CI 1.1- 7.2; $P=0.02$) were more at risk of SIADH. SIADH was not seen with acromegaly or Cushing's.
Conclusions
Transient fluid & sodium disorders occurred in majority of the patients undergoing pituitary-related surgeries. Polyuria & CDI were more common than SIADH. Re-operation, tumour size and the type of tumour could be predictors of post-operative fluid and sodium disorders. The findings of this real-world study add to the existing global literature and is the first such study conducted in Sri Lanka.

DOI: 10.1530/endoabs.81.EP757

EP758

Severe growth retardation due to pituitary stalk agenesis: a case report

Kaoutar Rifai, Manale Azriouil, Farah Kamel, Kaoutar Elmoatamid, Loubna Guissi, Hinde Iraqi & Mohamed Elhassan Gharbi
Ibn Sina University Hospital, Endocrinology, Rabat, Morocco

Introduction
Growth retardation is considered severe when the height of the child is -3 standard deviation (SD) below the average height in reference to the growth curves of children of the same sex and age. Pituitary stalk interruption syndrome (PSIS) is one of the most common conditions in children with short stature.
Case report
We report the case of a 12-years old boy with no clinical history of perinatal injury or traumatic birth, who was admitted for short stature. Physical examination showed that his height was 105 cm (-4 SD), his weight was 15 kg (-4 SD), and Tanner stage was 1. A complete pituitary hormone profile was performed, which showed picture of hypopituitarism with low T4: 0,46 ng/ml, and low morning baseline cortisol: 28 ng/ml. His IGF1 level was under 10 ng/ml. His bone age was 2 years according to the Greulich and Pyle. Magnetic resonance imaging (MRI) examination showed an agenesis of the pituitary stalk which was not visualized; however; anterior pituitary and posterior pituitary were normally identified.
Discussion
PSIS is characterized by the presence of a thin or absent pituitary stalk, associated to hypoplastic anterior pituitary and ectopic posterior pituitary on MRI. However, there are variations in MRI appearances of this syndrome that includes the form of the pituitary stalk (interrupted, thin, or absent), the height of the anterior pituitary (from absence to normal) and the appearance of the posterior pituitary (ectopic, absent, or normal) The clinical presentation of PSIS varies with the age of diagnosis; manifestations may include neonatal hypoglycemia, prolonged neonatal jaundice, or short stature in older children. The clinical findings are related to isolated growth hormone deficiency; or combined multiple pituitary hormone deficiency.
Conclusion
PSIS is a rare syndrome of congenital abnormalities involving hypothalamic-pituitary structures. It should be considered in the differential diagnosis of a child presenting with short stature or delayed puberty.

DOI: 10.1530/endoabs.81.EP758

EP759

About two cases of adipsic hypernatremia in adults, one with proven blood antibodies against subfornical organ (SFOAb).

Lilia Charfi[1], Hippolyte Dupuis[1], Szuwarski Lucile[1], Gillot Christine[2], Utsunomiya Akari[3] & Marie-Christine Vantyghem[1,4,5]
[1]Chu De Lille, Lille, France; [2]Hospital Center De Béthune Beuvry, Beuvry, France; [3]Hiroshima Prefectural Hospital, Hiroshima, Japan; [4]Inserm, Lille, France; [5]CHRU Lille, France

Adipsic hypernatremia, a rare hypothalamic disorder characterized by a loss of thirst in response to hypernatremia is more often reported in children. An autoimmune mechanism has been recently demonstrated. We report two cases.
Case1
A lean 67-year-old female, with a history of multilocular sclerosis, was admitted, for severe hypernatremia (162 mmol/l) with low ADH level (0.5 pmol/l; N: 0.5-2). She did not complain of thirst, despite ideomotor slowing and a skinfold. Diuresis was 1.40 l/24 h. Pituitary assessment showed mild hyperprolactinemia, a Nugent test at 11.5 mg/dl (n <1.8 mg/dl) with low TSH level (0.08 uU/ml (n 0.4-3.6)). MRI showed pituitary stalk nodular thickening. Etiological research only showed SFOAb. Treatment with desmopressin allowed improvement of ideo-motor slowing and natremia (145 mmol/l). The pituitary stalk thickening had partially regressed one year later.
Case2
An overweighed 38-year-old lady, was referred for a first hypernatremia episode (160 mmol/l) in 2013 after an acute pancreatitis complicated with cardiovascular collapse. She had no polyuria-polydipsia, did not feel thirst, and was irregularly menstruated. Initial pituitary assessment showed gonado-somatotropic insufficiency, mild hyperprolactinemia, normal thyroid and adrenal function. Keeping diagnosis was possible pituitary ischemia. The patient was advised to drink at least 2 liters/day and remained asymptomatic except for infertility. Three other episodes of pancreatitis occurred, the only identified cause being heterozygosity for a *CFTR*

variant. In 2021, a new work-up showed similar pituitary profile as in 2013, hypernatremia (150 mEq/l), negative autoimmune panel, and normal CRP, IgG4 and pituitary MRI. A month later, a 5th pancreatitis with severe bradycardia (30-35/bpm) , hypothermia, low blood pressure and severe hypernatremia 170 mmol/l (ADH: 0.8 pmol/l) required ICU admission. Cortisol and thyreotrope deficit were present, with persistent hyperprolactinemia and somato-gonadotropic insufficiency. She initially improved with rehydration, hydrocortisone 200 mg/day and levothyroxine. Polyuria or thirst were absent. Hypernatremia worsened as soon as rehydration/hydrocortisone were tapered. Desmopressin allowed clinical improvement with a 10 mmol/day natremia decrease. On day 3, a seizure revealed brain hematoma and CT signs of vasculitis. Vasogenic edema finally leds to death.
Conclusion
These two cases of adipsic hypernatremia in adult female patients are possibly related to an autoimmune neurohypophysitis in the context of MS in case1 and systemic inflammatory/autoimmune disease explaining both the hypothalamic and pancreatic involvement in case2 Despite the lack of polyuria-polydipsia syndrome, desmopressin treatment improved clinical status and natremia, but should perhaps be used more cautiously than usually recommended. Autoimmune causes can today be proven and may help to adjust the treatment.

DOI: 10.1530/endoabs.81.EP759

EP760

Features of the incidence of postoperative complications in patients with transsphenoidal pituitary adenectomy

Gulmira Inomova[1], Zamira Halimova[2] & Yayrahon Kuldasheva[3]
[1]223 Bog'ishamol Ko'chasi, Endocrinology with Pediatric Endocrinology, Tashkent, Uzbekistan; [2]Republican Specialized Scientific and Practical Medical Center of Endocrinology named after academician Ya.Kh.Turakulov, Neuroendocrinology, Tashkent, Uzbekistan; [3]Andijan State Medical Institute, Endocrinology with Hospital Therapy, Tashkent, Uzbekistan

Target.
To study the incidence of postoperative complications in patients with transsphenoidal pituitary adenoectomy.
Materials and research methods
180 cases of PA subjected to TPA for the period from 2018 to 2020 were analyzed. Of these, 102 (56.6) women, 78 (43.3) men, patients were divided into two alternative groups: the first group - 93 (51.6%) patients with macroadenomas - 42 (45.2%) men, women 51 (54.8%), the second (comparison group) - 87 (48.4%) with microadenomas of men - 35 (40%), women - 52 (60%) of the pituitary gland. The age of the patients ranged from 30 to 59 years. The levels of hormones STH, IGF-1, ACTH, cortisol, prolactin, TSH, fT4, LH, FSH, estradiol, progesterone according to indications, MRT/CT of the chiasmal-sellar area and the state of the organ of vision were studied.
Results
Patients were distributed as follows: depending on the hormonal activity of patients with adrenocorticotropic hormone secreting Cushing's syndrome-60, acromegaly-60, inactive pituitary adenoma-60; depending on the size of the formation: 93 (51.6%) were with macroadenomas, 87 (48.3%) with pituitary microadenomas. An analysis of the incidence of postoperative complications in the short term (1 month) revealed that in 81 (45%) patients with hypopituitarism; hypothyroidism in (70)39%; hypogonadism in 50(28%); diabetes insipidus in 7(4%); transient diabetes insipidus in 11(6%); visual acuity deterioration in 2 (1.2%) patients and liquorrhea in 3 (5.4%) patients. At the same time, there was a normalization of elevated hormone levels in 133 (74%) patients; 30% improvement in vision; lack of disease dynamics in 47 (26%). Despite the persistent phenomena of hypopituitarism 47(26%) and diabetes insipidus 11(6%), which were mainly observed in 165(92%) patients with macroadenomas and did not depend on the organ activity of the formation (against 54(30%) cases with microadenomas). In the long-term follow-up of patients after TPA (t 3 months to 1 year), an improvement in pituitary function was noted in the form of restoration of gonadotropic insufficiency, phenomena of transient diabetes insipidus and improvement in hypertensive cephalgia.
Conclusion
The frequency of immediate and long-term complications in most cases is observed in pituitary macroadenomas and does not depend on the hormonal activity of the adenoma.

DOI: 10.1530/endoabs.81.EP760

EP761

Skeletal complications in Cushing's disease (CD)

Dragana Miljic[1,2], Sandra Pekic Djurdjevic[1, 2], Mirjana Doknic[1, 2], Marko Stojanovic[1, 2], Marina Nikolic Djurovic[1, 2], Zvezdana Jemuovic[1], Nevena Radić[2], Sara Radovic[2] & Milan Petakov[1,2]
[1]Clinic for Endocrinology, Diabetes and Diseases of Metabolism, University Clinical Centre of Serbia, Belgrade, Serbia; [2]University of Belgrade - Faculty of Medicine, Belgrade, Serbia

Introduction
Structural and functional damage of the skeletal system resulting in fractures is a common complication of CD. Due to major effect of glucocorticoids on the trabecular bone, vertebral fractures are a common and severe complication which can lead to disability.
Goal
To investigate the prevalence of skeletal complications (osteoporosis, osteopenia, presence of fragility fractures) in patients with Cushing's disease, as well as gain insight into the potential risk factors for their development.
Material and methods
Cross-sectional study was carried out analyzing electronic medical histories of 52 patients (41 female, 11 male), diagnosed with CD treated between 2009 and 2019.
Results
The study shows that bone demineralization is present in 52% of patients, 32% of whom were diagnosed with osteoporosis, 20% with osteopenia. A correlation between bone demineralization and age or age of CD diagnosis is shown. Bone fractures were present in 17.3% of the patients, of which 77.8% were vertebral and 22.2% peripheral. Patients who had bone fractures were more prone to bone demineralization ($P=0.02$), and more specifically, there was a significant association between osteoporosis and skeletal fragility fractures ($P=0.003$).
Conclusion
Patients with CD have high prevalence of bone demineralization and osteoporosis. Patients with reduced bone mineralization are at higher risk of fracutres, most commonly vertebral fractures, which is why early diagnosis and treatment are necessary.

DOI: 10.1530/endoabs.81.EP761

EP762

Feasibility and effectiveness of switching patients with acromegaly receiving long-acting octreotide to lanreotide (Somatulin Autogel)

Olga Zanozina
Privolzhsky Research Medical University, Regional Clinical Hospital named after N. A. Semashko, Endcrinology, Nizhny Novgorod, Russian Federation

Medical therapy of patients with acromegaly is an important addition to surgical treatment or an alternative to it when it is impossible to use the latter. Long-acting synthetic analogues of somatostatin (octreotide and lanreotide) act on the same subtypes of somatostatin receptors, but the drugs have been shown to differ in efficacy and tolerability.
Objective
to achieve complete clinical and laboratory remission in patients with acromegaly, which did not reach it when using prolonged octreotide.
Materials and methods
12 patients with acromegaly who did not have clinical and laboratory remission during treatment with octreotide Depo (Long), while only 3 patients had incomplete clinical and laboratory remission. Of these, surgical treatment was performed in 9 patients. The mean age of the patient is 52.3 years. The patients were switched from octreotide Depo (Long) 30 mg (5 people) and octreotide Depo (Long) 40 mg (7 people) to Somatulin Autogel 120 mg somatulin. The interval between injections was 28 days. Controlled the level of growth hormone (GH) and insulin-like growth factor 1 (IGF-1)
Results
During 6 months of therapy, 10 patients showed a significant decrease in growth hormone ($P=0.024$) and IGF-1 ($P=0.041$), while the level of IGF-1 was completely normalized in 3 people, and growth hormone - in 3 people. After 12 months, complete clinical and laboratory remission was observed in 4 patients, partial - in 4 patients. Thus, after a year of observation, 8 out of 12 patients achieved remission.
Conclusions
Patients who have not achieved remission on long-acting octreotide should be switched to long-acting lanreotide (Somatulin Autogel)

DOI: 10.1530/endoabs.81.EP762

EP763

Abstract Withdrawn

DOI: 10.1530/endoabs.81.EP763

EP764

Clinical characteristics, treatment and outcomes of well-differentiated gastroenteropancreatic G3 NET

Marta Opalinska[1], Anna Sowa Staszczak[2], Anna Kurzyńska[2], Karolina Morawiec-Sławek[2], Agnieszka Stefańska[1] & Alicja Hubalewska-Dydejczyk[2]
[1]University Hospital in Krakow, Department of Endocrinology, Oncological Endocrinology and Nuclear Medicine, Kraków, Poland; [2]Jagiellonian University Medical College, Chair and Department of Endocrinology, Krakow, Poland

Background
Although gastroenteropancreatic neuroendocrine tumors G3 (GEP-NET G3) and neuroendocrine cancers (GEP-NEC G3) are characterized in histopathological examination by Ki67 > 20% or > 20 mitoses/10HPF their management and prognosis is substantially different. Despite the WHO introduces the novel well-differentiated neuroendocrine tumour of high grade (NET G3) classification in 2017 the clinical management of them is still challenging due to high NET G3 heterogeneity and limited data in regards to best therapeutic strategies.
Material and Methods
We review clinical characteristics, treatment options, and outcomes in cohort of patients with gastroenteropancreatic NET G3 (GEP-NET) managed at our centre since implementation of the new WHO classification (2017 – 2021).
Results
There were 9 cases of GEP-NET G3 (4 women and 5 men, mean age at diagnosis 62,6 years, range 47-80 years). 8 of them had disease stage IV at diagnosis (with liver, lymph nodes, bone, adrenal, brain and peritoneal metastases) and 1 stage IIB with loco-regional lymph node metastasis. The tumours originate from: pancreas (3 cases), stomach (2 cases), small intestine (2 cases), large intestine (1 case) and in 1 case the primary site was unknown. Mean Ki67 was 35% (range 25-70%). In 4 cases there was good or very good somatostatin receptor expression (SSTR) (Kenning score 3 and 4) in somatostatin receptor imaging. Treatment options included combination of surgery, somatostatin analogues (SSA), Peptide Receptor Radionuclide Therapy (PRRT) or chemotherapy (temozolomide/capecitabine or platinum-based regimens). Mean overall survival was 17,2 months (range 3,0 - 46,6 months).
Conclusion
NET G3 management is challenging due to the their heterogeneity and relatively poor prognosis. Further research is needed to optimize/personalize NET G3 therapy with regard to differences in their organ of origin, stage, grading and SSTR expression status.

DOI: 10.1530/endoabs.81.EP764

EP765

Head and neck paragangliomas: the belfast trust experience

Milad Darrat[1], Neil Bailie[2], Susie Hampton[2], Stephen Cooke[3], Philip Weir[3], Louis Lau[4], Brian Herron[5], Patrick J Morrison[6] & Philip Johnston[1,1]
[1]Royal Victoria Hospital, Belfast, Regional Centre for Endocrinology and Diabetes, Belfast, United Kingdom; [2]Royal Victoria Hospital, Belfast, Department of Otolaryngology, Belfast, United Kingdom; [3]Royal Victoria Hospital, Belfast, Department of Neurosurgery, Belfast, United Kingdom; [4]Royal Victoria Hospital, Belfast, Department of Vascular Surgery, Belfast, United Kingdom; [5]Royal Victoria Hospital, Belfast, Department of Pathology, Belfast, United Kingdom; [6]Belfast City Hospital, Department of Clinical Genetics, Belfast, United Kingdom

Background
Head and neck paragangliomas (HNPGL) are rare, usually benign slow-growing tumours arising from neural crest-derived tissue. Definitive treatment strategies for HNPGL have not been clearly defined.
Aims
To provide a comprehensive review of our institutional experience of the clinical features, investigations, management and follow up of this cohort.
Methods
Baseline clinical information was taken from a prospectively maintained HNPGL database between January 2017 to January 2022. Further clinical, radiological and laboratory data as well as outcomes were obtained from electronic medical records (NIECR).
Results
There were 21 patients; 10 M; 11F with a mean age of 54 years (range 17-76). Seven (33.3%) patients had glomus jugulare tumour, six (28.5%) had carotid body tumour, four (19%) had glomus tympanicum, four (19%) were in other locations. Tumour size ranged from 20 mm to 5 cm. Thirteen (61.9%) patients had a pre-operative scans, six of which had octreotide avid scans. To date five (23%) patients had SDHD gene mutation and three (14%) patients had SDHB gene mutation identified. All tumours were non-functioning with normal urine metanephrines. Ten (47%) patients underwent surgical resection with five subsequently receiving adjuvant radiotherapy. Recurrence was present in three patients who had surgery for jugulare tumours. Four (19%) patients were deemed not suitable candidates for surgery either due to their extensive disease burden, tumour location or the presence of multiple co-morbidities. Three (14%) patients received monthly sandostatin/Octreotide-therapy. Two of these three patients had stable tumour size without any significant growth since they started on Octreotide-therapy. The remaining four patients (19%) were managed conservatively with serial imaging and observation.
Conclusion
Management of patients with HNPGL requires a multidisciplinary approach and should be individualized and tailored to each patient. Consideration for primary surgical treatment should consider performance status, tumour location and size. Initial surgery still provides excellent outcomes for patients, with adjunctive radiotherapy as second line treatment. The role of Octreotide therapy should be studied in a larger cohort to determine longer term outcomes.

DOI: 10.1530/endoabs.81.EP765

EP766

A paradox in clinical practice: the case of a hidden tubercoloma

Matteo Parolin[1], Matteo Parisotto[1, 2], ambra uliana[1], Paola Sartorato[1] & Ernesto De Menis[1]
[1]ULSS 2 Treviso, Dipartimento di Medicina, Treviso, Italy; [2]University of Padua, Dipartimento di Medicina, Padova, Italy

Introduction
A potential cause of panhypopituitarism could be cerebral tubercular lesions, that are often misdiagnosed. Hormonal effects could be related directly to primary tubercular lesions, or after starting antitubercular therapy. Paradoxical reaction (PR) in tuberculosis is defined as clinical or radiological worsening of pre-existing tuberculous lesions or development of new lesions after beginning an appropriate antitubercular therapy (ATT). It has been suggested that the mechanism underlying a PR is an excessive immune response.
Case Report
A 26-year-old man presented to the Emergency Department with a two-week history of fever, headache, visual impairment and fatigue. He was known to have a *Mycobacterium tuberculosis* axillary adenopathy treated with ATT consisting of rifampicin, isoniazid, ethambutol and pyrazinamide, shifted to a maintenance therapy with Isoniazide and Rifampicine three months before. The patient was taking his medication regularly. On examination all clinical parameters were normal; general physical evaluation was unremarkable except for visual loss. Initial laboratory investigations revealed anterior hypopituitarism, (secondary adrenal, gonadal and thyroid failure) without central diabetes insipidus. Cerebrospinal fluid analysis did not show abnormal findings (in particular acid fast bacilli stains on liquor, cultures, PCR for M. tuberculosis and cryptococcal antigens were negative). A chest x-ray was negative. An MRI of the brain with gadolinium enhancement showed a polylobate cystic suprasellar lesion with thickening of pituitary peduncle. The lesion showed ring enhancement with gadolinium, compatible with a flogistic lesion. Visual perimetry examination showed bilateral temporal deficit. Due to the clinical worsening while on ATT and the absence of secondary infection, a paradoxical reaction to ATT was suspected and the patients was managed with high dose dexamethasone (8 mg daily) added to standard therapy for hypopituitarism showing gradual response to the treatment. There was a complete regression of visual deficit and a partial reduction of the intracranial lesion (an MRI was repeated). The patient was

discharged after ten days in good general conditions, with the indication to continue corticosteroids for two months.
Conclusions
Our patient's neurological finding after the beginning of ATT may have been a new development or a progression of intracranial tuberculoma. A paradoxical reaction to ATT should be suspected in any patient in ATT who present with neurological findings and hypopituitarism. Paradoxical tuberculomas are observed in approximately 1% of all active tuberculosis cases. Corticosteroids are the only anti-inflammatory drug that can be used in the management of PR.

DOI: 10.1530/endoabs.81.EP766

EP767

'The efficiency of the treatment by Sandostatin-Lar in patients with non-functional pituitary macroadenomas'

Malika Mirtukhtaeva[1], Ashley Grossman[2], Nitin Leekha[3], Alisher Akbutaev[4] & Urmanova Yulduz[5]
[1]Republican Specialized Scientific Practical Medical Center of Endocrinology of Public Health Ministry named by acad. Ya.Kh. Turakulov, Tashkent, Uzbekistan; [2]University of Oxford Senior Research Fellow, Green Templeton College, United Kingdom; [3]Jaypee Hospital, Sector 128, Noida, India, Oncology Department, Noida, India; [4]Republican Specialized Scientific Practical Medical Center of Endocrinology of Public Health Ministry named by acad. Ya.Kh. Turakulov, Department of Neurosurgery, Tashkent, Uzbekistan; [5]Tashkent Pediatric Medical Institute, Department of Endocrinology, Tashkent, Uzbekistan

The purpose of the study
Is to study the efficiency of the treatment by Sandostatin-Lar in patients with non-functional pituitary macroadenomas (NFPA)
Material and methods.
Under our observation there were 20 patients with NFPA, of whom women were 8, men - 12. The average age of patients was 29,2/36.4 years. All patients were subjected to transnasal adenomectomy of pituitary gland (TAG) in our clinic. The whole patients were performed by research complex, which included Chemilyuminiscent hormonal (STH, IGF-1, Prolactin, LH, FSH, TSG, ACTH, Cortizol, etc.), ophthalmological (Eye bottom, field of view) and X-ray studies (CT, MRI of the Turkish saddle).
Results
According to our data, In all 20 patients, the average sizes of the pituitary tumor before TAG were in range 3.1 x 3.4 x 3.0 cm. Patients were divided into 2 groups: patients of 1 st group received after TAG the treatment by Sandostatin-Lar during 3 months, patients of 2 nd group not received Sandostatin-Lar.. The Sandostatin-Lar was prescribed 20 mg every 4 weeks for 3 months. The preliminary results showed the stabilization of the tumor residue in 7 of 10 patients (70%) in the group of combined treatment compared to 10 patients from 2 nd group who did not received Sandostatin-Lar.
Conclusions
It is necessary further continuation of research, taking into account immuno-cytochemical studies and biomarkers.

DOI: 10.1530/endoabs.81.EP767

EP768

Clinical, paraclinical, therapeutic and evolution profile of pituitary adenomas: about 92 cases

Wahiba Abdellaoui[1], Imane Assarrar[2], Lamiae Zarraa[1], Soumiya Berrabeh[1], Siham Rouf[1, 2] & Hanane Latrech[1,2]
[1]Mohammed VI University Hospital, Medical School, Mohammed the First University, Department of Endocrinology-Diabetology-Nutrition, OUJDA, Morocco; [2]Laboratory of Epidemiology, Clinical Research and Public Health, Faculty of Medicine and Pharmacy of Oujda, Mohammed the First University, Oujda, Morocco

Introduction
Pituitary adenomas represent about 10 to 20% of all intracranial tumors. They are usually classified according to their size into pico-adenomas, micro-adenomas and macro-adenomas, but can also be classified according to their secretory properties into secreting or nonfunctional adenomas. In this study, we describe the clinica, paraclinica, therapeutic and evolution features of pituitary adenomas in our center.
Material and methods
A retrospective and descriptive study, over a period of 6 years, including 92 patients with pituitary adenoma, followed-up in the Endocrinology-Diabetology and Nutrition department of Mohammed VI University Hospital Center of Oujda, Morocco.
Results
The mean age of the patients was 44 years with a sex ratio (F/M) of 1.6. The clinical features were dominated by headaches and/or visual changes and were reported in 59.8% of patients. Radiologically, macroadenomas were by far the most frequent (70.7%). Hypopituitarism was found in 28.3% of cases. In our study, non-functional adenomas were the most frequent etiology (26.1%), followed by Cushing's disease (22.8%) and prolactinomas (20.6%). Somatotropic adenomas were found in 17.4% of cases. Fifty-eight percent of the patients underwent transphenoïdal surgery, of which 9.8% received radiotherapy. Medical treatment was considered in 63% of patients.
Conclusion
The management of pituitary adenomas must be multidisciplinary engaging neurosurgeons, endocrinologists, radiologists and ophthalmologists. The decision of the therapeutic choice is taken according to several criteria including: size, secreting or functional character, invasive character and response to medical treatment... [1]. All the files of our patients were discussed in a multidisciplinary meeting entitled 'Staff of the pituitary gland'.
Bibliography
[1] Molitch ME. Diagnosis and Treatment of Pituitary Adenomas: A Review. JAMA. 2017 Feb7;317(5):516-524

DOI: 10.1530/endoabs.81.EP768

EP769

A challenging case of sheehan syndrome

Ana Rita Elvas[1], Inê s Vieira[2], Miguel Melo[2], Dí rcea Rodrigues[2], Maria Leonor Gomes[2] & Isabel Paiva[2]
[1]Portuguese Oncology Institute of Coimbra, Endocrinology, Coimbra, Portugal; [2]Coimbra Hospital and University Center, Department of Endocrinology, Diabetes and Metabolism, Coimbra, Portugal

Introduction
Sheehan Syndrome (SS) is a cause of hypopituitarism resulting from postpartum pituitary infarction. Its frequency is decreasing worldwide, particularly in developed countries due to advances in obstetric care.
Case report
A 50-year-old female patient was admitted to the emergency department with complains of progressive pain in the lower hemithorax and abdomen. She also referred constipation, weight gain and asthenia. The initial laboratory tests showed raised creatinine kinase (4661 U/l [<145]) and aminotransferases (AST 86 U/l [<31]; ALT 36 U/l [<36]). Thyroid function was assessed revealing thyroid stimulating hormone (TSH) of 0.27 uIU/ml [0.4-4.0] and free thyroxine <0.40 ng/dl [0.7-1.5]). Assessment of anterior pituitary function was carried out indicating pan-hypopituitarism: FSH 3.8 mIU/ml; LH 0.6 mIU/ml; Prolactin <0.8 ng/ml [5.2-26.5]; ACTH 16 pg/ml [9-52]; Cortisol 2.1 mg/dl [5-25]; GH <0.1 µg/l [<1]. A brain magnetic resonance imaging (MRI) was performed, revealing the presence of an intrasellar arachnoidocele. She was started on replacement therapy with hydrocortisone and later levothyroxine with symptomatic improvement. The patient had a past medical history of a stillbirth at 28 years old, in Guinea-Bissau, due to postpartum haemorrhage requiring transfusion support. Afterwards a combined oral contraceptive was started, which she maintained for 11 years. After discontinuing the drug at the age of 39, she remained amenorrhoeic.
Discussion
This case fulfils the classic criteria of Sheehan's syndrome with severe postpartum haemorrhage requiring transfusion; postpartum oligomenorrhea; hypopituitarism and the presence of arachnoidocele at brain MRI. Stillbirth in an underdeveloped country is also frequently described and related to a diagnostic latency. The diagnosis was obtained 26 years after the incident, with unspecific symptomatology. The fact that the corticotropic axis tends to be affected later in these cases, may explain the absence of significant consequences. This illustrates a difficulty in diagnosing Sheehan's syndrome outside the acute context and highlights the need to be alert for this entity.

DOI: 10.1530/endoabs.81.EP769

EP770

A case with primary autoimmune hypothyroidism causing pituitary enlargement mimicking pituitary macroadenoma and secondary adrenal insufficiency

Mustafa Burak Yaşar[1], Zehra Yagmur Sahin Alak[2], Pinar Uzgec Guller[1], Metin Guclu[1], Fatih Aydemir[3] & Sinem KIYICI[1]
[1]Health Sciences University, Yuksek Ihtisas Research and Training Hospital, Endocrinology and Metabolism, Bursa, Turkey; [1]Health Sciences University, Yuksek Ihtisas Research and Training Hospital, Endocrinology and Metabolism, Bursa, Turkey; [3]Health Sciences University, Bursa Sehir Hospital, Neurosurgery, Bursa, Turkey

Introduction
In primary hypothyroidism, the increase in TRH may cause hyperplasia in the pituitary gland. It has been reported that long-standing hypothyroidism might also cause irreversible pituitary damage, which may lead to a deficiency in one or more pituitary hormones. Herein, we report a case with primary autoimmune hypothyroidism causing pituitary enlargement mimicking pituitary macroadenoma and secondary adrenal insufficiency.
Case
A 17-year-old female patient was diagnosed with primary hypothyroidism when she was 12 years old and levothyroxine-sodium treatment was started. Three years ago, she applied to a tertiary medical center with headache. A solid mass lesion in pituitary gland measuring approximately 15 mm diameter was reported at magnetic resonance imaging (MRI). After hormonal evaluation the mass was considered as a non-functioning macroadenoma and follow-up was recommended. Secondary adrenal insufficiency was observed in follow-up and hydrocortisone treatment was added. She referred to neurosurgery for the operation. Repeated MRI of the sella reported that there was a 10 x 10 mm nodular lesion suspicious for macroadenoma, and pituitary hyperplasia and hypophysitis should be considered in the differential diagnosis. Serum TSH was found suppressed while ft4 and ft3 were in normal range. The patient referred to our center for a differential diagnosis. The patient had fatigue and hair loss complaints. She had regular menstrual cycle and no galactorrhea. The visual field examination was normal. She was using levothyroxine-sodium and hydrocortisone. Macroadenoma wasn't considered when the serial MRI of sella was reevaluated. Pituitary hyperplasia or hypophysitis was suspected as a primary diagnosis. No signs of systemic disease were found clinically in terms of hypophysitis. Serum acute phase reactants and IGG4 levels were normal, and the anti-PIT 1 antibody was negative. Thyroid autoantibodies were positive. Serum TSH level was found increased (>100 uIU/ml) while serum fT4 was low. The hypothalamic-pituitary-adrenal axis couldn't be evaluated due to long-term steroid usage. Other pituitary hormones were normal. We found out that she didn't use levothyroxine-sodium regularly. Previous TSH measurements were occasionally >300 uIU/ml. Pituitary hyperplasia due to irregular replacement was considered. She was warned about regular usage. It was planned to taper and discontinue hydrocortisone during follow-up and reevaluate the pituitary-adrenal-axis.
Discussion
Despite the recent advances in MRI examinations, it might be still difficult to differentiate pituitary adenoma, hyperplasia and hypophysitis. Therefore, the patient's medical history, clinic and laboratory results should be evaluated together carefully. Accurate identification of such patients is important for avoiding unnecessary surgery and costly MRI follow-up.

DOI: 10.1530/endoabs.81.EP770

EP771

The management of hypophysitis in Covid-19

Sara Menotti, Miriam Veleno, Antonella Giampietro, Sabrina Chiloiro, Pier Paolo Mattogno, Quintino Giorgio D'Alessandris, Liverana Lauretti, Simona Gaudino, Francesco Doglietto, Alfredo Pontecorvi, Laura De Marinis & Antonio Bianchi
Agostino Gemelli University Policlinic, Endocrinology, Roma, Italy

Introduction
Literature has already described some cases of hypophysitis related to acute respiratory syndrome coronavirus 2 (SARS-Cov2). The pituitary is indeed target for the virus due to the angiotensin-converting-enzyme-2 expression. Hypophysitis patients present with mass effect and pituitary dysfunction related symptoms. ACTH and TSH deficiencies are the most reported, along with central diabetes insipidus (CDI). The best way to manage these hypophysitis is still undefined. However, it must be considered that the prompt correction of Glucocorticoid (GC) therapy in Adrenal insufficiency (AI) is aimed at saving the life of the patients. We describe our experience in the management of hypophisitis in patients who tested positive for SarsCov2, focusing on its two most challenging presentations: adrenal insufficiency and diabetes insipidus.
Discussion
If COVID-19 infection was mild and without fever, we chose to conservatively treat AI patients, with surveillance of symptoms of the onset of adrenal crisis, as nausea, vomiting, abdominal pain and hypotension. Furthermore, we suggested to the patients to monitor their body temperature and to take a careful water balance. If COVID-19 infection was moderate and in any patients at risk of adrenal crisis, we immediately increased the dose of Hydrocortisone to 100 mg (i.m. or i.v) and hospitalized the patients. We raised the GC dose up to Hydrocortisone 300 mg/day for those patients whose clinical condition worsened into acute respiratory distress syndrome (ARDS). In severe COVID-19, the patients who developed central DI may be vulnerable to life-threatening hypernatremia. Patients with severe dehydration were treated with hypotonic fluids, either enterally (using water) or intravenously (using 5% Glucose solution). Desmopressin was administered as occurred, according to the evaluation of the fluid balance, the dosage of natriemia and of plasmatic and urine osmolality. We measured the plasma sodium at frequent intervals (every 12 hours). We accepted mild hypernatraemia (<155 mmol/l) as the price of preventing pulmonary oedema. No patient developed secondary consequences linked to both corticosteroid insufficiency and fatal hypernatremia/hyponatriemia. In hospitalized patients thyroid function was tested at least weekly or more frequently when clinically indicated.
Conclusion
Because of the AI, hypophysitis patients present an increased risk of worsening of COVID-19 infection and developing ARDS. When associated with the central diabetes insipidus, this increases the risk of mortality in these patients. According to our experience, in order to avoid the deterioration of their clinical conditions, it is necessary to keep these patients under strict endocrinological control even when they are hospitalized.

DOI: 10.1530/endoabs.81.EP771

EP772

Case of a giant prolactinoma presenting as a clival mass

Pinar Uzgec Guller[1], Mustafa Burak Yaşar[1], Zehra Yagmur Sahin Alak[1], Metin Guclu[1], Fatih Aydemir[2] & Sinem Kiyici[1]
[1]University of Health Sciences, Bursa Yuksek Ihtisas Research and Training Hospital, Endocrinology and Metabolism, Turkey; [2]University of Health Sciences, Bursa Sehir Hospital, Neurosurgery, Turkey

Introduction
Giant prolactinomas are rare tumors accounting for 2–16% of all prolactinomas. They may be aggressive and invasive. Rarely, they might not have a suprasellar component and grow downward. Such extension can make it difficult to distinguish pituitary adenoma from other skull base tumors. We present a case that was considered to be chordoma based on clinical and radiological imaging features, but was diagnosed as prolactinoma by pituitary biopsy.
Case
A 67-year-old male patient with headache, dizziness admitted to the emergency department. There was no pathological finding in his physical examination. Cranial MRI demonstrated a large mass (5 x 3 x 3.5 cm) which destroyed the clivus, extending anteriorly towards the sphenoid sinus, and surrounding both cavernous sinuse. He was referred to neurosurgery department and underwent transsphenoidal biopsy for the differential diagnosis of clival tumors such as chordoma. The histopathological examination revealed it to be pituitary adenoma and immunohistochemical study showed a strong positive staining for the prolactin. He was diagnosed with giant prolactinoma and referred to our outpatient clinic. He reported reduced libido and difficulties in erection. Visual field examination was normal. Hormonal evaluation revealed that serum prolactin level was significantly increased (6290 ng/ml) and serum IGF-1 level was compatible with age and sex. Serum total testosterone level was decreased (115 ng/dl) while FSH and LH levels were within the reference ranges. The pituitary-adrenal and pituitary-thyroid axis were intact. He was started a dose of cabergoline 500 micrograms once weekly. Then the dose increased to 500 micrograms twice weekly as tolerated. He responded well to the medical treatment. Serum prolactin levels dramatically decreased. Pituitary MRI in 12 weeks intervals showed a remarkable reduction in mass.
Conclusion
This case highlights the importance of including invasive pituitary macroadenomas with infrasellar extension in the differential diagnosis of skull base

tumors. Initially, evaluation of clinical signs and hormonal tests in patients with sellar-parasellar masses, can prevent unnecessary invasive procedures.

DOI: 10.1530/endoabs.81.EP772

EP773

Clinical and paraclinical features of pituitary metastases: Report of five cases

Cyrine Chehaider, Ibtissem Oueslati, Meriem Yazidi & Melika Chihaoui
La Rabta University Hospital, Department of Endocrinology, Tunis, Tunisia

Introduction
The sellar region is known as a low-risk brain metastasis area. The prevalence of pituitary metastasis represents 1% of all surgical tumors of the pituitary gland. In most cases, pituitary metastasis is identified in patients with a prior history of cancer. In a few cases, it can reveal the primary tumor. The aim of this study was to assess clinical and paraclinical features of pituitary metastasis.
Methods
This was a retrospective and descriptive study including patients with pituitary metastasis admitted to our department. Clinical, hormonal, and radiological data were collected.
Results
Five patients (four women and a man) with a mean age of 51.4 years [extremes: 32-68] were enrolled in this study. Three women had a history of metastatic ductal breast carcinoma. Two women presented with polyuria-polydipsia syndrome and the third one presented with headaches, blurred vision, and decreased visual acuity. Hormonal investigations revealed disconnection hyperprolactinemia ($n=2$), central diabetes insipidus ($n=2$), and hypopituitarism ($n=3$). Pituitary magnetic resonance imaging (MRI) revealed, in both women with polyuria-polydipsia syndrome, a heterogeneous thickening of the pituitary stalk. The third patient presented a large heterogeneous pituitary mass of 27 mm with supra-sellar extension and infiltration of the optic chiasm. In two patients, the primary cancer was revealed by the pituitary metastasis. The first was a 50-year-old woman who presented with headaches, visual disorders, weakness, nausea, vomiting, and hypoglycemia. Pituitary MRI showed a large mass extending from the sella turcica to the sphenoid sinus, optic chiasm, and nasopharynx. Endoscopic biopsy confirmed the diagnosis of undifferentiated nasopharyngeal carcinoma with intracranial extension. Biological investigations revealed hypopituitarism and disconnection hyperprolactinemia. The patient was put on hormone replacement therapy. After corticosteroid treatment initiation, a diabetes insipidus was revealed. The second patient was a 68-year-old man, who presented with polyuria-polydipsia syndrome. The diagnosis of central diabetes insipidus with disconnection hyperprolactinemia and hypopituitarism was established. Pituitary MRI showed a tumor of a 12 mm involving the pituitary stalk and infundibulum. The patient was diagnosed with metastatic small-cell lung cancer.
Conclusion
The hypothalamic-pituitary area is a rare site of metastasis. Clinical presentation and pituitary MRI are the key in guiding the diagnosis. Signs of dysfunction of both the anterior and the posterior pituitary gland are often present. Diabetes insipidus is the most frequent symptom.

DOI: 10.1530/endoabs.81.EP773

EP774

Cushing's syndrome due to adrenocorticotropic hormone-secreting metastatic neuroendocrine pancreatic tumor: diagnostic workup and management

Giada Cosentino[1], Luca Manetti[1], Giulia Marconcini[1], Ugo Boggi[2], Riccardo Marconcini[3], Isabella Lupi[1], Daniele Cappellani[1], Claudio Urbani[1] & Fausto Bogazzi[1]
[1]Clinical and Experimental Medicine University of Pisa, Endocrinology, Pisa, Italy; [2]Division of General and Transplant Surgery, University of Pisa, Pisa, Italy; [3]Unit of Medical Oncology 2, Azienda Ospedaliera-Universitaria Pisana, Department of Translational Research and New Technologies in Medicine and Surgery, University of Pisa, Italy

We report the clinical history of a 21-years old young female who, in February 2021, presented abdominal pain and biliary vomiting that lasted for two months. An esophagus-gastroduodenoscopy revealed a duodenal ulcerative lesion and proton pump inhibitory therapy was started with clinical benefit. One month later, the patient presented a facial acneiform rush with hirsutism for which she was referred to our attention. An abdominal MRI documented a well-circumscribed hyper-vascular round mass in the pancreatic head with a maximum diameter of 3.5 cm. The fine needle aspiration of the lesion revealed a well-differentiated neuroendocrine tumor, grade 2 (MIB1: 10%). Immunohistochemistry was positive for CK-CAM 5.2, chromogranin, sinaptofisin and a diffuse staining for ACTH in more than 50% of neoplastic elements was detected. Laboratory examination revealed high serum cortisol and ACTH concentrations, respectively 41,1 mcg/dl and 262 ng/l, associated with hyperglycemia and hypokalemia. Futhermore, the 68 Ga DOTA(0)-Phe(1)-Tyr(3)-octreotide (DOTATOC) positron emission tomography (PET) computed tomography demonstrated radiotracer activity within the pancreatic mass with high somatostatin receptor 2 and 5 (SSTR2-5) expression. The hormonal work up was conclusive for ectopic Cushing syndrome (EAS). Hence, the patient was discharged on Ketoconazole (KTZ) 200 mg PO twice a day with clinical and biochemical benefits. In June, the patient underwent duodenocefalopancreasectomy robot assisted surgery with resection of the pancreatic mass, peripancreatic lymph nodes and gallbladder. Histopathological exams confirmed the neuroendocrine origin of the tumor with a Ki67 of 15% and diffuse ACTH staining (pT3 N1 G2 R1). Three months after surgery, the CT scan revealed multiple hepatic metastases while the hormonal exams showed the hypercortisolism relapse. Hence, a double therapeutic approach was planned: oral therapy with osilodrostat (4 mg increased to 10 mg per day) and lanreotide (120 mg monthly). Urinary free cortisol (UFC) declined progressively and clinical signs of CS regressed during therapy. Unfortunately, the subsequent morphologic evaluation with CT, revealed a progression of the hepatic disease. According to the mild hepatic uptake of ^{68}Ga and the extension of the hepatic disease, a radioreceptor therapy or a novel surgery approach were excluded. In December, capecitabine combined with temozolomide (CAPTEM) was started with no adverse events. The second cycle was stopped because of Sars-Cov2 infection of the young patient. In conclusion, EAS is a severe condition that requires rapid management of hypercortisolism; the choice of treatments must be performed in a multidisciplinary team, individualized for each patient, using a shared decision-making approach.

DOI: 10.1530/endoabs.81.EP774

EP775

Distribution of E- and N-cadherin in subgroups of non-functioning pituitary neuroendocrine tumours

Kristin Astrid Berland Øystese[1,2], Olivera Casar-Borota[3,4], Jon Berg-Johnsen[5], Jens Petter Berg[2] & Jens Bollerslev[1,2]
[1]Oslo University Hospital, Oslo, Norway; [2]University of Oslo, Institute of Clinical Medicine, Oslo, Norway; [3]Uppsala University Hospital, Department of Clinical Pathology, Uppsala, Sweden; [4]Department of Immunology, Genetics and Pathology, Uppsala University, Uppsala, Sweden; [5]Oslo University Hospital, Department of Neurosurgery, Oslo, Norway

Purpose
Clinically Non-Functioning Pituitary Neuroendocrine Tumours (NF-PitNETs) present a varying degree of aggressiveness, and reliable prognostic markers are lacking. We aimed to characterize the distribution of E- and N-cadherin in corticotroph, PIT1 and null-cell NF-PitNETs, and link it to the clinical course of the tumours.
Methods
We investigated the distribution of E- and N-cadherin by immunohistochemistry in a retrospective cohort of thirty tumours of the less common NF-PitNETs (corticotroph ($n=18$), PIT1 ($n=8$) and null-cell PitNETs ($n=4$)). Immunoreactive scores were compared to previously presented cohorts of gonadotroph NF-PitNETs and corticotroph functioning PitNETs.
Results
We found a low immunoreactive score (IRS) for the extracellular domain of E-cadherin, a medium to high IRS for the intracellular domain of E-cadherin and a high IRS for N-cadherin throughout the cohort. The corticotroph NF-PitNETs presented a higher IRS for the extracellular (median 0 (IQR 0-2) and the intracellular (median 9 (IQR 6-12) domain of E-cadherin, and a lower proportion of tumours presenting nuclear E-cadherin (17%) compared to the previous presented gonadotroph NF-PitNETs (P-value < 0.001 for all three comparisons). Presence of nuclear E-cadherin was associated with a weaker staining for the intracellular domain of E-cadherin by the cell membrane (median 4 (IQR 0.5-6) and 9 (IQR 9-12) for tumours with and without nuclear E-cadherin respectively,

P-value <0.001). None of the eight patients presenting tumours with nuclear E-cadherin went through reintervention, while 9 out of 21 without nuclear E-cadherin went through reintervention (*P*-value 0.03).
Conclusion
The immunohistochemical staining for N-cadherin was high throughout the presented cohort. The IRS for E-cadherin varied between subtypes of NF-PitNETs. Nuclear E-cadherin was associated with a lower IRS of the intracellular domain of E-cadherin by the membrane, and with a low rate of reintervention. Considering our results and the benign course of NF-PitNETs, we suggest that a high N-cadherin and downregulation of membranous E-cadherin are not associated with an aggressive clinical course in NF-PitNETs.

DOI: 10.1530/endoabs.81.EP775

EP776

Primary cilia in Pituitary neuroendocrine tumours and their association with aggressiveness

Rebeca Martínez-Hernández[1], Ana Serrano-Somavilla[1], Miguel Sampedro-Nuñez[2], María Calatayud[3], Almudena Vicente[4], Gonzalo García-de-Casasola[5], Ancor Sanz-Garcia[6], Manel Puig-Domingo[7] & Monica Marazuela[1]
[1]IIS Princesa, Universidad Autónoma de Madrid, Endocrinology, Madrid, Spain; [2]Hospital La Princesa, Endocrinology, Madrid,; [3]Hospital Universitario 12 de Octubre, Endocrinology, Madrid, Spain; [4]Hospital Virgen de la Salud, Endocrinology, Toledo, Spain; [5]Hospital Universitario Infanta Cristina, Pathology, Parla, Spain; [6]IIS Princesa, Methodology Unit, Madrid, Spain; [7]Germans Trias i Pujol Research Institute and Hospital, Endocrinology, Barcelona, Spain

Purpose
Although growing evidence supports the role of primary cilia (PC) in the regulation of cancer development, their possible role has not yet been studied in pituitary neuroendocrine tumours (PitNETs). The study of cilia could serve as a diagnostic tool providing new insights into the mechanisms of tumorigenesis and aggressiveness of PitNETs.
Methods
A total of 86 patients with PitNETs (28 functioning and 58 non-functioning [NF-PitNETs]) and 12 controls were evaluated by immunofluorescence and immunohistochemistry in tissue microarrays (TMA) and by western blot in PitNETs protein extracts. The frequency of ciliated cells was estimated using a cilia index score based on the length of cilia and the percentage of ciliated area in the tissue. The distribution of PC and its correlation with several clinical parameters and aggressiveness was analysed.
Results
PC were present only in scattered cells of control pituitary tissues, whereas PitNET cells showed robust staining for ciliary markers. Interestingly, the number and /or length of ciliated cells was significantly higher in non-functioning PitNETs, including null cell adenomas and gonadrotropinomas, when compared to functional tumours. Remarkably, PC were significantly increased in non-functioning-PitNETs. In addition, the presence of cilia was associated with tumour invasion, aggressiveness and recurrence in PitNETs.
Conclusions
PC are present in PitNETs, especially in non-functioning PitNETs and may represent an important contributor to aggressiveness. PC may serve as a novel diagnostic marker for predicting tumour behaviour and as a potential target for drug therapy.

DOI: 10.1530/endoabs.81.EP776

EP777

Cushing's disease in MEN 4 syndrome

Dina Rebrova[1], Ekaterina Zgoda[1], Leonid Krasnov[1], Vladimir Rusakov[1], Ilya Sleptsov[1], Roman Chernikov[1], Arseny Semenov[1, 2], Elisey Fedorov[1], Igor Chinchuk[1], Ilya Sablin[1], Shamil Shihmagomedov[1] & Ilya Shcherbakov[1]
[1]Saint Petersburg State University, Saint Petersburg State University Hospital, St. Petersburg, Russian Federation; [2]Saint Petersburg State University, Medical Faculty, Saint-Petersburg, Russian Federation

In 2000 female, 28 y.o., admitted endocrinologist with headache, high blood pressure, dark skin and muscle weakness. Lab data showed high levels of ACTH and cortisol, low potassium level. According to MRI scans, pituitary gland seemed normal. On CT in right adrenal was found 32 mm mass with the native density of 20 HU. Diagnosed ACTH-dependent Cushing syndrome (CS). As Mitotane was not available in Russia at that time, she received ketokonazole due to progression of CS but it was canceled later due to intolerance. So, right adrenalectomy was performed. Histology: adrenal adenoma with adrenal hyperplasia. The cortisol level decreased and symptoms diminished. In 2002 pituitary adenoma of 6 mm appeared on MRI. It was resected endoscopically by transsphenoidal approach. Histology: chromophobe adenoma. However, the hypercortisolism and high level of ACTH remained. Later in 2002 she underwent the proton beam surgery with following disease remission. At 2012 the patient had noticed the deterioration of health: skin darkening, high levels of blood pressure, hyperglycaemia. In 2015 the relapse of hypercortisolism was confirmed. According to MRI there were signs of pituitary adenoma relapse (partial empty sella). CT scan showed two adrenal masses up to 23 mm and 10 mm in the left adrenal. Second transsphenoidal partial removal of pituitary adenoma was performed, complicated by liquorrhea, purulent meningitis, secondary hypothyroidism. Second relapse of hypercortisolism with high level of ACTH with no signs of pituitary regrowth on MRI scan occurred in 2018. Ketoconazole therapy was tried once again with bad tolerance and no effect. Right adrenalectomy was performed. The patient is prescribed with adrenal replacement therapy (hydrocortisone 45 mg and fludrocortisone 0,1 mg daily), levothyroxine 100 mkg daily. Levels of ACTH are still persistently high. In 2020 the patient was diagnosed with papillary thyroid cancer and primary hyperparathyroidism. She received right hemithyroidectomy with central neck lymph node dissection, selective parathyroidectomy (lower right and higher left glands). No mutations in MEN1 gene were found. It is known that patient's mother was operated on thyroid gland due to papillary cancer. MEN4 syndrome was described in 2010. We present the patient with 3 MEN4 tumors in absence of MEN1 gene mutations, burdened family history.

DOI: 10.1530/endoabs.81.EP777

EP778

Acromegaly with negative pituitary magnetic resonance imaging: a case report

Anis Grassa, Ibtissem Oueslati, Meriem Yazidi, Elyes Kamoun & Melika Chihaoui
La Rabta University Hospital, Department of Endocrinology, Tunis, Tunisia

Introduction
Acromegaly is a rare endocrine disorder. In 95% of cases, it is caused by a GH-secreting pituitary adenoma. Rarely, acromegaly is due to ectopic production of GH or growth hormone-releasing hormone (GHRH). Herein, we report a case of acromegaly with negative pituitary magnetic resonance imaging (MRI) and discuss its possible etiology and management.
Observation
A 75-year-old woman was referred to our department for the exploration of acquired acrofacial dysmorphic syndrome. Her past medical history included type 2 diabetes mellitus and hypertension. She presented with paraesthesia of the left hand, arthralgia, and nocturnal snoring. Neither headache nor visual impairment was reported. On physical examination, she had a body weight of 69 kg, a body height of 1 m 68, corresponding to a body mass index of 24.4 kg/m^2, an enlargement of facial features and hands, and a loss of dental articulation. Hormonal investigations revealed an IGF1 level of 424 ng/ml (nr = 55-212), a nadir of GH under oral glucose tolerance test of 7.1 ng/ml (> 1 ng/ml), a TSH level of 1.3 mIU/l (nr:0.35-4,95), a FT4 level of 0.97 ng/dl (nr: 0,7-1,5), a FSH level of 43.9 IU/l, a LH level of 14.64 IU/l, and a prolactin level of 7 µg/l. The peak of cortisol level in response to the insulin-induced hypoglycemia test was 19.7µg/l. Further explorations showed carpal tunnel syndrome, thyroid nodule, and a mild obstructive sleep apnoea syndrome. The chest x-ray and the abdominal ultrasound were normal. Initial and repeat pituitary MRI showed a normal-sized pituitary gland with no evidence of an adenoma. Work-up for ectopic GH-secreting tumor was planned (cervical-thoraco-abdominal computed tomography scan and octreotide scintigraphy).
Conclusion
Acromegaly may be a curable cause when a pituitary adenoma is evident. However, its extra-pituitary origin remains a real challenge as to its localization and management.

DOI: 10.1530/endoabs.81.EP778

EP779

TSH-secreting pituitary neuroendocrine tumor revealed after total thyroidectomy, a case study

Bessaid Khadidja[1] & Mouna Mezoued[1,2]
[1]Public Hospital Establishment of Bologhine, Algiers, Algeria; [2]Bologhine Hospital, Endocrinology, Algiers, Algeria

Introduction
TSH-secreting pituitary neuroendocrine tumor (TSH-PitNET) is the rarest pituitary tumors. Most TSH-PitNETs are secreting, with a biological profile of inappropriate TSH secretion (moderately elevated TSH, elevated FT3 and FT4).
Observation
We report the case of a 69-year-old patient, with a history of total thyroidectomy in 2014 for multinodular goiter, hospitalized for suspected levothyroxine pseudo-malabsorption. Despite doses above 2 µg of levothyrox, the TSH always remains high above 10 mIU/l with high FT4. Clinically the patient presents some signs of hyperthyroidism.
Discussion
The diagnosis of pseudo malabsorption is unlikely, despite constantly elevated peripheral hormones the TSH remains elevated. Faced with a biological profile associating elevated peripheral hormones with an unrestrained TSH, the main differential diagnoses are thyroid hormone resistance syndrome and TSH PitNET. The age, sex and level of clinical thyroid functional tests are similar in the two pathologies. Thyroid hormone resistance syndrome is eliminated by a normal preoperative assessment. Hypothalamic pituitary MRI showed a 7.5 mm right pituitary microadenoma. A somatostatin analog braking test at 90 mg/28day was performed, after 2 months of treatment, TSH decreased to 1 mIU/l with reduced doses of levothyrox. The diagnosis of TSH-PitNET is retained in our patient despite the normality of the preoperative assessment which can be explained by a cyclic secretion, or a lifting of inhibition already described in the literature.

DOI: 10.1530/endoabs.81.EP779

EP780

Null cell adenoma with low Ki-67 presenting as recurrent pituitary mass

Leo Tiu & Carolyn Montano
Makati Medical Center, Section of Endocrinology, Diabetes and Metabolism, Makati City, Philippines

Background
Approximately one-third of pituitary adenomas are identified as nonfunctioning pituitary adenomas (NFPA) which have a heterogenous profile and an increased potential for relapse one to five years after pituitary surgery. In a retrospective analysis by Almeida et al, multiple surgical resections, elevated ki-67 and cavernous sinus invasion were predictive of recurrence. They typically present with symptoms of mass effect and most are macroadenomas at time of diagnosis.
Clinical Case
A 65-year-old female initially presented with bitemporal hemianopsia, galactorrhea and amenorrhea 28 years prior. She subsequently underwent transsphenoidal hypophysectomy with resolution of symptoms postoperatively. She was clinically stable until 12 years after whenshe had peripheral visual field loss. Upon reevaluation, she was diagnosed with non-functioning pituitary macroadenoma for which she underwent a repeat transsphenoidal pituitary surgery. Her vision improved and she remained asymptomatic thereafter. Sixteen years after her second surgery, she developed blurried vision. Cranial MRI was done which showed lobulated, heterogeneous hyperdense sellar-suprasellar mass measuring 55 x 36 x 47 mm extending to the bilateral sphenoid and ethmoid sinuses, left pterygopalatine fossa, left superior orbital fissure, probably the left foramen lacerum, and left cavernous sinus with encasement of the left internal carotid artery and associated erosion of the adjacent osseous structures. Visual field testing showed mild reduction in field sensitivity with consideration of media opacity and/or uncorrected error of refraction. Baseline hormonal work up was unremarkable. Hence, endoscopic endonasal transphenoidal, transethmoidal parasellar excision of sellar mass, with reconstruction via Hadad Flap was done. There were no intraoperative nor postoperative complications. The specimen was sent for histopathology with provisional anatomic diagnosis of pituitary adenoma. Immunohistochemistry stained negative for chromogranin and any of the pituitary hormones which was consistent with null cell adenoma. The Ki-67, an independent marker of tumor progression and recurrence, was low at less than 1%. However, after 1 month, repeat MRI showed no significant change in the heterogeneously enhancing mass centered in the sellar-suprasellar region. Thus, she received adjuvant radiotherapy with total dose of 5040 cGy divided in 28 fractions and was advised close monitoring of pituitary MRI and development of any new symptoms.
Conclusion
In this case, although with low Ki-67, the presence of multiple surgery and high Knosp grade were recognized as risk factors for its recurrence. Treatment of recurrent NFPAs is multimodal which includes re-operation, radiosurgery and radiation therapy. A multidisciplinary team approach is required for its comprehensive management and long-term follow-up.

DOI: 10.1530/endoabs.81.EP780

EP781

Discordant GH and IGF-1 values in a surgically treated acromegaly patient: a management conundrum

Theodor Mustata[1,2], Carmen Sorina Martin[1, 2], Ovidiu Parfeni[2], Bianca Dumea[2], Florina Andrada Predescu[2] & Fica Simona[1,2]
[1]Carol Davila University of Medicine and Pharmacy, Endocrinology Department, Bucharest, Romania; [2]Elias University Emergency Hospital, Endocrinology Department, Bucharest, Romania

Introduction
Remission after transsphenoidal surgery in patients with acromegaly is confirmed by biochemical assays of growth hormone (GH) and insulin-like growth factor-1 (IGF-1). Although their levels are usually closely correlated, discordant results of these tests have been noted, making the follow-up of acromegaly patients particularly challenging.
Case report
We present the case of a 35 year old female diagnosed with acromegaly at the age of 32 years. At the time of diagnosis a 20.9 x 17 x 16 mm macroadenoma was found on pituitary MRI. IGF-1 was 408 ng/ml (normal age and sex-matched values 115-307), serum nadir GH during a 75 g oral glucose tolerance test (OGTT) was 5.61 ng/ml and prolactin levels were 51.92 ng/ml (normal values < 26.53). She underwent endoscopic transsphenoidal surgery, with immunohistochemistry analysis revealing a mixed somatotroph-lactotroph pituitary adenoma, with a Ki 67 index of 6%. Analysis of GPR101 and AIP genes mutations was negative. She developed transient postoperative SIADH with hyponatermia (sodium values of 118 mEq/l). Postoperative evaluation 3 months after surgery showed no tumor remnant on pituitary MRI, normal IGF-1 [257 pg/ml (normal age and sex-matched values 115-307)], but a lack of inhibition of GH after OGTT (nadir values of 0.733 ng/ml). At this moment the chosen approach was biochemical evaluation every 6 months and annual pituitary MRI. For the next two and a half years the patient had the same biochemical profile of normal IGF-1 but unsuppressed GH during OGTT and no tumor remnant visible on MRI. However, at the last evaluation in January 2022 we found elevated levels of IGF-1 (341.3 ng/ml, 1.23 x upper limit of normal), serum nadir GH during OGTT of 2.55 ng/ml and no changes on pituitary MRI. Taking into account the marginally elevated IGF-1 and the patient's desire to undergo an in-vitro fertilization procedure in the near future, we opted for initiation of therapy with cabergoline until pregnancy is obtained and we are considering referring the patient for a ^{11}C-methionine PET/CT for accurate localization of a potential residual/recurrent pituitary adenoma.
Conclusions
Management of surgically treated acromegaly patients with discordant GH and IGF-1 values is a challenge. Close biochemical evaluation is needed and an individualized approach is warranted, but further studies are needed to asses the risk of disease recurrence and the impact on the patient's quality of life.

DOI: 10.1530/endoabs.81.EP781

EP782

Screening of IGF-1 level in patients with Prolactinomas

Yulia Ukhanova & Irena Ilovayskaya
Moscow Regional Research and Clinical Institute named by M.F. Vladimirsky, Neuroendocrine Unit, Department of Endocrinology, Russian Federation

Objective
to determine the need for screening for IGF-1 levels in patients with prolactinomas and without obvious symptoms of acromegaly.
Matherials and methods
A pilot cross-sectional study, based on the analysis of medical records of patients with confirmed prolactinoma, who applied to the Moscow Regional Research and Clinical Institute named by M.F. Vladimirsky. A total of 88 patients were included in the study. The frequency of studying the level of IGF-1, and the frequency of detecting cases of acromegaly were evaluated in patients with prolactinoma. The level of IGF-1 was determined in 60/88 patients with prolactinoma. Among patients with prolactinoma, women with microadenoma (Fmi) - 17, women with macroadenoma (Fma)- 16, men with microadenoma (Mmi) - 7, men with macroadenoma (Mma) - 20. The median level of prolactin at the onset of the disease was 2330 mU/l (1010; 4389) in Fmi, 10006.5 mU/l in Fma (1917.6;95106.3), in Mmi 2017.52 mU/l (1626;4382), in Mma 6080 mU/l (14000;104700).
Results
Among patients with a known level of IGF-1, its increase was recorded in 6/60 patients with prolactinomas. An oral glucose load (OGL) was performed in all 6 patients. The diagnosis of acromegaly was confirmed in 2 Fmi. The percentage of excess of the IGF-1 levels above the upper limit of the normal in patients with a negative test – 20.1%, 45.58%, 46.09% and 115.1%, in patients with diagnosed acromegaly – 70.8% and 217.6%.
Conclusions
In real clinical practice, the level of IGF-1 was determined in 68.2% of patients with prolactinomas. At the same time, the proportion of identified patients with acromegaly among the examined patients with prolactinomas but without obvious clinical signs of acromegaly, was 3.33%. Considering the obtained results, the question of the necessity of screening the level of IGF-1 in patients with prolactinomas requires further study.

DOI: 10.1530/endoabs.81.EP782

EP783

Polyuria-polydipsia in an athletic teenager

Mihaela Rosu[1], Felicia Baleanu[1], Taujan Georgiana[1], Olga Kosmopoulou[1], Blerta Papadopoulou[1], Luiza Gambini[2] & Iconaru Laura[1]
[1]CHU Brugmann, Department of Endocrinology, Brussels, Belgium; [2]Kanton Spital Aarau, Department of Endocrinology, Aarau, Switzerland

Introduction
Central diabetes insipidus is characterized by partial or total ADH deficit of various origins. The clinical picture is dominated by massive polyuria with diluted urine, increased thirst and daily water consumption reaching impressive quantities.
Case report
We report the case of a 16 year-old male teenager presenting with excessive thirst and water intake of 8 -10 l/day and voiding large quantities of diluted urine. Symptoms started gradually over the past 3 years. He attributes his increased thirst to increased transpiration during his recently restarted judo-training and he states he can abstain from drinking water if he has to, especially during school-time. He denies headaches and troubled vision. Physical examination was unremarkable, except for a grade 1 obesity (BMI 32 kg/m^2) of recent onset (interruption of regular training during first COVID lock-down). Personal history is devoid of chronic diseases and head trauma and he denies consumption of medication or recreational drugs. Family history is positive for type 2 diabetes in all his four grandparents. Lab tests including electrolytes and pituitary axis returned normal. A thirst test was undertaken, starting at 23.00 h and conducted until 12 p.m. next day. Sodium concentration increased from 140 to 143 mEq/l, serum osmolality increased from 284 to 294 mOsm/l, while urine osmolality raised slightly from 602 to 679 mOsm/kg. No signs of dehydration and no hypotension occurred during the test. At the final blood draw copeptine was measured at an external laboratory. Patient was discharged with no treatment awaiting the results of hypophysis IRM and copeptine. At the follow-up, he still reports a water intake of 3 to 7 l per day. The IRM of the hypophysis and IgG4 level were normal. Copeptine measured at 1.7 pmol/l for a osmolality of 294 mOsm/l (normal range 2.3-24.5 pmol/l for osmolality between 291 and 295 mOsm/kg) thus showing insufficient increase and suggesting a partial deficit of ADH. Arginin- vasopressin was initiated at a dose of 25 microg/day sublingual in the morning. At one–week follow-up water consumption decreased to 1.5-2 l/day, urine output normalized, while maintaining normal sodium and serum osmolality.
Conclusion
The copeptine value and the response to the therapeutic trial of arginine-vasopressin helped diagnosing a central partial ADH deficit which we considered idiopathic, however repeated minor head trauma during his years-long judo-training may have also played a role in the onset of the disease.

DOI: 10.1530/endoabs.81.EP783

EP784

A novel population of activated cytotoxic T cells infiltrate pituitary neuroendocrine tumour subytpes

Oriana Mazzitelli[1], Jean Paul Ebejer[2, 3], Nikolai Paul Pace[4], Mark Gruppetta[4, 5], Josanne Vassallo[4, 5] & David Saliba[1]
[1]University of Malta, Faculty of Health Sciences, Msida, Malta; [2]University of Malta, Centre for Molecular Medicine and Biobanking, Msida, Malta; [3]University of Malta, Faculty of Information & Communication Technology, Msida, Malta; [4]University of Malta, Faculty of Medicine and Surgery, Msida, Malta; [5]Mater Dei Hospital, Neuroendocrine Clinic, Msida, Malta

Non-functional pituitary adenomas (NFPA) are non-hormone secreting pituitary tumours while growth hormone-secreting pituitary adenomas (GHPA) are active pituitary tumours causing acromegaly. Since immunotherapy is becoming the preferred therapeutic strategy in cancers, understanding the diversity of immune cells infiltrating the tumour microenvironment is warranted. However, little is known about the immune landscape of pituitary tumours. We validated an acoustic-assisted hydrodynamic focusing cytometer based method (Attune, Thermofisher) to identify rare immune cell populations in NFPA ($n=6$) and GHPA ($n=3$) obtained from patients undergoing transphenoidal surgery. We unravelled key cellular populations of myeloid (macrophages and monocytes) and lymphocytic (CD4 and CD8 T cells) origin using a multi-colour panel of antibodies against cell surface (CD45, CD163, CD64, CD11b, CD3, CD56, CD19, CD4 and CD8) and intracellular (CD68, T-bet, GATA-3 and FOXP3) antigens and assessed the degree of T-cell activation using the CD44 marker. We also checked for the expression of immune checkpoint and exhaustion markers PD1 and TIM-3 respectively. In all samples, lymphocytic infiltrates were detected. In all except 1 NFPA and in all GHPA the CD8:CD4 ratio was greater than 1 ranging from 1.88 - 5.74 in NFPA and 1.35 - 5.21 in GHPA with no statistical difference between NFPA and GHPA. This method also revealed novel populations of activated, cytotoxic T cells in all pituitary adenomas analysed. We are currently characterising the function of these cells in such tumours and how their presence correlates with the patients' clinical data and tumour characteristics.

DOI: 10.1530/endoabs.81.EP784

EP785

Clinical case of syndrome of inappropriate secretion of antidiuretic hormone (SIADH) with uncertain localization

Ekaterina Pigarova, Larisa Dzeranova, Nino Katamadze, Khava Fargieva, Natalya Malysheva, Larisa Nikankina & Elena Przhiyalkovskaya
Endocrinology Research Centre, Moscow, Russian Federation

Introduction
The syndrome of inappropriate secretion of antidiuretic hormone (SIADH) is characterized by hypotonic and euvolemic hyponatremia along with urinary hyperosmolarity, resulting from antidiuretic hormone (ADH) release in the absence of adequate stimuli.
Case report
A 59-year-old woman, presented with complaints of constant thirst, general weakness, memory loss, episodes accompanied by headaches, leg cramps,

increased blood pressure. From the anamnesis-for the first time hyponatremia 114-123 mmol/l (135-145), was revealed during hospitalization for fainting 5 years ago, this episodes repeated several times a year. At the same time, a pituitary non-active macroadenoma of 22*12*9 mm (Knosp 2) was found, without indications for surgical treatment during yearly observation by MRI. All diagnostic criteria for SIADH were met in the form of repeatedly confirmed hypotonic hyponatremia with urine osmolality exceeding the blood plasma osmolality (412-520 mOsm/kg), and normal urinary sodium excretion of 92-162 mmol/l and GFR > 60 ml/min. Hypothyroidism and adrenal insufficiency were excluded. Cardiac, hepatic and renal functions were normal. Medications included azilsartan 40 mg and amlodipine 5 mg. To search for the source of a possible ADH-secreting tumor, an oncological search was performed with ultrasound of the thyroid gland, abdominal cavity, CT of the lungs with contrast, gastro- and colonoscopy. She also underwent PET/CT 'whole body' with 68Ga-DOTATATE, according to which no pathological formations were detected. According to the results of which, a node of the right lobe of the thyroid gland 11 x 10 mm was revealed, with a fine-needle aspiration biopsy - Bethesda II. Drinks about 2000 ml (of which 300-400 ml is 0.9% saline), releases 1700-1800 ml of urine per day. Copeptin (Phoenix) -1.659 ng/ml (0.178-2.578 ng/ml), Oxytocin (BMA Biomedicals) -2.668 ng/ml (0-12.821 ng/ml), Apelin-12 (Phoenix) -2.026 ng/ml (0.620-2.095 ng/ml), BNP (RayBiotech)-981.63 pg/ml (646.3-2033.4 pg/ml). Since the synthesis of ADH occurs in the nuclei of the hypothalamus, and the hormone is only stored and secreted in the posterior lobe of the pituitary gland, then the pituitary adenoma per se presumably cannot be a source of ADH (the patient refused the proposed adenectomy).
Conclusions
The modern diagnostic arsenal is not sufficient to identify the source of inadequate secretion of ADH. Fluid restriction and oral saline administration are effective and well tolerated long-term therapeutic interventions.

DOI: 10.1530/endoabs.81.EP785

EP786

Epidemiological data of prolactinomas in the Republic of Uzbekistan

Zamira Khalimova & Mijgona Safarova
[1]Republican Specialized Scientific Medical Center of Endocrinology, Neuroendocrinology, Tashkent, Uzbekistan

Objective
To create a national register of prolactin-secreting pituitary adenomas to assess the prevalence of various forms and the effectiveness of therapy.
Material and research methods
National register of patients with pituitary prolactinomas in the Republic of Uzbekistan, includes 172 cases with pituitary prolactinomas, of which 61% (105 women) and 37.2% (64 men), aged 17-74 years, mean age 38.5 ± 12.6 years and 3 (1.7%) children and adolescents. All 172 patients underwent studies of somatic, endocrine, gynecological status, the levels of prolactin, LH, FSH, TSH, free T4, progesterone, estradiol, testosterone, IHLA method, MRI of the chiasmatic - selar region were studied.
Results
Prolactinomas were more common in women (62.7%) than in men (37.2%), with a predominance of their frequency in women aged 21-30 years (66.7%), in men aged 41-50 years (59, 3%). Depending on the size, the patients were distributed as follows: microadenomas 98 (5.7%), macroadenomas -53 (30.8%), giant adenomas with aggressive growth 21 (12.2%). Prolactin levels varied from 7.8 to 530 ng/ml on average in men 94 ± 3.7 in women - 162 ± 9.4 ng/ml. According to the applied methods of treatment: 128 patients (74.4%) are on drug therapy with modern drugs of dopamine agonists, transsphenoidal adenomectomy in 44 patients (25.6%), including 21 with giant (12.2%), 12 with macroadenoma (7%)) and 10 with resistant prolactinomas (5.8%). Treatment outcomes were euprolactinemia in 142 (82.5%), persistent hyperprolactinemia against the background of SPTS in 31 (18%), panhypopituitarism in 28 (16.3%), remission was not achieved in 8 (4.6%)), fertility disorders in 57 (33.1%), including 8 men and 49 women, continue to occur.
Conclusion
Pituitary prolactinoma affects young women and men, predooming them to long-term medication and are a serious cause of infertility in both sexes.

DOI: 10.1530/endoabs.81.EP786

EP787

The Nelson's Syndrom (about 3 cases)

Lionel Stève Kamgain Simeu, Nassim Essabah Haraj, Siham El Aziz & Asma Chadli
Ibn Rochd University Teaching Hospital, Endocrinology, Diabetology, Metabolic Disease and Nutrition, Casablanca, Morocco

Introduction
The Nelson's syndrom (NS) is defined by the development of an ACTH pituitary adenoma. Complication of bilateral adrenalectomy performed in some cases of Cushing's disease.
We report the observation of three patients.
Case1
34-year-old patient, followed for Cushing's disease with pituitary microadenoma, having undergone pituitary surgery, then bilateral adrenalectomy due to surgical failure. Presented two years later an SN associating skin hyperpigmentation, high level of plasmatic ACTH and a pituitary adenoma measuring 10 mm. Having undergone a pituitary adenomectomy. Because of surgical failure and given the difficulty of surgical revision, a treatment associating Cabergoline with stereotactic radiotherapy was instituted.
Case2
21-year-old patient, followed for ACTH-dependent Cushing's syndrome with bilateral thickening of the adrenal glands on CT scan. Patient having benefited from a bilateral adrenalectomy, complicated Nine months later by an NS associating skin hyperpigmentation, high level of plasmatic ACTH and a pituitary microadenoma. In failure after two surgical revisions, he benefited from stereotactic radiotherapy.
Case3
48-year-old female patient, followed for Cushing's disease with pituitary microadenoma, having undergone pituitary surgery, then bilateral adrenalectomy due to surgical failure. Present Ten years after an NS, associating skin hyperpigmentation, high level of plasmatic ACTH, and a pituitary adenoma measuring 20 mm. She underwent a pituitary adenomectomy. Faced with the persistence of the NS after surgery, a treatment associating Cabergoline with stereotactic radiotherapy was instituted.
Conclusion
The management of the NS despite the therapeutic advance, remains heavy and associated with significant morbidity, hence the interest of early detection.

DOI: 10.1530/endoabs.81.EP787

EP788

Case report in a patient with insulinoma

Katerina Cheshlaroska Markushoska[1], Biljana Todorova[2], Hristina Cheshlaroska[3] & Belma Bilaloglu Jovanoska[2]
[1]General Hospital Borka Taleski, Internal Medicine, Prilep, Macedonia; [2]University Clinic of Endocrinology, Diabetes and Metabolic Disorders, University Clinic of Endocrinology, Diabetes and Metabolic Disorders, Skopje, Macedonia; [3]Faculty of Medicine, Internal Medicine, Skopje, Macedonia

Introduction
An insulinoma is a neuroendocrine tumor, deriving mainly from pancreatic islet cells, that constantly produces insulin even when blood sugar is very low. Insulinomas are the most common cause of hypoglycemia resulting from endogenous hyperinsulinism. Biochemical diagnosis of insulinoma is established during prolonged fasting test (up to 72 hours) in 95 % of patients, 90-95% of insulinomas can be diagnosed during 48 hours of prolonged fasting. After biochemical confirmation of the existence of insulinoma, imaging studies are used to localize the tumor.
Material and methods
A female patient aged 54 years, mother of two children, no smoker. In menopause from 3 years ago. She has arterial hypertension from the past disease, regulated by an angiotensin receptor blocker. The patient consults the ambulant of Endocrinology Clinic due to symptoms of malaise, fatigue and tingling in the mouth, which occurred episodically and improved after ingestion of carbo-hydrates. During one such episode, glycaemia was measured at 2 mmol/l. She gives information that she does not remember events from the recent past. On one occasion she lost consciousness. These symptoms were started a year ago, so the patient was examined by a neurologist and the existence of neurological disease

has not been established. From the outpatient analysis fasting plasma glucose 3.1 mmol/l, HbA1C: 4.4 %, OGTT: O min: 4.6 mmol/l, 120 min: 1.5 mmol/l, due to suspicion of insulinoma the patient is hospitalized for additional examination.
The diagnosis is made by a prolonged fasting test and a computed tomography scan with contrast to localize the insulinoma. Multiple endocrine neoplasia type 1 is excluded due to other laboratory analyses – parathyroid hormones, the hormones of the hypophysis, ionized Calcium which are in the referent values. The patient was referred for surgery and the histopathological examination confirmed the diagnosis of insulinoma. Postoperative patient without symptoms, with glycaemia in reference values.
Conclusion
When we have a case of insulinoma we need to determine whether it is an isolated case or is part of multiple endocrine neoplasia type 1 (MEN 1). In the case of the patient we are treating we concluded that it is an isolated case of insulinoma.
Because 90 % of insulinomas are benign and long-term cure with a total resolution of preoperative symptoms is expected after complete resection.

DOI: 10.1530/endoabs.81.EP788

EP789

GH provocative tests stimulate the growth in children without GH deficiency

Anna Tortora[1], Vincenzo Marotta[2], Giulia Izzo[2], Domenico Rocco[3], Gennaro Clemente[4] & Mario Vitale[3]
[1]Clinica Endocrinologica e Diabetologica, Salerno, Italy; [1]Clinica Endocrinologica e Diabetologica, Salerno, Italy; [3]Dipartimento di Medicina e Chirurgia, Salerno, Italy; [4]IRPPS Consiglio Nazionale delle Ricerche, Penta di Fisciano, Italy

Introduction
GH deficiency (GHD) is a clinical disorder characterized by pathological short stature in the child, altered body composition, impaired psychological well-being and reduced quality of life. These alterations are almost always reversible after recombinant human GH (rhGH) administration, which is currently the only accepted treatment for the subjects with GHD. Secretory dysfunction is confirmed when GH peak does not reach the established cut-off in at least two different stimulus tests performed in two different days. When tests response is considered adequate, the short stature is considered idiopathic and no GH replacement therapy is advised.
Objective
To determine the effect of GH provocative tests on growth rate in children without GH deficiency.
Design and Methods
Children of both gender with pathological short stature (h< 3°percentile) and/or annual growth rate <-2 SDS but with normal response to two GH provocative tests, were selected. Diagnosed endocrinopathies, other organ dysfunction, autoimmune diseases, genetic syndrome or current drug therapies were excluded. Height, mid-parental height, body weight, and body mass index were registered. The height and annual growth rate were converted to percentiles and Standard Deviation Score using reference ranges standardized for age and sex and were recorded pre and post stimulus tests and during subsequent follow-up over time. GH provocative tests employed arginine or clonidine as secretagogues.
Results
Twenty-one children of both genders were enrolled. Heights were measured at test time and at a mean time prior and after the tests of 209 days and 192 days respectively. Children displayed a 5-fold increase of their annual growth rate. The mean growth rate of children pre- and post-tests were -4.3 SDS and +2.0 respectively ($P<0.0001$). In 9 children the height was measured two times after the tests at an average time of 228 days and 887 days. All children displayed a stimulated growth also in the second time interval after the tests, with a decremental in some.
Conclusions
Two sequential somatotropic axis provocative tests increase the growth rate in non-GHD children with pathological short stature and that this effect persists for several months.

DOI: 10.1530/endoabs.81.EP789

EP790

Sarcopenia and frailty in acromegalic patients

Kader Ugur[1], Hasan Eryeşil[2], Ramazan Fazıl Akkoç[3] & Ahmet Karatas[4]
[1]Faculty of Medicine, Firat University, Department of Internal Medicine (Endocrinology and Metabolism Diseases), Elazığ, Turkey; [2]Faculty of Medicine, Firat University, Department of Radiology, Elazığ, Turkey; [3]Faculty of Medicine, Firat University, Department of Anatomy, Elazığ, Turkey; [4]Faculty of Medicine, Firat University, Department of Rheumatology, Elazığ, Turkey

Introduction
Acromegaly is a clinical syndrome associated with excess growth hormone. The present study aimed to investigate sarcopenia and frailty, which could affect mortality and morbidity, in patients with acromegaly.
Method
Twenty outpatients diagnosed with acromegaly were included in the study. The hand muscle strength of the patients was measured by electronic hand dynamometer (Model EH101, Zhongshan Camry Electronic Co. Ltd. China). Computed tomography, imaging at the L3 level was used to measure the abdominal muscle mass area (cm2). Measurements for the skeletal muscle mass index abdominal muscle mass area were expressed in (cm2)/height (m2). Normal values for men and women were considered >52.4 cm2/m2 and >38.5 cm2/m2, respectively. The Tilburg Frailty Indicator was used to determine the frailty of the patients. The Social Sciences Version 26.0 software was used to perform analyses in line with appropriate statistical methods.
Results
Thirteen patients were female and 7 were male. The mean age and time of diagnosis were 45.65±9.7, 10.4±6.4 years respectively. Sixteen patients received medical treatment, while 4 did not. Eighteen patients underwent surgical treatment. While 17 patients were in remission 3 patients had active disease under treatment. The mean body mass index of the patients was 29.95±5.1 kg/m^2. The mean hand muscle strength of the patients was 37.36±13.8 kg. 14 of all patients had frailty. Hand muscle strength in patients with and without frailty was 37.2±14.6 kg and 37.6±13 kg, respectively ($P=0.953$). Furthermore, there was no statistical difference in frailty between the patients by the remission status ($P=0.891$). Mean cross-sectional skeletal muscle area was 145.8±33.7 cm^2. The mean skeletal muscle index (SMI) was 53.1±9.7 cm^2/m^2. While sarcopenia was detected in 1 female patient, there was no difference in SMI levels between the groups in terms of SMI by the remission status ($P=0.794$).
Conclusion
The risks associated with sarcopenia and frailty increase as a result of increased intra-muscle fat storage due to increased insulin resistance, extended duration of the disease, accompanying hormonal changes, and decreased mobility due to joint pain. In the present study, patients with acromegaly had higher levels of frailty. In conclusion, it is important to carry out routine assessments for frailty and sarcopenia, which are associated with multifactorial causes, and to take timely measures based on a multidisciplinary approach in order to improve the quality of life and prevent the comorbidities of the aging population with acromegaly, which may induce high mortality and morbidity.

DOI: 10.1530/endoabs.81.EP790

EP791

A mini case series of hypophysitis with atypical presentation

Rukiye Dilara Tekin Uzman[1], Ş eyma Aksoy[1], Sebnem Burhan[1], Mutlu Niyazoğlu[1] & Esra Şüheda Hatipoğlu[1]
[1]Başakşehir Çam ve Sakura Şehir Hastanesi, Endocrinology and Metabolism Diseases, Istanbul, Turkey

Introduction
Hypophysitis is a rare condition characterized by inflamation of the pituitary gland, causing mass effect and hypopituitarism. The incidence is estimated to be 1in9 million/year. The diagnosis of hypophysitis is based on clinical and laboratory findings, imaging methods and histopathology in selected cases. The aim of the treatment is to eliminate the compression effects of the mass and to treat hypopituitarsim. The first choice in medical treatment is immunsupressive drugs. Surgical treatment can be considered for patients with progressive visual defects unresponsive to medications. Certain cases may be followed without immunesupression or surgical intervention. Here in we present cases with hipophysitis of atypical presentation.

Clinical Cases

Case 1:

A 20-year female presented with headache, blurred vision, oligomenorrhea and galactorrhea. Basal cortisol was 1.89μg/dl, other anterior pituitary hormones were in referance ranges. A 22 x 17 mm hemorrhagic atypical macroadenoma was present on the pituitary MRI. The stalk thickness was not increased. The patient underwent transsphenoidal surgery; pathologic specimen showed infiltration with lymphocytes, plasmacells and CD68(+) histiocytes; which were evaluated as xantamatous hypopysitis. After the operation the patient's complaints regressed. However glucocorticoid replacement was continued.

Case 2:

A 55-year male presented with headache, vomiting, fever, diplopia, polyuria and polydipsia for 10 days. Laboratory findings at first presentation showed hypocortisolemia, partial central diabetes inspidus, central hypothyroidism and lymphopenia. On the pituitary MRI, a 22 x 17 mm macroadenoma was observed. Initially an adenoma was suspected based on imaging, however hypophysitis was considered in the differantial diagnosis due to a spontaneous decrease in dimensions to 17 x 9 mm (>50%) and increased stalk thickness in control imaging. Lymphopenia improved spontaneously. For the differantial diagnosis laboratory invesitgations including inflammatory markers, IgG4, Covid-PCR and antibodies and, investigations for other infectious and inflammatory/infiltrative diseases showed only increased Covid antibody (IgG>250 U/ml). Patient was evaluated as a secondary hypophysitis after an unrecognised Covid infection.

Case 3

A 35-year male with acute onset headache, double vision and 6th cranial nerve palsy had 16 x 18 x 21 mm cystic lesion (macroadenoma) with increased stalk thickness on pituitary MRI. Pituitary hormones and other laboratory findings were within normal levels. Hipophysitis was considered, however with the acute presentation of mass effects transsphenodial surgery was performed. The intraoperative mass had a purulent apperance, and the pathology was evaluated as abscess and lymphocytic hypophysitis. The microbiologic evaluation confirmed a sterile abscess. Postoperatively the patients complains regressed completely and there was no need for any hormonreplacement therapy.

Conclusion

Hypophysitis is a rare condition with variable presentations. Diagnostic and treatment modalities may vary for each case. Not all cases require immunesupressive treatment and, a case based specific approach is necessary.

DOI: 10.1530/endoabs.81.EP791

EP792

The natural course of hypopituitarism at diagnosis and following therapy in non-functioning pituitary macroadenomas

Ziad HUSSEIN[1,2,3], Hani J Marcus[4], Joan Grieve[4], Neil Dorward[4], Peirre Bouloux[3] & Stephanie Baldeweg[3,5]

[1]University College London Hospitals NHS Foundation Trust, London, United Kingdom; [2]Sheffield Teaching Hospitals NHS Foundation Trust, United Kingdom; [3]University College London, United Kingdom; [4]National Hospital for Neurology and Neurosurgery, United Kingdom; [5]University College Hospital, United Kingdom

Background

Non-functioning pituitary macroadenomas (NFPMs) may present with hypopituitarism. Pituitary surgery and radiotherapy pose an additional risk to pituitary function.

Aims

The aim of this study was to assess the incidence of hypopituitarism preoperatively and the impact of surgery and radiotherapy on pituitary function.

Methods

All patients treated with surgery and radiotherapy for NFPMs between 1987 and 2018 with more than 6 months follow-up were identified. A retrospective case note review was performed.

Results

Overall, 383 patients were identified, 256 patients (256/383; 67%) were men. The median age was 57 years (IQR 48-67) with median follow-up of 5 years (IQR 2-9). 58 patients (58/377, 15%) presented with pituitary insufficiency, however, on endocrine evaluation, 235 patients (235/377; 62%) had evidence of pituitary impairment. Growth hormone deficiency occurred in 115 patients (115/273; 31%), hypogonadotropic hypogonadism in 161 patients (161/375; 43%), 132 patients (132/375; 36%) recorded to have adrenal insufficiency and 157 patients (157/375; 42%) developed secondary hypothyroidism. Anterior hypopituitarism was reported in 100 patients (100/377; 26%). With regards to treatment modality; 318 patients (318/383; 83%) were treated with surgery alone and 65 patients (65/383; 17%) were treated with surgery and radiotherapy. Histological analysis showed gonadotroph adenomas in 271 patients (371/383; 97%) and plurihormonal adenomas in 12 patients (12/383; 3%). At latest follow-up, 105 patients (105/383; 27%) had no evidence of pituitary impairment post therapy while 278 patients (278/383; 73%) suffered endocrine dysfunction. Patients who were treated with surgery and radiotherapy had a greater degree of partial and complete adenohypophysial hormone deficit than those treated with surgery alone as demonstrated in the table:

Conclusion

Non-functioning pituitary macroadenomas are associated with significant degree of hypopituitarism at time of diagnosis as well as post therapy. The combination of surgery and radiotherapy are associated with higher risk of pituitary dysfunction. Regular endocrine evaluation and lifelong follow-up is required following NFPMs treatment to screen for hormone deficiency and provide appropriate replacement therapy.

Table 1

	Total	Surgery	Surgery and radiotherapy	P value
GH	165/383 (43%)	118/318 (37%)	47/65 (72%)	<0.0001
FSH/lH	178/383 (46%)	136/318 (43%)	42/65 (65%)	0.001
ACTH	156/383 (41%)	111/318 (35%)	45/65 (69%)	<0.0001
TSH	206/383 (54%)	151/318 (47%)	55/65 (85%)	<0.0001
Anterior hypopituitarism	133/383 (35%)	90/318 (28%)	43/65 (62%)	0.0001

DOI: 10.1530/endoabs.81.EP792

EP793

Importance of neurosurgical expertise and multidisciplinary approach in pituitary patients

Simone Pederzoli[1,2], Maria Laura Monzani[1, 2], Sara De Vincentis[21, 2], Bruno Madeo[4], Chiara Diazzi[1] & Vincenzo Rochira[1,2]

[1]Unit of Endocrinology, Department of Medical Specialties, Azienda Ospedaliero-Universitaria of Modena, Modena, Italy; [2]Unit of Endocrinology, Department of Biomedical, Metabolic and Neural Sciences, University of Modena and Reggio Emilia, Modena, Italy

Background

Multidisciplinary approach to pituitary disease is highly recommended; it requires a close relationship between expert pituitary surgeons and endocrinologists together with several specialists (e.g. neuroradiologists) in order to provide a high-level standard of care. Although there is evidence that neurosurgeons' expertise is a key element to achieve better outcomes, also endocrinologists' role is fundamental but it may sometimes encounter real-life barriers.

Aim of the study

To explore from a real-life database the impact of neurosurgical centre expertise on post-surgical outcomes in pituitary patients attending a tertiary academic medical centre.

Methods

A retrospective, observational, single-centre study was carried out including all patients attending the Endocrinology Unit of Modena (Italy) that underwent pituitary surgery from January 1995 to December 2020. For each patient, preoperative features of the pituitary lesion, surgery information and post-surgical outcomes (i.e. residual neoplasia, surgery-related complications and pituitary function) were collected from record charts. Patients were grouped according to the expertise degree of the centre where they underwent surgery: Group1 included patients treated in neurosurgical centres with high expertise in pituitary surgery (defined as ≥50 transsphenoidal pituitary surgeries per year); Group2 included patients treated in neurosurgical centre performing <50 transsphenoidal pituitary surgeries per year.

Results
A total of 132 patients (67 men, 65 women; mean age at surgery 50.4 ± 16.8 years) were included. Considering the histological diagnosis, 114 patients (86.4%) had a pituitary adenoma, 11 patients (8.3%) had a craniopharyngioma, and 7 patients (5.3%) had other rarer diagnoses. Group1 included 63 patients (47.7%) and Group2 included 69 patients (52.3%). A pre-surgical endocrinological evaluation was performed in almost all patients with adenoma (89.3%), and just only in 37.5% of patients with craniopharyngioma ($P < 0.001$). Interestingly, patients without a pre-operative endocrinological evaluation were significantly more frequent in Group2 (26.3%) than Group1 (1.9%) ($P < 0.001$). We analysed post-surgical outcomes focusing on pituitary adenoma patients. Patients in Group2 had an almost eight-fold increased likelihood to have residual neoplasia (OR: 8.53; 95% CI: 3.45-21.09) and five-fold increased likelihood to have hypopituitarism (OR: 5.53; 95% CI: 2.41-12.73), while no difference was found for post-surgical complications (9.6% in Group1 vs 22.4% in Group2; $P = 0.070$).
Conclusions
This study confirms that high pituitary neurosurgical expertise is essential to achieve better post-surgical outcomes. The lack of pre-operative endocrinological evaluation is significantly associated to surgery performed in a not-experienced centre. A close multidisciplinary cooperation between experienced endocrinologists and neurosurgeons is required both before and after surgical procedures.

DOI: 10.1530/endoabs.81.EP793

EP794

Pituitary deficiencies after brain injury: a practical approach to evaluation and management

Tamara Wexler[1,2]
[1]NYU Langone, New York,; [2]University of Pennsylvania, Philadelphia,

While increasing attention is being paid to the health effects of brain injury, the role that neuroendocrine dysfunction may play in patients' health after traumatic brain injury (TBI) remains underappreciated. Pituitary deficiencies are seen at a high rate in patients who have sustained TBI, with reports of chronic pituitary dysfunction in 15-60% of adults after TBI, and up to 42% of children and adolescents. Deficiencies may resolve over time, or develop years after injury, and may occur after mild or severe injury. While there is a large and growing body of literature on the risk of pituitary dysfunction after brain injury, differences in assays and definitions account in part for the broad range of reported prevalence, and highlight the importance of a rigorous review of the evidence. Given the large number of people with a history of TBI, there has been much investigation into features that may predict neuroendocrine dysfunction. Studies have investigated biomarkers, imaging characteristics, and types of injury, but no consistent clinically useful association has been described**.** Thus, we rely on signs and symptoms to determine whom to screen**.** The overlap in symptoms seen in pituitary deficiencies and following TBI, and the potential clinical benefit of identifying hypopituitarism, make it particularly important to be aware of patterns that suggest pituitary dysfunction. Symptoms from hypopituitarism include cognitive, physical, and emotional effects, and overlap with symptoms from other etiologies including TBI itself. Clinical symptoms may include difficulties with executive function, increased anxiety and irritability, irregular menses, sexual side effects, and fatigue, and delay physical and neurorehabilitation efforts. It is particularly important to be aware of patterns that suggest pituitary dysfunction in patients with persistent symptoms after TBI, as replacement of deficient hormones can ameliorate or reverse the effects of hypopituitarism. In addition, there are indications that the cognitive issues and fatigue that may be seen as part of "Long Hauler" syndrome after COVID-19/SARS-CoV- infection may be related to pituitary deficiencies. This presentation will review the current understanding of pituitary dysfunction following TBI and the clinical relevance of pituitary axes, and offer a practical approach to evaluation and treatment; emerging information regarding other forms of brain injury will be included, and specific populations (military, children, women) will be highlighted.

DOI: 10.1530/endoabs.81.EP794

EP795

Response to classic dynamic tests of a corticotropinoma due to Nelson's syndrome

Foteini Adamidou, Paraskevi Komzia, Efstathios Divaris, Athanasios Panagiotou & Marina Kita
Ippokration General Hospital, Department of Endocrinology, Thessaloniki, Greece

Introduction
Nelson's syndrome is a rare complication of Cushing's disease treated with bilateral adrenalectomy. There is no effective medical treatment yet. Nelson's patients respond to hypothalamic stimuli distinctly from patients with Cushing's disease and those with Addison's disease. We describe the responses to standard ACTH stimulation tests in a patient with Nelson's syndrome.
Case report
A 42-year-old woman presented with ACTH dependent Cushing's syndrome. Pituitary MRI was suggestive of a lesion on the left side, measuring 4 x 3 mm and an ectopic source of ACTH was excluded. Following an unsuccessful transphenoidal surgery in 2013, she was placed on pasireotide 0.6 mg twice daily for one year. Partial response was seen on pasireotide, but she developed severe hyperglycemia. Fluconazole 200 mg daily was tried for 6 months, in conjunction with cabergoline 1 mg twice weekly, with little benefit. The patient finally had a bilateral adrenalectomy in3/2016 and was replaced with hydrocortisone 20 mg am-10 mg pm and fludrocortisone 0.1 mg/d, while maintaining all other pituitary axes intact. Two years later (2/2018), a pituitary tumor was visible on the right lateral pituitary, which grew further in the next 32 months to 10 mm (10/2020). Gradual skin hyperpigmentation was noticeable since 2018. The patient remained hyperglycemic but managed well with GLP-1R agonist and metformin. Her ACTH levels gradually increased since 2016, reaching am levels of 1886 pg/ml (7-64) and late evening levels of 1235 pg/ml (5-30) in late 2021. The patient had an exaggerated response to desmopressin stimulation with ACTH > 2000 pg/ml (dilutions were not performed) to x3 above baseline at 15', remaining at this level beyond 120'. An exaggerated response was noted following CRH stimulation, with ACTH rising from 1741 pg/ml to > 2000 pg/ml at 15', returning to baseline at 120'. ACTH decreased to 134 pg/ml following overnight suppression with 8 mg dexamethasone.
Conclusions
Abnormal and distinct hypothalamic-pituitary dynamics underlie the pathophysiology of Nelson's syndrome, which cannot be explained solely on lack of adrenal negative feedback. In patients with otherwise intact pituitary function repeat neurosurgery or radiotherapy are not desirable options and pasireotide use is similarly limited. A case for blockade of CRH receptor blockade can be a rational therapeutic option in this clinical situation.
References
1 Barber TM et al, European Journal of Endocrinology (2010) 163 495–507
2 Patel J et al, Neurosurg Focus 38 (2):E14, 2015
3 He X & Spencer-Segal JL: Clinical Diabetes and Endocrinology (2020) 6:22
Oldfield EH et al, J Clin Endocrinol Metab 62: 1020,1986

DOI: 10.1530/endoabs.81.EP795

EP796

Incidental discovery of pituitary insufficiency after non-pituitary surgery

Tamari Khutsishvili[1], Irine Lomtadze[2] & Miranda Baratashvili[3,4]
[1]Todua Clinic, Endocrinology, Tbilisi, Georgia; [2]Aversi Clinic, Endocrinology, Tbilisi, Georgia; [3]Endocrinology, Tbilisi, Georgia; [4]Helsicore, Endocrinology, Tbilisi, Georgia

Introduction
Pituitary Insufficiency is life threatening condition, that can lead or manifest by any stressful situation (surgery, infections, intoxication and etc)
Case report
A 70-year-old man diagnosed with Bladder Cancer had underwent surgery - Cystoplasty. The operation was performed without complications, but, after the intervention, the general condition of the patient sharply declined. There appeared strong general weakness, blurred consciousness, frequent abdominal pains, bradycardia, lowering of T/A(< 80/50 mmHg), fever. His condition required intensive care.
Laboratorial tests:
Na – 133-135 (130-152)mmol/l, K – 3.7 (3.6-5.2)mmol/l, CRP – 173 (< 5)mg/l, creatinine – 132 μmol/l, CBC - Leukocytosis, Urine total - bacteria – 205 cell/ul (< 11.4), Consultations with a Neurologist, Infectionist, Endocrinologist were conducted. TSH, FT4 tests were prescribed, we got a remarkable results – TSH - 1.25 (0.4-3.7) mIU/l, FT4-4.72 (12-22) pmol/l. Besides that, based on the recommendation of a Neurologist, the patient underwent MRT examination of the

brain. An introspectively revealed changes (adenoma?) was seen as the result of examination that is more likely to be Pituitary apoplexy (P/A). According to the findings, there was a doubt that it could be Central Hypothyroidism. The following studies have been scheduled: Cortisol, ACTH in Blood. So we have got worrisome results again: Cortisol – 3,9 (4,3-22,4) mg/dl, ACTH -3.36 (1.6-10.21) pmol/l.According to lab tests (Low Ft4, normal TSH, low cortisol, MRT results) patient was likely to have pituitary hypofunction, that causes central hypothyroidism and central hypocorticism. The patient was diagnosed with the following: Pituitary Hypofunction (E27) Pituitary damage, unspecified (E27.3) Other hypothesized hypothyroidism (E03.8), Malignant tumor of the bladder, unspecified (Ch 67.9)
Prescription
-Hydrocortisone 20 mg/day, In two days - Euthyrox 37 mcg/day 2-3 days after the medication administration patient's condition improved dramatically, T/A, pulse, temperature had been normalized (Antibiotic therapy due to urine infection was going). Patient got active, started adequate speech, movement and communication. We have checked Patient's lab tests in 10 days – TSH -1.8 (0.4-3.7) mIU/l, FT4- 8(12-22) pmol/l, Cortisol –13 (4,3-22,4) mg/dl, he was discharged home. Repeated examination of MRT of the brain, monitoring Pituitary, thyroid hormones, electrolytes is planned. Patient should be under constant supervision of an Oncologist and Endocrinologist.

DOI: 10.1530/endoabs.81.EP796

EP797

Severe heart failure in a young male with unrecognized hypopituitarism

Bojana Caric[1,2], Marko Stojanovic[3, 4], Gabrijela Malesevic[1, 2], Siniša Nikolić[5], Aleksandra Grbic[1, 2] & Dragana Miljić[6,7]
[1]University Clinical Centre of the Republic Srpska, Clinic of Internal Diseases, Department of Endocrinology, Banja Luka, Bosnia and Herzegovina; [2]School of Medicine, University of Banja Luka, Banja Luka, Bosnia and Herzegovina; [3]Clinic of Endocrinology, Diabetes and Metabolic diseases, Clinical Centre Serbia, Department of Neuroendocrinology, Belgrade, Serbia; [4]Faculty of Medicine, University of Belgrade, Serbia, Belgrade, Serbia; [5]Department of Physical Medicine and Rehabilitation 'Dr Miroslav Zotović', Banja Luka, Bosnia and Herzegovina; [6]Clinic of Endocrinology, Diabetes and Metabolic Diseases, Clinical Centre Serbia, Department of Neuroendocrinology, Belgrade, Serbia; [7]Faculty of Medicine, University of Belgrade, Serbia, Belgrade, Serbia

Background
The partial or complete hypopituitarism is described as late complication of hemorrhagic fever with renal syndrome (HFRS). Imaging methods of pituitary gland examination in the chronic phase showed pituitary atrophy, but a precise pathogenic mechanism that causes pituitary damage in HRFS remains unclear. While hypopituitarism in HFRS is rarely described, cardiac failure as a known complication of hypopituitarism is even more rarely described. We present a case of severe heart failure in a young male patient with unrecognized hypopituitarism consequent to HFRS and undiagnosed hemochromatosis.
Case Presentaton
42-year-old male patient was admitted at the Department of Endocrinology of University Clinical Centre of Republic of Srpska with suspected hypopituitarism. He managed to walk with the help of another person, and his speech was incoherent and with difficulties. The patient was pale, facial and body hairless with adynamia, myxedema, hypotension, and bilateral gynecomastia with decreased libido and impotency. Echocardiography verified a global reduction in myocardial contractility, dilated left atrium and ventricle, with low ejection fraction (10-15%). Results of hormone tests confirmed diagnosis of panhypopituitarism, and replacement therapy (hydrocortisone, levothyroxine and testostreone) was started. MRI of the pituitary gland was performed and it showed an "empty sella". On the third day after the therapy was introduced, the patient started to speak clearly and mental status was stabilized. The patient was independently mobile after seven days. Echocardiography performed a month after the replacement therapy was introduced showed an improvement in myocardial contractility with normal dimensions of the atrium and ventricle and estimated EF of 40%. Additionally, the diagnose of chemochromatosis was confirmed by genetic analysis of the HFE gene and presence of homozygosity for mutation pH63D (c 187 >G), but the specific therapy was not initiated. At follow-up visit, 6 months after introduction of replacement therapy, the patient felt well, performed usual physical activities, male type of facial and body hair distribution recovered, his sexual function normalized, and he had a normal mental status. Echocardiography was completely normal 6 months after introduction of replacement therapy (the left ventricle with normal dimensions, EF 58%).
Conclusion
The heart failure is extremely rare complication of hypopituitarism, but it is usually reversible when hormonal therapy is replaced. According to significant relationship and a high prevalence of hypopituitarism as a consequence of HFRS, endocrinological investigation should be considered in patients with HFRS and clinical signs and symptoms suggestive of hypopituitarism.

DOI: 10.1530/endoabs.81.EP797

EP798

Silent somatropic adenoma in young girl about a case

Charlene Ludwine Bifoume Ndong[1,2], Fatima Zahra El Jaafari[1,2], Sana Rafi[2], Ghizlane EL Mghari[2] & Nawal EL Ansari[2]
[1]Department Of Endocrinology, Metabolic Diseases and Diabetology, University Hospital Of Mohammed VI, Marrakech, Morocco

Introduction
Clinically non-secreting pituitary adenomas are rare in children We report a case of a silent somatotropic adenoma revealed by anatomopathology.
Case
A 13 year-old patient with no prior history of sudden onset intracranial hypertension syndrome. Clinical examination showed no dysmorphic Syndrome, no galactorrhea, no delay or statutory advance, Tanner P1S3. The MRI reveals a heterogeneous tumor process intra and suprasellar of 30 mm *15 mm of large axes, containing pockets of necrosis exerting a mass effect on neighboring structures and in particular on the optic nerves and quiasma evoking a priori craniopharyngioma. Initial hormonal balance: T4: 17,1 pmol/l;Cortisol:8,85 g/dl Prolactina:10,25 ng/ml, FSH: 2,2 UI/l; LH:0,1 UI/l; Eostradiol:8,2 ng/l and visual fields bitemporal hemianopsia. Partial transsphenoidal pituitary surgery performed in emergency with simple surgical follow-up and supplemented thyreocorticotropic deficit. The anatomopatho-immunohistochimical study concludes to a tumor proliferation with round cells whose morphological aspect first evokes pituitary adenoma secreting GH with Ki67 to1%. Before this and the normal initial IGF-1 at 360.1 ng/ml (90-581) a GH braking test under HGPO is performed with a GHnadir at 2.03 ng/ml confirming hypersecretion ofGH. Patient scheduled for surgery.
Discussion
Pituitary adenomas are rare tumors in children and adolescents whose most common type is prolactinoma followed by somatotropic as our case. The clinical expression of somatotropic adenoma is correlated with the early age of GH hypersecretion in relation to the welding or not of the epiphyses giving way to acromegalogigantism or gigantism. None of these dysmorphia have been found in our case thus signing the silent character of this somatotropic. The initial hormonal balance doesn't direct to any pituitary hypersecretion especially with a normal IGF-1 for age. Our presentation by ICHT syndrome, radiological elements as well as age were all in favor of craniopharyngioma which remains the most common tumor at this age. Only anatomopathological examination with positive immuno-labeling for GH supplemented by a GH braking test under HGPO initially not performed allowed to retain the diagnosis. The treatment is surgery with possible treatment by somatostatin analogous in case of no cure hence the surgical resumption planned for our case.
Conclusion
Before any sellar tumour any clinico-radiological presentation in children the anatomopathological study is the sole guarantaor of specific treatment.
References
1-Abe T, et al. Clinicallynonsecreting pituitary adenomas in childhood and adolescence. Neurosurgery. 1998 Apr;42(4):744-50
2-Chanson P, Salenave S. Diagnosis and treatment of pituitaryadenomas. Minerva Endocrinol. 2004 Dec;29(4):241-75.

DOI: 10.1530/endoabs.81.EP798

EP799

Endocrine dysfunction in hemochromatosis

Ben Salem Maram, Wafa Grira, Nadia Khessairi, Meriem Yazidi & Melika Chihaoui
Hospital La Rabta, Departement Of Endocrinology, Tunis, Tunisia

Introduction
Hemochromatosis is associated with iron overload that is responsible of iron deposit causing multiple organ dysfunctions which affects especially endocrine glands.

Methods
We report four cases of pituitary hemochromatosis responsible of endocrine dysfunction.
Results
Three women and one man were included, aged respectively 28, 19, 26 and 35 years old. These patients were suffering from ß-thalassemia and treated with multiple blood transfusions. All patients had delayed puberty with primary amenorrhea and erectile dysfunction. Hormonal screening showed hypogonadotropic hypogonadism with all the patients. They were treated with hormonal substitution. Two patients presented inaugural diabetic ketosis and were treated with insulin for the diabetes mellitus. One patient was diagnosed with corticotroph deficiency and was treated with hydrocortisone. Thyrotropic and somatotropic axis were normal with all patients. No cardiac or hepatic dysfunction was found with these patients.
Discussion and conclusion
Secondary hemochromatosis is responsible of multiple endocrine dysfunctions. The most endocrine dysfunction in hemochromatosis is diabetes mellitus and hypogonadotropic hypogonadism. The other endocrine dysfunctions are rare. Screening for endocrine dysfunction must be systematic and so a regular follow-up for all patients with hemochromatosis.

DOI: 10.1530/endoabs.81.EP799

EP800

Hyperprolactinemia, thyrotropic and corticotropic insufficiency in a patient with end-stage renal failure

Yasmine Mouelhi, Nadia Khessairi, Ameni Terzi, Meriem Yazidi & Melika Chihaoui
Rabta Hospital, Endocrinology, Tunis

Introduction
Hyperprolactinemia is a condition of elevated prolactin levels in blood which could be physiological, pathological, or idiopathic in origin. Some cases of hyperprolactinemia have been reported in patients with renal failure. We present a case of hyperprolactinemia, thyrotropic and corticotropic insufficiency in a patient with end-stage renal failure.
Case presentation
The patient was 27 years old, with a history of hypertension, renal insufficiency at the stage of haemodialysis, tertiary hyperparathyroidism and thyrotropic insufficiency. She was admitted to our endocrinology's department, in October 2021, for further exploration of the other pituitary axes. She had no functional complaints. The physical examination showed a weight of 49 kg with a body mass index of 20.3 kg/m^2. BP was 150/80 mmHg and there were galactorrhea on breast examination .
The biological investigations showed :
- Thyrotropic insufficiency : TSH : 0.099 mUI/l [usual values : 0.35-4.95]; FT4 : 0.69 ng/dl; FT3 :2,39 pg/ml [usual values:1.71-3.71];
- FSH :4.8 UI/l, LH :45.31 UI/l;
- Hyperprolactinemia was confirmed PRL : 229.66 and 255.03 mg/l
- Testosterone : 2.04 mmol/l;
- PTH : 1877.8 ng/dl [15-68]; Calcemia : 2.46 mmol/l
- A corticotropic insufficiency had been confirmed by a hypoglycemia test, and a treatment by hydrocortisone was started.
A Hypothalamic pituitary MRI was performed and showed no abnormalities.
Conclusion
This case confirmed that pituitary function is abnormal in patients receiving haemodialysis. Hyperprolactinemia is common and may be a factor in the infertility and sexual dysfunction in patients with end-stage renal disease.

DOI: 10.1530/endoabs.81.EP800

EP801

PE in Surgically Treated Cushing's Disease: A Case Report

Ketevan Gvazava[1], Nino Zavrashvili[1], Ketevan Chanturishvili[1], Natia Shonia[1], Natia Margvelashvili[1], Qetevan Gvazava[1], Nino Zavrashvili[1], Natia Margvelashvili[2], Natia Shonia[2] & Ketevan Chanturishvili[2]
[1]Tbilisi Institute of Medicine, Endocrinology, Tbilisi, Georgia; [1]Endocrinology Department, Tbilisi Institute of Medicine

Title
Pulmonary Embolism in Surgically Treated Cushing's Disease: A Case Report
Authors
Qetevan Gvazava1, Nino Zavrashvili1, Natia Margvelashvili2, Natia Shonia2, Ketevan Chanturishvili2 Endocrinology Department, Tbilisi Institute of Medicine
Background
Cushing's disease is the most common cause of Cushing's syndrome but can be very difficult to diagnose and to treat. as we know it has numerous health effects on patients and long-term health and quality of life in these patients often remains suboptimal, despite treatment. patients with CS have about ten times the risk for VTE. 2019 meta-analysis encompassed 7142 patients with endogenous CS (including Cushing's disease) undergoing transsphenoidal surgery or adrenalectomy, and their risk of unprovoked VTE was almost 18 times higher in comparison with a healthy population. The aim of this case report is to underline the clinical significance of increased VTE in endogenous Cushing's syndrome and to keep high clinical suspicion after undergoing transsphenoidal surgery.
Case Description
We report 57 years old women, who was hospitalized in our hospital with declining health for 6 months. Patient complained of weight gain, discomfort in chest area, face and neck edema, muscle weakness and overall low energy. Upon physical examination and appropriate laboratory work-up, this patient was diagnosed with ACTH dependent Cushing's syndrome. Head MRI later confirmed Cushing's disease and patient was set up for transsphenoidal surgery for removal of pituitary adenoma. Few weeks post-op patient presented in ER with tachycardia, shortness of breath, chest pain. PE was diagnosed and patient was started on anticoagulative therapy, oxygen therapy and close monitoring. It also needs to be mentioned that the patient had a history of hypertension and valve replacement, as well as Covid-19 disease.
Conclusion
In conclusion we want to highlight that CS is a risk factor for VTE/PE, which is often overlooked. It is important to keep high clinical suspicion and continue close monitoring of CS patients even after transsphenoidal surgery treatment. Physicians who treat VTE/PE cases should also be aware of increased risk associated with Cushing's disease.

DOI: 10.1530/endoabs.81.EP801

EP802

Hypothalamic neuropeptides as biomarkers for water-electrolyte disturbances

Nino Katamadze, Aleksandra Shutova, Ekaterina Pigarova, Larisa Dzeranova & Khava Fargieva
Endocrinology Research Centre, Moscow, Russian Federation

Hypothalamic neuropeptides as biomarkers for water-electrolyte disturbances. Introduction Diabetes insipidus is a rare condition characterized by excretion of large amounts of dilute urine and increased thirst. Nephrogenic diabetes insipidus (NDI) is caused by the inability of the kidneys to concentrate urine in response to vasopressin.
Aim
The aim of our case report is to present the patient with NDI and to report the data on physiological changes in hypothalamic neuropeptides such as copeptin, oxytocin, apelin, brain natriuretic peptide (BNP) in patient with NDI.
Material and methods
21-year-old male patient was admitted to the hospital with chief complaint of increased thirst and urinary frequency.
Results
In accordance with the results of indirect water-deprivation test NDI was diagnosed in our patient due to maximum urine osmolality of less than 76 mOsm/kg, plasma osmolality 302 mOsm/kg, maximum plasma sodium was 148 mmol/l, and no change in urine osmolality after administration of 2 mg of s.c. desmopressin. Copeptin, oxytocin, apelin, BNP after 8-h fluid restriction accounted for: 0.844 ng/ml (0.178-2.578 ng/ml), 5.694 ng/ml (0-12.821 ng/ml), 1.476 ng/ml, (0.620-2.095 ng/ml),1225.86 pg/ml (646.3-2033.4 pg/ml) and at the peak of dehydration (for 16 h) accounted for: 1.058 ng/ml, 6.176 ng/ml, 1.346 ng/ml, 973.93 pg/ml.
Conclusion
Our data confirm a commensurate increase in the levels of copeptin and oxytocin with a reciprocal decrease in the concentrations of apelin and BNP against the background of additional dehydration, which can later be used for differential diagnostic procedures for the syndrome of polydipsia-polyuria.

DOI: 10.1530/endoabs.81.EP802

EP803

Hashimoto's encephalopathy : a case report

Zineb Mhamdi, Kaoutar Rifai, Hinde Iraqi & Mohamed Hassan Gharbi
Ibn Sina University Hospital, Department of Endocrinology and Diabetology, Rabat, Morocco

Introduction
Hashimoto's encephalopathy or SREAT (steroid-responsive encephalopathy associated with auto-immune thyroiditis) is a rare autoimmune disorder that is particularly corticosensitive and whose pathogenesis remains poorly understood. It is associated with high levels of antithyroid antibodies in plasma and/or CSF. Clinical manifestations are deceptive and may include cognitive and behavioral disturbances, seizures or abnormal movements.
Case report
We report the case of a 54-year-old female patient who presented with progressive abnormal movements with balance disorders. The clinical examination revealed a cerebellar syndrome, a cerebellar dysarthria with an abolition of the osteotendinous reflexes. Brain MRI was without abnormalities. The electroencephalogram showed a diffuse slowing of the background rhythm without paroxysmal figure. Lumbar puncture revealed a clear cerebrospinal fluid without pleocytosis with hyperproteinorachy at 1.01 g/l. Antithyroglobulin and antithyroperoxidase antibodies were positive (anti-TPO antibody: 493 IU/ml and anti-TG antibody: 20 IU/ml) with a normal TSH. The diagnosis of Hashimoto's encephalopathy was retained after ruling out other causes, including metabolic, vascular, toxic, infectious and neoplastic. Intravenous corticosteroid therapy at a dose of 1 g of methylprednisolone per day was started for 3 days, followed by oral corticosteroid therapy at a dose of 1 mg/kg for one month and then gradually tapered off over 2 months. The patient was controlled with prednisone 2.5 mg per day with good improvement of her neurological symptomatology.
Discussion and conclusion
Hashimoto's encephalopathy is often underdiagnosed. The revealing neurological signs are polymorphic. Its pathophysiology is controversial, an autoimmune cerebral vasculitis is evoked. It should be systematically investigated in cases of unexplained encephalopathy, by looking for anti-TPO antibodies in the CSF even in cases of euthyroidism. This case highlights the different and often confusing clinical presentations of Hashimoto's encephalopathy but also its particular corticosensitivity.
References
S. Bannier, F. Taithe, C. Solmon, P. Thieblot, P. Clavelou. Corticosensitive encephalopathy associated with autoimmune thyroiditis: current data. Annals of Endocrinology. Volume 68, Issues 2-3. 2007. Pages 167-172. H. Tibar, W. Regragui, E. Aitbenhaddou, A. Benomar, M. Yahyaoui. Hashimoto's encephalopathy: a rare cause of status epilepticus. Revue Neurologique. Volume 171, Supplement 1. 2015. Page A105. I. Oueslati, A. Melki, N. Ben Ali, N. Mchirgui, I. Ben Nacef, K. Khiari, N. Ben Abdallah. Hashimoto's encephalopathy: about a case. Annals of Endocrinology (2015) 412-453.

DOI: 10.1530/endoabs.81.EP803

EP804

Gestational diabetes insipidus: about a case

Amal Elkhomri, Bensbaa Salma, Nassim Essabah Haraj, Siham El aziz & Asma CHADLI
CHU Ibn Rochd, Endocrinology-Diabetology and Metabolic Diseases Department, Casablanca, Morocco

Introduction
Diabetes insipidus during pregnancy is rare (4/100,000 pregnancies) generally occurring in the last two trimesters. It can be a previous diabetes insipidus, revealed by pregnancy, or a gestational diabetes insipidus. It would be secondary to the plasma degradation of antidiuretic hormone by placental vasopressinase.
Observation
We report the case of a 34-year-old patient, with no history of head trauma, radiation, infiltrative or autoimmune disease. who presents for a polyuro-polydipsic syndrome evolving since the second trimester of her pregnancy, with inputs at 5 liters per day and outputs at 7 liters. At the paraclinical level: Natremia at 134 mmol/l, with normal serum potassium at 4.4 mmol/l, low natriuresis at 20 mmol/24 h, plasma osmolarity at 285 mOsmo/l, and low urinary osmolarity at 160 mOsmo/l, Hypothalamo-pituitary MRI was without abnormalities, the patient was started on desmopressin nasally, the pregnancy was carried to term, with a cesarean delivery without insidents, giving birth to a new born female of 3500 g the postpartum evolution was marked by the disappearance of the polyuro-polydipsic syndrome after the second week
Conclusion
Gestational diabetes insipidus is therefore a polyuro-polydipsic syndrome which appears in pregnant women due to a deficiency in antidiuretic hormone. Rather rare, it usually disappears within three weeks after delivery.

DOI: 10.1530/endoabs.81.EP804

EP805

Endocrinopathy behind the facemask

Sandhi Nyunt[1], Parizad Avari[1], Giridhar Tarigopula[1], Niamh Martin[2], Catherine Mitchell[1] & Yong Yong Ling[1]
[1]Hillingdon Hospital, Diabetes and Endocrine, London, United Kingdom; [2]Charing Cross Hospital, Diabetes and Endocrine, United Kingdom

A 44-year-old gentleman presented to the Emergency Department with a 2-week history of fevers and rigors. Past medical history was unremarkable other than an earlier diagnosis of hypertension. He was noted to have new onset atrial fibrillation with rapid ventricular response, and a new diagnosis of hypertrophic obstructive cardiomyopathy (HOCM) was made on echocardiography. In addition, a vegetation was identified on the mitral valve. Treatment for infective endocarditis (Streptococcus oralis) was initiated and he was subsequently transferred to a specialist centre for mitral valve replacement surgery. During the admission, a history of chronic headaches was investigated. MRI pituitary revealed a 3.8 x1.9 cm pituitary macroadenoma with suprasellar extension. There was no cavernous sinus invasion. He was further evaluated in the outpatient endocrine clinic. On removal of his facemask, examination revealed typical acromegalic features with supraorbital ridge prominence, significant underbite and macroglossia. Visual fields were normal to confrontation testing and no organomegaly was present on bedside examination. Urgent endocrine investigations including baseline pituitary function testing were performed. IGF-1 was significantly elevated at 140.3 nmol/l (range 8.5-31.0), 9am cortisol was 352 nmol/l (range 200-750), prolactin 1119 mU/l (range 60-300), TSH 1.98 mU/l (range 0.34-5.60), FSH $<$0.U/l (range 1.7-8.0) and testosterone 8.7 (range 10.0-30.0). Acromegaly was confirmed with an oral glucose tolerance test showing a paradoxical rise in growth hormone. Glucose levels remained normal throughout the OGTT. The patient was commenced on monthly Lanreotide injections and referred to the specialist neuro-endocrine clinic to determine the best course of further management. Unfortunately, this gentleman's endocrine management was further complicated by a second hospital admission with persistent bacteraemia. Further redo of his mitral valve replacement is being considered, and safety of pituitary surgery at this stage remains a concern. In this case, radiotherapy could be a more suitable treatment option for acromegaly. This case highlights the requirement for early diagnosis and treatment to prevent further complications, as well as the need for individualisation of complex treatment decisions within a multidisciplinary setting. Cardiovascular complications including HOCM, arrhythmias, arterial hypertension and valvulopathy, as well as colonic benign neoplasms such as polysis, are common complications of acromegaly. For people presenting with 'idiopathic' HOCM, a IGF-1 may be considered to screen for acromegaly. Finally, the requirements for facemasks and virtual telephone consultations during the Covid-19 pandemic have likely compounded potential delays in diagnosis.

DOI: 10.1530/endoabs.81.EP805

EP806

Pituitary hypertrophy secondary to primary hypothyroidism (one case report)

Lionel Stève Kamgain Simeu, Nassim Essabah Haraj, Siham El Aziz & Asma Chadli
Ibn Rochd University Teaching hospital, Endocrinology, Diabetology, Metabolic Disease and Nutrition, Casablanca, Morocco

Introduction
There are several causes of sellar and suprasellar mass, and pituitary hyperplasia secondary to primary hypothyroidism has been reported in the literature.
Case report
20-year-old patient, born from a consanguineous marriage, presenting with failure to thrive. Patient reporting no tumor syndrom. Clinical examination: Height at 88 cm ($<$-4 SD), weight at 18 kg ($<$3rd percentile), BMI at 23 kg/m2. TANNER at G2P0, micropenis length of 5 cm ($<$-2.5 DS), infantile voice, elf-like features,

with periorbital puffiness, flat nasal bridge, short upturned nose with bulbous tips, large mouth with everted and broad lower lips. Patient with friendly behaviour. Thyroid not palpable, no clinical signs of pituitary hypersecretion. Paraclinical findings: TSHus >500 mIU/l (0.35-4.94) >100 times normal T4L: 2.81 pmol/l (10.6-19.4). IGF-1: 19.26 ng/ml (27-114). Cortisolemia before 10 hrs: 8.5 ng/dl (3.7-19.4) Prolactinemia: 118 ng/ml (3.6-19.4). Cervical ultrasound: heterogeneous thyroid gland without detectable nodules. Bone age: 1 year 6 months RISSER test: 0 Pituitary MRI: pituitary hypertrophy, without clearly detectable nodule. The patient benefited from a substitution by Levothyroxine and Somatostatin analogue with a good evolution.
Conclusion
Pituitary enlargement secondary to primary hypothyroidism should be considered as a differential diagnosis of solid pituitary masses, especially when associated with growth and pubertal retardation. Adequate care helps to avoid no need surgeries.

DOI: 10.1530/endoabs.81.EP806

EP807

Giant prolactinoma in an adolescent girl revealed by visual impairment

Hind Asbar, Hind Ouakrim, Sana Rafi, Ghizlane EL MGHARI & Nawal EL ANSARI
Chu Mohamed Vi Marrakesh - Drh, Department of Endocrinology, Diabetes, Metabolic Diseases and Nutrition, Marrakech, Morocco

Introduction
Pituitary adenomas are rare in infants and adolescents. Prolactinomas account for 50% of these pituitary adenomas. In adolescent girls, it is usually a microprolactinoma revealed by puberty delay or amenorrhea. We report a rare case of a macroprolactinoma in an adolescent girl revealed by visual impairment.
Case presentation
A 15-year-old adolescent girl presented with loss of vision over a long period of time. Magnetic resonance imaging revealed an expansive sellar and suprasellar mass measuring 48x47x37 mm consisting of cystic and solid components in favor of craniopharyngioma. Patient underwent transsphenoidal surgery for tumor resection. Post operative labroratory findings were in favor of a hyperprolactinemia with prolactine of 600 ng/ml and a thyrotrope deficiency. Histological assessment confirmed diagnosis of prolactinoma. Pituitary MRI control revealed a 20x9x17mm residual macroadenoma. Patient was started on cabergoline resulting in lowering prolactin levels and tumor shrinkage.
Discussion
Prolactinomas are rarely found in adolescents. Tumoral syndrome with visual impairment can be seen in large tumors in males. In girls, the most frequent presentation is a microprolactinoma revealed by amenorrhea. Less frequently, it can be revealed by pubertal delay or short stature. In our case, the patient presented with a macroprolactinoma revealed by visual impairment that was initially accounted for a craniopharyngioma. Medical treatment by dopamine agonists like in adults is the first line therapy as it's effective in up to three quarters of cases.
Conclusion
Prolactin levels should be measured in every child or adolescent with visual impairment and a large suprasellar tumor to rule out a prolactinoma that can be successfully managed by medical therapy.

DOI: 10.1530/endoabs.81.EP807

EP808

Inappropriate antidiuretic hormone secretion syndrome associated with covid 19 pneumonia

Amani Mezzi, Najla Bchir, Zouaoui Chedia, abderrahim yosra, chhida anaam & Ouertani Haroun
The Principal Military Hospital of Instruction of Tunis, Tunisia

Introduction
Hyponatremia is a commonly associated with atypical pneumonia. One of its pathophysiological mechanisms is inappropriate antidiuretic hormone secretion(-SIADH). We describe the case of a patient presenting an SIADH caused by COVID19 infection.
Observation
We report a case of a 70-year-old man, known to have well-controlled hypertension, with a medical history of cavum's neoplasia treated with radiotherapy and hypothyroidism post thyroidectomy for multinodular goiter. He was admitted in the intensive care unit for 'status epilepticus' caused by severe hyponatremia (120 mmol/l). The hormonal investigation showed a normal thyroid function test (TSH:2.06 uU/ml FT4 11.4 pmol/l) and a normal stimulated cortisol at 524 nmol/l. Therefore, the diagnosis of SIADH was retained. It was based on euvolemic hyponatremia with concurrent low serum and high urine osmolality (265 mosm/l and 338 osmol/24h, respectively) and high urine sodium (75 mmol/24h). Concerning the etiological investigation, we evoked the disorders of the central nervous system caused by cerebral radiotherapy but it goes back to 6 years during which the natremia was normal. Negative tumor markers, absence of tumoral process on the CT-scan and the normal bronchial fibroscopy infirmed paraneoplasic syndromes. Nasopharyngeal RT-PCR and abnormal chest CT-scan depicting bilateral infiltrates and bilateral pleural effusion confirmed COVID-19 infection. The course was marked by pneumonia's healing at the expense of SIADH's persistence. Currently, the patient is on fluid restriction, his natremia varies between 120 and 137 mmol/l.
Discussion
SIADH may be the only presentation of covid19. This association has been reported in the literature, but the course of the hyponatremia after pneumonia's healing was not mentioned. The pathophysiology is unknown. Several theories were suggested: hypoxemia, stress, nausea, IL6 secretion. However, none of those theories explains the persistence of SIADH after recovering from pneumonia.

DOI: 10.1530/endoabs.81.EP808

EP809

Association between uncontrolled acromegaly and nasopharyngeal tumor-case presentation

Valeria Nicoleta Nastase[1], Burcea Iulia-Florentina[1,2], Amalia Raluca Ceausu[3], Anca Maria Cimpean[3], Marius Raica[3] & Catalina Poiana[1,2]
[1]'C.I. Parhon' National Institute of Endocrinology, Pituitary and Neuroendocrine Pathology, Bucureşti, Romania; [2]Carol Davila University of Medicine and Pharmacy, Endocrinology, Bucureşti, Romania; [3]Victor Babeş University of Medicine and Pharmacy, Department of Microscopic Morphology/Histology and Angiogenesis Research Center, Timişoara, Romania

Introduction
Acromegaly is characterized by elevated levels of growth hormone (GH) and insulin-like growth factor 1 (IGF-1), most often due to a pituitary tumor. Persistent high levels of these hormones lead to a constellation of signs and symptoms and systemic complications associated with increased mortality. A potential association between acromegaly and cancer has been hypothesized regarding colorectal, thyroid, and prostate cancers, but there are few or no descriptions for other kinds of tumors.
Case presentation
Male, 49 years old, presented with headache, multiple episodes of loss of consciousness, joint pain, profuse sweating. Clinical examination revealed acral enlargement, generalized thickening of the skin, prominent supraorbital ridges, nose enlargement, prognathism. Hormonal assessment showed increased levels of IGF-1 (2.8 x upper limit of normal, ULN) and high levels of nadir GH in the oral glucose tolerance test (OGTT, 10.3 ng/ml). All others anterior pituitary hormones were within normal range. Pituitary MRI revealed a hypophyseal mass with heterogenous signal (23/14 mm). The patient underwent surgical removal of the pituitary macroadenoma using transsphenoidal resection. The immunohistochemical (IHC) examination showed positivity for GH and prolactin (PRL). Three months after surgery, the patient presented active disease (IGF-1 = 1.8 x ULN, nadir GH in OGTT = 3.24 ng/ml), with a small pituitary remnant (9/7 mm). The disease persisted uncontrolled after two years of treatment with Octreotide LAR up to 40 mg/28 days, Cabergoline up to 3 mg/week and Pegvisomant up to 40 mg/week (associated in the last three months, with good control of GH secretion). The patient developed severe obstructive sleep apnea documented using polysomnography. Fibroscopy reported a glossy, smooth tumor occupying completely the choanal quadrant and pegvisomant was withdrawn. Surgical intervention was performed, and the histopathological examination described a sessile polyp on the background of a chronic erosive rhinopharyngitis. IHC analysis revealed a positive cytoplasmic reaction for GH in tumoral cells. Two months after the nasopharyngeal tumor resection, IGF 1 was within normal range on somatostatin analogue and dopamine agonist.
Conclusion
Active acromegaly defined by GH excess and increased levels of IGF-1 contributes to mitogenesis, delayed apoptosis and malignant proliferation. In the current case, uncontrolled acromegaly was associated with a nasopharyngeal

tumor presenting IHC positive expression for GH. This aspect could partially explain the decreased IGF-1 levels after surgical intervention and a better therapeutical response to standard medical treatment and could raise the hypothesis of a tumor invasion.

DOI: 10.1530/endoabs.81.EP809

EP810

Hypopituitarism in adults - the importance of clinical suspicion

Ana Rita Elvas[1], Mariana Lavrador[2], Miguel Melo[2], Luí sa Barros[2], Maria Leonor Gomes[2] & Isabel Paiva[2]
[1]Portuguese Oncology Institute of Coimbra, Endocrinology, Coimbra, Portugal; [2]Coimbra Hospital and University Center, Department of Endocrinology, Diabetes and Metabolism, Coimbra, Portugal

Introduction
Hypopituitarism is a rare entity that can have different aetiologies. Symptoms are usually progressive and non-specific; therefore, many patients are under-diagnosed and untreated. We present a clinical case of a patient presenting septic shock, hyponatremia and central hypothyroidism.
Case report
A 46-year-old man was admitted in ICU for septic shock of unknown origin and multiorgan failure. Hormonal profile showed central hypothyroidism, prolactin and gonadotropins deficiency. The integrity of corticotropic axis could not be assessed due to the immediate introduction of glucocorticoids, with a significant improvement in clinical status. An MRI was performed, which revealed increased dimensions of the sella turcica, with an apparent bone discontinuity of the sella turcica floor; it was not possible to visualize the right lobe of the adenohypophysis and the remaining pituitary gland had reduced dimensions. He was discharged home medicated with hydrocortisone and levothyroxine and was referred to Endocrinology outpatient clinic. He presented an history of previous traumatic brain injury (TBI) eighteen years earlier, requiring medical observation and an episode of intense headache with associated vomiting, eight years before when he started his complaints of asthenia, reduced libido, pale skin and decreased body hair began. Its fertility was unknown as he had no wish for procreation. Laboratory study control revealed panhypopituitarism: FSH 2.3 mIU/ml [< 15]; LH 0.7 mIU/ml [< 9.0]; 1.2 ng/ml prolactin [3.5-19.4]; Total Testosterone 0.1 ng/ml [2.7 - 11.0]; TSH 1.0 uUI/ml [0.4 - 4.0] Free T4 0.60 ng/dl [0.7 - 1.5]; ACTH 14 pg/ml [9-52]; Cortisol 0.4 mg/dl [5-25]; IGF1 22 ng/ml [53-215]. He was medicated with hydrocortisone 15 mg daily, levothyroxine 75µg/day and testosterone 250 mg IM every four weeks. At the time of the last observation, he reported a significant improvement in his general condition, normalized sexual activity and body hair growth.
Discussion
Discovering the cause of hypopituitarism can be a challenging. TBI can caused hypopituitarism several years after the event, and can even occur after minor trauma. The onset of symptoms of hypopituitarism after the episode of severe headache and vomiting also raises the possibility of another concomitant event, namely pituitary ischemia/haemorrhage. The hospitalization with septic shock, the detailed clinical evaluation and follow-up of the patient were crucial to detect the occurrence of this condition, associated with high morbidity and whose hormone replacement significantly improved the prognosis and quality of life.

DOI: 10.1530/endoabs.81.EP810

EP811

Non-functional pituitary adenomas: clinical and paraclinical aspects

Anis Grassa[1], Cyrine Chehaider[2], Nadia Khessairi[1, 2], Meriem Yazidi[2], Ibtissem Oueslati[2] & Melika Chihaoui[1]
[1]Hopital La Rabta, Endocrinology, Tunis, Tunisia; [2]Hopital La Rabta, Tunis, Tunisia;

Introduction
Non-functional pituitary adenomas (NFPAs) represent 30% of all pituitary adenomas and not associated with clinical evidence of hormonal hypersecretion. The aim of our study was to describe the clinical and paraclinical aspects of NFPAs.
Methods
This is a retrospective descriptive study concerning 40 patients who were hospitalized in the endocrinology department of Rabta hospital in Tunis between January 2014 and December 2020. Clinical and paraclinical data were taken from medical records.
Results
Our population had a mean age of 51.8 ± 15.9 [21-80] years. Patients were 40% male and 60% female, sex ratio was 0.66. The circumstances of discovery were mainly: pituitary incidentaloma (12,5%), headache (50%), visual impairment (45%), endocrine manifestations (10%) and epilepsy (2,5%). Five had a pituitary apoplexy at the time of diagnosis (12.5%). On pituitary imaging, the mean size of the adenomas was 23 mm (4mm-52mm) and were classified: 4 microadenomas and 36 macroadenomas. The optic chiasm and pituitary stalk were invaded in 29 cases (72.5%), the cavernous sinus in 15 cases (37.5%) and the sphenoidal sinus in 6 cases (15%). The main symptoms were headache, visual impairment, asthenia, weight loss, psychomotor retardation and hypoglycaemic discomfort found in 27 (67.5%), 24 (60%), 21 (52.5%), 8 (20%), 7 (17.5%), 4 (10%) cases respectively. Decreased libido was found in 12 patients (30%). Seven women had secondary amenorrhea and 10 men had erectile dysfunction. Axillary-pubic depilation was noted in 5 persons. For the visual impact, an alteration of the visual field was found in 24 (60%) cases, a pathological fundus in 7 cases (17.5%), papilledema in 4 cases and optic atrophy for the rest. A decrease in visual acuity was observed in half of the subjects (50%). Hormonal deficiencies were corticotropic, thyrotropic, gonadotropic insufficiency, disconnection hyperprolactinemia and central diabetes insipidus in 80%, 32.5%, 42.5% and 15% respectively.
Conclusion
NFPAs in addition to their incidental discovery, are usually diagnosed lately as macroadenoma which commonly present with symptoms related to the mass effect on surrunding structures. They put at risk the vital and visual prognosis.

DOI: 10.1530/endoabs.81.EP811

EP812

Hypopituitarism induced Radiotherapy for nasopharyngeal carcinoma: a case report

Meriem Adel[1], Ibtissem Ben Nacef[2], Elyes Kamoun[2], Sabrine Mekni[2], Youssef Lakhoua[2], Nadia Mchirgui[2], Imen Rojbi[2] & Karima Khiari[2]
[1]Charles Nicolle Hospital, Endocrinology, Tunis, Tunisia;

Introduction
Since the hypothalamic-puituitary axis (HPA) is a radiosensitive region, cranial radiotherapy for head and neck malignancies represents a major risk factor for the development of endocrine complications particularly hypopituitarism.
Case report
A 22 years old girl with a history of a undifferentiated carcinoma of nasopharyngeal type UCNT at the age of 09 years old treated with radiotherapy and chemotherapy was referred to the endocrinology department for investigation of short stature and primary amenorrhea. The patient presented with short stature, height of 146 cm (–3 standard deviations), with normal weight (body mass index 24 kg/m2), Breast Development Scale stage 4 and Pubic Hair Scale stage 4. Radiography of the left hand revealed a bone age of 15 years. Dynamic growth hormone evaluation showed unstimulated levels. The Endocrine investigation was consistent with hypopituitarism (corticotropic insufficiancy, gonadotrop insufficiancy, central hypothyroidism and GH deficiency). However, Prolactin levels were normal. Pituitary MRI showed hypotrophic pituitary gland with partial intrasellar arachnoidocele, and a bilateral postradic demyelination of temporal white matter. Pelvic MRI revealed an uterine and ovarian atrophy. Hormonal substitution therapy with glucocorticoids levoT4 and sex steroids was started.
Discussion
RIH (radiotherapy induced hypopituitarism) is a slow-developing process. Its development dependens on RT per fraction dose, post-RT interval radiation dose, age, the volume of the HPA irradiated. In addition, the incidence of RIH increases with the total dose. However, it should be noted that this incidence does not have a specific threshold dose since cases with doses as low as 20 gy were documented. This further highlights the importance of early detection. Some studies have suggested that the growth hormone deficiency is the first manifestation of RIH followed by deficiencies in gonadotropin, ACTH, and TSH. Moreover, the dysfunction of the hypothalamus leads to the reduction of dopamine release. Hence, hyperprolactinemia, which contributes to gonadal dysfunction, can be present on a case by case basis. Despite the fact childhood cancer survival rates

have improved across all measures, survivors are still at risk of developping endocrine disorders, even years removed from therapy. This accentuates the importance of lifelong surveilance.
Conclusion
RIH worsens the quality of life and reduces the life span of patients. Thus, successefull management depends greately on early detection and hormone replacement therapy.

DOI: 10.1530/endoabs.81.EP812

EP813

Cushing Disease with COVID-19: Protective or Dangerous?

Zehra Yagmur Sahin Alak[1], Pinar Uzgec Guller[1], Mustafa Burak Yaşar[1], Metin Guclu[1], Fatih Aydemir[2] & Sinem KIYICI[1]
[1]Health Sciences University, Bursa Yuksek Ihtisas Research and Training Hospital, Endocrinology and Metabolism, Bursa, Turkey; [2]Health Sciences University, Bursa Sehir Hospital, Neurosurgery, Bursa, Turkey

Introduction
Coronavirus disease-19 (COVID-19) pandemic renders high morbidity and mortality. Glucocorticoid excess is characterized by increased susceptibility to infections due to impairment of the innate and adaptive immune system. Manifestations of Cushing disease (CD) including diabetes mellitus (DM), hypertension, and obesity are risk factors for severe COVID-19 disease. We present three CD patients with different clinical courses of COVID-19. The patients' general characteristics are summarized in table 1.
Case-1
The patient was a 27-year-old woman with recurrent CD after transsphenoidal surgery. She had DM, hypertension, and obesity. She tested positive for SARS-CoV-2 with dyspnea, cough, chest pain, and fever. She hospitalized at intensive care unit (ICU). A CT scan showed bilateral diffuse ground-lass opacities of both lungs. Significant clinical improvement was achieved on the 13th day of ICU. She discharged from the hospital on 17th day.
Case-2
A 23-year-old woman was diagnosed with CD recently. She had obesity. The COVID-19 nasopharyngeal PCR was positive during preoperative evaluation. Lung involvement wasn't observed. She survived the COVID-19 disease without symptoms.
Case-3
A 55-year-old woman with CD had a transsphenoidal surgery 2 months ago. She had DM and obesity. She was admitted to our clinic with adrenal insufficiency. She tested positive for SARS-CoV-2 with cough and shortness of the breath. A CT scan showed bilateral pleural effusion and bilateral diffuse ground-glass opacities. She died on the 18th day while treated in ICU.
Conclusions
Cushing disease-associated glucocorticoid excess, immunosuppression and co-morbidities may alter the severity and the course of COVID-19. In contrast, glucocorticoids have shown improve COVID-19 associated mortality in randomized controlled trials. It was also reported that COVID-19 disease infection can be worsened by concomitant hypocortisolism. Herein we report three cases with different prognosis. Thus, patients with CD should be followed more carefully during COVID-19 disease.

Table 1

Patient	1	2	3	References
Diabetes mellitus	Yes	No	Yes	
Hyperten-sion	Yes	No	No	
Basal ACTH	78.9	79	1.6	7.2–63.3 pg/ml
Basal corti-sol	15	21	3.2	5-20 mg/dl
LDDST	16	7.9	-	$<$1.8 mg/dl
24-h urinary free cortisol	153	144.5	-	$<$45 mg/24 h
Hemoglobin A1c	11.7	5.8		%5.7-6.4
Hemo-globin	10.5	13.0	11.4	12.0–15.5 g/dl
WBC	10.12	12.79	13.15	3.5–10.5$\times$109/μL
Lympho-cyte count	1.05	2.79	0.27	0.9–2.9$\times$109/μL
Creatinin	0.6	0.78	0.85	0.57–1.11 mg/dl
C-reactive protein	304	14.7	360	$<$5 mg/l
Ferritin	88.8	19.30	1188	4.63–204 ng/ml
D-dimer	1.04	0.2	2.39	0-0.5 μg/mL
COVID-19 Vaccine	No	No	No	

DOI: 10.1530/endoabs.81.EP813

EP814

Exploring a new entity of monotherapy pembrolizumab-associated hypophysitis

Eric Balti[1], Sarah Verhaeghe[1], Vibeke Kruse[2], Stijn Roels[3] & Peter Coremans[1]
[1]VITAZ Hospital, Department of Endocrinology and Diabetes, Sint-Niklaas, Belgium; [2]VITAZ Hospital, Department of Onco-Hematology, Sint-Niklaas, Belgium; [3]VITAZ Hospital, Department of Radiology, Sint-Niklaas, Belgium

Background
There are increasing number of reports on immune checkpoint inhibitors induced adverse events including hypophysitis. Hypophysitis tends to occur more with CytotoxicT-lymphocyte-associated protein 4 inhibitors (12-15% of cases) which is a different entity compared to those associated to anti-program death 1 (anti-PD1) inhibitors.
Aim
We describe a case of pembrolizumab-associated hypophysitis and conduct a discussion based on a systematic review of the literature.
Case presentation
A 55-year-old woman presented with headache, nausea and fatigue 3.5 months (5 cycles) after initiation of adjuvant pembrolizumab for a stage 3b (TNM) melanoma. Endocrine profile was consistent with secondary adrenal failure, thyrotropic insufficiency and defective gonadotrophin secretion. Progressive decline of thyroid stimulating hormone and free tetraiodothyronine occurred three months prior to diagnosis. Imaging study showed an enlarged pituitary gland with homogeneous enhancement of the gland and pituitary stalk. After interruption of anti-PD1 therapy and administration of adrenal and thyroid hormonal substitutions improvement was observed. Magnetic resonance study showed declining pituitary mass three months later.
Discussion
Systematic search of literature identified 16 studies reporting 19 patients with single use pembrolizumab-associated hypophysitis. Most patients were treated for melanoma (n=7, 35%) and urogenital or breast neoplasia (n=7, 35%). Time to onset of pituitary insufficiency was most frequently 6 months (range 1.5 to 39.0 months) after treatment initiation. The most prevalent hormonal defect was isolated adrenocorticotropic hormone deficiency. Two studies reported multiple central hormonal defects. In those patients and in our case, increased pituitary mass was observed.
Conclusion
In contrast with the majority of other cases of pembrolizumab monotherapy associated hypophysitis, our case has distinct features. These include early disease onset, after pembrolizumab initiation, panhypopituitarism and increased pituitary mass. Whether or not this is a new clinical entity warrants further investigation. Until then, clinicians should be aware that pembrolizumab monotherapy associated hypophysitis might cover a heterogeneous clinical spectrum.

DOI: 10.1530/endoabs.81.EP814

EP815

The impact of adenoma size on the clinical course of acromegaly : a comparative study

Faten Haj Kacem Akid, Wafa Belabed, Abdelmouhaymen Missaoui, Dhoha Ben Salah, Mouna Elleuch, Fatma Mnif, Nabila Mejdoub & Mohamed Abid Hedi Chaker University Hospital, Endocrinology Department, Sfax, Tunisia

Introduction
Acromegaly is a chronic, slowly progressing disease caused in most cases by growth hormone (GH)- producing pituitary adenoma. This rare disorder is associated with a spectrum of various clinical manifestations and treatment outcomes differ between patients. The aim of this study was to evaluate the impact of adenoma size on comorbidities and biochemical status at the diagnosis of disease.
Methods
This is a one-centre cohort study conducted among adult patients with confirmed acromegaly. Baseline data regarding biochemical and radiological status were collected retrospectively. We performed a comparative analytical analysis between two subgroups:
• G1: patients with pituitary adenoma larger than 20mm ($n = 17$)
• G2: patients with pituitary adenoma smaller than 20mm ($n = 12$)
Results
29 adult patients were included with a mean age at diagnosis of 45,8 $\pm$ 12,4 years. Both genders and age did not differ between the two subgroups. Adenoma size greater than 20 mm (G2) was significantly associated with a higher GH level. Furthermore, there was a positive and significant ($P < 0.05$) correlation between baseline GH level and adenoma size. All patients in G2 had an intact gonadotropic axis, whereas more than half of those in G1 had gonadotropic insufficiency ($P <$ 0,05). The differences in the occurrence of hyperprolactinemia, of corticotropic and thyrotropic insufficiencies were not statistically significant between the two subgroups.
Conclusion
According to our results, the clinical course of acromegaly is influenced by adenoma size at the onset of symptoms. This difference should be considered when treating patients with acromegaly.

DOI: 10.1530/endoabs.81.EP815

EP816

Clinical and demographic features of acromegaly in tunisian patients: a monocentric retrospective study

Faten Haj Kacem Akid, Wafa Belabed, Dhoha Ben Salah, Abdelmouhaymen MISSAOUI, Fatma Mnif, Mouna Elleuch, Nabila Mejdoub & Mohamed Abid
Hedi Chaker University Hospital, Endocrinology Department, Sfax, Tunisia

Background and Aims
Acromegaly is a rare condition caused by an excessive secretion of growth hormone (GH) and insulin-like growth factor1 (IGF-1), which are responsible for exaggerated somatic growth and distorted proportions. The objective of the current work was to investigate the clinical and demographic features of acromegaly in Mediterranean patients.
Patients and Method
From 1997 to 2021, 29 patients with acromegaly were diagnosed and followed up at the Endocrinology Department of Hedi Chaker University Center, Sfax, Tunisia. We retrospectively reviewed the medical charts of all patients to assess their clinical and demographic characteristics.
Results
We noted a slight male predominance with a sex-ration of 1.07. The mean age at diagnosis was 45.8 $\pm$ 12.4 years old. The diagnosis of acromegaly was more delayed in females (male: 44.1 $\pm$ 11.2 vs female: 47.7 $\pm$ 13.7 years old). Symptoms related to tumoral mass effects such as headache and visual impairment were the leading causes of consultation in 31.0%. Changes in appearance brought only 17.2% of patients who had acromegaly to seek medical care. In 27.6% of cases, patients with dysmorphic features were referred by their physicians to the Endocrinology department for further hormonal assessment. The worsening of some nonspecific symptoms such as snoring (10.3%), glycemic imbalance (6.9%), and secondary amenorrhea (6.9%) led to the diagnosis of acromegaly. The mean weight was 82.5 $\pm$ 13.0 kg. The average height was 167.3 $\pm$ 11.2 cm (extremes:146-191). The mean BMI was 28.0 $\pm$ 7.2 kg/m^2. Obesity was found in 40.7%. Dysmorphic features were observed in all patients with variable degrees. The dermatologic examination noticed frequently thickening skin (69.0%) and hyperhidrosis (65.5%). A horsely voice was found in 48.3%. Patients with acromegaly reported asthenia, lower back pain, and arthromyalgia in 41.4%, 20.7%, and 10.3%, respectively. The principal general comorbidities associated with this condition were diabetes (34.4%), hypertension (13.7%), and dyslipidemia (10.3%).
Conclusion
Acromegaly is an insidious disease that impacts equally both genders with a prevalence ranging between 2.8 and 13.7 cases per 100,000 people. Clinical manifestations include skeletal and soft tissue deformities, along with cardiorespiratory, neuromuscular, and metabolic disturbances. Most patients are diagnosed at an advanced stage after the onset of tumoral mass effect signs. Better recognition of the clinical landscape of acromegaly by first-line physicians may help in its precocious diagnosis and thus improve its therapeutic outcomes.

DOI: 10.1530/endoabs.81.EP816

EP817

Pituitary Stalk Interruption Syndrome in a 22-year old Filipino Male : A case report

Irene Kei Bariuad-Garcia & Cecille Dela Paz
East Avenue Medical Center, Internal Medicine, Section of Endocrinology, Quezon City, Philippines

Background
Pituitary Stalk Interruption Syndrome (PSIS) is a rare congenital anomaly affecting the pituitary gland with characteristic MRI findings of small or absent anterior pituitary gland, misplaced or absent posterior pituitary gland and very thin or interrupted pituitary stalk (1). Patients with PSIS often presents with signs and symptoms of either isolated growth hormone deficiency or multiple anterior pituitary hormone deficiency and symptoms differ according to age at diagnosis (2). We report a case of pituitary stalk interruption syndrome in a 22-year old Filipino male presenting with micropenis.
Case
A 22-year old Filipino male was referred to endocrinology service for evaluation of micropenis. His birth history was unremarkable. Developmental milestones were at par with age. Both parents and 3 siblings were healthy. On examination, his BP was 90/60 mmHg with a height of 139.7 cm, weight of 32 kg, with a eunuchoid proportion. Facial, axillary and pubic hair were absent. His testes were 1 ml in size, with a 1.5 cm-at-stretch penis. Laboratory findings showed: Total testosterone 0.11 ng/ml (NV: 2.80-8 ng/ml), FSH 0.18 mIU/ml (NV: 1.5-12.40 mIU/ml), LH $<$ 0.100 mIU/ml (NV: 1.70-8.60 mIU/ml), FT4 8.63 pmol/l (12-22 pmol/l), TSH 6.17 uIU/ml (NV: 0.27-4.20 uIU/ml), IGF 1 13.23 ng/ml (120-388 ng/ml), Prolactin 191.40 mIU/l (NV: 86-324 mIU/l), Estradiol $<$ 5 pg/ml (NV: 25.80-60.70 pg/ml), DHEAS 0.07 umol/l (NV: 6.50-14.60 umol/l). ACTH stimulation test was done, baseline cortisol was 78. 27 nmol/l (NV: 172-497 nmol/l), 30 minutes and 60 minutes post ACTH cortisol levels were 290 nmol/l and 60 minutes cortisol: 343. 20 nmol/l respectively indicating intact adrenal gland. His bone age was 14 years. Pituitary MRI results were consistent with pituitary stalk interruption syndrome.
Conclusion
Despite being a rare syndrome, pituitary stalk interruption syndrome should be one of the differential diagnosis in patients presenting with micropenis and short stature. Importance of early recognition of the disease is important because it associated with permanent hormonal deficiencies leading to significant morbidity and mortality.
References
1. Gutch M, Kumar S, Razi SM, Saran S, Gupta KK. Pituitary stalk interruption syndrome: Case report of three cases with review of literature. *Journal of Pediatric Neurosciences*. 2014; 9(2):188-191.
2. El Chehadeh-Djebbar S, Callier P, Masurel-Paulet A, Bensignor C, Méjean N, *et al*. (2011) 17q21.31 microdeletion in a patient with pituitary stalk interruption syndrome. Eur J Med Genet 54: 369–373

DOI: 10.1530/endoabs.81.EP817

EP818

Hypopituitarism in tropical countries

Lakshman kumar Ega[1], rakesh sahay[2] & neelaveni kudugunti[3]
[1]Osmania Medical College, Endocrinology, Hyderabad, India; [2]Osmania Medical College, Endocrinology, Hyderabad, India; [3]Osmania Medical College, Hyderabad, India

Background
Etiology of hypopituitarism differs in tropical countries compared to the West and includes pituitary abscess, snake bite, HIV infection, Sheehan syndrome, road traffic accidents, iron overload states etc.
Aims and Objectives
The present case series highlights the spectrum of hypopituitarism in tropical countries.

Case Details
1. C1: 23 y/o female presented with loss of consciousness, unrecordable BP and hypoglycemia. H/O spontaneous pre term delivery at home with significant PPH with lactational failure. 2. C2: 21 y/o male came with c/o poor height and weight gain and poor development of secondary sexual characteristics. Examination revealed a large healed scar over foot which developed after snake bite in past. 3. C3: 41 y/o female with h/o recurrent episodes of altered sensorium. H/o PPH, lactational failure, amenorrhea following home delivery. 4. C4: 30 y/o female presented with h/o delivery with PPH, followed by amenorrhea, lactation failure with sparse axillary, pubic hair. MRI pituitary was normal in C1 and showed empty sella for C2, C3 and C4
Conclusion
The etiology and clinical features of hypopituitarism are variable. Awareness and early recognition in these cases is necessary for optimal management of the patient.

DOI: 10.1530/endoabs.81.EP818

EP819

Demonstration of the effects of asprosin on the sense of smell in female rats with hidden cookie test

Zeynep Dila Öz[1], Gö khan Zorlu[2], Fatih Tan[1], Gaye Gö ksu Avcu[1], Emine Kacar[1], Abdullah Yasar[3], Ihsan Serhatlioglu[2], Haluk Kelestimur[1] & Bayram Yilmaz[4]
[1]Firat University Faculty of Medicine, Physiology, Elazig, Turkey; [2]Firat University Faculty of Medicine, Biophysics, Turkey; [3]Fırat University, Vocational School of Health Services, Turkey; [4]Yeditepe university, School of Medicine, Turkey

Purpose
Asprosin is a novel glucogenic adipokine produced by the fibrillin 1 (FBN1) gene that is generated and released by white adipose tissue during fasting. Asprosin hormone has been shown to improve the sense of smell in wild-type mice by activating the OLFR734 receptor and decreasing the time it takes for them to discover hidden food. The purpose of this study was to determine the effects of asprosin on the sense of smell in female rats through the use of a hidden cookie test.
Materials and methods
Twenty-four female Sprague-Dawley rats were randomly divided into 2 groups ($n=12$) as control and asprosin. Asprosin and saline were intraperitoneally given at a dose of 500 ng/kg and 1 ml/kg to asprosin and control groups, respectively at 14.00 every day for eight weeks. The hidden cookie test was performed four times a day during ad libitum feeding, and the final experiment was repeated 24 h after fasting when all animals were in the estrous phase. Cookies (Chocapic, Nestle) were buried at a depth of 3 cm. They were recorded from 4 angles for 10 minutes. The finding time of the cookie was scored in seconds. T-test was used for the evaluation of the data. In all analyses, $P<0.05$ was considered statistically significant.
Results
In the hidden cookie test, the meantime of the control group was 445.29 ± 64.58 seconds while it was 450.45 ± 63.46 seconds in the asprosin group ($P>0.05$). Twenty-four hours after fasting, the average time in the asprosin group was 379.58 ± 55.04 while it was 208.83 ± 58.28 seconds in the control group ($P<0.05$).
Conclusion
It was found that there was no significant difference in the hidden cookie test performed when female rats were fed. However, asprosin hormone significantly increased the sense of smell due to the test performed after 24 h after fasting. Key words: Asprosin, adipokine, smell, hidden cookie test
Acknowledgment
This study was supported by TUBITAK (Project:220S744).

DOI: 10.1530/endoabs.81.EP819

EP820

Pre-validation study of alternative developmental neurotoxicity test using Sox1-GFP cell.

YongIn Kim, Sunhwa Jeong, Jimin Lee, KangMin Kim, Minsu Lee & Eui-Bae Jeung
Chungbuk National University, Laboratory of Veterinary Biochemistry and Molecular Biology, College of Veterinary Medicine, Cheongju-si, Chungcheongbuk-do, Rep. of South Korea

The chemically induced disturbance during the neurodevelopment stage could cause a serious disease. *In vivo* study is useful to discriminate against neurotoxic substances but is time-consuming and ethically problematic. So, we have previously established, developmental neurotoxicity test (DNT) *in vitro* method using Sox1-GFP. In this study we aimed to increase the predictability of discriminant function. The equation was statistically improved using thirty additional chemicals. Concomitantly, we conduct reproducibility assessment; inter- and intra- studies were carried out for fifteen chemicals by three experimenter and three independent laboratories. In this study, we correlated our prediction model with wider range of chemicals; 20 toxicants and 10 non-toxicants data was newly added to secure analytical accuracy. To establish a discriminant function, two factors, half inhibition concentration for cell viability (IC50) and half inhibition concentration for neuro-sphere area (ID50), were used. IC50 value was obtained by performing CCK-8 assay after chemical treatment on undifferentiated cells for 2 days. ID50 value was obtained by measuring both GFP intensity and neuro-sphere areas of differentiated cells as neural form which cell was exposed to chemical for 4 days. From the inter result obtained using the stated discriminant function gave 100% accuracy and from intra test it gave 96% accuracy. Inter- and intra- experiments were able to classify chemicals as toxic or non-toxic very equally. Conclusively we have established animal alternative DNT and showed that this test is a transferable, reproducible and accurate method. Therefore, we suggest that this method will be able to be a standardizing method as animal alternative.
Keyword: Developmental neurotoxicity test, *in vitro*, Sox1-GFP cell

DOI: 10.1530/endoabs.81.EP820

EP821

Preference of acromegaly patients for treatment attributes in Spain

Carmen Fajardo-Montañana[1], Cristina Álvarez Escolá[2], Betina Biagetti[3], Rogelio Garcí a Centeno[4], Raquel Ciriza[5], Laura Sanchez[6] & Marcos Díaz[6]
[1]Hospital Universitario de La Ribera, Endocrinology Department, Alzira (Valencia), Spain; [2]'La Paz' University Hospital, Endocrinology Department, Madrid, Spain; [3]Vall d'Hebron University Hospital and Vall d'Hebron Research Institute (VHIR), Universidad Autónoma de Barcelona, Diabetes and Metabolism Research Unit, Barcelona, Spain; [4]Gregorio Marañon Hospital, Endocrinoloy Department, Madrid, Spain; [5]Spanish Acromegaly Patient Association (Asociación de pacientes Afectados por Acromegalia), Huesca, Spain; [6]Pfizer S.L.U, Medical Affairs Department, Alcobendas (Madrid), Spain

Background
Acromegaly is a slowly progressive rare disease caused by an increase in growth hormone secretion that causes a subsequent rise in insulin-like growth factor (IGF-1), both contributing to the excessive growth of the extremities, soft tissues and organs, in addition to other comorbidities directly interfering with patient's quality of life. Acromegaly patients are concerned about their disease and their treatments, however, publications about patient's opinion towards their disease and treatments are scarce.
Objective
The aim of this study was to gain further insight into the Spanish acromegaly patients' perspective on their disease, unmet needs and treatment preferences.
Methods
A qualitative study was carried out to determine the attributes and levels of the quantitative. Two-hour-group interviews, comprising 4 and 5 adult patients each, took place in Madrid and Barcelona (September 2019). The group dynamics were conducted by an experienced moderator. The quantitative study was designed as a discrete choice experiment.142 patients were initially invited to complete the online survey; however, only 67 patients completed the questionnaire. Choice-based conjoint analyses were used to estimate the utilities and values for treatment attributes. Subject preferences were estimated at aggregated levels. Using a Bayesian hierarchical modelling, the percentage of levels and attributes were transformed in utilities.
Results
QoL stood out as the most important attribute for respondents (37%), and IGF-1 together with glucose blood level and tumour size control (Table. 1), were the most important attributes according to participants. The pain associated to the treatment administration method was a secondary attribute. Diarrhoea, administration methods and storage conditions were the less important attributes according to participants and were only relevant for the treatment choice.
Conclusion
Despite acromegaly patients showing a high degree of awareness about the importance of IGF1 levels and tumour size control, our results point out the great relevance that patients award to Health-Related Quality of Life. Notably, patients showed great concern about glycemic level alteration, as well as the

Table 1 Utilities summary

Importance of the choice	Attribute	Choice (%)
Key Attribute	Quality of life	37%
	IGF-1 level control	20%
Main attributes	Glucose levels control in blood	17%
	Tumour control	13%
Secondary attributes	Pain associated to the administration method	7%
	Adverse events: diarrhea	2%
	Administration methods	2%
	Storage conditions	2%

levels of IGF-1 and the tumor size. Patients' opinion should be taken in consideration when prescribing a treatment, as these patients show high knowledge and awareness about the management of their condition.

DOI: 10.1530/endoabs.81.EP821

EP822

Sheehan Syndrome effects on cardiovascular risk

Ameni Salah, Amel Maaroufi, Rihab Ajili, Asma Benabdelkarim, Maha Kacem Njah, Yosra Hasni & Koussay Ach
University Hospital Center Farhat Hached, Endocrinology Department, Sousse, Tunisia

Introduction
Sheehan syndrome has been for a long time the most frequent cause of hypopituitarism among women in developing countries, including Tunisia. Apart from hormonal deficits caused by SS, young women with SS are exposed to an increased risk of cardiovascular mortality. In this study, we aimed to evaluate the cardiovascular risk in patients with SS.
Patients and methods
This is a descriptive cross-sectional study. It was carried out in the Endocrinology department of the University Hospital Farhat Hached in Sousse, Tunisia, over a period of nine months, from July 2019 to March 2020. The estimation of the cardiovascular risk was made in patients who had no proven cardiovascular disease at the time of the diagnosis of SS, based on the Framingham score.
Results
Sixty five patients were included to the study. The mean age at diagnosis of SS was 48.2 $\pm$ 12.4 years. Thyrotropic and corticotropic insufficiency were present in 86.2% of our patients, followed by gonadotropic and lactotroph insufficiency in 72.3% and 38.5% of patients, respectively. Somatotropic insufficiency was explored by a dynamic test in only 8 patients, concluding with somatotropic deficiency in 10.8% of cases. A cardiovascular accident among first-degree relatives was noted in 10.7% of cases (5 cases of cerebrovascular accidents and 2 cases of myocardial infarction). Four patients had already proven cardiovascular disease at the time of SS diagnosis. The estimation of cardiovascular risk, using the Framingham equation, involved 39 patients. A very low, low or moderate cardiovascular risk was noted in 26.2%, 16.9% and 10.8% of patients, respectively. However a high cardiovascular was noted in 6,2% of patients. Four patients presented with coronary heart disease during follow-up. Three of the four patients, whose cardiovascular risk was considered moderate or high, presented with proven cardiovascular disease during follow-up. Furthermore, none of the patients whose cardiovascular risk was considered very low or low presented with subsequent cardiovascular disease. The difference between the two groups estimated using Fisher's exact test was statistically significant ($P=0.01$).
Discussion-Conclusion
Cardiovascular mortality is markedly increased in adults with hypopituitarism, and women are more affected than men. A number of factors contribute to the excess cardiovascular mortality including GH deficiency and untreated gonadotropin deficiency.

DOI: 10.1530/endoabs.81.EP822

EP823

Prevalence of benign and malignant tumors in patients with acromegaly

Iulia-Ştefania Plotuna[1,2], Daniela-Georgiana Amzar[1,2], Melania Balas[1,2], Ioana Golu[1,2] & Mihaela Vlad[1,2]
[1]Victor Babeş University of Medicine and Pharmacy, Timişoara, Romania; [2]Timiş County Emergency Clinical Hospital, Timişoara, Romania

Introduction
Acromegaly is an endocrine disease associated with an abnormal growth-hormone (GH) and insulin-like growth factor 1 (IGF-1) excess. Multiple studies demonstrated an association between these factors and pathways that play a major role in tumor proliferation, survival and resistance to anti-cancer therapies in many human malignancies.
Objectives
We wanted to study the incidence and types of tumors which are associated with Acromegaly.
Material and Method
We analyzed the data from all the patients who were diagnosed with Acromegaly between 2001 and 2021 in our Department of Endocrinology. Patient's data was collected retrospectively and included personal history, clinical examination, laboratory assessment and magnetic resonance imaging results. The study-group included 32 patients, aged between 20 and 64 years, 9 men (28,12 %) and 23 women (71,87 %). The mean age at Acromegaly diagnosis was 50+/-5,41 years old and mean age when the first tumor was diagnosed: 46+/-10 years old. GH and IGF-1 mean levels at diagnosis were 21,31 ng/ml and 639 ng/ml respectively. Acromegaly was controlled in 50 % of the patients after therapy.
Results:
Twenty-three(75 %) acromegalic patients were diagnosed with different forms of tumors and 15% of these were malignant. Four (44 %) men were diagnosed with tumors and all were benign. The most frequent tumors were multinodular goiter and benign prostatic hyperplasia. Eighteen (75 %) women were diagnosed with tumors, from which 20% (5 cases) were malignant. The most common benign tumor was multinodular goiter and the most frequent malignant tumor was papillary thyroid carcinoma. Acromegaly and diagnosis of tumors coincided in 52 % of the patients, most likely because screening for thyroid pathology was implemented. Among women diagnosed with cancer, one patient died as a result of this pathology.
Conclusions
Both women and men diagnosed with Acromegaly suffered more frequently form benign nodular goiter and only among women there were cases of malignant tumors.
Keywords: Acromegaly, Pituitary, Thyroid, Tumors

DOI: 10.1530/endoabs.81.EP823

EP824

What factors predict a favorable response to hormonal therapy in congenital growth hormone deficiency?

Nabila Rekik Majdoub, Kawthar El ARBI, Asma Zargni, Dhoha Ben Salah, Wafa Benothman, Mouna Elleuch, Mnif Fatma, Nadia Charfi, Mouna Mnif, Faten Haj Kacem Akid & Mohamed Abid
Hedi Chaker Hospital, Department of Endocrinology, Sfax, Tunisia

Introduction
Growth hormone (GH) treatment in congenital growth hormone deficiency (CGHD) is indicated to improve the prognosis of the statural prognosis. The aim of this study is to identify the predictive factors of a favorable response to GH therapy.
Patients & Methods
This is a retrospective study, conducted over a period of 27 years, including 30 patients with CGHD treated with hormonal therapy.
Results
The CGHD was diagnosed at a mean age of 8.8 $\pm$ 3.6 years with a male predominance. Only 2/22 patients reached the target height. The mean stature gain in standard derivations (SD) was 1.8 $\pm$ 1.07 SD. Severe growth retardation (86.7%) was positively correlated with stature response (2 vs 0.75 SD; $P=0.049$). The gain under hormonal treatment did not depend on the GH peak during stimulation tests, nor on the combined (33.3%) or total (73.3%) character of CGHD. The radiological assessment showed a significant association between pituitary stem abnormalities and a better response to GH (2.6 vs. 1.6 SD; $P=0.019$). The dose and duration of treatment as well as the target size did not influence the evolution under treatment. Only chronological age and delayed bone age at treatment initiation were positively correlated with a good response ($P=0.022$ and 0.042 respectively).

Conclusion
The results of GH treatment were more satisfactory on final height than on target height. Large-scale prospective studies are needed to validate the factors that seem to be involved in the statural response.

DOI: 10.1530/endoabs.81.EP824

EP825

Binasal hemianopsia with pituitary adenoma in a 15-year-old girl

Elyes Kamoun[1, 2], Imen Rojbi[1, 2], Sabrine Mekni[1, 2], Houaida Smadhi[3], Youssef Lakhoua[1], Ibtissem Ben Nacef[1, 2] & Karima Khiari[1,2]
[1]Hospital Charles Nicolle, Endocrinology Department, Tunis, Tunisia; [2]Faculté de Médecine de Tunis, Tunis, Tunisia; [3]Hopital Regional de Beja, Beja, Tunisia

Introduction
Pituitary adenomas represent 10 to 20% of intracranial tumors. In children, craniopharyngioma are the most common tumor of the sellar region. The symptoms can include headache, vomiting, pituitary deficiency and in pituitary adenomas, hormonal excess. The visual examination can find a visual field defect such as a bitemporal hemianopsia. We present a rare case of a pituitary adenoma in a 15-year-old girl with binasal hemianopsia.
Observation
A 15-year-old girl presented frontal headaches and vomiting occurring for a year before her referral to our department. At physical examination, she had a normal blood pressure, and clinical visual field assessment suggested an inferior and right nasal quadrianopsia. Firstline imaging investigations with cerebral tomography discovered a pituitary adenoma. A biopsy with immunohistochemistry was performed confirming the diagnosis of a plurihormonal LH and prolactin sparsely granulated pituitary adenoma. The magnetic resonance imaging confirmed intra and suprasellar adenoma measuring 26.4*20*21mm abutting optic chiasma and the third ventricule. On hormonal investigations, she had a corticotropin deficiency with a peak cortisol after insulin tolerance test at 300 nmol/l and ACTH levels at 26 pg/ml. She didn't have thyrotropin deficiency nor diabetes insipidus. Her menses were irregular, with a secondary amenorrhea of one year at three years after menarche. There wasn't any sign of hormonal excess, the prolactin levels were at 33µg/l, probably secondary to the pituitary stalk compression. A type 1 multiple endocrine neoplasia was excluded as there were no family history of endocrine disease and parathormone levels were normal. The visual field assessment concluded to bilateral defects with a pattern of an incomplete binasal hemianopsia. She was put on 15 mg of hydrocortisone and was referred to surgery.
Conclusion
The suprasellar extension of pituitary adenoma abutting the optic chiasma is responsible of a bitemporal hemianopsia as the optic nerves in the chiasma are responsible for the vision in those fields. A binasal defect can be seen in ophthalmologic pathology, but is extremely rare in pituitary adenoma. Pituitary adenoma prevalence in children and adolescents is less than 5%. This case represents an unusual clinical presentation of a pituitary tumor confirmed to be a pituitary adenoma in a 15-year-old girl with an exceptional optic defect.

DOI: 10.1530/endoabs.81.EP825

EP826

Looking for a safe and effective drug: the troubled journey of a Cushing's Disease patient

Angelo Milioto[1], Francesco Cocchiara[2], Giuliana Corica[2], Keyvan Khorrami[1], Federica Nista[1], Diego Criminelli[3], Gianluigi Zona[3], Diego Ferone[1] & Federico Gatto[2]
[1]University of Genoa, Department of Internal Medicine and Medical Specialties, Endocrinology Unit, Genova, Italy; [2]IRCCS Ospedale Policlinico San Martino, Endocrinology Unit, Genova, Italy; [3]IRCCS Ospedale Policlinico San Martino, Neurosurgery Unit, Genova, Italy

Cushing's Disease (CD) is severe clinical condition due to an ACTH-secreting pituitary tumor. Here we present the case of a 25-years old male who came to our attention for hypertension, moon face, acanthosis nigricans, abdominal purple striae and central obesity. The diagnosis of CD was based on the presence of high plasma cortisol after dexamethasone suppression test and elevated urinary free cortisol levels (UFC, 6-fold higher the upper limit of normality (ULN)). The pituitary MRI revealed a small lesion (5.5 mm), which was removed by transsphenoidal surgery, and it was later on confirmed as a corticotroph tumor at the pathology report. Surgery led to a slight improvement of symptoms. However, two months after the intervention, the patient experienced a worsening of the clinical picture, and the following biochemical assessment was suggestive of an early disease relapse. First, pasireotide was administered, although with low efficacy in reducing cortisol secretion. Then, a novel steroidogenesis-inhibitor, available only for investigational use in the context of a clinical trial, was started, but the patient withdrawn due to safety concerns. Therefore, low dose metyrapone was prescribed. However, severe gastrointestinal side effects occurred, and the drug was discontinued after few months. Furthermore, during imaging follow-up, the suspicion for a recurrent pituitary lesion was raised. Following a multi-disciplinary discussion, inferior petrosal sinus sampling was performed, confirming the disease recurrence. Based on the expected low success rate, the team avoided a second surgery. Ketoconazole (600 mg/day) was then administered, leading for the first time to UFC normalization. Unfortunately, the patient developed severe nausea, headache and fatigue, and the dosage was reduced (400 mg/day). As expected, cortisol levels raised and cabergoline (1 mg/week) was then added. Combination therapy led to partial disease control, but a further disease relapse was observed. Therefore, radiosurgery was performed, and the newly available steroidogenesis-inhibitor, osilodrostat, was started as bridge therapy due to persistent hypercortisolism. Osilodrostat was titrated up to 5 mg/day, leading to biochemical control (UFC normalization) with no side effects. At 7-months follow-up, the patient is currently proceeding with this latter treatment schedule, with no safety issues. Our case report highlights the difficulties encountered during the management of CD. The patient underwent surgery, radiotherapy and six different types of drugs before achieving disease control without adverse events. Therefore, clinical predictors of drug safety and efficacy are strongly needed in a challenging disease such as CD.

DOI: 10.1530/endoabs.81.EP826

EP827

Management of SIADH in patients with acute admissions to hospital: a single centre experience

Vinit Shah, Francesca Neale, Dorina Condurache, Saranya Baleswaran, Amy Price & Ian Seetho
London North West University Healthcare NHS Trust, United Kingdom

Background
Hyponatraemia is a common electrolyte abnormality that is associated with significant morbidity and mortality in patients admitted to hospital. Fluid restriction is the recommended treatment option for syndrome of inappropriate antidiuretic hormone secretion (SIADH), a common cause of hyponatraemia with limited evidence for alternative treatment options. The aim of our study was to share the experience of our hospital in the successful management of SIADH where we also use oral sodium chloride and urea salts in addition to fluid restriction.
Methods
We collected data for patients with severe hyponatraemia (Serum $Na^+ < 125$ mmol/l) identified by our biochemistry lab from all samples they received. Suitable patients were identified over a two-week period. We included all those patients who were admitted to our hospital for any diagnosis and excluded those who were discharged from the emergency department or for tests completed as out-patients. Relevant data was collected from medical paper notes and drug charts with laboratory data available from patients' electronic patient records. The treatment protocol for SIADH is set out by the hospital guidelines with fluid restriction as first line followed by addition of oral sodium chloride and/or urea salts as second line treatment options. Successful treatment is defined as improvement in serum sodium to >125 mmol/l.
Results
Thirty-eight patients with a mean age of 77 years were identified. The most common reason for admission was confusion and falls (24% and 18% respectively). Approximately one-third of the cases of hyponatraemia was due to SIADH ($n=14$). For patients with SIADH, successful treatment with fluid restriction alone was required in 43% of cases, combined with oral sodium chloride in another 43% of cases and only 7% required triple treatment combination of fluid restriction, oral sodium chloride and urea salts.
Conclusion
SIADH is a common cause of hyponatraemia in patients with acute hospital admissions. Fluid restriction alone is an effective treatment strategy in many of these patients. Additional solute intake is thought to increase renal free water

clearance and increase electrolyte diuresis. The study demonstrates that additional solute intake in the form of oral sodium chloride or urea salts are potential additional treatment options in those resistant to fluid restriction alone to correct hyponatraemia and their potential role in management of complex cases where strict fluid restriction is contraindicated.

DOI: 10.1530/endoabs.81.EP827

EP828

The third case report of pituitary apoplexy complicated by a subarachnoid hemorrhage and ventricular extension

Carlien De Herdt[1], Kamerling Niels[2] & Christophe De Block[1]
[1]Universitary Hospital of Antwerp, Endocrinology-Diabetology-Metabolism, Edegem, Belgium; [2]Universitary Hospital of Antwerp, Neuro-Endocrinology, Edegem, Belgium

Introduction
Pituitary apoplexy is a rare endocrine emergency due to hemorrhage of the pituitary gland. The clinical presentation depends on the extent of bleeding and can deteriorate into a life-threatening condition if complicated by a subarachnoid hemorrhage, as previously described in 2 cases.
Case Description
A 60-year-old woman presented herself at the emergency department because of confusion for several hours. Clinical examination revealed anisocoria with mydriasis of the right pupil in an agitated woman able to move her four limbs but unable to execute commands. Seven months earlier, a macroprolactinoma with a craniocaudal diameter of 28 mm and compression of the optic chiasma was diagnosed, resistant to treatment with cabergoline and complicated by panhypopituitarism. CT scan of the brain was urgently performed and revealed an extensive suprasellar hemorrhagic mass and a subarachnoidal bleeding with extension to the lateral, third and fourth ventricles. The patient was sedated to enable placement of an external ventricular drain. CT angiography excluded an arterial aneurysm. The day after admission the patient awakened and executed commands. Visual field examination revealed bitemporal hemianopsia. MRI of the pituitary one month after admission showed a heterogenous suprasellar mass with a craniocaudal diameter of 28 mm. Endoscopic transsphenoidal resection of the pituitary mass was performed and anatomopathological examination showed necrotic tissue. Pituitary MRI 3 months postoperative revealed an important resorption of the hemorrhagic zone with a residual collection at the bottom of the sella turcica. Whether this collection is residual hematoma or adenoma could not be differentiated. Visual field examination 3 months postoperatively showed improvement, but was not normal with a bitemporal quadrantanopia. Panhypopituitarism persisted.
Conclusion
This case report described a woman with a pre-existing macroprolactinoma and a life-threatening presentation of pituitary apoplexy complicated by a subarachnoid bleeding with ventricular extension. Besides having a macroprolactinoma, this patient had no predisposing factors for apoplexy since it has shown that dopamine agonists are not associated with an increased incidence of apoplexy. Pituitary apoplexy has to be considered in an angiographically negative subarachnoid hemorrhage. However in every patient presenting with a subarachnoid bleeding, even if a medical history of a pituitary adenoma, a cerebral aneurysm always have to be excluded since this is much more frequent. The endocrine prognosis is poor because of frequently irreversible pituitary damage. This is the third case of a pituitary apoplexy complicated by a subarachnoid hemorrhage and ventricular extension with a cerebral aneurysm being excluded.

DOI: 10.1530/endoabs.81.EP828

EP829

Hormonal and regional complications of craniopharyngomas

Khadra Faraoun[1] & Chentli Farida[2]
[1]Université Oran 1, Endocrinology, Oran, Algeria; [2]Algier University, Oran, Algeria

Background
The craniopharyngioma is a non-endocrine tumor, developed along the infundibulo-pituitary axis, from the 3rd ventricle to sphenoid, histologically benign but locally invasive. It is a tumor with serious complications because of its location, its considerable potential for extension, its tendency to recur, and its adhesions to neighbouring structures. Our aim is to assess hormonal, neuro-ophthalmological and metabolic complications at the diagnosis of craniopharyngiomas.
Patients and methods
It is a multicentre Cross-sectional descriptive study in the town of Oran, with prospective and retrospective data collection. MRI, hormonal, biochemical and ocular tests, made the diagnosis. Data entry and analysis were performed with CDC Epi Info version 6 (USA), SPSS 20, Statistica10.
Results
In our study, we collected 86 non-adenomatous tumours, among them 26 craniopharyngiomas (35%), sex ratio men/women at 1.3. Average age at 17.3 ± 13.5 years (2-56). Mean consultation time 20.5 ± 25.3 (1-96) months (range). Circumstances of discovery: headaches - visual disturbances (79.8%), growth retardation (15.4%) and hypogonadism in adults (20.4%). Average dimensions (mm ± SD): average height 39.1 ± 17.4, transverse diameter 32.2 ± 14.9, antero-post diameter 36.0 ± 17.5, extremes 15-95 mm. Extensions (percentage): Supra sellar (88.5), Infra sellar (46.2), posterior (23.1), Multidirectional extensions (38.5). Anterior pituitary insufficiency 96.1%, multiple anterior pituitary deficiencies 77.5%, hypothalamic syndrome 30.8%, epilepsy 11.5%, diabetes insipidus 23%. Neuropsychiatric complications (55.1%), ophthalmological (79.8%), blindness 23%, hydrocephalus 68.7%.
Discussion
Craniopharyngiomas are accompanied by significant pituitary, hypothalamic and neuro-visual morbidity. The consequences of a delay in diagnosis increases the frequency and severity of complications, hence the need for early diagnosis in order to control this morbidity, the burden of which is considerable on the health system.

DOI: 10.1530/endoabs.81.EP829

EP830

'Features of cardiovascular complications in patients with cushing syndrome in the republic of uzbekistan (register data)'

Gavhar Jabborova[1] & Zamira Khalimova[1]
[1]Republican Specialized Scientific Practical Medical Center of Endocrinology of Public Health Ministry named by acad. Ya.Kh. Turakulov, Tashkent, Uzbekistan

The purpose of the study
Is to study features of cardiovascular complications in patients with Cushing syndrome in the Republic of Uzbekistan (RUz).
Material and research methods
In the period of 2002 to 2021, 317 patients were installed with the following clinical forms of Cushing syndrome (CS): 1) ACTH-dependent CS (ACTH-DCS) - 258 (81.3%) patients, of which women -174 (54.8%), men - 84 (26.4%), 2) ACTH independent CS (ACTH-iCS) -51 patients (16.08%) of women - 41 (12.9%), men - 10 (3.15%). 3) Ectopic CS (ACTH-ECS) -8 patients (2.5%) of women-5 (1.5%), men-3 (0.94%). The average age during the manifestation of men amounted to 26.38 ± 3.4 years, women - 27.58 ± 3.4 years. The illness of the disease ranged from 4 months to 25 years. 10 patients amounted to a control group. The study used clinical and biochemical, hormonal studies (serum, urine), functional tests, as well as instrumental (neurophthalmological, radiological - MRI pituitary gland, MSCT of adrenal glands, X-ray absorption densitometry and statistical techniques.
Results
The most frequent complications of the CS were cardiovascular complications (CVC), which developed in 113 (48.9%) patients with a predominance of female 74 (61.3%).. Among them, malignant arterial hypertension, acute vascular disasters in the form of myocardial infarction took place more often. In the 1st group of patients with ACTH- DCS total in men, the CVC frequency was 45 (53.5%), and among women - 80 (45.9%), only 125 cases out of 258 (48.4%). In the 2 group of patients with ACTH-iCS among men the CVC frequency was 2 (20.0%), and among women - 13 (31.7%), only 15 cases out of 51 (29.4%). And, finally, in a 3group of patients with ACTH- ECS in men, the CVC frequency was 1 (33.3%), and among women - 1 (31.7%), only 2 cases of 8 (20%).
Conclusions
Of 317 patients with CS in 142 (44.8%) cardio-vascular complications were recorded and more often in the 1 st group of patients.

DOI: 10.1530/endoabs.81.EP830

EP831

Acromegaly in the elderly patients

Dayssem Khelifi, Nadia Khessairi, Ameni Terzi, Wafa Grira & Melika Chihaoui
Rabta's University Hospital, Endocrinology's Department, Tunis, Tunisia

Introduction
Pituitary adenomas in people over 65 represent less than 10% of all pituitary adenomas, 80% of which are non-functional. Somatotropic adenomas remain very rare. The interest of our study is to describe the clinical, paraclinical and therapeutic profile of cases of senile acromegaly.
Patients and methods
This is a retrospective study of four senile acromegaly patients followed in our endocrinology's department.
Results
We report four cases of acromegalic patients, one woman and three men, respectively aged 75, 68, 65 and 69 at the time of diagnosis. Two had been diabetic and hypertensive for 05 years. The circumstances of discovery were a tumor syndrome in two patients, a dysmorphic syndrome in one patient and digestive symptoms secondary to a tumor process in another patient. The diagnosis was confirmed by elevated IGF1, a paradoxical GH response on OGTT and a disturbed GH cycle (two diabetics). Radiological exploration by pituitary MRI showed that it was a macroadenoma in 100% of cases with invasion of the cavernous sinuses and compression of the optic chiasm in two cases. The impact assessment revealed: corticotropic insufficiency (2 cases), bilateral visual field impairment (2 cases), moderate to severe sleep apnea syndrome (4 cases), hypertrophic heart disease (2 cases), arthropathy peripheral (2 cases), hypertriglyceridemia (1 case), a stenotic tumoral process inaugurating the disease in one patient and polyposis colon in two other patients, a multinodular goiter (1 case) and a TIRADS 2 nodule (2 cases). Therapeutically, the patient was treated surgically via the transphenoidal approach with simple post-operative follow-up. Given the operative risk and the non-motivation of the two other patients for surgery, they were put on a somatostatin analogue with a favorable outcome. The fourth patient was lost to sight.
Conclusion
Somatotropic adenomas in the elderly patients are rare, characterized by a diagnostic delay. Surgery, if possible, remains the treatment of choice for acromegaly in the elderly, but somatostatin analogues have also shown their effectiveness in the treatment of these patients.

DOI: 10.1530/endoabs.81.EP831

EP832

Features of the incidence of postoperative complications in patients with transsphenoidal pituitary adenectomy

Gulmira Inomova & Zamira Khalimova
TashPMI, Tashkent, Uzbekistan

Target
To study the incidence of postoperative complications in patients with transsphenoidal pituitary adenoectomy.
Materials and research methods
180 cases of PA subjected to TPA for the period from 2018 to 2020 were analyzed. Of these, 102 (56.6) women, 78 (43.3) men, patients were divided into two alternative groups: the first group - 93 (51.6%) patients with macroadenomas - 42 (45.2%) men, women 51 (54.8%), the second (comparison group) - 87 (48.4%) with microadenomas of men - 35 (40%), women - 52 (60%) of the pituitary gland. The age of the patients ranged from 30 to 59 years. The levels of hormones STH, IGF-1, ACTH, cortisol, prolactin, TSH, fT4, LH, FSH, estradiol, progesterone according to indications, MRT/CT of the chiasmal-sellar area and the state of the organ of vision were studied.
Results
Patients were distributed as follows: depending on the hormonal activity of patients with adrenocorticotropic hormone secreting Cushing's syndrome-60, acromegaly-60, inactive pituitary adenoma-60; depending on the size of the formation: 93 (51.6%) were with macroadenomas, 87 (48.3%) with pituitary microadenomas. An analysis of the incidence of postoperative complications in the short term (1 month) revealed that in 81 (45%) patients with hypopituitarism; hypothyroidism in (70)39%; hypogonadism in 50(28%); diabetes insipidus in 7(4%); transient diabetes insipidus in 11(6%); visual acuity deterioration in 2 (1.2%) patients and liquorrhea in 3 (5.4%) patients. At the same time, there was a normalization of elevated hormone levels in 133 (74%) patients; 30% improvement in vision; lack of disease dynamics in 47 (26%). Despite the persistent phenomena of hypopituitarism 47(26%) and diabetes insipidus 11(6%), which were mainly observed in 165(92%) patients with macroadenomas and did not depend on the organ activity of the formation (against 54(30%) cases with microadenomas). In the long-term follow-up of patients after TPA (t 3 months to 1 year), an improvement in pituitary function was noted in the form of restoration of gonadotropic insufficiency, phenomena of transient diabetes insipidus and improvement in hypertensive cephalgia.
Conclusion
The frequency of immediate and long-term complications in most cases is observed in pituitary macroadenomas and does not depend on the hormonal activity of the adenoma.

DOI: 10.1530/endoabs.81.EP832

EP833

'The frequency of postoperative hypopituitarism in patients with non-functional pituitary adenomas (NFPA) after transnasal hypophysectomy'

Malika Mirtukhtaeva[1] & Urmanova Yulduz[2]
[1]Republican Specialized Scientific Practical Medical Center of Endocrinology of Public Health Ministry named by acad. Ya.Kh. Turakulov, Tashkent, Uzbekistan; [2]Tashkent Pediatric Medical Institute, Tashkent, Uzbekistan

The purpose of the study
is to study the frequency of postoperative hypopituitarism after transnasal hypophysectomy (THE) in patients with pituitary adenomas.
Material and methods
Under our observation there were 24 patients with NFPA, of whom women were 14, men - 10. The average age of patients was 36.4 years. Total of 24 patients were performed for the period from 2016 to 2021 33 surgery in the neurosurgery department., of which THE - 32, 1 - bifrontal craniotomy. At the same time, 3 patients were 2 THE, in 3 - 3 THE, 4 patients with TGE also received radiation therapy. The whole patients were performed by research complex, which included radioimmune hormonal (STH, IGF-1, Prolactin, LH, FSH, TSG, ACTH, Cortizol, etc.), ophthalmological (Eye bottom, field of view) and X-ray studies (CT, MRI of the Turkish saddle).
Results
According to our data, postoperative panhibitionituitarism (deficiency of STH, LH, FSH, ACTH + Diabetes insipidus) developed in 6 patients (25%), postoperative partial hypopituitarism (deficiency of STH, LH, FSH) developed in 11 (45.8%) and 7 - STH deficiency (29.1%) developed. Thus, the most pronounced neuroendocrine disorders after THE were detected in 6 (25%) patients.
Conclusions
1) In patients with adenomas of pituitary gland subjected to THE, it is recommended to monitor the levels of all tropic and peripheral hormones of pituitary glands both in the early and later postoperative periods. 2) patients with pituitary adenomas after THE need substitution hormone therapy with appropriate drugs depending on the level of hormones (desmopressin, sex and thyroid hormones, corticosteroid preparations, growth hormone).

DOI: 10.1530/endoabs.81.EP833

EP834

'Case of re-growth of aggressive giant non-functional pituitary adenoma with panhypopituitarysm in 28-years old woman'

Urmanova Yulduz[1] & Malika Mirtukhtaeva[2]
[1]Tashkent Pediatric Medical Institute, Tashkent, Uzbekistan; [2]Republican Specialized Scientific Practical Medical Center of Endocrinology of Public Health Ministry named by acad. Ya.Kh. Turakulov, Tashkent, Uzbekistan

The purpose of the study
Is to research case of re-growth of non-functional giant pituitary adenoma (NFPA) with panhypopituitarysm in 28-years old woman
Material and research methods
Patient Karimova N, was born in 1994 in Namangan region. Clinical diagnosis: Non-functional giant pituitary adenoma with total variant of growth. Status after transnasal selective adenomphysisectomy (12.04.16). Re-growth of tumor. Second transnasal selective adenomphysisectomy (26.11.2021). Complications. Panhypopituitarysm. Secondary hypogonadism, hypocorticism, hypothyroidism. Growth hormone deficiency. Bitemporal hemianopsia. Functional

hyperprolactinemia. Primary infertility. Secondary amenorrhoea. The patient considers himself to be ill from 2015 year after marriage. She was operated on the occasion of pituitary adenoma with supra-infra-latero-sellar growth. Micro-cellular chromophobe adenoma was histologically determined. In early post-operative period the improvement of vision was marked. In late postoperative period neuroendocrine disorders were left without dynamics. As the patient wasn't observed regularly, she received Kabergolin 5 mg twice in week during 6 months. The patient refused from radiotherapy. The worsening of state was marked for the last 6 months, when the above mentioned complaints increased.
Results of the study
Height is 156 sm, weight is 55 kg. BMI = 24, 4 kg/m2. The skin coverings are pale, dry, clean. A/*P* = 110/70 mm.mer.e. Puls rate = 72 beats per min. In blood plasma GH – 0,13 ng/ml (norma 2-5 ng/ml), IGF-1 - 88 nmol/l (norma 300 nmol/l), FSH-0,94 Med/l, LH – 0, 46 MEd/l (norma 3-8 mME/l), cortisol in the morning – 55,1 nmol/l (norma 260-720 нмоль/л,), prolactin – 307 ng/ml (norma 7-8 ng/mi), estradiol – 17, 4 pg/ml. Ophthalmologist. Bitemporal hemianopsia on white color, absence of visual fields on green and red colors from both eyes. MRI : Pituitary macroadenoma with the size 5,6 sm x 4,3 sm x 5,4 sm The patient was operated again in our clinic. In the early postoperative period the patient was marked improving of visual fields.
Conclusions
1. For NFPA with small cellular chromofobe cells in patients of reproductive age it is typical aggressive re-growth of tumor. 2. For prevention of re-growth of giant pituitary tumor after surgery it is necessary to conduct for patient radiotherapy.

DOI: 10.1530/endoabs.81.EP834

EP835

Cushing syndrome and disease: A doctor of philosophy study conducted by a patient

Margaret McBride
Lancaster University, School of Medicine & Health Sciences, Bailrigg, United Kingdom

Introduction
Prior to and since the onset of my Doctorate study in 2019, a plethora of on-going research including my own has been conducted into the diagnosis, treatment, and management of Cushing syndrome (CS), and disease (CD). These conditions continue to challenge physicians not only in the diagnosis but how to treat their patients. The wide clinical spectrum of CS and CD produces a medical dilemma as patients' symptoms, can vary. The typical Cushingoid features which are referred to as the classic symptoms are not always obvious when a patient presents. There are population groups which have increased incidence of CS which includes obesity, diabetes, and osteoporosis. The diagnostic approach is a 3-step investigative process and includes *a)* a physician's knowledge of the signs and symptoms, which is crucial to make *b)* a definitive diagnosis of CS. The third step of this process is *c)* to identify the reason for excess cortisol.
Learning Process
The learning process during this study has been exponential and led to a clearer understanding as to why it took so long for my physicians to make a definitive diagnosis of initially CS and then CD. This personal Cushing's journey of study revealed the reasons for the twists and turns on the 'bumpy,' road to diagnosis, treatment and then remission. Comparing other patients experiences during my study with my own, provided an understanding why we experience pain, changes in our personality, fatigue, a reduction in quality of life (QoL), and in most cases, irreversible comorbidities, my own being osteoporosis. During the process of study, I endeavoured to use my knowledge and skills as a Health Professional, promoting awareness through conference presentations and publications. On the long road to remission, I discovered the importance for Health Professionals, particularly General Practitioners and the public, to recognise patients' unmet needs.
Study Conclusions
By taking a more patient-centred approach including time to listen to their patients, in parallel with the well-established biochemical and imaging tests would increase early diagnosis and treatment.
Recommendations
Recommendations included identifying target audiences, examples women's clinics, and methods of screening obese and diabetic patients. Increase in using advanced technologies such as artificial intelligence in identifying early signs, example osteoporosis. Virtual learning platforms for educating Health Professions, extensive use of thematic analysis in QoL questionnaires and media coverage to raise awareness.

DOI: 10.1530/endoabs.81.EP835

EP836

Metabolic abnormalities profile of non-functioning pituitary adenomas

Wahiba ABDELLAOUI[1], Imane Assarrar[1], lamiae zarraa[1], soumiya berrabeh[1], Siham ROUF[1, 2] & Hanane Latrech[1,2]
[1]Mohammed VI University Hospital, Medical School, Mohammed the First University, Department of Endocrinology-Diabetology-Nutrition, OUJDA, Morocco; [2]Laboratory of Epidemiology, Clinical Research and Public Health, Faculty of Medicine and Pharmacy of Oujda, Mohammed the First University, Oujda, Morocco

Introduction
Metabolic abnormalities are common in pituitary adenomas and metabolic targeting is becoming a new therapeutic approach to the management of most tumor pathologies, especially pituitary tumors. The objective of this work was to assess the metabolic profile of non-functioning pituitary adenomas.
Material and methods
A retrospective and descriptive study, over a period of 6 years, conducted in the Endocrinology-Diabetology and Nutrition department of Oujda in the eastern of Morocco. The study included 24 patients with histologically confirmed non-functional pituitary adenoma.
Results
The mean age was 50 ± 11.2 years, with a female predominance (58.3% of cases). The average duration of the disease was 1.9 ± 3.6 years. The clinical examination found 50% of the patients to be overweight and 20.8% were obese. The metabolic work-up showed type 2 diabetes in 20.8% of cases and pre-diabetes in 33.3%. Hyperuricemia was found in 16.6% of patients. On the lipid panel, mixed dyslipidemia was revealed in 20.8% of the patients, hypertriglyceridemia and hypoHDLemia < 0.35 g/l were confirmed respectively in 25% of cases and hypercholesterolemia in 12.5% of patients.
Conclusion
Metabolic abnormalities associated with non-functioning pituitary adenomas are correlated with disease progression and prognosis. The evaluation of metabolic status should be emphasized during treatment of pituitary adenoma and control of metabolic abnormalities should be added to their current therapies.
Bibliography
Metabolic abnormalities in pituitary adenoma patients: a novel therapeuthic target and prognostic factor; YangDiabetes MetabSyndr Obes. 2015; 8: 357361

DOI: 10.1530/endoabs.81.EP836

EP837

Kallmann's Syndrome: case report

Rokya Abdel Aziz, Heba Moustafa, Soad Sultan, Randa Salam, Ola El Garhi, Iman Tohamy, Aya Taraby & Amira Nashat
Cairo University, Internal Medicine, Endocrinology, Cairo, Egypt

Introduction
Kallmann syndrome, a rare genetic disorder, refers to the association between hypogonadotropic hypogonadism and anosmia or hyposmia due to abnormal migration of olfactory axons and gonadotropin-releasing hormone producing neurons It can be autosomal dominant, autosomal recessive, or X-linked inheritance.
Case report
A 16-year-old male student, presented to endocrinology unit with delayed puberty. He was born to consanguineous parents and had normal delivery. He had normal developmental mile stones. Bilateral cryptorchidism was discovered at age six, associated with hyposomia but no hearing defect or oral cavity abnormalities. He was diagnosed with anosmia. Skull magnetic resonance imaging (MRI) revealed hypo plastic olfactory bulbs and shallow olfactory grooves, along with a normal pituitary gland and a normal pituitary stalk. No history of deepening of voice or morning erection Physical examination: Height : 164 cm, arm span was 169 cm, BMI: 17, no gynecomastia Genital examination showed Tanner stage 1 (penis 3 cm, empty scrotum at time of examination with no corrugation & absent axillary & pubic hair) Neurologic examination was otherwise unremarkable except for decreased sense of smell.
Investigations
ACTH:12 pg/ml(10-60), TSH:3 mIu/l(0.4-5), PRL was 13 ng/dL(N: < 20 ng/dl), FSH : 0.71 IU/ml (1.4-18), LH :0.1 IU/ml (Adult:1.7-8.6, prepubertal up to 6), Total Testosterone:1.79 ng/ml (> 2.5 ng/ml) Scrotal ultrasound revealed: both testes are ectopic in location rt :at the RT inguinal canal, LF seen in left scrotal neck, both tests are small in size for patient age RT 13x5.8x13.6 mm/lF 10x5x11.3 mm Chromosome analysis showed 46, XY He was prescribed human chorionic gonadotropin 5000 IU weekly for 6 weeks and testosterone cream daily, with a 25 mg of intramuscular testosterone injection and were then increased by

25 mg every two weeks Regular follow-up showed a change in voice and appearance of coarse pubic hair. Morning erections was reported, the testes and penis increased in size respectively (testes = 2 cc, phallus = 4 cm). Serum testosterone increased to 1.5 ng/ml
Conclusion
Clinical abnormalities during childhood such as cryptorchidism, anosmia or pubertal delay should be considered warning signs to start diagnosing Kallmann's syndrome. Early diagnosis triggers the initiation of multidisciplinary care in Pediatrics and adolescent medicine Timely treatment is relevant to restore metabolic, bone, sexual balance and psychosocial effects. Gonadotropin and pulsatile GnRH therapy are the treatment of choice to induce fertility Spermatogenesis can be induced in the majority of these patients and fertility rates are above 50%.

DOI: 10.1530/endoabs.81.EP837

EP838

'The functional status of pituitary-gonads-cortex axis in women on fertile age with ACTH-depended Cushing syndrome'

Zamira Khalimova[1] & Oydin Irgasheva[1]
[1]Republican Specialized Scientific Practical Medical Center of Endocrinology of Public Health Ministry named by acad. Ya.Kh. Turakulov, Tashkent, Uzbekistan

Aim
– to study the functional status of pituitary-gonades-cortex (PGC) axis in women with Cushing syndrome (CS)
Materials and methods
Weevaluated 25 women with ACTH-depended CS without other associated pathology. Mean age of patients was 28,3 years-old.. All patients have complaints to amenorrhea and primary infertility. Control group constituted by 20 healthy women with same age All patients underwent clinical and biochemical evaluations including endocrine check, lipids profile, hormonal profile in 14 day of menstrual cycle (LH, FSH, prolactin, free testosterone, estradiol, progesterone, etc), genitalia ultrasonography, electroencephalography (EEG), height, weight, BMI, waist circumference (WC), hip circumference (HC), waist-hip ratio, questioning and other studies.
Results
The investigation ofhormonal profileshowed anovulation in 19 patients (76%) (mean LH ranged 3,7 ± 1, 2 mIU/l, FSH 4,4 ± 1,5 mIU/l) in 14 day of the menstrual cycle and high range of free testosterone levels (mean 3,6 ± 0,3 ng/ml). Besides that, all patients have hypercortisolemia. ($P < 0{,}05$). The investigation of levels of estradiol and progesterone in 7,14, 21 days of menstrual cycle showed of their partial decrease. Most of the patients had central obesity with BMI > 35 kg/m^2. WC was in normal range 104,3 ± 7, 4 cm, HC = 85, 6 ± 5,3 cm, whereas waist-hip ratio > 1, 22. Blood tests showed dyslipidemia in all patients (100%).
Conclusions
Mostfertilewomen with ACTH-DCS (76%) have anovulation with high range of free testosterone in all patients with partial decrease of estradiolum, progesterone (secondary hypogonadism).

DOI: 10.1530/endoabs.81.EP838

EP839

Diagnosis of Kallmann syndrome in adulthood

Elyes Kamoun[1, 2], Sabrine Mekni[1, 2], Meriem Adel[1], Imen Rojbi[1, 2], Ibtissem Ben Nacef[1, 2], Nadia Mchirgui[1, 2] & Karima Khiari[1,2]
[1]Hospital Charles Nicolle, Endocrinology Department, Tunis, Tunisia; [2]Faculté de Médecine de Tunis, Tunis, Tunisia

Introduction
Kallmann syndrome is a rare genetic condition characterized by the association of a hypogonadotropic hypogonadism and anosmia. It results from the failure of GnRH cells to migrate to the hypothalamus and lack of development of the olfactory bulb. The main symptom of Kallmann syndrome is delayed or incomplete puberty usually associated with an impaired sense of smell. We herein describe a case of Kallmann syndrome discovered at the age of 57 years old.
Observation
We report the case of a 57 years old man, with a history of a pathologic fracture, referred to our department for exploration of gynecomastia. The patient didn't reveal any symptoms such as erectile dysfunction or reduced sex drive, only an anosmia lasting since his youth. Physical examination revealed a grade 2 bilateral gynecomastia, a blood pressure of 150mmHg over 90mmHg. Examination of the external genital organs showed normal pubic hair, a micropenis measuring 5 cm and hypotrophic testis. On hormonal investigations, his testosterone levels were at 0,442 ng/ml, his LH levels were at 0,05 mUI/ml and his oestradiol levels were at 20,55 pg/ml (< 62 pg/ml in male). His prolactin levels were normal at 2,68µg/l. Corticotropin and thyrotropin deficiency were excluded. On imaging investigations, he had an osteoporosis with a T-score at -5,2 and hypotrophic non nodular testis. The magnetic resonance imaging of the brain couldn't be performed as the patient has metallic orthopedic devices. He was put under calcium, vitamin D, bisphosphonates and testosterone therapy after eliminating contraindication.
Conclusion
This case highlights a non-classical presentation of a Kallmann Syndrome discovered during the investigations of gynecomastia. The delay of diagnosis was due to the reluctance of the patient, explaining with the spontaneous onset of puberty, the late diagnosis at this age. The psychological impact of this disease could have been prevented with an early treatment.

DOI: 10.1530/endoabs.81.EP839

EP840

Evaluation of neuroendocrine dysfunction in the diagnosis of depressive and non-depressive alcohol-dependent persons

Shaibal Guha[1], Anand Shankar[2], Amit Kr Das[3] & Subhash Kumar[4]
[1]Positive Health Care Center, Diabetes, Patna, India; [2]Shankar Diabetes Care and Research, Diabetes, Patna, India; [3]SHMC Muzaffarpur, Diabetes, Muzaffarpur, India; [4]Diabetes and Obesity Care Center, Patna, India

Introduction
Acute and chronic alcohol intake and alcohol withdrawal induce dysfunction of neuroendocrine and other regulatory systems. The expression 'neuroendocrine dysfunction' alludes to an assortment of conditions brought about by imbalances in the body's chemical creation straightforwardly connected with the pituitary, nerve center, and their tomahawks following TBI.
Aims
This study aimed to assess a possible hypothalamo-pituitary-adrenal (HPA) axis dysfunction in a population of alcoholics, using a dexamethasone suppression test (DST).
Methods
For this study, 90 participants had been selected, among whom 65% of participants were depressive and 35% of are non-depressive alcoholics.
Discussion
The serum and urinary cortisol were compared between the groups of 89 male patients (65% depressive and 36% non-depressive alcoholics) (Hamilton test), before and after DST. In non-depressive patients, 49% was non-suppressive in DST. In depressive patients, 47% was suppressive in the DST test (serum cortisol). Twenty-four hours urinary excretion in a group of non-depressive patients was suppressed in 79% of cases; depressive patients showed 50.9% non-suppressors. Basal serum cortisol secretion was significantly lower in a group of non-depressive than depressive patients. Also, serum concentrations at 16 h were significantly higher in a group of depressive non-suppressive patients. Basal urinary cortisol excretion was in the normal range in all patients, but after dividing the patients into suppressible and non-suppressible groups, significantly higher ($P < 0.002$) basal urinary cortisol concentrations were found in the latter.
Conclusion
Based on the DST test and the basal cortisol measurement, the findings reveal that the neuroendocrine dysfunction of alcoholic patients could be present even if the depression is pronounced.

DOI: 10.1530/endoabs.81.EP840

EP841

Descriptive study of the acromegaly disease activity according to ACRODAT® in a tertiary Hospital in Spain

Juan Carlos Percovich Hualpa[1], Roberto Añez[1], Rogelio Garcí a Centeno[1], Laura Gonzalez Fernandez[1], Diego Munoz[1], ALEJANDRA MARICEL RIVAS MONTENEGRO[1], Elisa Fernández Fernández[1], Crystal Guerrero[2] & Olga González Albarrán[1]

[1]Hospital General Universitario Gregorio Marañón, Endocrinology and Nutrition, Madrid, Spain; [2]University of Virginia, Charlottesville, United States

Background
The goals of acromegaly treatment are to achieve long-term biochemical control, control tumor size and decrease the risk of developing systemic comorbidities. Moreover, from the patient's perspective, symptoms and QoL are critical parameters of disease control and should be assessed routinely. To aid in the global clinical management of acromegaly, a holistic clinical decision support tool, the Acromegaly Disease Activity Tool (ACRODAT®) was developed.
Objectives
To describe and analyze the acromegaly disease activity according to ACRODAT®.
Methods
Observational, cross-sectional study conducted in a Spanish tertiary hospital (Hospital General Universitario Gregorio Marañón). The ACRODAT® tool was used to assess disease activity entering the data collected in the study.
Results
In total, 42 acromegaly patients were enrolled. 26 patients were female (61.9%). The average age was 59.66 years (SD 15.22), the BMI was 31.85 Kg/m^2 (SD 20.53), % body fat mass was 36.93 (7.52), % truncal fat mass was 36.93 (7.52). IGF-1 levels were within normal limits in 64,3% of patients, between ULN and 1.2xULN in 21.4% of patients and $>$1.2 ULN in the 14.3% of patients. 100% of patients showed a stable tumor size. The most frequent comorbidity was cardiac disease (57.14%), followed by sleep apnea (40.48%) and diabetes (35.71%). According to ACRODAT®, 61.9% ($n=26$) of patients were classified as stable (S), 23.8% ($n=10$) as having mild disease activity (M-DA) and 14.3% ($n=6$) as having significant disease activity (S-DA). 100% of S-DA patients showed IGF-1 levels $>$1.2ULN, 83.3% suffered from cardiac disease ($n=5$), 50% from diabetes ($n=3$) and 16.7% from sleep apnea ($n=1$). 66.7% ($n=4$) of S-DA patients showed not-controlled comorbidities, 50% ($n=3$) poor controlled of the symptomatology and 16.7% ($n=1$) poor QoL. In the total cohort of patients, in terms of comorbidities, patients were classified as controlled in 33.3% of patients, partially controlled in 33.33% of patients ($n=14$) and not controlled in 30.2% ($n=13$). Symptomatology was classified as stable in 31% of cases ($n=14$), 55.8% of cases ($n=24$) as mild activity and 9.3% of the patients ($n=4$) as significant disease. 58.1% of patients showed minimal or no impairment of QoL, mild impairment in 25.6% of patients and 14% with significant impairment.
Conclusions
ACRODAT® is a validated tool to monitor acromegaly disease activity that incorporates patient-centric parameters such as QoL and symptomatology.

DOI: 10.1530/endoabs.81.EP841

EP842

Central precocious puberty in a young boy associated with bilateral optic pathway glioma in neurofibromatosis Type 1: a case report

Muhammad Saleem[1], Saad Farooq[1] & Imran Ulhaq[2]
[1]Aga Khan University Hospital, Department of Medicine, Section of Diabetes, Endocrinology and Metabolism, Karachi, Pakistan; [1]Aga Khan University Hospital, Department of Medicine, Section of Diabetes, Endocrinology and Metabolism, Karachi, Pakistan

Background and Importance
Precocious puberty refers to sexual characteristics development before the normal age for its development. Neurofibromatosis Type 1 is an autosomal dominant condition with wide spectrum of clinical phenotype of which precocious puberty is common. This case report highlights the importance of recognizing this disease in patient presenting with precocious puberty and screening for optic pathway gliomas should be done and treat it to prevent the future chances of permanent blindness, neurological disability and gonadotropin deficiency.
Clinical Presentation
9 years old male came with chief complains of decreased/blurring of vision from the age of 3 to 4 years, increased pubic hair growth and multiple regions of skin lesions noticeable for the last 1 year. Clinical examination of the patient revealed classic features of precocious puberty. Hormonal workup showed significantly raised testosterone levels and mildly raised FSH levels. MRI brain was done which showed abnormally thickened bilateral optic nerves and optic chiasma, suggestive of optic nerve glioma. Final diagnosis of Neurofibromatosis Type 1 manifesting as Central Precocious Puberty in association with bilateral optic pathway Glioma was made.
Conclusion
By this case report, physician's attention is directed towards the importance of recognizing this disease with precocious puberty and screening for optic pathway glioma should be done, even when patient don't have any visual symptoms and treat it early which will help in preventing the complications of optic pathway glioma in long term and ultimately shall benefit patients in part of their increased survival, satisfaction and decreasing morbidity.

DOI: 10.1530/endoabs.81.EP842

EP843

Acromegaly-related dysmorphic syndrome In Mediterranean Patients: A monocentric retrospective Survey

Faten Haj Kacem Akid[3], Wafa Belabed[3], Elleuch Mouna[3], Cyrine Chehaïdar[3], Dhoha Ben Salah[3], Fatma Mnif[3], Nabila Mejdoub[3] & Mohamed Abid[3]
[1]Hedi Chaker University Hospital, Endocrinology Departement, Sfax, Tunisia; [2]Hedi Chaker University Hospital, Department of Endocrinology, Sfax, Tunisia; [3]Hedi Chaker University Hospital, Endocrinology Department, Sfax, Tunisia

Background and Aims
Acromegaly is an insidious disease related to hypersecretion of growth hormone (GH) that leads to several cardiovascular, respiratory, and metabolic comorbidities. The onset of dysmorphic body changes is one of the earliest signs of this condition. The objective of the current work was to describe the clinical manifestations of dysmorphic modifications characterizing Mediterranean patients diagnosed with acromegaly.
Patients and Method
We conducted a retrospective study that included all patients diagnosed with acromegaly who have been followed up, from 1997 to 2021, at the Endocrinology Department of Hedi Chaker University Hospital, Sfax, Tunisia. The review of medical charts provided a detailed description of dysmorphic features in the investigated population.
Results
Our sample included 29 with a mean age at diagnosis of 45.8 $\pm$ 12.4 years old (extremes: 23-72). No significant gender differences was reported (sex-ratio = 1.07). Dysmorphic features were observed in all patients with variable degrees. Patients diagnosed with acromegaly presented with facial changes in 96.5% of cases. Cranial ridges (41.1%), frontal skull bossing (48.3%), and enlarged nose (75.9%) were frequently recorded. Similarly, jaw and oral deformities were very common among the studies population such as prognathism (72.4%), enlarged lips (55.2%), and mandibular overgrowth with maxillary widening and teeth separation (37.9%). Macroglossia was found in 48.3% of cases. Acral modifications occurred in more than 80% with swelling thin-skinned hands in 51.7% and enlarged shoe size in 82.8% of cases. Skeletal axial involvement was present in 24.1% including kyphoscoliosis and diffuse skeletal hyperostosis.
Conclusion
Comorbidity and mortality rates in acromegaly are significantly higher compared with healthy subjects due to its delayed diagnosis and therapeutic difficulties [1]. Unlike North America and Northern Europe, acromegaly remains largely underdiagnosed, especially in the southern Mediterranean countries. Dysmorphic modifications are one of the earliest symptoms of this disease [2]. Raising awareness about acromegaly and its dysmorphic syndrome in the general population and among physicians in the Mediterranean region could aid in the early detection of undiagnosed cases.
References
1. Colao, Annamaria, *et al*. 'Acromegaly.' Nature Reviews Disease Primers 5.1 (2019): 1-17.
2. Lavrentaki, Aikaterini, *et al*. 'Epidemiology of acromegaly: review of population studies.' Pituitary 20.1 (2017): 4-9.

DOI: 10.1530/endoabs.81.EP843

EP844

Cushing's disease in a 14 year old child: A real diagnostic and therapeutic challenge

Trigui Souleima, Lassoued Najoua, Mrabet Houcem, Boubaker Fedia, Alaya Wafa & Sfar Mohamed Hbib
Mahdia, Endocrinology, Sfax, Tunisia

Introduction
Cushing's disease (CD) is a rare but serious pathology in children and adolescents. It differs from adult pathology by the mode of presentation and

management. We report a case of CD in a 14-year-old child whose diagnosis was confirmed only after 2 years.
Observation
This was a 14-year-old female patient with a family history of consanguineous marriage and personal history of nephrotic syndrome who presented with delayed stature, delayed puberty and obesity. On initial examination, she had Cushing's syndrome with facio-truncular obesity, buffalo hump, spontaneous bruising, and purple stretch marks. Her Weight was +2SD, her height was -4SD, with BMI of 33.5 kg/m2.Tanner score was A2P2S2R0. The diagnosis of ACTH-dependent Cushing's syndrome was made in view of an abolished cortisol cycle, an elevated CLU of 182 mg/24h and a low post-braking cortisol level of 140 ng/ml with an elevated ACTH of 97 pg/ml. Investigations to decide between a central origin and ectopic ACTH secretion were initially discordant. In favor of CD: Positive desmopressin test, elevation of Cortisolaemia of 30% higher, and ACTH of 20%higher, no carcinoid tumor on thoracic CT scan and no pathological fixation on Octreoscan. Negative strong braking (Cortisol level at 170 ng/ml) andHypothalamic-pituitary MRI without abnormalities were in favor of ectopic ACTH secretion. A second hypothalamic-pituitary MRI was performed 6 months after the diagnosis of CS, showing a right anterolateral microadenoma of 3. 4 *5 mm with a small dehiscence of the sellar floor, There was no evidence of multiple endocrine neoplasia. Thoracoabdomino-pelvic CT scan showed bilateral adrenal hypertrophy predominantly on the left. The patient received a preparation with ketoconazole and then was operated: A complete excision of the friable microadenoma and all the surrounding parenchyma was passed without incidents. Immediately postoperatively, the patient presented with central diabetes insipidus and recurrent bacterial meningitis. An osteomeningeal breach was surgically repaired in a second stage. She presented panhypopituitarism and was substituted with Lthyroxine and hydrcortisone.Currently, at one and a half years post-operatively, the patient retains signs of hypercorticism with faciotruncal obesity. The 8-h cortisol level is less than 2 ng/ml confirming corticotropic insufficiency, a key biological marker of remission. Discussion/Conclusion: Our case illustrates the diagnostic and therapeutic difficulty of CD in an adolescent girl. Since the cure rate is lower than in adults with a higher risk of recurrence and a shorter median recurrence time, a long term follow-up and a cardiovascular, metabolic and bone assessment in our patient is crucial.

DOI: 10.1530/endoabs.81.EP844

EP845

Clinical, biological and radiological particularities of acromegaly: Experience of the Endocrinology Department of the EPH Bologhine of West Algiers

Aicha Bouzid, Hanane Kherrab, Meskine Djamila & Malha Azzouz
Medical University of Algiers, Endocrinology & Metabolism Laboratory Algiers 1, Endocrinology Department of the EPH Bologhine, Algiers, Algeria

Introduction
Acromegaly is caused by chronic hypersecretion of GH and IGF-1. Chronically elevated GH and IGF-1 levels lead to a complex spectrum of signs.
Objectives
To describe the clinical, hormonal and radiological profile of acromegaly at the time of diagnosis.
Materials and methods
Retrospective study including 67 patients hospitalized in the Endocrinology Department of the EPH Bologhine
Results
There were 40 men and 27 women (Sex ratio M/F:1,48), the average age at the time of diagnosis of the patients was 43years, a partial or total anteropituitary insufficiency was found in 38,8% of the cases. This was global in 10.4% and partial in 28.35%. 7.4% of the patients had intestinal polyps, 2 of the 67 acromegalic patients had a thyroid cancer neoplasia and a colonic adenocarcinoma. Metabolically, 15% of the patients had diabetes mellitus Radiologically, a macroadenoma was found in 83.5% of cases, a microadenoma in 13.43% of cases. Hyperplasia was noted in one patient. In one case the pituitary gland was normal and the etiological investigation in search of an ectopic secretion was negative.
Conclusion
Our results agree with the data described in the literature, although acromegaly is more frequent in women. An early diagnosis is necessary in these acromegalic patients.

DOI: 10.1530/endoabs.81.EP845

EP846

Case report: Kallmann syndrome associated with a non-functional pituitary microadenoma

Sanaa Bammou, Sana Rafi, Ghizlane EL MGHARI & Nawal EL ANSARI
Mohamed VI University Hospital Center, Department of Endocrinology, Diabetology, Metabolic Diseases Nutrition, Marrakech, Morocco

Introduction
Kallmann syndrome (KS) is a rare disorder. It is now designated as olfactogenital dysplasia with an association between agenesis of the olfactory bulbs and hypogonadism. The association of KS with a pituitary microadenoma has not been well described in the literature.
Case report
It's a 16-year-old and 6 months, admitted for evaluation of a micropenis, he has as ATCDs an orchidopexy performed at the age of 3 years, infertility in the maternal uncle. During the interrogation a growth retardation was noticed from childhood, anosmia since the age of 7 years. The clinical examination revealed a a eunuchoid body proportion Body mass index (BMI) of 24.52 kg/m^2, gynecomastia without galactorrhea. Tanner scale: G1P2. He had micropenis (stretched phallus length 3.5 cm). Hormonal assays identified a hypogonadotropic hypogonadism profile with total testosterone 0,58 ng/ml, luteinizing hormone 0.1 IU/ml and follicle-stimulating hormone 1 IU/ml. prolactin (PRL) and the cortisol blood test are within normal limits. She had normal Thyroid function Karyotyping showed 46XY pattern. MRI of the brain showed hypoplasia of the olfactory bulb, especially on the left. MRI also revealed a 4 mm pituitary microadenoma. Androgen replacement is planned for patient
Discussion
We report a case of a rare association of KS with a non-functional pituitary microadenoma. KS is an isolated form of hypogonadotropic hypogonadism in combination with a defect in sense of smell. It is due to defects in olfactory structures (bulbs, grooves, tracts) and altered migration of GnRH-secreting neurons into the preoptic and hypothalamic regions. The patient's clinical presentation seems to be concordant in the literature, with the classical association of hypogonadotropic hypogonadism and anosmia. MRI is highly valuable in evaluating suspected KS. Data suggest that, in hypogonadotropic hypogonadism, MRI being a non-irradiating technique, should be the first radiological step for investigating the pituitary gland as well as abnormalities of the ethmoid, olfactory bulb and tracts. The central finding in the present case is the MRI finding of a non-functioning pituitary microadenoma in association with KS. This association has been previously reported by Bolu *et al*. in their MRI assessment of 120 male patients with idiopathic hypogonadotropic hypogonadism.
Conclusion
Olfactory MRI imaging may aid in the diagnosis of KS in patients with suggestive clinical findings. Pituitary adenoma is a rare association with the KS. This emphasizes the need to image the pituitary region in KS patients to assess for hypoplastic pituitary malformations or adenomas incidentaloma.

DOI: 10.1530/endoabs.81.EP846

EP847

Acromegaly revealed by pituitary apoplexy : a case report About 2 cases

Aicha Bouzid, Hanane Kherrab, Meskine Djamila & Malha Azzouz
Medical University of Algiers, Endocrinology & Metabolism Laboratory Algiers 1, Endocrinology Department of the EPH Bologhine, Algiers, Algeria

Introduction
Pituitary apoplexy is a rare endocrine emergency that can occur due to pituitary infarction or hemorrhage. There are conflicting data regarding the type of pituitary adenoma prone to apoplexy. Prolactinomas seem to have the highest risk. We report 2 cases of apoplexy of a somatotropic adenoma not medically treated
Case 1
Patient aged 45 years, with a history of chronic headaches, hospitalized in the emergency room for management of a meningeal syndrome with violent headaches associated with vomiting, a significant decrease in visual acuity, exophthalmos and ptosis of the left eye. The patient was treated with antibiotics and underwent a brain scan which returned normal. In front of the observation of a dysmorphic syndrome typical of acromegaly, she was referred to the endocrinology department where the diagnosis of acromegaly was confirmed biologically, the pituitary imaging revealed a necrotic pituitary adenoma. The evolution was marked by a recurrence of the macroadenoma 6 years later.

Case 2
A 57-year-old patient was admitted to a neurology emergency room for intense headaches that were resistant to analgesics, with decreased visual acuity and diplopia. The pituitary CT scan showed a macroadenoma of 2 x 1.6 cm with erosion of the sellar floor. The evolution is marked by the spontaneous appearance of an empty sella turcica with progressive installation of an antehypophyseal insufficiency with therapeutic normalization of GH levels under medical treatment (somatuline and cabergoline) and substitution of hormonal deficits.
Conclusion
Pituitary apoplexy is a rare complication of pituitary adenomas, it must be suspected in front of brutal headaches with ophthalmologic disorders. Its management must be multidisciplinary.

DOI: 10.1530/endoabs.81.EP847

EP848

Chronic diarrhea: the diagnostic process

Paraskevi Floroskoufi[1], Eirini Vourlioaki[1], Papazoglou George[2], Stergos Koukias[2] & Aikaterini Stamataki[1]
[1]Venizeleio General Hospital of Heraklio, Endocrinology Department, Greece; [2]Venizeleio General Hospital of Heraklio, Pathology Department, Greece

Introduction
Neuroendocrine tumors (NETs) are a heterogeneous group of rare neoplasms that originate from endocrine cells with the ability to secrete amines and hormonal polypeptides. Pancreatic neuroendocrine tumors (PNETs) can be functional or non-functional. Functional PNETs secrete common hormones such as gastrin, insulin and glucagon and much less frequent hormones such as vasoactive intestinal peptide (VIP). Their clinical characteristics depend on the peptide secreted. It is estimated that up to 10% of all pNETs being associated with MEN1.
Case report
We present the case of a 45-year-old woman who came to the emergency department with diarrhea, dehydration and electrolyte disorders (severe hypokalemia and hypercalcemia). The patient reported ~5 daily episodes of diarrhea without mucus or blood for 7 months while the last month she mentioned an increase to ~15 daily episodes of diarrhea with fatigue, polydipsia and polyuria. Due to the hypercalcemia, further testing was compatible with the diagnosis of primary hyperparathyroidism. 99 Tc-sestamibi scanning for parathyroid gland evaluation revealed features suggestive of parathyroid adenoma. Contrast-enhanced computed tomography of the abdomen, as part of the workup for the chronic diarrhea, showed 3 masses in the pancreatic body and tail. Biopsy guided by ultrasound was performed and the cytological examination revealed a neuroendocrine carcinoma of the pancreas. Given this history and imaging findings, a workup for MEN1 was initiated. Magnetic resonance imaging (MRI) of pituitary gland showed a pituitary macroadenoma measuring 16 × 17 x 13 mm while the laboratory investigation was compatible with the diagnosis of acromegaly. The genetic test was positive for MEN 1 syndrome both for the patient and her three children.
Conclusion
Multiple endocrine neoplasia type 1 (MEN1) is a rare autosomal dominant hereditary tumor syndrome with a high degree of penetrance, that is caused by inactivating mutations of the tumor suppressor gene *MEN1*, and is characterized by a predisposition to a multitude of endocrine and nonendocrine tumors Our patient demonstrates a classic example of MEN1 syndrome with tumors in all 3 defining endocrine organs, including pituitary macroadenoma, parathyroid adenoma, and pancreatic neuroendocrine tumors. When the diagnosis of the syndrome is done, genetic testing of first-degree relatives is considered necessary

DOI: 10.1530/endoabs.81.EP848

EP849

Features of a clinical flow and diagnostics of patients with the family anamnesis of inactive adenomas of hypophysis (IAH)

Dilorom Xolova[1]
[1]Republican Scepialized Scientific Medical Center of Endocrinology, Neuroendocrinology, Tashkent, Uzbekistan

Objective was to study features of clinical semiology, their value for differential diagnostics in population of patients with the sporadic and family IAH anamnesis.
Materials and methods.
71 IAH patients with intracellar adenoma of a hypophysis. Patients with IAH were divided into two alternative groups: the 1st group - 50 (70,4 %) patients with environmental factors without the burdened family anamnesis and 2nd - 21 (29,6 %) with the burdened family anamnesis, including with a panmiksiya - 9 (2,7 %) and an inbriding - 12 (16,9 %) patients. Average patients age was 18-70 years (44,5±3,85 years). At the same time the greatest number of the arrived IAH patients to fall on age from 35 (23,9 %) to 40 (25,4 %) years and to a lesser extent be elderly to 30 (18,3 %) and 55 (5,6 %) and is more than years that will be coordinated with literary data. It should be noted that at patients of 2-group with hereditary IAH signs is more often than patients of 1-group - without hereditary signs prevail frequency of clinical signs, such as sexual violations - 26,5 %, decrease in sight - for 40,2 %, headaches - for 26,5 %, doubling in eyes - for 15,0 %, visual discomfort - for 12,5 %, olfactory violations - for 19,8 %, vegetative crises - for 12,3 %, duration of a disease among women 5-20 years - for 12,3 and 24,6 %, but to a lesser extent till 20 and more than 21 years - for 23,2 and 15,2 %, and among men of such difference it is not revealed. Frequency of complaints in 1-group on visual violations it is revealed, decrease in visual acuity at IAH patients with a tumor to 10 mm at 10 % surveyed, to 20 mm - 70,0 %, with huge - 100 %, at patients of 2-groups - 50,0 %, 87,5 % and 72,7 %. At patients with the family it is IAH the main clinical symptoms of a disease associate: - visual, sexual, headaches, vegetative crises, climax come aged till 20-25 years, and time of establishment of the diagnosis - 10-20 years; - adenomas > 10 мм which progress quicker, in huge adenomas, with the heavy course of a disease more often come to light, than at patients from the single is IAH; - the IAH family form and development of clinical symptoms at early age should be object of diagnostic screening.

DOI: 10.1530/endoabs.81.EP849

EP850

Polyuro-polydipsia syndrome revealing a craniopharyngioma in a 60-year-old female patient following a surgery

Zineb Mhamdi, Ikram Amira, Kaoutar Rifai, Hinde Iraqi & Mohamed El Hassan Gharbi
Ibn Sina University Hospital, Department of Endocrinology and Diabetology, Rabat, Morocco

Introduction
Craniopharyngioma is a benign, slow-growing epithelial tumor of embryonic origin, originating in the pituitary stem or pituitary gland and developing in the sellar and/or suprasellar region. It is characterized by its considerable potential for extension, its tendency to recur, and its adhesions to surrounding structures.
Case report
We report the case of a 60-year-old female patient with secondary amenorrhea at the age of 38 years, neglected and never explored, and who installed after surgery for intestinal obstruction on colonic tumor, a polyuria with polydipsia with 4 nocturnal awakenings and estimated input-output of 4 liters per day. The first-line workup was without abnormalities. The hypothalamo-hypophyseal MRI showed a 17 x 13 mm tumor that corresponds to a craniopharyngioma. This craniopharyngioma was complicated by a panhypopituitarism with 8 o'clock cortisol : 15 ng/ml, FT4 : 0.63 mUI/ml and hypogonadotropic hypogonadism profile with low FSH, LH and estradiol. The patient was put on Desmopressin with a good improvement of the polyuro-polydipsic syndrome. She was also put on Hydrocortisone and Levothyroxine.
Discussion and conclusion
Craniopharyngioma is a rare and benign epithelial tumor of the central nervous system, affecting mostly children. It is rarely observed in adults. Its diagnosis remains late despite the development of imaging techniques resulting in significant morbidity and poor survival. This is why it is essential to take each symptom seriously.

DOI: 10.1530/endoabs.81.EP850

Reproductive and Developmental Endocrinology

EP851

Eunuchoid skeletal proportions in male hypogonadism: a comparative analysis of anthropometric measures between men with congenital hypogonadotropic hypogonadism (CHH) and Klinefelter Syndrome (KS)

Sara De Vincentis[1,2,3], Rossella Corleto[1, 2], Alessio Bellelli[1, 2], Lucia Zirilli[2], Emanuele Santamaria[1], Antonio Granata[2] & Vincenzo Rochira[1,2]
[1]Unit of Endocrinology, Department of Biomedical, Metabolic and Neural Sciences, University of Modena and Reggio Emilia, Modena, Modena, Italy; [2]Unit of Endocrinology, Department of Medical Specialties, Azienda Ospedaliero-Universitaria Policlinico of Modena, Modena, Italy; [3]Clinical and Experimental Medicine PhD Program, University of Modena and Reggio Emilia, Modena, Modena, Italy

Background
Patients with CHH and KS have eunuchoid body proportions of the skeleton compared to normal male subjects, characterized by tall stature, and reduced upper-to-lower segment ratio (U/l). *Vice versa*, steroids exposure deeply differs between CHH and KS at puberty, with both testosterone and estradiol being very low only in CHH. At present, body skeletal proportions comparison between CHH and KS is not available.
Aim
To compare anthropometric measurements of adult male CHH patients to adult KS patients.
Methods
A prospective, cross-sectional, observational study was carried out. CHH patients were subdivided into 2 subgroups according to the timing of treatment start (testosterone replacement therapy [TRT] or gonadotropins): CHH1) CHH patients who started treatment late after 18 years; CHH2) CHH patients who started treatment on time before 18. All KS patients did not start TRT before 18 since KS do not usually delay puberty. The following anthropometric measurements were collected by using a digital scale and stadiometer (Seca gmbh&co®): height, weight, sitting height, total arm span. Legs length was obtained by subtracting sitting height from stature; U/l was calculated dividing sitting height for legs length.
Results
A total of 70 CHH and 45 KS age-matched patients were enrolled (mean age 33.7 ± 13.7 and 35.3 ± 13.7 years, respectively). CHH1 showed a longer arm span compared to CHH2 ($P=0.001$) and KS ($P=0.003$), and a shorter sitting height compared to KS ($P=0.008$). On the contrary, legs length was shorter in CHH2 compared to CHH1 ($P<0.001$) and KS ($P=0.011$). Accordingly, U/l and upper-to-height ratios were lower in CHH1 compared to CHH2 ($P<0.001$) and KS ($P=0.001$). Furthermore, the arm span-to-height ratio was higher in CHH1 compared to CHH2 ($P<0.001$) and KS ($P=0.008$).
Conclusions
Under the same definition of eunuchoid body proportions, the traditional hallmark of male hypogonadism, more fine differences are observed comparing adult CHH to KS patients. CHH patients who delayed treatment showed longer arm length and lower U/l in comparison to CHH patients receiving treatment on time at pubertal age and KS. This suggests a different mechanism involved in the eunuchoid skeleton development between CHH and KS confirming a major role for estrogen/androgen deficiency in the former (leading to disproportional growth of both legs and arms due to delay in epiphyseal closure that could benefit from on time replacement treatment) and a possible role of genetic supernumerary X in the latter, displaying a disproportional growth only at the legs site since infancy.

DOI: 10.1530/endoabs.81.EP851

EP852

Investigating the prevalence of hypogonadism and associated cardio-vascular risk of males presenting with infertility: Results from a diverse and multi-ethnic UK patient cohort

Vina Soran[1], Abigail Knell[1], Tharu Tharakan[2], Axel Cayetano-Alcaraz[2], Channa Jayasena[3] & Suks Minhas[2]
[1]Imperial College London, United Kingdom; [2]Imperial Healthcare NHS Trust, Charing Cross Hospital, Urology, London, United Kingdom; [3]Imperial College London, Section of Endocrinology and Investigative Medicine, London, United Kingdom

Background
Hypogonadism is estimated to account for over 10% of male-factor infertility. However, due to conflicting data regarding the relationship between testosterone levels and sperm quality, hormone evaluation is not consistently requested during initial assessment of the infertile male. Hypogonadism is associated with cardiovascular disease (CVD) and has been linked to an increased risk of mortality The aim of this study was to investigate the prevalence of hypogonadism and cardiovascular risk in a cohort of infertile men.
Methods
This was a single-centre retrospective analysis of all patients presenting with male-factor infertility between January 2015 and December 2020. Biochemical hypogonadism was defined as a morning serum testosterone level <10 nmol/l according to local reference range. Semen analyses were compared between hypogonadal and eugonadal males. Lipid-profiles were compared between both cohorts. Patient demographic and clinical data were used to calculate the Charlson Comorbidity Index (CCI) and QRISK®3 scores.
Results
Of 855 patients, hypogonadism was present in 284 (33.22%) of patients. The median (IQR) testosterone level in eugonadal males was 15.5 (12.7-20.68), compared to 7.3 (5.25-8.60) in hypogonadal males ($P<0.0001$). A significantly greater proportion of hypogonadal males were found to be azoospermic compared to eugonadal males (57.6% vs. 42.2%, $P<0.0001$). Moreover, eugonadism was more prevalent amongst patients from a White-Background (30.8%, vs 20.1%, <0.0001). Whereas hypogonadism was more common amongst patients from an Asian-Background (22.5% vs. 12.6%, $P<0.0001$). Accordingly, median testosterone levels were significantly lower in Asian males compared to white males (10.3 vs. 13.5, $P=0.000162$). A higher BMI was observed in hypogonadal males compared to eugonadal males (28.9 vs. 26.4, $P<0.0001$) and had significantly higher serum cholesterol (5.00 vs. 4.7, $P=0.031$), triglycerides (1.73 vs. 1.09, $P<0.0001$) and non-HDL cholesterol (3.90 vs. 3.49, $P=0.001$) compared with eugonadal males., However, HDL-Cholesterol levels were higher in males with normal testosterone (1.06 vs. 1.25, $P<0.0001$). Median QRISK®3 scores were significantly higher in hypogonadal males than eugonadal males (1.40% vs. 1.10%, $P=0.0004$). A significantly greater proportion of hypogonadal males had a CCI score of 1 compared to eugonadal males (15.1% vs. 7.2%, $P=0.0002$).
Discussion and Conclusions
This study demonstrated a high prevalence of hypogonadism within a cohort of infertile males compared to existing literature. Whilst an association between testosterone and sperm quality was not established, hypogonadism was shown to be associated with raised lipid parameters and an increased risk of CVD. All infertile men should undergo endocrinological evaluation and follow-up to mitigate the risks of dyslipidaemia and CVD.

DOI: 10.1530/endoabs.81.EP852

EP853

Hereditary syndromes in children with short stature

Olga Gumeniuk & Yuriy Chernenkov
Saratov State Medical University, Saratov, Russian Federation

Short stature is a clinical sign noted in genetic syndrome.
Purpose
Molecular genetic characterization of children with short stature.
Objects and methods
The study involved 7 patients 3-15 yrs (3 boys and 4 girls) with short stature. Full clinical and molecular genetic research (Whole Exome or Genome Sequencing) was conducted.
Results
SDS height was from -2 to -4. All patients had multiple stigmas of dysembriogenesis, autistic behavior disorders, mental and speech development delay. In boys KBG syndrome (heterozygous mutation in the ANKRD11 gene on chromosome 16q24), Wiedemann-Steiner syndrome (mutation in the KMT2A gene on chromosome 11q23.3), Coffin–Siris Syndrome, type VI (mutation in the ARID*A* gene on chromosome 12q12) were diagnosed. In girls De Grouchy syndrome, Yunis–Varon syndrome (mutation in the FIG4 gene on chromosome 6q21) was diagnosed. Two children with pronounced skeletal deformities and growth retardation were diagnosed with Brooke's syndrome.
Conclusion
Short stature in children combined with stigmas of dysembriogenesis, autistic behavior disorders, mental and speech development delay is it is an indication for molecular genetic examination in order to diagnose rare genetic syndrome.

DOI: 10.1530/endoabs.81.EP853

EP854

The kiss of metabolism and reproduction: is kisspeptin the key?

Mihaela Poterasu[1] & Simona Fica[1,2]
[1]Carol Davila University of Medicine and Pharmacy, Bucharest, Romania; [2]Elias Emergency Hospital, Bucharest, Romania

Background
The relationship between energy balance and reproduction is U-shaped, meaning that both a negative and a positive energy balance have a detrimental effect on reproductive function. In a world increasingly burdened by the growing prevalence of obesity, we turned our attention to the negative extremity of weight, by exploring anorexia nervosa (AN) and constitutional thinness (CT) metabolic and reproductive features. Kisspeptin (kiss-1) is a relatively recently discovered neurohormone with implications in the onset of puberty, sex steroid feedback and brain sexualization. More recent data show a possible involvement of kisspeptin in the metabolic processes, with a role in regulating the homeostasis of blood glucose, insulinemia and appetite, as well as regulating fat deposits, but these still need confirmation in further studies.
Objectives
The aim of this study was to evaluate the particularities of the indicators of reproductive function and look for possible implications in this regard of the neurohormone kiss-1 in normal and underweight patients, with or without eating disorders such as AN. In particular, the study focuses on the role of kisspeptin in amenorrhea induced by dietary restriction in patients with AN.
Material and Methods
We included in this cross-sectional and observational study a cohort of 34 young female patients gathered in 4 similar-sized groups, as it follows: AN and underweight, AN and normal weight, CT, and healthy, normal weight patients. Anamnestic, anthropometric and biological data were recorded, as well as the total fat percentage (TFP) data from the whole-body DXA scan.
RESULTS
Kiss-1 was significantly higher in patients with atypical AN subjects than in underweighted, typical AN patients (1.24 ± 0.15 vs 0.96 ± 0.17 ng/ml, $P=0.03$). No significant associations were found between kiss-1 levels and clinical-biological factors of reproduction, even though kiss-1 was significantly correlated with TFP throughout the cohort ($P=0.03$, $r=0.365$). Menses are significantly associated with the diagnosis of AN ($r=0.625$, $P<0.001$), weight ($r=0.448$, $P=0.005$), TFP ($r=0.457$, $P=0.007$) as well as with gonadotropins and thyroid hormones levels (FSH $r=0.353$, $P=0.007$, LH $r=0.474$, $P=0.005$, TT3 $r=0.472$, $P=0.006$, fT4 $r=0.625$, $P<0.01$).
Conclusions
Kiss-1 increases in atypical AN patients, who, despite their psychiatric diagnosis, have a normal weight and are not in such deteriorating physical health condition, probably in an attempt to maintain viable reproductive function for as long as possible. This result, together with the correlation of this neurohormone with TFP, sheds light on the involvement of kiss-1 in both reproductive and metabolic regulation of the study population.

DOI: 10.1530/endoabs.81.EP854

EP855

Maternal prolactin-levels in pregnancy and offspring body composition at 7 years. Odense Child Cohort

Freja Pelck Hansen[1], Anders Grøntved[2], Richard C Jensen[1], Frederik D Højsager[2], Ivan Brandslund[3], Henriette Boye[4], Tina Kold Jensen[4, 4], Marianne Andersen[1] & Dorte Glintborg[1]
[1]Odense University Hospital, Endocrinology, Odense, Denmark; [2]University of Southern Denmark, Odense, Denmark; [3]Vejle Hospital, Hospital Lillebælt, Vejle, Denmark; [4]Odense University Hospital, Odense, Denmark

Background
Prolactin is associated with metabolic risk inside and outside of pregnancy. Maternal prolactin levels could be associated with offspring body composition.
Aim
To investigate if maternal prolactin-levels were linked to offspring body composition at seven years of age.
Design
Prospective observational cohort study (the Odense Child Cohort).
Methods
Maternal fasting blood samples were assessed during 1st (prolactin) and 3rd trimester (prolactin and glucose). Prolactin ratio was defined as 3rd trimester/1st trimester prolactin. Offspring body composition at seven years of age was assessed by Dual-Energy X-ray Absorptiometry (DXA)-scan, BMI and waist circumference. A total of 854 mother-child-pairs were included. Gestational diabetes mellitus (GDM) was defined by WHO13-criteria (fasting glucose ≥ 5.1 mmol/l). Oral glucose tolerance test (OGTT) was performed around gestation week 28 in 180 women with risk factors for GDM and in 168 randomly included women. Multiple regression analyses investigated associations between maternal prolactin (continuous and quartiles) and offspring body composition stratified by offspring sex and models were adjusted for maternal age, parity and BMI.
Results
Median (quartiles) maternal age was 30 (27–33) years and pre-gestational BMI 24.5 (21.3; 26.5) kg/m^2. In boys ($n=301$), maternal prolactin-ratio (4th quartile) was positively associated with fat percentage (Adjusted $\beta=0.09$, $P=0.02$, and gynoid fat percentage (Adjusted $\beta=0.08$, $P=0.04$). In boys born of mothers with risk of GDM ($n=135$), the association between maternal prolactin-ratio (4th quartile) and fat percentage (Adjusted $\beta=0.13$, $P=0.026$) and android fat percentage (Adjusted $\beta=0.22$, $P=0.032$) was attenuated. Maternal prolactin was not associated with body composition in girls.
Conclusions
Maternal prolactin-ratio was positively associated with fat percentage and android fat percentages in boys born of mothers at risk for GDM.

DOI: 10.1530/endoabs.81.EP855

EP856

Nijmegen breakage syndrome with unusual presentation: a case report

Teodora Dumitru[1], Miruna Anisia[1], Diana-Cristina Andrei[1], Cristina Preda[1,2], Caba Lavinia[3] & Maria Christina Ungureanu[1, 2]
[1]Emergency University Hospital "Saint Spiridon", Endocrinology, Iasi, Romania; [2]'Gr. T. Popa' University of Medicine and Pharmacy, Endocrinology, Iasi, Romania; [3]'Gr. T. Popa' University of Medicine and Pharmacy, Medical Genetics, Iasi, Romania

Introduction
Nijmegen breakage syndrome(NBS) represents a rare autosomal recesive disorder, characterized by severe chromosomal instability. It is caused by mutations in the NBN gene, which product, nibrin, belongs to the hMre11/hRad50 protein complex, critical for processing DNA double-strand breaks during mitotic and meiotic recombination. The hallmarks of NBS are growth retardation, microcephaly, premature ovarian failure(POI) in females, immunodeficiency and predisposition for malignancy.
Case report
A 9-year-old girl presented in the Department of Endocrinology Iasi with a history of two vaginal bleeding episodes and recurrent respiratory infections. Her clinical features were short stature (G=23 kg, T=127 cm, -1.78 SD->Pascanu), craniofacial dysmorphia with microcephaly, up-slanting palpebral fissures, long nose, sloping forehead, micrognathia and Sutton's nevi, no clinical signs for secondary sexual characteristics development, borderline intellectual ability. Biological tests were normal, but the hormonal assessment showed hypergonadotrophic hypogonadism (increased FSH=69,9 mUI/ml and LH=13,3 mIU/ml and low estradiol< 20 pg/ml). The pelvic ultrasonographic (US) examination reveals small uterus and ovarian sizes, regardless of age, without ovarian follicles. The karyotype and MLPA for SHOX gene deletion were normal. The two episodes of vaginal bleeding were interpreted in a mild pelvic traumatic injury context (falling from the bicycle). Six months later, she developed extensive vitiligo lesions on her lower body. The suspicion for Nijmegen Breakage Syndrome was confirmed by the Sanger sequencing, which identified the mutation of the Nibrin gene (NBN) in exon 6: c.657_661delACAAA, in a homozygous state. When she was 12 years old, we started the treatment for pubertal induction with low doses of transdermic estradiol.
Discussions
NBS is caused by mutations in the NBN gene, which product, nibrin, belongs to the hMre11/hRad50 protein complex, critical for processing DNA double-strand breaks during mitotic and meiotic recombination. The hallmarks of NBS are growth retardation, microcephaly, premature ovarian insufficiency (POI) in females, immunodeficiency and predisposition for malignancy. Our case is an unusual presentation for the NBS – suspicion of precocious puberty with vaginal bleeding. In the literature, NBS is associated with premature ovarian failure. The pathomechanism of hypoplastic ovaries or streaks gonadal is explained by genome instability.

DOI: 10.1530/endoabs.81.EP856

EP857

Clinical and biochemical markers of premature ageing in young hypopituitary women with untreated hypogonadism

Irena Ilovayskaya & Anna Loktionova
Moscow Regional Research and Clinical Institute, Neuroendocrinology, Moscow, Russian Federation

Hypogonadotropic hypogonadism as a part of hypopituitarism can be a cause of persistent amenorrhea and hypoestrogenemia in women of reproductive age as it is observed in postmenopause. We know that premature and early menopause leads to accelerated aging with such markers as decreased quality of life, phyco-emotional deprivation, dyslipidemia, bone mineral density and others. We hypothesized that untreated hypogonadism in young women with hypopituitarism could cause premature aging. Clinical symptoms, hormonal levels, lipid and mineral metabolism, BMI, BMD and quality of life (GHQ-28) were evaluated in young women with hypopituitarism ($n=49$, 25[22;31] y.o.), healthy age-matched young women (YW $n = 53$, 24[23;28] y.o.) and middle-aged women with natural postmenopause (PM $n = 50$, 56[53;59] y.o.) were compared. Duration of amenorrhea and postmenopause was similar (median 5 and 6 years, $P=0.9$). Hypopituitarism group included patients with organic pituitary lesions, hypothyroidism and hypocortisolism were compensated. The prevalence of general, neurovegetative and psychoemotional symptoms was significantly higher in women with hypopituitarism than in YW though it was similar to PM. In contrast, common to the postmenopause vasomotor symptoms were observed less frequently in hypopituitarism. Concentrations of E2, T and DHEAS, total cholesterol, triglycerides, calcium and alkaline phosphatase as well as quality of life in women with hypopituitarism were not typical of YW but were comparable to PM. Frequency of increased BMI was higher in women with hypopituitarism (51%) than in YM (11%) and comparable to PM (48%). BMD in lumbar spine and femur was even lower in young patients with hypopituitarism than in postmenopausal women. Thus, clinical and biochemical abnormalities revealed in women with untreated hypogonadism at young age were similar in many aspects to those in postmenopausal women at middle/old age in spite of the age difference and various reasons for hypoestrogenemia. These findings could be considered as markers of premature ageing because the biological changes attributable to postmenopause occurred well in advance.

DOI: 10.1530/endoabs.81.EP857

EP858

Perceptions and experiences of women with polycystic ovary syndrome-a systematic review

Gar Mun Lau[1], Mirna Elghobashy[1], Mansi Thanki[2], Shirley Ibegbulam[2], Helena Gleeson[3], Lynne Robinson[4], Pallavi Latthe[4], Caroline D. T Gillett[5], Wiebke Arlt[3, 5], Antje Lindenmeyer[6], Punith Kempegowda[3, 5] & PCOS SEva Working Group[5]
[1]College of Medical and Dental Sciences, University of Birmingham, Birmingham, United Kingdom; [2]School of Pharmacy, University of Birmingham, Birmingham, United Kingdom; [3]Department of Endocrinology, Queen Elizabeth Hospital, University Hospitals Birmingham NHS Foundation Trust, Birmingham, United Kingdom; [4]Birmingham Women's Hospital, Birmingham Women's and Children's NHS Foundation Trust, Birmingham, United Kingdom; [5]Institute of Metabolism and Systems Research, University of Birmingham, Birmingham, United Kingdom; [6]Institute of Clinical Sciences, University of Birmingham, Birmingham, United Kingdom

Introduction
With a global prevalence of around 10%, polycystic ovary syndrome (PCOS) is a common endocrine condition affecting women. Despite its prevalence, limited evidence exists around the condition and its impact on patients. Qualitative research provides insights into symptoms and experiences faced by women with PCOS that can affect management and compliance.
Aim
A systematic review was undertaken to evaluate the current literature on the experiences, perceptions and opinions of women with PCOS, with an aim to highlight key areas for improvement in the standard of care and education on PCOS.
Methods
A comprehensive search of seven electronic databases was conducted between July 2021 and October 2021. Studies focusing on both adolescent and adult patients with PCOS were considered for inclusion. The quality of individual studies was assessed by adaptation to the Critical Appraisal Skills Program (CASP) quality assessment tool. 1615 articles were screened and 34 full-text articles were used in the systematic review and subsequently coded using NVivo 12 software.
Results
Thematic analysis revealed 5 domains: *Signs/Symptoms of PCOS, Diagnosis, Management, Improving Outcomes, Perceptions of women with PCOS regarding their care.*Common themes included poor mental health (25/34 studies), subfertility (16/34 studies), and frustration or dissatisfaction with their diagnostic journey (16/34 studies). There were a number of concerns regarding the symptoms experienced by women, particularly difficulty losing weight and irregular menstruation. The majority of the literature reported negative experiences towards the standard of care. Issues surrounding diagnosis, such as a delay and under-diagnosis, led to cynicism towards healthcare providers and poor health outcomes. Only four studies suggested that a diagnosis of PCOS was a relief for patients. The main barrier perceived by patients was a lack of knowledge amongst healthcare professionals. Additionally, uptake of management advice was poor for most patients, as they experienced personal, educational and healthcare professional related barriers. Research indicated that empowering women with information helped with professional interactions and subsequent reduction of symptoms as women take a more patient-centered role in their management.
Conclusion
Despite its prevalence, women with PCOS feel under-supported by healthcare professionals and society in general. Prompt diagnosis and provision of appropriate information about the condition and its long term impact are required. Enhancing educational opportunities and access may empower women with PCOS and lead to improved clinical outcomes and reduced morbidity.

DOI: 10.1530/endoabs.81.EP858

EP859

Therapeutic management in transsexual women infected by VIH: about a case

Daniel Medina Rivero[1, 2], Isabel Mateo Gavira[2] & Laura Larrán Escandón[2]
[1]Hospital San Carlos San Fernando, San Fernando, Spain; [2]Hospital Universitario Puerta del Mar, Cádiz, Spain

A 38-year-old transsexual woman, with no known drug allergies, active tobacco smoker, ICAT 2. As diseases of interest, stage A2 human immunodeficiency virus (HIV) infection with current negative viral load. Lúes in 2012 treated. In treatment with Stribild (elvitegravir 150 mg/ cobicistat 150 mg/ emtricitabine 200 mg/ tenofovir disoproxil fumarate 245 mg). She went to the Transsexual Persons Care Unit due to gender inconsistency since childhood with the adoption of the female role for years. She now expresses her desire to start hormonal and surgical treatment to try to accommodate her secondary sexual characteristics to the desired sex. After the directed anamnesis and carrying out of complementary tests according to the recommendations of the Assistance Process of Attention to Transsexual People in Andalusia, cross-hormonal therapy is started. Antiandrogenic treatment was prescribed with cyproterone acetate 50 mg/day and estrogenic treatment with estradiol valerate at progressive doses up to a final dose of 6 mg/day (maximum recommended dose). However, despite adequate adherence to treatment and the high doses of estrogen used, plasma levels of estradiol remained low. Given the suspicion of possible interaction between antiretroviral treatment and estradiol valerate, Internal Medicine was consulted, deciding to change treatment to Triumeq (dolutegravir 50 mg/abacavir 600 mg/lamivudine 300 mg). Six months after the change in treatment, the target plasma estradiol levels were reached, even allowing the dose of estradiol valerate to be reduced to 4 mg/day. A prevalence of 19.1% of HIV-infected transsexual women is estimated. Several studies have associated the use of ritonavir-boosted protease inhibitors or cobicistat with a decrease in exogenous estrogen levels. The use of non-analog reverse transcriptase inhibitors (nevirapine, efavirenz) with decreased estrogen levels has also been described. Therefore, based on current evidence, the best option as antiretroviral treatment in transsexual women with cross-hormonal therapy could be a nucleoside reverse transcriptase inhibitor (such as abacavir, lamivudine) together with an integrase inhibitor (dolutegravir, raltegravir) without booster.

DOI: 10.1530/endoabs.81.EP859

EP860

A 20-steroid LC-MS/MS panel to investigate classical and backdoor pathways of androgen biosynthesis in the Leydig cells

Matteo Magagnoli[1], Marco Mezzullo[1], Silvia Limoncella[2], Alessia Tommasini[1], Daniele Santi[2], Carla Pelusi[1], Manuela Simoni[2], Uberto Pagotto[1], Livio Casarini[2] & Flaminia Fanelli[1]
[1]Alma Mater University of Bologna, Unit of Endocrinology and Prevention and Care of Diabetes - Center for Applied Biomedical Research - Department of Medical and Surgical Sciences, Bologna, Italy; [2]University of Modena and Reggio Emilia - Baggiovara Hospital, Unit of Endocrinology, Department of Biomedical, Metabolic and Neural Sciences - Center for Genomic Research, Modena, Italy

Background
The classical steroidogenic route to the synthesis of dihydrotestosterone in Leydig cells involves delta-5 and delta-4 precursors. Besides, the "backdoor pathway", encompassing progesterone metabolites, is gaining increasing interest in fetal development and men pathophysiology. Nowadays, liquid chromatography/tandem mass spectrometry (LC-MS/MS) is the ideal technique to simultaneously quantify large panels of steroids with elevated sensitivity and specificity.
Aim
We developed and validated a LC-MS/MS method measuring 20 among androgens, precursors and metabolites pertaining to both the classical and the backdoor pathways in the steroidogenic mouse Leydig tumor cell line 1 (mLTC1).
Methods
Steroidogenesis of serum-starved mLTC1 cells was induced by 100μM choriogonadotropin (hCG). Steroids released in 500μL cell medium were extracted with 2mL N-hexane:ethyl-acetate (8:2) spiked with 100μL internal standards in methanol. The organic phase was dried and samples were reconstituted with 100μL of 75% methanol before 10μL were analyzed. The platform included the Serie200 HPLC (Perkin Elmer) and the API-4000 QTrap (Sciex) operated in multiple reaction monitoring mode. 16OH-progesterone, 11-deoxycortisol, androstenedione, 11-deoxycorticosterone (21OH-progesterone), testosterone, androstenediol, 17OH-progesterone, 17OH-pregnenolone, dehydroepiandrosterone, androstanedione, epitestosterone, dihydrotestosterone, 17OH-dihydroprogesterone, progesterone, androstanediol, androsterone, pregnenolone, 5α-dihydroprogesterone, 17OH-allopregnanolone and allopregnanolone were separated in 13-min gradient operated on a Luna C8 100x3 mm, 3 μm column, equipped with 4x2.0 mm guard column (Phenomenex), termostated at 45°C, using 100μM ammonium fluoride and methanol as mobile phases. Analytes were revealed by quantitative and qualitative transitions and quantified by isotopic dilution.
Results
Isobaric compounds were separated to ensure selectivity. The dynamic range was between 3 and 5 orders of magnitude. Functional sensitivity was between 0.012 and 38 nmol/l. Intra-assay and inter-assay imprecision and trueness, valued at low, medium and high levels, were below 9.1 and 10.0%, and within 93.4-122.0%, respectively. Recovery and matrix factor were within 55.6-104.1% and 76.4-106.3%, respectively. Levels (nmol/l) of 16OH-progesterone (20.7 ± 4.2), 11-deoxycortisol (0.924 ± 0.115), androstenedione (727 ± 89), 11-deoxycorticosterone (3.69 ± 0.40), testosterone (52.8 ± 10.1), 17OH-progesterone (6.58 ± 0.75), androstanedione (774 ± 164), epitestosterone (26.1 ± 4.4), dihydrotestosterone (9.61 ± 2.51), progesterone (4.79 ± 0.60), androsterone (379 ± 80) and 17OH-allopregnanolone (4.30 ± 0.58) were within the measurement range. Levels of 17OH-dihydroprogesterone (0.844 ± 0.107), androstanediol (21.5 ± 5.9) and dihydroprogesterone (0.791 ± 0.136) were slightly above the limit of detection, whereas other compounds were undetectable.
Conclusions
We validated a LC-MS/MS method including a broad number of androgens, precursors and metabolites. Medium secretion levels from mLTC1 cells were measured effectively for most of the steroids, however, levels of some neutral and delta-5 steroids were below method's sensitivity. Nonetheless, we provided a powerful tool to simultaneously characterize the gonadal classical and backdoor steroidogenic pathways.

DOI: 10.1530/endoabs.81.EP860

EP861

Associations of serum AMH levels and hormonal, metabolic and cardiovascular parameters in adult men

Veronika Tandl[1], Caterina Colantonio[2], Christoph W Haudum[1], Barbara Hutz[1], Ewald Kolesnik[2], Albrecht Schmidt[2], Andreas Zirlik[2], Nicolas Verheyen[2], Thomas R Pieber[1] & Barbara Obermayer-Pietsch[1]
[1]Medical University of Graz, Division of Endocrinology and Diabetology, Graz, Austria; [2]Medical University of Graz, Division of Cardiology, Graz, Austria

Background
Anti-Müllerian hormone (AMH) is well known for its association with ovarian follicular count and ovarian reserve in general as well as for its recruitment of primordial follicles in women. With an explicit decrease in menopause, it is mainly used for clinical questions from in-vitro-fertilisation to polycystic ovary syndrome. Interestingly, AMH levels in men are quite high during lifetime, but there is only few data about its relevance and potential effects in adult men. The aim of our study was to investigate and describe AMH levels in men in association with a number of hormonal, metabolic and cardiovascular parameters and whether there are links to physiological or pathophysiological functions.
Methods
We analysed data from the BioPersMed cohort (Biomarkers for Personalized Medicine), a prospective cohort of asymptomatic subjects at cardiovascular risk. Clinical parameters, past medical history, AMH, hormonal profiles including androgens, fasting glucose and insulin values as well as oral glucose tolerance tests, lipid measurements including high- (HDL) and low-density (LDL) lipoproteins, inflammation markers such as C-reactive protein (CRP) and others were analysed as well as anthropometric parameters, DXA(dual energy X-ray absorptiometry)-derived body composition.
Results
Out of $n = 1022$ healthy volunteers, we identified 389 men (38% of the cohort) with a mean age 58 +/- 9 years. While AMH was BMI-dependent ($P = 0.0113$), and decreased slightly with age ($P = 0.03$), it was inversely associated with pituitary hormones LH (luteotropic hormone, $P = 4.5e\text{-}5$) and FSH (follicle stimulating hormone, $P = 1.6e\text{-}10$). The highest AMH quartiles showed an inverse association with C-peptide, but also HDL, while androgens or SHBG were not significantly different between groups, in contrast to pronounced differences of these parameters according to BMI categories.
Conclusion
AMH in men is an interesting, however neglected biomarker with a number of potential associations with hormonal, but also metabolic and potentially cardiovascular risk profiles. Its clinical value has to be determined in follow-up studies, but AMH in men might become an important health marker and needs further investigation.

DOI: 10.1530/endoabs.81.EP861

EP862

Hormonal profile in idiopathic male infertility

Dinu Draganescu Daniela[1], Anca Botezatu[2], SUZANA VILMA VLADOIU[1], Fudulu Alina[2], Albulescu Adrian[2], Oana-Monica Popa[1], Andrei Muresan[1], Plesa Adriana[2], Iancu Iulia Virginia[2], Dinu Draganescu Daria[3], Cristina Stancu[1], Velicu Alexandru[1], Purice Mariana[1], Padure Adriana[1], Udrea Luminita[1], Kremer Andreea[1], Dumitrica Alina Elena[1] & Corin Badiu[1]
[1]C.I. Parhon National Institute of Endocrinology, Bucureşti, Romania; [2]Ştefan S. Nicolau Institute of Virology, Molecular virology, Bucharest, Romania; [3]University Medical Center Groningen, Groningen, Netherlands

Male infertility arises as a global public health in the context of the dramatic decrease in birth rates, within a complex picture of hormonal, genetic and epigenetic factors. However, the underlying causes of male infertility remain unknown in many cases. Our study included samples ($n = 82$, median: 34 years, range 20–55 years) obtained from men investigating couple infertility and from a normal control group ($n = 11$, median: 29 years, range 21–55 years). Blood and seminal fluid were harvested after 3–5 days of sexual abstinence. Hormonal profile was evaluated, including FSH, LH, testosterone, estradiol, inhibin B and prolactin. Exclusion criteria: Radiotherapy and/or pelvic chemotherapy (over the last 6 months), known genetic aberrations, endocrine diseases, urogenital infections, bilateral orchiectomy, vasectomy and occupational exposure to harmful organophosphorus hydrocarbons, ionizing radiation, heavy metals. Inclusion criteria: spermatic parameters according to WHO 2010 Standards (Word Health Organization, 2010). The infertile group was divided in three subgroups: azoospermia (AZO $n = 23$), oligoasthenozoospermia/severe oligoasthenozoospermia (OAS/OASS $n = 14$), oligoasthenoteratozoospermia/-severe, oligoasthenoteratozoospermia (OATS/OATSS $n = 41$). The analysis of hormonal profile displayed statistically significant differences for FSH ($P = 0.0003$), LH ($P = 0.0092$), prolactin ($P = 0.043$), and inhibin B (0.0003). Moreover, a significant difference between azoospermia and control group was noted regarding FSH/E2 ratio (median: 0.4532 vs 0.152; $P = 0.00163$). A similar

pattern was displayed by the FSH/E2 ratio between subjects with <1 million spermatozoa/ml and control group (median: 0.420 vs 0.152; $P=0.00174$). The motility/E2 ratio was significantly lower in the azoospermia group compared to the control group (median: 0.000 vs 2.064; $P=0.034$). Sperm concentration/E2 ratio displayed a significant difference between the selected groups vs the control group (median: AZO-0; OAS/OASS-63328; OATS-70998; control-1453000). Investigating the LH/T and T/LH ratio, it was observed a significant difference between azoospermia and control group (median:2.207 vs 1.097, $P=0.0094$; respectively median:0.373 vs 0.912; $P=0.0388$). Subtle imbalances of reproductive hormones levels, revealed by disturbed evaluated ratios might be one of the causes of inappropriate sperm production mechanism. It appears that estrogen activity as reflected in the investigated ratios, is important with regards to proper fertility in males, since the spermatogenesis is modulated by estrogen at the level of HPG axis. In conclusion, investigated ratios could serve as a potential instrument in the diagnosis and management of male infertility, since these hormones cooperate to maintain the semen quality, stability and feedback control of the system.

DOI: 10.1530/endoabs.81.EP862

EP863

Does iron homeostasis influence gonadal axis in men with obstructive sleep apnea ?

Barbara Bromińska[1], Nadia Sawicka-Gutaj[1], Aleksandra Hernik[1], Ewelina Szczepanek-Parulska[1], Halina Batura-Gabryel[2] & Marek Ruchala[1]
[1]University of Medical Sciences in Poznań, Department of Endocrinology, Metabolism and Internal Disease, Poznań, Poland; [2]University of Medical Sciences, Department of Pulmonology, Allergology and Respiratory Oncology, Poznań, Poland

Introduction
Obstructive sleep apnea syndrome (OSAS) is characterized by chronic inflammation. Hepcidin is an acute-phase protein involved in iron metabolism. Increase in hepcidin has been shown in OSAS. Testosterone probably exerts inhibitory effect on hepcidin levels and even trump iron and inflammation-mediated mechanism in chronic inflammatory state. On the other hand iron balance may influence gonadal axis. The aim of this study was to assess whether hypogonadism in OSAS could be associated with iron metabolism.
Material and Methods
We recruited 92 males. Mean age was 61 years old. Sixty nine were diagnosed with OSAS, based on polysomnography. This group was divided into two subgroups. First comprised of 45 eugonadal men (g1), while the second included 24 hypogonadal patients (g2). Control group consisted of 23 patients with normal testosterone levels and normal sleep pattern (g3). We measured multiple parameters, among them: serum testosterone, LH, CRP, insulin levels and irone balance parameters.
Results
We have found significant differences in testosterone ($g1>g2$, $g3>g2$; $P<0.0000$), iron ($g3>g1$, $g3>g2$; $P=0.0378$), CRP ($g2>g3$; $P=0.0389$), BMI ($g1>g3$, $g2>g3$; $P=0.0065$), insulin ($g2>g1$; $g2>g3$; $P=0.0153$) and hemoglobin ($g3>g1$, $g3>g2$, $P<0.0000$) between groups. There was a tendency toward statistically significant difference in hepcidin levels ($g1>g2$, $g1>g3$; $P=0.0513$). On linear regression in a whole group testosterone level was inversely associated with hepcidin ($P=0.0152$; $\beta=$ -0,1804), insulin ($P=0.0024$; $\beta=$ -0,1409) and BMI ($P=0.0042$; $\beta=$ -0,3589). On multiple regression BMI and hepcidin were independent factors negatively influencing testosterone levels ($P=0.0009$).
Conclusion
Changes in testosterone in males with OSAS might be at least partially attributed to hepcidin concentration. Metabolic factors such as insulin and BMI negatively influence gonadal axis. The exact mechanism of potential mutual relationship between iron homeostasis and gonadal status in men with OSAS remains to be elucidated.

DOI: 10.1530/endoabs.81.EP863

EP864

Is there seasonal variation in testosterone levels? Data from a large cohort of men

Taiba Zornitzki[1], Sagi Tshori[1], Galit Shefer[1], Shira Mingelgrin[1], Carmit Levy[2] & Hilla Knobler[1]
[1]Hebrew University of Jerusalem, The Faculty of Medicine, Diabetes, Endocrinology and Metabolic Disease Institute, Rehovot, Israel; [2]Department of Human Genetics and Biochemistry, Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

Context
Several previous studeis suggested seasonal variation in testosterone levels. However, these studies were limited by either their small sample size or by variability in baseline characteristics and confounders such as: differences in age and weight distribution, co-existent illness, time in the day in which testosterone was measured and by differences in geographic location and climate conditions. Ultraviolet (UV) exposure is one of the main environmental stimuli. In a recent study (Parikh R, *et al*, Cell Rep. 2021, 36(8): 109579), we explored a novel skin-brain-gonad axis triggered by UV and mediated by skin p53. Through the use of various mouse models, we found that UV exposure led in male and female mice to increased hypothalamus-pituitary-gonadal axis hormone levels and to increased sexual responsiveness and attractiveness. These data provide for the first time an underlying mechanism for seasonal variability in testosterone levels.
Objectives
To evaluate in a large cohort of males with a wide-range of age, metabolic status and co-existent morbidities, whether month of blood test performance was associated with total and bioavailable testosterone levels independent of age, body-mass index (BMI), existing cardiovascular disease (CVD) and CVD risk factors.
Methods
Cross-sectional study including data from computerized medical records of 27,328 men aged 20-70, treated by the largest health care organization in Israel, who underwent testosterone measurement. In 7,940 subjects with available sex-hormone-binding globulin levels, bioavailable testosterone was calculated.
Results
Total and bioavailable testosterone levels gradually decreased with age and BMI ($P<0.001$) and were significantly lower in men with diabetes, hypertension, hyperlipidemia and known CVD ($P<0.001$). Intrigungly, testosterone levels were higher in current smokers compared with non-smokers ($P<0.001$). We stratified total and bioavailable testosterone levels according to the month in which the test was performed and observed a peak of total and bioavailable testosterone levels during August to October. After October, total testosterone and bioavailable testosterone started to decline reaching a nadir in March. Overall, total and bioavailable testosterone levels were significantly lower in March compared to August-October ($P<0.001$). In a linear regression analysis, age, BMI, current smoking, and month of testing were independently associated with both total ($P<0.001$) and bioavailable testosterone levels ($P=0.002$).
Conclusion
In a large cohort of men with a wide-range of age, BMI and co-morbidities, month of testing was independently associated with total and bioavailable testosterone levels. These data provide compelling evidence that seasonal variation has to be considered in clinical practice.

DOI: 10.1530/endoabs.81.EP864

EP865

A new, accurate and time-saving, two-step intracavernosal injection procedure to diagnose psychological erectile dysfunction

Giorgia Spaggiari[1], Antonio Raffaele Michele Granata[1], Manuela Simoni[1, 2] & Daniele Santi[1,2]
[1]Azienda Ospedaliero-Universitaria of Modena, Unit of Endocrinology, Department of Medical Specialties, Modena, Italy; [2]University of Modena and Reggio Emilia, Department of Biomedical, Metabolic and Neural Sciences, Modena, Italy

Background
The recognition of the erectile dysfunction (ED) pathogenesis is essential to identify the appropriate ED management. Since vascular ED (vED) could be a manifestation of a systemic arterial damage, the watershed in the ED diagnostic framework is the discrimination between psychological (pED) and vED. However, reliable tools to directly diagnose pED are currently lacking.
Aim of the study
To identify which parameters could predict pED. Moreover, we suggest a new intracavernosal injection (ICI) procedure to optimize the ED diagnostic work-up.
Methods
A retrospective, real-world analysis was carried out including all men who underwent ICI procedure at the Andrology Unit of Modena (Italy) from 2018 to 2021. Data about previous medical history and ED characteristics were collected. A first ICI procedure with 5 μg of prostaglandin E-1 (PGE-1) was performed. In

the absence of a full drug-induced erection (immediate or delayed), an echo-color doppler penile evaluation after administration of PGE-1 10 μg was conducted, measuring intracavernosal blood flows, to document a possible vascular etiology. Hormonal measurements, including testosterone, luteinizing hormone, follicle-stimulating hormone, estradiol, prostate-specific antigen, prolactin and thyroid-stimulating hormone serum levels, were performed to rule out a possible hormonal DE etiology.
Results
Out of 179 enrolled patients, 70.4% showed pED, 21.7% vED and 7.8% hormonal genesis. Multinomial logistic regression analysis identified absence of cardio-vascular disease ($P=0.017$), presence of spontaneous morning erections ($P=0.018$) and normal penile erections with masturbation ($P=0.035$) as predictors of pED. Clinically, normal ICI test response was detected in 86 patients and abnormal response in 93 subjects. Among the latter, 54 patients experienced a delayed response. The combination of ICI test with late penile erections evaluation was able to diagnose pED (sensitivity 97%, specificity 100%), avoiding unnecessary retesting.
Discussion
We propose a two-steps ICI procedure that allows to recognize pED with a high sensitivity/specificity, saving costs and time and limiting adverse events. Moreover, the presence of spontaneous morning erections and valid penile erections after masturbation could guide the diagnostic work-up, indirectly identifying those patients deserving of a deeper evaluation of vascular health.

DOI: 10.1530/endoabs.81.EP865

EP866

Effect of testosterone on body composition - randomised placebo-controlled study in hypogonadal men with uncontrolled type-2 diabetes - STRIDE STRUDY

Preethi Mohan Rao[1, 2], Alifyah Najefy[1] & T. Hugh Jones[1,2]
[1]Barnsley Hospital NHS Foundation Trust, Robert Hague Centre for Diabetes and Endocrinology, Barnsley, United Kingdom; [2]University of Sheffield, Human Metabolism and Oncology, Sheffield, United Kingdom

Objective
The objective of the study was to assess the effect of intra-muscular testosterone on body composition in men with hypogonadism and poorly controlled type 2 diabetes.
Research design and methods
This is a randomised double-blinded placebo-controlled add-on trial of intramuscular testosterone undecanoate administered every 12 weeks in 65 hypogonadal men with poorly-controlled diabetes. Phase 1 patients were randomly assigned to either treatment or placebo arm for 6 months of TRT. Phase 2 was an open-labelled phase for 6 months and patients on placebo moved on to the treatment group wherein patients in the treatment group continued. Body composition was measured by dual energy X-ray absorptiometry (DEXA scan). Outcomes were assessed at baseline and every 3 months.
Results
Mean age of the cohort was 59 years. Baseline characteristics were comparable between active/placebo groups. Only 48 patients had DEXA scans both at baseline and at 6 months. Limb fat mass and percentage fat significantly correlated strongly and inversely with total testosterone(TT), calculated free testosterone (cFT) and bioavailable testosterone(cBT) and there was no correlation with limb lean mass. There was strong inverse correlation between total fat mass, total fat percentage and truncal fat percentage with TT, cFT and cBT($P<0.05$). Truncal fat mass correlated inversely with TT and cBT but did not correlate significantly with cFT. There was no significant correlation between lean mass and TT, cFT or cBT. These correlations remained significant after correcting for age, BMI and SHBG in linear regression model. There was a significant reduction in Left leg fat mass in the active group compared to placebo group. ($P=0.03$) after 6 months of TRT. There was no significant difference in either the fat mass or lean mass between the active and placebo group elsewhere including truncal area. There were no significant changes in either fat or lean mass before and after 12 months of treatment with testosterone in the active group
Conclusions
Testosterone levels strongly and inversely correlates with fat mass and has no correlation with the lean mass. There was significant reduction in left leg fat mass after 6 months of TRT. There were no significant changes in any other body composition at 6 or 12 months and it suggests that these changes may take more than a year to show positive changes.

DOI: 10.1530/endoabs.81.EP866

EP867

Real-world evidence of follicle stimulating hormone effectiveness in male idiophatic infertility

Marilina Romeo[1,2], Giorgia Spaggiari[1], Federico Nuzzo[1], Antonio R.M. Granata[1], Manuela Simoni[1, 2] & Daniele Santi[1,2]
[1]Unit of Endocrinology, Department of Medical Specialties, Azienda Ospedaliero-Universitaria of Modena, Modena, Modena, Italy; [2]Unit of Endocrinology, Department of Biomedical, Metabolic and Neural Sciences, University of Modena and Reggio Emilia, Modena, Modena, Italy

Introduction
Male idiopathic infertility represents a therapeutic challenge for physicians, since a targeted aetiological treatment does not exist. Several hormonal and non-hormonal therapies have been proposed so far to increase pregnancy rates. Among hormonal therapies, exogenous follicle-stimulating hormone (FSH) administration shows the most convincing physiological rationale in the face of a clinical efficacy below expectations. Indeed, from evidences available in the literature, it was calculated that 10 to 18 men have to be treated to achieve one only pregnancy. This result comes from the published controlled clinical trials, but only few data are currently available on the real FSH effectiveness in clinical practice.
Aim
To assess the effectiveness of FSH administration in male idiopathic infertility in a clinical setting.
Methods
An interim analysis of a retrospective, observational, monocentric, real-world study was performed. All consecutive male outpatients attending the Andrology Unit of Modena (Italy) for couple infertility were enrolled. According to the reimbursement rules of the Italian Health System, FSH could be prescribed to men with idiopathic infertility and FSH serum levels <8 UI/l. Collected data included medical history, physical and andrological examinations, sex steroid hormones, conventional semen analysis and therapeutic choice.
Results
201 infertilemen were enrolled (mean age 37.6 ± 6.2 years), presenting mostly (91.2% of cases) for primary couple infertility. At baseline, 17 patients (12.4%) showed normozoospermia, 25 subjects resulted azoospermic (12.5%), while a variable degree of semen parameters impairment was recorded in 159 men (75.1%). Among 161 patients potentially eligible for exogenous FSH administration, 54 patients (33.1%) received hormonal therapy. FSH-treated patients showed significantly lower baseline FSH levels (3.5 ± 1.8 vs 8.9 ± 10.9 IU/l), sperm concentration (8.2 ± 8.4 vs 29.7 ± 26.5 millions/ml) and sperm motility (5.1 ± 8.6 vs $25.7\pm18.9\%$) compared to FSH-untreated men. Comprehensively, nine pregnancies were obtained in FSH-treated patients (16.7%), one spontaneous and eight after assisted reproduction procedures.
Conclusion
From our single centre experience on FSH treatment in male idiopathic infertility, it emerged that FSH is currently administered to men with low baseline FSH levels and impaired semen parameters. Our experience suggests that FSH empirically administered leads to pregnancy in 1 on 6 patients treated. Despite this study lacks a control group in a real world setting, the number of patients required to achieve a pregnancy seems to be lower than what calculated on published data.

DOI: 10.1530/endoabs.81.EP867

EP868

The FSH administration to men with idiopathic infertility improves sperm DNA fragmentation index together with testosterone serum levels increase

Daniele Santi[1,2], Giorgia Spaggiari[1], Monica Lispi[3, 4], Drakopoulos Panagiotis[3] & Manuela Simoni[1,2]
[1]University of Modena and Reggio Emilia, Department of Biomedical, Metabolic and Neural Sciences, Modena, Italy; [2]Azienda Ospedaliero-Universitaria di Modena, Unit of Endocrinology, Department of Medical Specialties, Modena, Italy; [3]Merck KGaA, Global Medical Affairs Fertility, Research and Development, Darmstadt, Germany; [4]University of Modena and Reggio Emilia, Clinical and Experimental Medicine PhD Program, Modena, Italy

Background
Testicular overstimulation is the pursued therapeutic goal when exogenous follicle-stimulating hormone (FSH) is empirically administered to men with idiopathic infertility. Although a robust physiological rationale theoretically supports the FSH use in male idiopathic infertility, useful markers to evaluate its

efficacy are still far from being detected. While pregnancy rate remains the strong outcome in couple infertility management, the identification of reliable, and possibly early, markers of therapeutic response to FSH in males is mandatory. Randomized controlled clinical trials (RCTs) on the topic focused, on the seminiferous component, not considering the potential involvement of the testosterone-secreting compartment.
Aim of the study
The evaluation of the potential relationship between testosterone serum levels and semen quality measured through sperm DNA fragmentation (sDF) index before and after FSH administration in male idiopathic infertility.
Methods
A retrospective post-hoc re-analysis was performed on raw data of RCTs in which idiopathic infertile men were treated with FSH and both testosterone serum levels and sDF were reported among primary and/or secondary endpoints. Additional data regarding couple infertility history, age, anthropometric variables, FSH treatment scheme and semen variables were included in a single dataset.
Results
Two RCTs (Colacurci *et al*. 2012 and Simoni *et al*. 2016) were included accounting for 148 patients (median age 37, 25-52 years). After three months of FSH administration, a significant increase was observed in FSH levels ($P<0.001$), inhibin B ($P=0.012$), sperm concentration ($P=0.003$), total sperm number ($P=0.021$), progressive motility ($P<0.001$) and normal sperm morphology ($P<0.001$). Moreover, an overall sDF index reduction was confirmed after treatment ($P=0.002$). SDF resulted significantly inversely related to sperm concentration both at baseline and after FSH treatment (Rho -0.325, $P<0.001$ and Rho -0.316, $P=0.001$, respectively). Interestingly, sDF index after treatment showed a significant inverse correlation with testosterone serum levels (Rho -0.327, $P=0.002$). Multivariate stepwise linear regression analyses using sDF index as dependent variable identified testosterone as a predictor for sDF index change ($P=0.005$). Similarly, logistic regression analysis highlighted testosterone and SHBG levels as predictive of sDF reduction after FSH administration ($P=0.043$ and $P=0.005$, respectively).
Conclusion
Combining raw data of published RCTs investigating FSH administration to idiopathic infertile men, a significative improvement of conventional semen parameters together with a reduction in sDF were confirmed. Intriguingly, a potential correlation between testosterone serum levels and sDF was highlighted for the first time, opening a completely unexplored way in the identification of potential early predictors of FSH therapy response in male idiopathic infertility.

DOI: 10.1530/endoabs.81.EP868

EP869

Procoagulant imbalance in male hypogonadism and effect of short-term testosterone replacement therapy

Rita Indirli[1], Marigrazia Clerici[2], Valeria Lanzi[1], Eriselda Profka[3], Biagio Cangiano[4], Marco Bonomi[4], Maura Arosio[1], Giovanna Mantovani[1], Armando Tripodi[2] & Emanuele Ferrante[3]
[1]University of Milan, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Department of clinical sciences and community health, Endocrinology Unit, Milan, Italy; [2]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Angelo Bianchi Bonomi Hemophilia and Thrombosis Center, Milano, Italy; [3]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Endocrinology Unit, Milan, Italy; [4]University of Milan, IRCCS Istituto Auxologico Italiano Milan, Department of Medical Biotechnology and Translational Medicine, Department of Endocrine and Metabolic Medicine, Milan, Italy

Introduction
The effects of testosterone on coagulation have not yet been clarified. In particular, it is still controversial whether male hypogonadism, or testosterone replacement therapy (TRT), may slightly increase the risk of venous thromboembolism, in particular during the first months of therapy. This study aimed to assess the hemostatic balance in hypogonadal men before and after short-term TRT, compared to healthy controls.
Methods
Thrombin generation assay (TGA) was performed in 38 hypogonadal men (10 primary hypogonadism, 19 organic central hypogonadism, 9 functional hypogonadism) before and 6 months after the initiation of TRT (transdermal testosterone gel, $n = 36$; long-acting i.m. testosterone undecanoate, $n = 2$), and in 38 age-matched healthy controls (median age 55.1 and 54.7 years respectively, $P=0.91$). Thrombophilia, Klinefelter syndrome, uncontrolled diabetes mellitus, anti-coagulant or anti-platelet therapy were exclusion criteria. TGA is based on the continuous registration of thrombin generation (mediated by procoagulants) and decay (mediated by anticoagulants) in platelet-poor-plasma. To make the procedure sensitive to imbalances in Factor (F)VIII–protein (P)C activities, thrombomodulin is added to the TGA assays. The following parameters are recorded: *thrombin peak* concentration; *endogenous thrombin potential (ETP*, the total amount of thrombin generated during the test); the *ETP-ratio*(ETP with/ETP without thrombomodulin) which accounts for FVIII-PC balance.
Results
Larger amounts of thrombin were generated in hypogonadal men at baseline (ETP 2173 ± 288 nMxmin) and during TRT (2166 ± 301) compared to controls (1947 ± 273, $P<0.001$ and $P=0.001$), with no significant change over 6 months in hypogonadal patients ($P=0.82$). Similar results were observed when thrombomodulin was added to TGA. The ETP-ratio was comparable in hypogonadal patients before (0.68 ± 0.23) and after TRT (0.68 ± 0.20, $P=0.73$), and in controls (0.61 ± 0.20, $P=0.17$ and $P=0.13$). Thrombin peak did not change from baseline to six months ($P=0.29$); however, it was significantly higher than controls only at baseline ($P=0.03$). ETP was inversely associated with total testosterone concentrations at baseline ($r=-0.44$, $P=0.008$) but not when on TRT.
Conclusion
A procoagulant imbalance is observed in hypogonadal men. This does not appear to involve the FVIII-PC axis and is not modified by short term testosterone therapy. Further studies are needed to clarify which coagulation factors drive the procoagulant imbalance, whether longer TRT can normalize it, and if platelets or endothelial cells are affected as well.

DOI: 10.1530/endoabs.81.EP869

EP870

Combined omic analysis revealed autism-linked NLGN3as new candidate gene associated to GnRH neuron development and disease

Roberto Oleari[1], Antonella Lettieri[2], Alyssa J.J. Paganoni[1], Federica Amoruso[1], Peter Scheiffele[3], Sasha Howard[4] & Anna Cariboni[1]
[1]Department of Pharmacological and Biomolecular Sciences, Milano, Italy; [2]University of Milan, Department of Health Sciences; [3]University of Basel, Biozentrum, Basel, Switzerland; [4]William Harvey Research Center, London, United Kingdom

During development, gonadotropin releasing hormone (GnRH) neurons are born in the nasal placode and migrate to the hypothalamus, where they position to regulate sexual reproduction by the pulsatile release of GnRH. Defective GnRH neuron development or action may lead to GnRH deficiency (GD) which is characterized by absent or delayed puberty (1). GD can also be present as a trait shared by several complex neurodevelopmental disorders (NDDs), such as cerebellar ataxia, developmental delay and autism spectrum disorder (ASD) (2). Interestingly, a recent register-based population study showed for the first time that patients with GD have increased risk for being diagnosed with ASD or other NDDs, but the underlying genetic correlation is unknown (3). Although more than 20 genes have been associated to GD pathogenesis (4), half of the cases are still idiopathic, suggesting the need of novel experimental approaches to identify the elusive genes. Here, we combined the transcriptomic analysis of primary and immortalized GnRH neurons with exome sequencing data from GD patients to identify novel candidate genes. As a proof-of-principle, we identified pathogenic variants in the autism-linked Neuroligin 3 (*NLGN3*) gene in two unrelated patients sharing GD and ASD. We demonstrated that NLGN3 is enriched in GnRH neurons at late developmental stages and its overexpression in a model of immortalized GnRH neurons (GN11 cells) promoted neurite extension. Further, the two identified NLGN3 mutations, which are both loss-of-function, formed prematurely truncated proteins that were retained in the endoplasmic reticulum thus preventing cell protrusion formation in GN11 cells. Overall, our results highlighted how the combination of gene expression and exome sequencing data is a reliable approach to identify novel candidate gene for GD such a NLGN3, an autism-linked gene that we found for the first time associated to GD.
References
1. Boehm U, Bouloux P-M, Dattani MT, *et al*. Expert consensus document: European Consensus Statement on congenital hypogonadotropic hypogonadism–pathogenesis, diagnosis and treatment. *Nat Rev Endocrinol*. 2015;11(9):547-564. doi:10.1038/nrendo.2015.112
2. de Roux N, Carel J-C, Léger J. Congenital Hypogonadotropic Hypogonadism: A Trait Shared by Several Complex Neurodevelopmental Disorders. In: *Endocrine Development*. Vol 29.; 2016:72-86. doi:10.1159/000438875
3. Ohlsson Gotby V, Söder O, Frisén L, *et al*. Hypogonadotrophic hypogonadism, delayed puberty and risk for neurodevelopmental disorders. *J Neuroendocrinol*. 2019;31(11). doi:10.1111/jne.12803
4. Oleari R, Massa V, Cariboni A, Lettieri A. The Differential Roles for Neurodevelopmental and Neuroendocrine Genes in Shaping GnRH Neuron

Physiology and Deficiency. *Int J Mol Sci*. 2021;22(17):9425. doi:10.3390/ijms22179425

DOI: 10.1530/endoabs.81.EP870

EP871

Endometrial cell-type-specific disease signatures and endometrial organoids in polycystic ovary syndrome

Gustaw Eriksson[1], Congru Li[1, 2], Han-Pin Pui[1], Sanjiv Risal[1], Angelica Lindé n Hirschberg[3], Sophie Petropoulos[4,5,6], Qiaolin Deng[1] & Elisabet Stener-Victorin[1]
[1]Karolinska Institutet, Department of Physiology and Pharmacology, Solna, Sweden; [2]Peking University Third Hospital, Department of Obstetrics and Gynecology, Beijing, China; [3]Karolinska Institutet, Department of Women's and Children's Health, Stockholm, Sweden; [4]Karolinska Institutet, Department of Clinical Science, Huddinge, Sweden; [5]Centre de Recherche du Centre hospitalier de l'Université de Montréal (CRCHUM), Immunopathology Axis, Montréal, Canada; [6]Université de Montréal, Department of Medicine, Montreal, Canada

Introduction
Polycystic ovary syndrome (PCOS) is the leading cause of female infertility and is associated with high degree of comorbidities including type 2 diabetes and endometrial cancer. Hyperandrogenemia is a hallmark of PCOS and contributes to endometrial-related dysfunctions, including implantation failure and miscarriage. Whether cellular heterogeneity contributes to the functioning of the endometrium is not previously studied. Therefore, the aim is to reveal cell-type-specific disease signatures in the endometrium in women with PCOS at the single-cell level and to validate the role of molecular targets in endometrial organoids (EOs).
Method
Single nuclei were extracted from frozen endometrial biopsies collected from women with PCOS ($n=12$) and healthy controls ($n=5$) at cycle day 7-10. The nuclei RNA libraries were prepared following the 10x genomics protocol allowing us to sequence ~10,000 cells per sample and ~20,000 reads per cell. Sequencing data is processed using Cellranger count for further data integration, quality control and analysis with the Seurat package. In parallel, 3-dimensional (3D) EOs are established from fresh endometrial biopsies that are enzymatically dissociated and collected at cycle day 7-10. The cells are resuspended in Matrigel droplet and organoids are generated and maintained in a defined medium. Following several passages, EOs are cryopreserved to create a biobank to be used for future functional analyses of identified molecular targets by single-cell RNA-sequencing, immunofluorescence microscopy and Seahorse metabolic analysis.
Results
Single-nuclei were extracted from 17 endometrial samples, 12 from women with PCOS and 5 from healthy controls for 10x snRNA-sequencing. Our initial bioinformatic analyses show that the endometrial tissue of women with PCOS has a distinct single-cell transcriptomic profile, with cell-type specific differentially expressed genes that differ from the healthy controls. The EO protocol has been established and EOs from four women with PCOS have been cryopreserved with EOs successfully reestablished after thawing. Validation with immunofluorescent staining shows that the 3D EOs consist of an intact proliferative epithelial membrane with a consistent polarity across the whole EO.
Conclusion
This rigorous mapping of endometrial tissue samples will increase the understanding of the cellular complexity and dysfunction and will be linked to phenotypic features in women with PCOS. By successive formation of 3D PCOS-EOs, we can further study cellular and molecular mechanisms causing PCOS-specific endometrial dysfunction.

DOI: 10.1530/endoabs.81.EP871

EP872

Assessment of early vascular changes in adult females with polycystic ovary syndrome in correlation with insulin resistance

Marwa Fathy[1], Mona Mansour[1], Aasem Saif[1], Alaa Mahmoud Abd Elhamid[2], Adel Mohamed[3], Mai Galal[2], Shrouk Moussa[1] & Samar Saad[4]
[1]Faculty of Medicine-Cairo University, Internal Medicine-Endocrinology Unit, Cairo, Egypt; [2]Faculty of Medicine-Cairo University, Internal Medicine-Vascular Unit, Cairo, Egypt; [3]Faculty of Medicine-Cairo University, Gynaecology and Obstetrics Department, Cairo, Egypt; [4]Faculty of Medicine-Cairo University, Clinical Pathology, Cairo, Egypt

Background
Polycystic ovary syndrome is a long lasting, complex, hormonal condition associated with microvascular endothelial dysfunction and strongly related to CIMT changes at an early age. ED represents an initial reversible step in atherogenesis development, so early clinical identification of ED may play a pivotal in the prevention or reversal of progression to atherosclerosis. Also, CIMT is considered as an early marker of atherosclerosis
Objective
to assess the early vascular changes in Egyptian women with PCOS marked functionally by measurement of endothelial dysfunction using brachial artery flow–mediated dilatation (FMD) andstructurally via CIMT using high resolution Doppler ultrasonography with correlation of such early vascular changes with HOMA-IR index. Also, to assess independent determinants of CIMT in PCOS patients for optimal control of all modifiable CV risk factors and targeted treatment protocols.
Material and Methods
In this study, Seventy Egyptian females were included and they were divided into **50** diagnosed to have PCOS using Rotterdam Criteria (PCOS group) and **20** in control group. Patients were recruited from General Gynecology Clinics and Endocrinology &Metabolic Diseases Outpatient Clinic at Cairo university hospitals during the period from 2019 to 2020. fasting insulin, fasting blood glucose, HbA1C, lipid profile, TSH, free testosterone, HOMA-IR, CIMT and endothelial function were assessed in all patients.
Results
HOMA-IR correlates positively with (BMI, waist circumference, SBP, DBP, TG, T. Cholesterol) and negatively with HDL in PCOS patients. We also found that CIMT was significantly higher in PCOS group (0.06 ± 0.01) than control group (0.05 ± 0.01) with $P < 0.001$. A more intense vasodilatation was observed in controls than in polycystic ovary syndrome (PCOS) patients ($P < 0.001$). The diagnosis of PCOS per se is a strong independent predictor of CIMT and endothelial dysfunction.
Conclusion
polycystic ovary syndrome is a condition associated with increased vascular risk as it is associated with microvascular endothelial dysfunction and strongly related to CIMT changes. For optimal control of all modifiable CV risk factors and targeted treatment protocols, we recommend screening of early stages of atherosclerotic diseases in PCOS women which may be possible causes of morbidity and mortality as PCOS is also associated with increased risk of different metabolic complications including HTN, insulin resistance, DM, CV diseases
Keywords
polycystic ovary syndrome;carotid-intima media thickness; endothelial dysfunction;insulin resistance; atherosclerosis.

DOI: 10.1530/endoabs.81.EP872

EP873

Gender affirming hormonal treatment in Danish transgender persons. A nationwide register-based study

Dorte Glintborg[1], Katrine Hass Rubin[1], Simon Bang Kristensen[1], Øjvind Lidegaard[2], Guy T'Sjoen[3], Malene Hilden[2] & Marianne Skovsager Andersen[1]
[1]Odense University Hospital, Odense, Denmark; [2]Copenhagen University, København, Denmark; [3]Ghent University Hospital, Gent, Belgium

Background
Gender affirming hormonal treatment (GAHT) is for many a cornerstone of transgender care. National data regarding use of hormonal treatment by transgender persons are limited.
Aim
To assess use of GAHT in transgender persons.
Design
National register-based cohort study in Danish transgender persons followed from 2000 until 2018. The main outcome measure was redemption of GAHT. Persons with an ICD-10 diagnosis code of "gender identity disorder" (CGI-cohort) and persons with legal sex change but without diagnosis (CPR-cohort) were included. In the CGI-cohort, transgender women were defined by prescription of estrogen and/or antiandrogens and transgender men were defined by prescription of testosterone after study inclusion. Discontinuation of GAHT was defined as no

redemption of GAHT ≥ 13 months or shift from feminizing to masculinizing hormone treatment, or vice versa.
Results
The cohort included 2770 transgender persons ($n=1700$, CGI-cohort and $n=1070$, CPR-cohort). The median age (interquartile range) at study inclusion was 26.0 (17.3) years for persons assigned male at birth ($n=1437$) and 22.5 (10.4) years for persons assigned female at birth ($n=1333$). In the CGI-cohort, the redemption rate for GAHT in transgender women increased from 4.0 (95% CI: [3.1; 5.2]) events per 100 person in year 2000-2005 to 20.5 [17.7; 23.6] between 2014 -2018. In transgender men, the event rate of GAHT increased from 4.2 [2.8; 6.2] to 18.9 [16.4; 21.7]. The rate of discontinuation of GAHT was 0.06 (95% CI 0.048; 0.071) per person year.
Conclusions
The event rate of GAHT increased during 2000-2018. Our data suggested high adherence to GAHT.

DOI: 10.1530/endoabs.81.EP873

EP874

Have we ignored red cell parameters in Turner Syndrome? Results from a single specialist centre

Katharina Beck[1], M d s a Dilrukshi[2], Matilde Calanchini[2], Noémi B A Roy[3] & Helen E Turner[2]
[1]University of Oxford, Medical Sciences Division, Oxford, United Kingdom; [2]Oxford Centre for Diabetes, Endocrinology and Metabolism, Department of Endocrinology, Oxford, United Kingdom; [3]Oxford University Hospitals, Department of Haematology, Oxford, United Kingdom

Introduction
Anaemia and other haematological disorders have been reported in Turner Syndrome (TS). TS-related comorbidities (premature ovarian insufficiency, autoimmune hypothyroidism, coeliac disease and liver diseases) and treatments (hormone replacement [HRT] and growth hormone) are possible explanations. We aim to investigate the prevalence of abnormal full blood count (FBC) in adult TS and assess associated clinical characteristics.
Methods
FBC parameters and clinical characteristics were retrospectively collected from the electronic patient records of 120 adult TS women attending a dedicated TS clinic.
Results
Median age was 34 years (IQR 27.25-49) and 45, X was the commonest karyotype ($n=46$, 38%). The most frequent abnormality in the most recent FBC was an elevated red blood cell (RBC) count in 25% ($n=30$), elevated mean cell haemoglobin (Hb) concentration in 19% ($n=23$) and/or elevated Hb in 9% ($n=11$). While some results were isolated when compared to previous FBCs, seven patients (6%) had elevated Hb and RBC count on more than one occasion. Associated conditions included primary hypothyroidism on treatment in 2, structural renal abnormalities in 2, and non-alcoholic fatty liver disease without significant liver impairment in 5. None were smokers or had a diagnosis of obstructive sleep apnoea. Six were of premenopausal age and on HRT (progestogens; medroxyprogesterone, levonorgestrel, or norethisterone; none received testosterone analogues) with 4 having regular withdrawal bleeding, while 1 patient was of postmenopausal age and no longer on HRT. Amongst TS patients on HRT, 51% had elevated Hb, haematocrit, RBC count, mean cell Hb and/or mean cell Hb concentration, compared to 45% not on HRT. Amongst TS patients who had NAFLD, 70% had elevated Hb, haematocrit, RBC count, mean cell Hb and/or mean cell Hb concentration compared to 44% amongst those without any liver disease. Six patients (5%) had recurrent anaemia (microcytic in 2, normocytic in 4). Half had a 45, X karyotype, 1/6 was on HRT, 4/6 had regular periods or withdrawal bleeds. Three women had been diagnosed with iron deficiency, associated with gastro-oesophageal reflux disease in 2.
Discussion
While our cohort shows a similar prevalence of anaemia in TS to a recent large observational study, the finding of elevated red cell parameters in the context of TS is novel and deserves further analysis in larger studies. Exploring the association between the abnormal red cell parameters and levels of sex hormones, EPO levels, Jak2 status as well as TS-associated conditions is warranted in the future.

DOI: 10.1530/endoabs.81.EP874

EP875

Multiple prolactinomas in a young man with Kallman syndrome and familial hypocalciuric hypercalcemia

Mojca Jensterle[1], Andrej Janez[1], Tina Vipotnik Vesnaver[2], Maruša Debeljak[3] & Magdalena Avbelj Stefanija[4]
[1]Department of Endocrinology, Diabetes and Metabolic Diseases, University Medical Centre Ljubljana, Ljubljana, Slovenia; [2]Clinical Institute of Radiology, University Medical Centre Ljubljana, Ljubljana, Slovenia; [3]Clinical Institute for Special Laboratory Diagnostics, University Children's Hospital, University Medical Centre Ljubljana, Ljubljana, Slovenia; [4]Department of Paediatric Endocrinology, Diabetes and Metabolic Diseases, University Children's Hospital, University Medical Centre Ljubljana, Ljubljana, Slovenia

Introduction
Kallmann syndrome (KS) is a rare congenital form of hypogonadotropic hypogonadism (HH) associated with anosmia, that occurs with an incidence of 1:48,000 (1:30,000 males). Multiple separate pituitary adenomas are also rare, identified in only 0.7 % of pituitary adenoma cases.
Case Presentation
A male Caucasian patient presented with absent puberty, small testicles (1 ml), microphalus, osteopenia and anosmia at age 15. Endocrine assessment confirmed HH. Based on concomitant olfaction dysfunction, he was diagnosed with Kallmann syndrome (KS). Hormonal replacement treatment was initiated for puberty induction with testosterone enanthate and then continued with testosterone undecanoate following local monitoring protocol. At age 26 the patient presented with mild headache. MRI revealed two separate pituitary adenomas along with the absence of the olfactory bulbs. Given the presence hyperprolactinemia (17x upper limit of the reference range) the diagnosis prolactinoma was made and treatment with cabergoline was started which resulted in complete biochemical response and in marked reduction of both adenomas in size. Hypogonadism persisted and testosterone replacement therapy was continued. Targeted genetic testing of genes associated with neuroendocrine tumors (AIP, *MEN1*, *NF1*, *PRKAR1A, RET, TSC1, TSC2, VHL*), and of 49 genes associated with HH and *TSHZ1*gene associated with isolated congenital anosmia using a next generation sequencing platform was negative. Mild concomitant hypercalcemia in accordance with familial hypocalciuric hypercalcemia (FHH) prompted mutation analysis of the *CASR* gene which yielded a pathogenic inactivating variant.
Discussion
Double separate prolactinoma in a patient with KS has not yet been reported in the literature. The effect of sex hormone treatment of KS patients on the possible development of prolactinoma is unknown at present. The relevance of the *CASR* gene mutation in our patient for the KS phenotype also needs further insights since CaSR is expressed in GnRH neurons in mouse brain and CaSR deficient mice have a reduced hypothalamic GnRH neuronal population. This would possibly point to a role for the CaSR pathogenic variant in the development of KS in our patient. On the other hand, no delayed puberty, infertility or central hypogonadism have been reported in FHH patients.
Conclusion
We are unaware of earlier reports of an ultra rare co-occurrence of KS and multiple prolactinomas and FHH. The role of an inactivating variant in *CASR* gene as well as the effect of sex hormone treatment on the patient's phenotype are uncertain at this stage.

DOI: 10.1530/endoabs.81.EP875

EP876

Reproductive endocrinology characteristics in young women with osteoporosis

Clara Kühner[1], Veronika Koeppen-Ursic[1,2] & Vanadin Seifert-Klauss[1]
[1]Klinikum rechts der Isar der Technischen Universität München : Frauenklinik der Technischen Universität München, Interdisciplinary Osteoporosis Center (IOZ) of the Technical University Munich (TUM), München, Germany; [2]Klinikum Freising GmbH, Orthopedics, Freising, Germany

Introduction
Premenopausal women that suffer from osteoporosis are under-diagnosed and many anti-osteoporotic medications are neither licensed for young women, nor

have they been established as safe or effective. Current guidelines on osteoporosis only address postmenopausal women, resulting in uncertainty and insufficient treatment for premenopausal women. To prevent bone fragility in young women, more knowledge and education about possible risk factors for osteoporosis in young age is needed.
Methods
Women under the age of 50 were recruited to fill out a questionnaire, if their T-values were osteoporotic, or if they presented with one or more fractures with a T-value of -2,0. They answered 42 questions on potential risk factors for bone fragility. Frequencies of risk factors were compared with published prevalences for the normal premenopausal population.
Results
Data of 104 women was analysed. The average age at first diagnosis of osteoporosis/osteopenia was 37 years *(range: 19-49)*, 78% had already sustained a fracture. 40% had been pregnant at least once, but only 74% of them had given birth. 16% of the patients had involuntary infertility, of these 82% had never been pregnant. Female infertility is estimated to affect 7,5% in the general population. 75% of the women had used or were on hormonal contraception, which is less than in the German population (87%). 14% had started hormonal contraception prior to 16 years of age. Hypermenorrhoea was more common amongst young osteoporosis patients than in the general female population (22% vs. 10%). Nearly half of the participants (45%) reported secondary amenorrhoea of more than 6 months at least once in their lifetime, much more than women without osteoporosis (1,5-3%). 22% of our patients stated having had an eating disorder for longer than one year. The lifetime prevalence for eating disorders in Germany ranges from 1,7-3,6% for anorexia nervosa and 2,6% for bulimia nervosa. 74% of the participants with an eating disorder also had amenorrhoea. Depression was more prevalent in young osteoporotic women (13%) than in the average population (8,2%), as was hypothyroidism (18% vs. 1-2%). 30% of the participants worked shifts or admitted to a chronic sleep disorder.
Discussion and conclusion
Compared to the normal population, some reproductive endocrine characteristics are more frequent in young women with osteoporosis, such as hyper- and amenorrhoea, eating disorders, hypothyroidism and depression.

DOI: 10.1530/endoabs.81.EP876

EP877

The endocrine disruptor Benzo[a]Pyrene inhibits gonadotropin-mediated steroidogenesis in a mouse Leydig tumor cell line

Samantha Sperduti[1,2], Neena Roy[1], Clara Lazzaretti[1], Elia Paradiso[1], Sara D'Alessandro[1,3], Elisa Mascolo[1], Lara Baschieri[1, 3], Daniele Santi[1, 4], Manuela Simoni[1,2,4] & Livio Casarini[1,2]
[1]University of Modena and Reggio Emilia, Unit of Endocrinology, Department of Biomedical, Metabolic and Neural Sciences, Modena, Italy; [2]University of Modena and Reggio Emilia, Center for Genomic Research, Modena, Italy; [3]University of Modena and Reggio Emilia, International PhD School in Clinical and Experimental Medicine (CEM), Modena, Italy; [4]Azienda Ospedaliero-Universitaria di Modena, Department of Medical Specialties, Modena, Italy

Introduction
Benzo[a]Pyrene (BaP) is an endocrine-disrupting chemical, which may impact reproduction. It is a polycyclic aromatic hydrocarbon generated by the incomplete combustion of organic compounds. BaP may be accumulated in the environment, achieving effective concentrations in the nanomolar range and exerting genotoxic effects in long-term exposed humans.
Aim
We evaluated the short-term impact of BaP on luteinizing-hormone (LH) /choriogonadotropin (hCG)-mediated functions in the steroidogenic mouse Leydig tumor cell line (mLTC1), *in vitro*.
Methods
mLTC-1 cells were treated with increasing BaP doses (range fM-μM), over 0-40 h, in the presence or in the absence of the maximal, non-saturating effective LH and hCG concentration (1500 and 300 pM, respectively). The maximal, non-cytotoxic BaP dose was evaluated by 3-(4,5-dimethylthiazol-2-yl)-2,5 diphenyl tetrazolium bromide (MTT) assay. 3-h intracellular cyclic adenosine monophosphate (cAMP) production was assessed by bioluminescence resonance energy transfer (BRET), in transfected cells overexpressing the specific biosensor. 10, 50 and 100 μM forskolin-treated cells served as controls. 15-min cAMP-response element binding protein (CREB), extracellularly-regulated kinases 1 and 2 (ERK1/2) and p38 mitogen-activated protein kinase (p38-MAPK) phosphorylation was evaluated by Western blotting. 8- and 24-h progesterone and testosterone levels were measured by immunoassay. Results were compared with those from gonadotropin- and BaP-untreated samples by Kruskal-Wallis test followed by Dunn's post-hoc test ($P<0.05$; $n = 6$).
Results
1 μM BaP was determined as the maximal, non-cytotoxic dose ($P\geq0.5$) and was used for cell treatments, as well as the environmentally available dose of 1 nM. LH/hCG-induced intracellular cAMP accumulation was dampened by 1 μM BaP (2.0-fold compared to BaP-untreated; $P<0.05$), with no gonadotropin-specific differences, while 1 nM BaP did not produce any effect. 1 μM BaP failed in inhibiting 10-100 μM forskolin-induced cAMP ($P\geq0.5$), excluding that the compound modulates adenylyl cyclase enzyme functioning. Consistently, BaP interfered with most of the downstream intracellular cAMP-dependent events. 1 μM BaP decreased LH/hCG-induced CREB phosphorylation ($P<0.05$) and increased basal ERK1/2 phosphorylation ($P<0.05$), while no perturbation of p38-MAPK phosphorylation was detected ($P\geq0.05$). The modulation of signal transduction is linked to interfering effects on steroidogenesis. LH/hCG-mediated, 24-h progesterone synthesis (1.5-fold BaP-untreated; $P<0.05$), as well as 8-h testosterone production (2.0-fold BaP-untreated; $P<0.05$), decreased significantly in the presence of 1 μM BaP.
Conclusions
These results demonstrated that a micromolar BaP concentration inhibits short-term steroidogenic signals in a mammal Leydig cell line, through an unknown molecular mechanism. These data suggest that BaP may potentially interfere with endocrine signals, dysregulating male gonadal and reproductive functions.

DOI: 10.1530/endoabs.81.EP877

EP878

Characteristics of male idiopathic hypogonadotropic hypogonadism (IHH) patients

Muhammad Saleem[1], Nanik Ram[1], Sajjad Ali Khan[1] & Muhammad Mustansir Mehdi Khan[2]
[1]Aga Khan University Hospital, Section of Diabetes, Endocrinology and Metabolism and Department of Medicine, Aga Khan University Hospital, Karachi, Pakistan, Karachi, Pakistan; [2]Aga Khan University, Pakistan

Background
Idiopathic Hypogonadotropic Hypogonadism (IHH) is a condition caused by deficiency or insensitivity to gonadotropin-releasing hormone where the pathology behind the mechanism is unknown and no secondary causes of hypogonadotropic hypogonadism are present. The condition not only effect sexual characteristic but can affect the physical and psychosocial development of a patient therefore making its prompt diagnoses and treatment necessary. The purpose of this study was to determine the sign, symptoms and laboratory parameters of the male IHH patients presenting in a tertiary setting.
Materials and Methods
This cross-sectional study was carried in Aga Khan University on male patients presenting with IHH to the Endocrinology clinic from December 2000 to December 2020. The patients presenting with signs or symptoms of hypogonadism, associated low sex steroid hormone and inappropriately low or normal gonadotropins with absent expansive hypothalamic or pituitary lesions or multiple pituitary hormone defects were included in the study. Quantitative variable was shown as Mean ± Standard Deviation while qualitative variables were shown as frequency and percentages.
Results
Data of 79 IHH patients was reviewed with Mean Age ± SD being 24.2 ± 7.5 years. Clinically 64 (81.0%) presented with small genitalia, 50 (63.6%) had absent secondary sexual characteristics, 53 (67.1%) presented with infertility, 44 (55.7%) had not attained puberty, 52 (65.8%) had erectile dysfunction, 46 (58.2%) with loss of libido, 11(13.9%) had a positive family history, 24 (30.3%) had gynecomastia, 9 (11.4%) had undescended testes and 6 (7.6%) had hyposmia or anosmia. The mean serum testosterone level of the patients was 26.3 ± 60 ηg/dl while mean FSH and LH level were 2.7 ± 5.0 and 1.3 ± 2.4 respectively.
Conclusion
It was observed that the primary complains of patients presenting with IHH were small genitalia, infertility, and absence of secondary sexual characteristics with a low serum testosterone level.
Keywords
Male Idiopathic Hypogonadotropic Hypogonadism (IHH), Infertility, Pakistan

DOI: 10.1530/endoabs.81.EP878

EP879

Daytime salivary androgen rhythm by LC-MS/MS in women affected by Polycystic Ovary Syndrome (PCOS) fulfilling the three Rotterdam diagnostic criteria

Flaminia Fanelli[1], James M Hawley[2], Marco Mezzullo[1], Alessia Fazzini[1], Laura Zanotti[1], Matteo Magagnoli[1], Uberto Pagotto[1], Brian Keevil[2] & Alessandra Gambineri[1]
[1]Alma Mater University of Bologna, Unit of Endocrinology and Prevention and Care of Diabetes - Center for Applied Biomedical Research - Department of Medical and Surgical Sciences, Bologna, Italy; [2]University Hospital South Manchester, Manchester NHS Foundation Trust, Department of Clinical Biochemistry, Manchester, United Kingdom

Background
Excess testosterone in PCOS is accompanied by increased levels of other ovarian and adrenal androgens and precursors. Recently, 11-oxygenated adrenal androgens have been postulated as major components of the circulating androgen pool in PCOS. Obesity is strictly connected with androgen excess and with the derangement of hormone circadian rhythmicity. To date, it has not been clarified whether hyperandrogenism in PCOS, either complicated by obesity or not, is accompanied by the dysregulation of androgen biorhythm.
Objective
To investigate the daytime rhythmicity of androgens and precursors in saliva of women with PCOS fulfilling the three Rotterdam diagnostic criteria, according to their BMI status.
Methods
PCOS patients (age 15-34y) showed oligo-amenorrhea, polycystic ovarian morphology and either clinical (hirsutism) or biochemical (elevated serum testosterone) hyperandrogenism. These were subdivided in overweight/obese (OB-PCOS; BMI $\geq$ 27 kg/m^2 $n = 8$) and non obese PCOS (NO-PCOS; BMI $<$ 27 kg/m^2 $n = 8$) and compared with age-matched non obese healthy women (NO-CTR; age: 23-32y; BMI $<$ 27 kg/m^2 $n = 16$). All were in follicular phase, had standardized meals and self-collected saliva every hour from 7 until 23am. Testosterone, androstenedione, 17OH-progesterone, dehydroepiandrosterone, 11OH-androstenedione and 11keto-testosterone were measured by LC-MS/MS.
Results
BMI was higher in OB-PCOS (31.1 (29.1-34.4)) compared to NO-PCOS (22.5 (20.2-27.2)) and NO-CTR (21.3 (20.7-22.9) kg/m^2) ($P<0.001$), but similar between NO-PCOS and NO-CTR. All women showed higher androgen and precursor levels at awakening, which decreased until bedtime (all $P<0.001$). Testosterone and androstenedione, at each time point, and 17OH-progesterone, at most time points, were higher in OB-PCOS and NO-PCOS vs NO-CTR women (all $P<0.050$). Testosterone was higher in OB-PCOS vs NO-PCOS at 8, 10, 11, 16 and 17am (all $P<0.050$). Dehydroepiandrosterone was higher in OB-PCOS compared to both NO-PCOS and NO-CTR at 9-13 and 16-17am (all $P<0.050$). PCOS women showed a trend for high 11-oxygenated androgens at mid-morning and afternoon, but lower at late night, only achieving significance at 10am, with 11OH-androstenedione higher in OB-PCOS vs NO-CTR; at 17am, with 11-ketotestosterone higher in OB-PCOS and NO-PCOS vs NO-CTR; and at 23am, with 11OH-androstenedione lower in OB-PCOS vs NO-CTR (all $P<0.050$).
Conclusion
Androgen biorhythm was preserved in PCOS. Excess secretion of androgens originating from both ovary and adrenal was maintained throughout the day in both PCOS groups. The overweight/obese PCOS phenotype is featured by a partial rhythm derangement with a more severe testosterone excess and enhanced adrenal tone, as featured by dehydroepiandrosterone, at mid-morning and afternoon. Interestingly, 11-oxygenated androgens did not show a specific alteration in the examined PCOS phenotypes.

DOI: 10.1530/endoabs.81.EP879

EP880

Cardiopulmonary capacity and muscle strength in transgender women in long-term gender-affirming hormone therapy: a cross-sectional study

Leonardo Alvares[1,2], Marcelo Rodrigues dos Santos[3], Francis Ribeiro de Souza[3], Lívia Marcela Santos[1], Elaine Maria Frade Costa[2], Berenice Bilharinho de Mendonça[2], Maria Janieire de Nazaré Nunes Alves[3] & Sorahia Domenice[2]
[1]Centro Universitário São Camilo, Brazil; [2]Faculdade de Medicina da Universidade de São Paulo, Unidade de Endocrinologia do Desenvolvimento, São Paulo, Brazil; [3]InCor - Instituto do Coração do Hospital das Clínicas da FMUSP, São Paulo, Brazil

Introduction
Effects of prior exposure to testosterone (T) during puberty on the performance of transgender women (TW) in estrogen therapy undergoing physical effort are not known, mainly about cardiopulmonary capacity (CPC). Objectives: To evaluate CPC and muscle strength in TW undergoing long-term gender-affirming hormone therapy (GAHT). Methods: A cross-sectional study was carried out with 15 TW (34.2 $\pm$ 5.2 yo), 13 cisgender men (CM) and 14 cisgender women (CW). TW were in hormone therapy for 14.4 $\pm$ 3.5 years. Bioimpedanciometry, handgrip test and CP exercise on a treadmill with an incremental effort were done. Results: The medium strength (kg) was 35.3 $\pm$ 5.4 in TW, 29.7 $\pm$ 3.6 in CW, and 48.4 $\pm$ 6.7 in CM (TWvsCW $P=0.0250$;TWxCM $P<0.0001$). About Median Strength/FFM (Free Fat Mass), a mean of 0.6 was observed in TW group and 0.7 in both others (TWvsCW $P=0.1432$; TWvsCM $P=0.0301$). Mean VO2peak (L/min) of TW was 2606 $\pm$ 416.9, of CW 2167 $\pm$ 408.8 and of CM 3358 $\pm$ 436.3 (TWvsCW $P=0.0238$; TWvsCM <0.0001; CWvsCM $P<0.0001$). Analysis of VO2 max/FFM (L/min/kg), TẂs rate was 47.7 $\pm$ 5.1, CẂs was 53.3 $\pm$ 8.3 and CḾs was 52.4 $\pm$ 5.8 (TWvsCW $P=0.0704$;TWvsCM $P=0.1357$). O2pulse of TW was intermediate between CW and CM (TWvsCW $P=0.0131$, TWvsCM $P<0.0001$) . There was high correlation of VO2peak and FFM/height2 (FFM/Hgt2) of TW ($r=0.7388$;$P=0.0017$) not seen in the other groups. Percentage predicted Heart Rate at effort was higher in TW (103.1) than in CW (96.5) ($P=0.0065$) and CM (99.2) ($P=0.1373$). Discussion: By integrating the data set we may conjecture that TW undergoing long-term GAHT could have an exacerbated ergoreflex and a decreased functionality of the muscular unit. Conclusion: Cardiopulmonary capacity, mainly peak VO2, is blunted in TW after long-term hormone therapy. However, TW still present slightly higher exercise performance when compared with CW.

DOI: 10.1530/endoabs.81.EP880

EP881

Noonan Syndrome, Dandy-Walker variant and delayed puberty- a rare association

Mariana Lavrador, Lú cia Fadiga, Mafalda Martins Ferreira, Luí sa Barros & Isabel Paiva
Centro Hospitalar e Universitário de Coimbra, Coimbra, Portugal

Introduction
The Dandy-Walker complex (DW) comprises a rare intracranial malformation of the posterior fossa and multiple organ anomalies. The association with endocrine pathology is rare - described in isolated cases (Kallman syndrome, primary hypothyroidism (PH) and central precocious puberty). Noonan syndrome (NS) is a genetic disease usually diagnosed at birth, with variable phenotype. Most cases have AD transmission, with the PTPN11 gene mutation responsible for 50%.
Case report
Male patient referred for consultation at 16 years due to short stature and delayed puberty. At 1st evaluation: height 148.5cm (-3.1 SD), weight 41 Kg, pubertal stage P3, testicular volume 10mL; facial dimorphisms (hypertelorism, bulbous nose, triangular face), and 5th finger's brachydactyly. Past medical history of congenital diaphragmatic hernia, intestinal occlusion at 11 months, strabismus, delayed developmental milestones and unilateral cryptorchidism (surgically corrected at 12y). Family target height of 165 cm. He denied olfactory dysfunction. Of the complementary diagnostic exams: bone age of 13y1month; FSH <0.3 mIU/ml; LH <0.1 mIU/ml; total and free testosterone (TT/FT) 2.2 ng/ml (2,7-11) and 3.3 pg/ml (13-40); LHRH stimulation test with FSH 15.7 mIU/ml and LH 14.5 mIU/ml post stimulation; primary hypothyroidism (TSH 5.7 uIU/ml; T4L 0.7 ng/dl – started LT4 25 mg); 46XY karyotype; brain MRI showed "patency of the olfactory bulbs, identifying both olfactory sulci, without hypothalamic-pituitary alterations; increase in fourth ventricle dimensions, focal increase in retrocerebellar extra-axial space - DW variant". Genetic study (CGH-array) without alterations. He started induction of puberty with testosterone enanthate 125 mg monthly, until 20y, with a final height of 162.1 cm (-2 SD), P5 Tanner stage, and testicular volume of 25mL. Lost of follow up until 30y. At 30y: FSH 11 mUI/ml, LH 4.5 mUI/ml, and TT 5,3 ng/ml; new genetic study by total exomic sequencing, with identification of the variant c.1472C $>$ T p.(Pro491Leu), in heterozygosity, in the PTPN11 gene, classified as pathogenic – Noonan Syndrome type 1.
Conclusion
This case illustrates the rare association of a patient with NS, DW variant and delayed puberty. The diagnosis of NS only at adulthood shows how genetic testing has improved over the years. The DW variant explains diaphragmatic

hernia, intestinal obstruction, hypertelorism, and eventually the PH. NS explains facial dimorphism, cryptorchidism and learning difficulties, as well as short stature and delayed puberty. Diagnosis of NS is of particular importance for surveillance of comorbidities and genetic counseling.

DOI: 10.1530/endoabs.81.EP881

EP882

Anti-müllerian hormone analysis as a predictor of the polycystic ovary syndrome diagnosis in romanian women

Nicoleta Baculescu[1,2], Laura Leonte[2], Serban Radian[1, 2], Monica Gheorghiu[1, 2], Andra Caragheorgheopol[1], Bianca Biban[1], Cristina Serban[1], Florin Grigorescu[2, 3] & Catalina Poiana[1,2]
[1]C.I. Parhon National Institute of Endocrinology, Bucharest, Romania; [2]Carol Davila University of Medicine and Pharmacy, Bucharest, Romania; [3]Institut du Cancer de Montpellier, Montpellier, France

Background
Higher anti-Müllerian hormone (AMH) values are associated with polycystic ovary syndrome (PCOS) and AMH is proposed as a marker of PCOS, however, the optimal diagnostic threshold is not yet defined.
Aim
To study the significant correlations of AMH in PCOS and the accuracy and threshold of AMH for the PCOS diagnosis in Romania.
Subjects and methods
Serum AMH, TT, LH, FSH, fasting glucose and insulin (Ins), HOMA-IR and BMI were analyzed in a cohort of 157 patients with PCOS selected by Rotterdam 2003 criteria and 166 controls, aged 18-35 years, recruited at the National Institute of Endocrinology, Bucharest, Romania. Receiver operator characteristic (ROC) curves were constructed to determine the diagnostic utility of different parameters.
Results
Serum AMH was positively correlated with oligo/amenorrhea ($P=0.0034$), TT ($P=0.0178$), LH ($P=0.0123$), LH/FSH ($P=0.0015$) and number of antral follicles per ovary ($P=0.0011$) in PCOS, while BMI ($P<$ -0.0001), fasting-Ins (P= -0.0209) and HOMA-IR (P= -0.0138) were negatively correlated with AMH in these patients. In stepwise linear regressions including as effects LH/FSH, TT, BMI, fasting-Ins or HOMA-IR and age, LH/FSH and BMI remained significant independent predictors of AMH values in PCOS ($P=0.0002$ and $P<$ -0.0001 respectively). In ROC curve analysis using all population of the study (PCOS and controls), the area under the curve (AUC) for AMH in the diagnosis of PCOS was 0.893 [95% confidence interval (CI): 0.834-0.953; $P<$ 0.0001], with the best compromise between sensitivity and specificity at a cut-off of 32.41 pmol/l (*i.e.*4.53 ng/ml) (Se=85.06%, Spe=80.65%). The AUCs for TT, LH, LH/FSH, fasting-Ins, HOMA-IR and BMI were 0.773 [95% CI: 0.717-0.830; $P<$ 0.001], 0.736[95% CI: 0.664-0.809; $P<$ 0.0001], 0.788 [95% CI: 0.715-0.862; $P<$ 0.001], 0.669 [95% CI: 0.598-0.741; $P=0.0004$], 0.615 [95% CI: 0.537-0.694; $P=0.005$] and 0.612 [95% CI: 0.546-0.678; $P=0.001$] respectively.
Conclusions
AMH values reflect both reproductive and metabolic dysfunction in PCOS. The optimal AMH threshold for PCOS diagnosis was 32.41 pmol/l (4.53 ng/ml) in the Romanian population of this study. The accuracy of serum AMH in PCOS diagnosis is greater than that of TT, gonadotropins or isulin-resistance quantified by HOMA-IR.

DOI: 10.1530/endoabs.81.EP882

EP883

Health related quality of life and symptoms of anxiety and depression in women with polycystic ovary syndrome in different weight categories

Josefin Kataoka[1], Marie Olsson[2], Ingrid Larsson[3], Johanna Schmidt[4] & Elisabet Stener-Victorin[2]
[1]Institute of Neuroscience and Physiology, Department of Physiology, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden; [2]Institute of Physiology and Pharmacology, Karolinska Institutet, Stockholm, Sweden; [3]Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden; [4]Institute of Clinical Sciences, Department of Obstetrics and Gynaecology, Sahlgrenska academy, University of Gothenburg, Gothenburg, Sweden

Background
Women with polycystic ovary syndrome (PCOS) have lower health related quality of life (HRQL) and more symptoms of anxiety and depression than women without PCOS, where a higher BMI is positively correlated to both lower HRQL and more symptoms of anxiety and depression. Studies on women with PCOS and severe obesity regarding symptoms of anxiety and depression are lacking.
Aims
To examine if women with severe obesity and PCOS have lower HRQL and more symptoms of anxiety and depression than women with severe obesity without PCOS, and evaluate the effect of a structured weight reduction program. Further, to compare HRQL and symptoms of anxiety and depression in women with and without PCOS in different weight categories.
Patients and methods
In total, 407 women from four studies were included (PCOS $n = 179$, non-PCOS $n = 228$). The main study included 246 women with severe obesity (BMI ≥ 35) (PCOS $n = 63$, non-PCOS $n = 183$). To compare weight categories, data from earlier studies were added, including 134 women with BMI < 35 (PCOS $n = 63$ non-PCOS $n = 51$). Questionnaires Short form (SF)-36 and Self-rating Scale for Affective Syndromes (CPRS-SA) were used to assess HRQL and symptoms of anxiety and depression. Women in the main study entered a weight reduction program, with a very low energy diet (VLED), and 73 women were left to follow-up (PCOS $n = 16$, non-PCOS $n = 57$).
Results
In women with severe obesity, HRQL and symptoms of anxiety and depression did not differ between women with and without PCOS. In women with normal- and overweight, women with PCOS had lower mental HRQL ($P=0.001$ resp. $P=0.004$) and more symptoms of anxiety ($P=0.001$ resp. $P=0.001$) and depression ($P=0.002$ resp. $P=0.012$) compared to women without PCOS. In women with severe obesity, significant weight reduction was achieved in both women with and without PCOS, and led to improved physical HRQL in both groups (PCOS: $P=0.011$, non-PCOS: $P=0.001$).
Conclusions
The difference in HRQL and symptoms of anxiety and depression seen between women with and without PCOS with normal- or overweight is not seen in women with severe obesity. Women with severe obesity benefits from losing weight to improve their physical HRQL. Keywords: Polycystic ovary syndrome, severe obesity, health related quality of life, anxiety, depression

DOI: 10.1530/endoabs.81.EP883

EP884

Obese patients with PCOS and prediabetes: two years follow up of the effects of metformin, pioglitazone and empagliflozin treatment on metabolic control, hormonal imbalance and ovulations

Nevena Ilic[1], Corrado Pasquali[2], Violeta Culafic-Vojinovic[3], Tatjana Eror[4] & Stanislava Zivkovic[5]
[1]Euromedik hospital, Endocrinology, Belgrade, Serbia; [2]Sant'Eugenio hospital, ICU, Rome, Italy; [3]Euromedik hospital, Belgrade, Serbia; [1]Euromedik hospital, Endocrinology, Belgrade, Serbia; [1]Euromedik hospital, Endocrinology, Belgrade, Serbia

Introduction
The role of metformin in PCOS is very well known and several studies reported effects of thiazolidinediones and SGLT2 inhibitors on metabolic parametars in these patients.
Objective
The aim of this study was to compare the effects of metformin, pioglitazone and empagliflozin treatment on metabolic control, hormonal imbalance, weight loss and ovulations in obese patients with PCOS and prediabetes.
Methods
BMI, waist circumference, HOMA index, leptin/adiponectin, LH/FSH, androstendione, testosterone, DHEAS, triglycerides, cholesterol, HDL, LDL and presense of ovulation were tested at the admission and 24 months after therapy.
Patients
146 overweight/obese patients (mean age $25 \pm 2,6$) with PCOS and prediabetes were divided in 3 groups based on medication they were treated with.
Results
Empagliflozin was superior to metformin in weight loss and metformin was superior than pioglitazone ($P<0,05$). Empagliflozin was superior to metformin and pioglitazone in reducing waist circumferences ($P<0.01$). Metformin was

superior to empagliflozin and pioglitazone in lowering LH/FSH and testosterone ($P<0,001$). Metformin and empagliflozin were superior in reducing androstendione than pioglitazone ($P<0,01$). Empagliflozin and pioglitazone were superior to metformin in raising SHBG and HDL ($P<0,01$) and lowering L/A ($P<0,05$), trilgycerides ($P<0,001$) and HOMA index ($P<0,01$). There was no difference between groups in ovulatory menstrual cycles regulation.
Conclusions
Empagliflozin and pioglitazone were superior to metformin in metabolic control while metformin was superior in resolving hyperandrogenism. Metformin, pioglitazone and empagliflozin were equally efficient in regulating menstrual cycles in patients with PCOS Pioglitazone and empagliflozin can be a second therapy of choice in patients with PCOS.

DOI: 10.1530/endoabs.81.EP884

EP885

Perrault syndrome in three Tunisian women

Faten Haj Kacem Akid, Wafa Belabed, Mouna Elleuch, Abdelmouhaymen MISSAOUI, Dhoha Ben Salah, Fatma Mnif, Nabila Mejdoub & Mohamed Abid
Hedi Chaker University Hospital, Endocrinology Department, Sfax, Tunisia

Introduction
Perrault syndrome (PS) is a rare disease characterized by the association of a premature ovarian failure (with primary or secondary amenorrhea) and a sensorineural deafness. In this context we report the case of three patients presenting the association of these two anomalies.
Cases
We report the cases of three females, including two sisters from a consanguineous marriage, aged 21, 16 and 23 years, respectively. The two cardinal signs of this syndrome made of premature ovarian failure and sensorineural deafness were present in the three patients, associated with a Parkinsonian syndrome in the third case. The examination did not show any dysmorphic syndrome or mental retardation. The audiometric exploration of the two sisters concluded to a deafness whose endocochlear nature was confirmed by the auditory evoked potentials. Hormonal exploration confirmed the presence of hypergonadotropic hypogonadism in all three patients. All three patients had a 46XX caryotype, thus eliminating Turner syndrome. The immunological investigation was negative. Pelvic ultrasound in all three patients showed hypoplastic ovaries and uterus. The brain MRI of the two sisters showed an aspect in favor of a leukodystrophy, never described in the literature. The family investigation revealed an isolated congenital deafness in a nephew of both sisters, also from a consanguineous marriage. Biomolecular study in search of genes involved in gonadal and endocochlear differentiation is in progress.
Conclusion
Ovarian dysgenesis associated with sensorineural hearing loss are the cardinal features of Perrault syndrome. A range of associated neurological and neuroradiological disorders are increasingly reported in the literature. Certainly, advances in molecular biology will be able to support the etiopathogenic link between gonadal, auditory and neurological involvement in this syndrome.

DOI: 10.1530/endoabs.81.EP885

EP886

Delayed puberty with a novel mutation in the p450 oxido reductase gene

Neelaveni Kudugunti[1], Dr Datta Reddy Aakiti[2] & Rakesh Sahay[1]
[1]Osmania Medical College, Hyderabad, India; [2]Yashoda Hospitals - Malakpet, Hyderabad, India

P450 Oxidoreductase (POR) deficiency is a rare autosomal recessive disorder of steroidogenesis with varied clinical presentation. POR is the electron donor for all microsomal enzymes involved in steroidogenesis namely P450c 17(17 hydroxylase/17,20 lyase), P450c 21 (21 –hydroxylase), and P450 aro(aromatase). POR deficiency can cause genital ambiguity in both sexes, impaired steroidogenesis and skeletal malformations. Here we present a patient with ovarian cysts and delayed puberty with a novel mutation in the POR gene. A 14 year old girl born of 3rd degree consanguineous marriage presented with acute abdominal pain, on evaluation found to have torsion of large right hemorrhagic ovarian cyst requiring surgical intervention with oophorectomy. 3 to 4 months later patient presented with recurrence of abdominal pain, investigation revealed large cyst in left ovary for which cystectomy was done, subsequent serial ultrasonography evaluation for the next 6months revealed increase in size of ovarian cysts. At this point endocrinology consultation was sought for not attaining menarche. History of acne eruption in the mother during pregnancy but no hirsutism. Her height was 164 cm (75-90th centile), weights 69 kg (90-97th centile), arm span – 171 cms, US/LS ratio-0.85:1. Sexual maturation is A1 P3 B1. No facial dysmorphism, no features of androgen excess, normotensive. Short 4th metatarsal left foot, no other skeletal deformities. Normal external genitalia. Karyotype is 46, XX. Prolactin is 12.8 ng/ml, FSH 13.8, LH 33.7, T3- 1.66, T4-10.5, TSH -1.10, Estradiol 24.22 pg/ml, AMH-0.45 ng/ml and testosterone 14.40 ng/dl. 8 AM serum cortisol is 12.62 mg/dl, 17 hydroxy progesterone 21.7 ng/ml, post ACTH stimulation serum 17 OHP is 22.8 ng/ml, serum cortisol 9.74 mgldl. Bone age-14 years. USG pelvis uterus 30x20x15 mm, ET 4.5mm, bulky left ovary with multiple cysts. Genetic testing showed homozygous mutation in POR (NM_000941.2), (Chr7:75615521); Exon 15; c.1860G>T (p.Trp620Cys). She was advised estrogen replacement and hydrocortisone cover during stress. In conclusion our case presented with normal genitalia, no skeletal abnormalities, no hyper androgenic features with large ovarian cysts and delayed puberty(suggestive of aromatase deficiency) with high 17(OH) progesterone and subnormal rise in cortisol and 17(OH) progesterone post ACTH stimulation consistent with POR deficiency. The wide range of phenotypic presentation may be explained by the differential inhibition of POR dependent enzymes. Given the varied clinical presentation and the risk of hypocortisolism, clinicians should be aware and alert to this diagnosis.

DOI: 10.1530/endoabs.81.EP886

EP887

Assessment of a new marker of polycystic ovary syndrome in morbidly obese women

Ibtissem Oueslati[1], Amani Terzi[1], Bassem Hammami[2], Hana Belhadj Hassen[1], Seif Boukriba[3], Habiba Mizouni[3], Moncef Feki[2] & Melika Chihaoui[1]
[1]La Rabta University Hospital, Department of Endocrinology, Tunis, Tunisia; [2]La Rabta University Hospital, Laboratory of Biochemistry, Tunis, Tunisia; [3]La Rabta University Hospital, Department of Radiology, Tunis, Tunisia

Introduction
Polycystic ovary syndrome is the most common cause of anovulatory infertility in women. Anti-Mullerian Hormone (AMH) was considered a reliable marker for the diagnosis of polycystic ovary syndrome (PCOS). However, AMH level is influenced by age and body mass index. The aim of this study was to analyze the performance of the (LH x AMH)/FSH ratio in the diagnosis of PCOS in women with morbid obesity.
Methods
This was a cross-sectional study including 50 women of reproductive age with morbid obesity (body mass index $\geq$ 40 kg/m2). Each patient underwent a clinical examination, biological and hormonal assays, and an ovarian ultrasound between the third and fifth day of the menstrual cycle. PCOS was diagnosed according to the Rotterdam criteria. (LH x AMH)/FSH ratio was calculated.
Results
Participants had an average age of 34.2 $\pm$ 7.5 years. PCOS was diagnosed in 20 women (40%). The (LH x AMH)/FSH ratio was positively correlated with Ferriman and Gallwey score ($r=0.602$, $P=0.002$), testosterone level ($r=0.586$, $P<10\text{-}3$), delta 4-androstenedione level ($r=0.343$, $P=0.01$), and ovarian volume ($r=0.442$, $P=0.004$). However, this ratio was not correlated with age, body weight, body mass index, and waist circumference. Its mean value was 3.34 in women with PCOS and 0.84 in those without PCOS ($P< 10^{-3}$). The area under the ROC curve for the diagnosis of PCOS was 0.807 for the (LH x AMH)/FSH ratio, 0.714 for the AMH level, and 0.788 for the LH/FSH ratio. A (LH x AMH) /FSH ratio $\geq$ 1 was positively associated with PCOS (Odds ratio= 10.2, $P=0.001$, 95%-CI: 2.39-43.5) with a sensibility of 85%.
Conclusion
Our results showed a significant association between (LH x AMH)/FSH ratio and PCOS. This new ratio was not influenced by age and obesity. Therefore, it may be a good screening tool for PCOS in women with morbid obesity.

DOI: 10.1530/endoabs.81.EP887

EP888

Significance of thyroid dysfunction on metabolism and pregnancy in women with polycystic ovary syndrome

Milena Brkic[1], Svetlana Vujovic[2], Radoslav Gajanin[3], Valentina Soldat Stankovic[4] & Gabrijela Malesevic[5]
[1]School of Medicine, University of Banja Luka, BanjaLuka, Bosnia and Herzegovina; [2]School of Medicine, University of Belgrade, Belgrade, Serbia, Department of Endocrinology, Clinical Center of Serbia, Beograd, Serbia; [3]School of Medicine, University of Banja Luka, Department of Clinical Pathology, University Clinical Center of the Republic of Srpska Banja Luka, BanjaLuka, Bosnia and Herzegovina; [4]School of Medicine, University of Banja Luka, Department of Endocrinology with General Internal Medicine, Banja Luka, BanjaLuka, Bosnia and Herzegovina; [5]School of Medicine, University of Banja Luka, University Clinical Centre of the Republic Srpska, internal medicine, Banja Luka, BanjaLuka, Bosnia and Herzegovina

Introduction
There is a significant overlap of symptoms between polycystic ovary syndrome (PCOS) and thyroid disease, despite the fact that they are two different diseases. Both diseases individually affect a woman's metabolic parameters and fertility, and their association makes them much more difficult to manage.
Objective
To investigate the effect of elevated thyroid stimulating hormone (TSH) concentrations on metabolic and endocrine parameters in women with PCOS. Analysis of the correction of TSH values and insulin resistance (IR) on pregnancy using levothyroxine with myo-inositol and d- hiro- inositol.
Methods
Examines between 25 and 35 years of age, diagnosed with PCOS were divided into 2 groups: women ($n=50$) with Hashimoto's thyroiditis, with TSH $\leq$6 mIU/l and regular thyroid hormone levels who did not conceive and women ($n=50$) without elevated serum TSH. Each exminee underwent hormonal analyses during the early follicular phase, glucose and insulin on an empty stomach for 30,60 and 120 minutes during an oral load test with 75 g glucose, body mass index, transvaginal ovarian ultrasound. The lipid profile was checked and homeostatic model assessment (HOMA). Women with PCOS and elevated TSH were divided into two groups ($n = 25$). One group took levothyroxine 0.25 g and myoinositol plus d chiro inositol for 6 months, and the other group ($n=25$) levothyroxine 0.25 mg. Both groups adhered to the same diet with exercise 3 times a week for 30 minutes. After 6 months, the same hormonal, biochemical analyses were checked.
Results
In women with elevated TSH and PCOS, the lipid profile and HOMA were significantly impaired compared to the control group ($P<0,01$)There was no statistical difference in androgen and prolactin concentrations between examines. In women with PCOS and elevated TSH after taking levothyroxine and myo-inositol, d-chiro -inositol combination therapy, there was a statistically significant correction of TSH, anti TPO, HOMA and pregnancy in relation (44:24%) in correlation with women who used only levothyroxine. In both groups of patients, there was a statistically significant correction of the lipid profile.
Conclusion
Hashimoto's disease in the range of subclinical hypothyroidism in combination with PCOS has a negative impact on the metabolic profile. Combination therapy of myo-inositol, D-chiro-inositol and levothyroxine has shown a significant effect on fertility rate and pregnancy by promoting insulin sensitivity and improving thyroid function. In women diagnosed with PCOS, especially those who want to become pregnant, it is necessary to examine the function of the thyroid gland at the first visit to the endocrinologist. Keywords:polycystic ovary syndrome, Hashimoto's thyroiditis

DOI: 10.1530/endoabs.81.EP888

EP889

Association of SPISE and HOMA-IR indexes with metabolic characteristics of different age groups of women with polycystic ovary syndrome

Milica Opalic[1], Sanja Ognjanovic[1], Bojana Popovic[1], Dusan Ilic[1], Jelica Bjekic - Macut[2], Valentina Elezovic[1], Lena Radic[1], Danijela Vojnovic Milutinovic[3], Olivera Stanojlovic[4] & Djuro P. Macut[1]
[1]Clinic for Endocrinology, Diabetes and Metabolic Diseases, University Clinical Centre of Serbia, Department for Endocrine Tumors and Hereditary Cancer Syndromes, Belgrade, Serbia; [2]CHC Bezanijska Kosa, Belgrade, Serbia; [3]IBISS, University of Belgrade, Belgrade, Serbia; [4]Institute of Physiology, Faculty of Medicine, University of Belgrade, Belgrade, Serbia

Introduction
Polycystic ovary syndrome (PCOS) is the most prevalent endocrinopathy among women during reproductive age. PCOS cardinal manifestations include hyperandrogenism, oligo/anovulation, and/or polycystic ovarian morphology, and is closely linked to metabolic disorders such as obesity and insulin resistance (IR). It was observed that single-point insulin sensitivity estimator (SPISE) index is associated with metabolic abnormalities and could predict glucose regulation during life. The aim of this study was to analyze metabolic and hormonal characteristics among two age groups of women with PCOS and their association with SPISE index and homeostatic model assessment of insulin resistance (HOMA-IR) index.
Subjects and methods
We analyzed 150 women with PCOS diagnosed using ESHRE/ASRM. Patients were divided into two age groups, younger/equal to 30 years (PCOS-A, $n = 74$, age: 23.3$\pm$3.1 years, BMI: 23.1$\pm$ 4.5 kg/m2), and older than 30 years (PCOS-B, $n = 74$, age: 35.7$\pm$4.9 years, BMI: 25.3$\pm$ 6.4 kg/m2). We measured lipids indices, glucose and insulin during oral glucose tolerance test (OGTT), while HOMA-IR and SPISE index were calculated. Statistical analysis was performed by SPSS software.
Results
Both groups had similar body mass index ($P=0.071$) and waist circumference (77.0$\pm$12.9 cm vs. 82.0$\pm$15.3 cm, $P=0.07$), but the incidence of obesity was higher in PCOS-B group (PCOS-A 5.9% vs. PCOS-B 23.5%, $P=0.004$). Women in PCOS-B in comparison to PCOS-A had higher total cholesterol ($P<0.001$), LDL cholesterol ($P=0.022$) and triglycerides ($P=0.012$). Incidence of impaired glucose tolerance was same in both groups, and no patient had diabetes. Although fasting glucose was statistically higher in PCOS-B group ($P<0.001$), there was no between-groups differences in levels of fasting insulin ($P=0.12$) and HOMA-IR ($P=0.151$). SPISE index was statistically lower in PCOS-B ($P=0.022$), showed negative correlation with HOMA-IR, baseline glucose and glucose in 120 minute of OGTT in PCOS-B (r=-0.483, $P=0.004$, r=-0.360, $P=0.007$, r=-0.337, $P=0.004$, respectively) and negative correlation with only fasting insulin in PCOS-A (r=-0.284, $P=0.024$).
Conclusion
PCOS is characterized by the existence of risk factors including obesity, elevated glucose and lipid concentrations all leading to an increased risk of cardiometabolic vascular disorders. The assessment of different indicators during time-line of PCOS could be used for prediction of long-term metabolic outcomes.

DOI: 10.1530/endoabs.81.EP889

EP890

Klinefelter syndrome associated with intellectual deficit, short stature and cardiac anomalies

YOSRA HASNI[1, 2], Hayfa Farid[1], Hamza Elfekih[1,2], Oumayma Zarrouk[1], Amel MAAROUFI[1, 2], Maha KACEM[1, 2], Molka CHADLI CHAIEB[1, 2] & Koussay Ach[1,2]
[1]Farhat-Hached University Hospital, Endocrinology-Diabetology Department, Sousse, Tunisia; [2]Faculty of Medicine Ibn El Jazzar, University of Sousse, Sousse, Tunisia

Introduction
Klinefelter syndrome is the most prevalent male chromosomal disorder, characterized by the presence of additional X chromosomes. Most males with Klinefelter syndrome have 47, XXY and normal intelligence. Intellectual disability occurs in males with Klinefelter syndrome variants, who have a higher number of X chromosomes. Here we report a rare case of a 49, XXXXY syndrome revealed by intellectual deficit and pubertal delay.
Observation
An 18-year-old male patient was presented in our department for pubertal delay associated with intellectual deficit. He showed dry mouth, polydipsia, and polyuria. On examination, he had short stature: height = 166 cm, weight = 67 Kg, BMI = 24.3 Kg/m^2, hypertelorism, gynecomastia, atrophic testes and micropenis. Biological examination showed diabetes mellitus and hypertriglyceridemia. Hormonal analysis confirmed a hypergonadotropic hypogonadism (Testosterone = 20 ng/dl, LH=29 IU/l, FSH= 55 IU/l). Thyroid function was normal and his IGF-1 level was low (170 [224-255 ng/ml]). Imaging examination showed a bone age of 16 years and cardiac anomalies: mitral and aortic *insufficiencies.* Genetic analysis exhibited a 49, XXXXY karyotype and the patient underwent testosterone therapy.
Conclusion
49, XXXXY syndrome is a rare variant of Klinefelter syndrome with an incidence of 1/85,000 male births. Its diagnosis is usually made postnatally because of growth deficiency and dysmorphism which wasn't the case for our patient.

Malformations and intellectual deficit are other characteristics of this syndrome that requires performing a karyotype.

DOI: 10.1530/endoabs.81.EP890

EP891

Effects of antiandrogen therapy of cyproteron acetate on androgen effects on the skin including androgenetic alopecia in menopausal women - case report: 10 years follow up -

Dragan Tesic, Milena Mitrovic, Tijana Icin, Dragica Andric & Mirjana Tomic
Clinics of Internal Diseases, Clinic of Endocrinology, Diabetes and Metabolic Disorders, Novi Sad, Serbia

Introduction
The term female pattern hair loss (FPHL) is commonly used synonymously with female androgenetic alopecia. While the the role of androgens and androgen receptor genes is well-defined in male androgenetic alopecia (AGA-M), its role in in the pathogenesis of FPHL is stil uncertain. More diffuse involvement, resulting in an oval-shaped alopecia surrounded by a rim of normal hair density (Ludwig's classification) might be a clinical challenge. The aim of case report is to present the menopausal patient with full blown signs of androgen excess such as acne, seborrhea, hirsutism (SAHA: seborrhea, acne, hirsutism, and alopecia), obesity and pronounced psychological consequences.
Case description
female, born in 1952y. Since 2000y. (menopausis in 2004y) she gained 35 kgs (85.1 kg), BH 158 cm and since 2010y. she started to notice increased hairiness (hirsutismus) and weakening and hair loss (FPHL), in 2016 Grade 3. At that time on adrenal CT it was detected adenoma on one gland. Cushing syndroma and Chon syndroma excluded, but among laboratory finding significant was LH 18 U/l, FSH 44.4 U/l, testosteron 13.8 nmol/l, insulin (fasting) 27.1 mU/l, post prandial 281.6 mU/l. Fasting triglycerides 0.95 mmol/l, HDL-cholesterol 1.8 mmol/l, total holesterol 5.56 mmol/l. In two years period (206-2018) she managed to reduce her body weight to 75 kg, insulinemia to 11.9 mU/l, testosteronemia to 5.8 nmol/l. Alopecia and hirsutisms had been without change, so we decided to introduce cyproteron acetate tbl. 2x50 mg. First drop in T was noticed 1 year later (2019y.), but even before that after a year on that therapy patient noticed changes in reduced alopecia and hirsutismus. After 2 ys od therapy in 2021y. we noticed futher drop in T between 1.44 and 3.04. Clinical improvement was manifested in alopecia removal of Grade 3 in to Grade 1. In these time DHT (Barts) has been 10.1-21.7 (reference -23) ng/dl.
Discussion
The aim of this case report is to emphasize the need of normalisation the testosteron level (refrence 2.6 nmol/l) for obtaining the effect of reducion of androgenization, meaning withdrawal of alopecia and hirsutism. If we consider hyperinsulinemia as a triger hormon change for the cascade of further androgenisation, its reduction seems not not to be enough for beneficial efects. More further, hyperinsulinism was assocociated only with hypertension but not with characteristic lipid consetalation that runs with insulin resistance, high triglycerodes and low HDL cholesterol.

DOI: 10.1530/endoabs.81.EP891

EP892

Effects of letrozole on reproductive organs of young and aged male rats

Alexander Reznikov[1], Olga Sachynska[1], Liubov Polyakova[1] & Oksana Faliush[2]
[1]VP Komisarenko Institute of Endocrinology and Metabolism, National Academy of Medical Sciences of Ukraine, Dept. of Endocrinology of Reproduction and Adaptation, Kyiv, Ukraine; [2]VP Komisarenko Institute of Endocrinology and Metabolism, National Academy of Medical Sciences of Ukraine, Kyiv, Ukraine

The aim of this work was to study the condition of the reproductive system after long-term administration of letrozole followed by its withdrawal in young males and against the background of involutive changes in aging males in a comparative aspect. The experiments were carried out on Wistar rats with an initial age of 5 months and 15 months, which have been gavaged by letrozole every other day at a dose of 1 mg/kg body weight for 3 months and then 2 months after its discontinuation. The blood plasma testosterone and estradiol levels were measured by immunoassays. The spermatozoa concentrations in epididymal washes were determined. The testicles and accessory sexual glands were weighed, and morphology of gonads and ventral prostate have been studied. The results of the study were compared with those of control animals of corresponding age. As the result of letrozole treatment, the ratio of testosterone and estradiol levels in blood plasma of aged rats increased. The spermatozoa content in epididymis rose up by 28% at average. The histological study revealed functional activation of Leydig cells, a significant retardation of involutive changes of their number and morphology. Some Leydig cells demonstrated the signs of functional exhaustion. Letrozole caused an increase of relative weights of the coagulation gland by an average of 40%, seminal vesicles by 31%, and ventral prostate by 33% compared with those of control animals. Two months after letrozole withdrawal, there were no any signs of difference between letrozole-treated and control animals. In young rats, the effects of letrozole were almost not detectable. Letrozole administration to male rats with age-related involution of the reproductive system increases testosterone/estradiol ratio in blood plasma, the spermatozoa content in epididymises and the weights of androgen-dependent accessory sexual glands. This is accompanied by slowing down of age-related changes of the gonad and prostate gland morphology. Letrozole-induced reproductive effects are reversible.
Keywords: letrozole, reproductive organs, male, rats.

DOI: 10.1530/endoabs.81.EP892

EP893

Mitochondrial uncoupling proteins (UCPs) regulate the mitochondrial activity of human sertoli cells

David F. Carrageta[1], Laís Freire-Brito[1], Bruno S. Monteiro[1], Bárbara Guerra-Carvalho[1,2,3], Raquel L. Bernardino[1], Pedro F. Oliveira[2], Mariana P. Monteiro[1] & Marco G. Alves[1]
[1]UMIB - Unit for Multidisciplinary Research in Biomedicine, ICBAS - School of Medicine and Biomedical Sciences, University of Porto, Porto, Portugal; [2]QOPNA & LAQV, Department of Chemistry, University of Aveiro, Aveiro, Portugal; [3]Department of Life Sciences, Faculty of Sciences and Technology, University of Coimbra, Coimbra, Portugal

Introduction
Mitochondrial uncoupling proteins (UCPs) are channel proteins present in the mitochondrial inner membrane which are responsible for the transport of protons between the mitochondrial intermembrane space and the matrix. Currently, six UCP homologues had been identified (UCP1-6). UCPs are major regulators of reactive oxygen species (ROS) production, general cellular redox state and metabolism. UCPs also exhibit specific functions, such as UCP1 and thermogenesis or UCP2 and regulation of insulin secretion in beta-pancreatic cells. Altered expression and function of UCPs have been linked with the onset of metabolic diseases, including obesity and diabetes mellitus and increased oxidative stress. Male infertility is an overlooked comorbidity related to metabolic diseases since the testis is susceptible to metabolic alterations and increased oxidative stress. However, the expression and function of UCPs in the human testis remain unknown.
Aim of the study
The main objective of this study was to identify the expression of the different UCPs homologues in human Sertoli cells (hSCs). In addition, the function of UCPs on the mitochondrial activity and metabolism of hSCs was analysed through its inhibition by genipin, a specific UCP inhibitor.
Matherials and methods
Primary cultures of human Sertoli cells from healthy men with conserved spermatogenesis were established ($n=6$). Total RNA was extracted and all UCP homologues (UCP1-6) mRNA expression was analysed by RT-PCR. UCP1-3 were detected by immunofluorescence. Then, UCPs were inhibited in hSCs by genipin, a specific UCP inhibitor, (0.5, 5, 50, and 100 μM). Cellular viability, proliferation, and ROS production were accessed after 24 h treatment. Mitochondria function was accessed by Seahorse XF Cell Mito Stress assay. Culture media were collected and analysed by ^{1}H-NMR.
Results
We were able to identify all UCPs homologues (UCP1-6) in hSCs. The inhibition of UCPs by high concentrations of genipin decreased hSCs proliferation but no cytotoxicity was observed. In addition, UCP inhibition by genipin decreased mitochondrial activity in a dose-dependent manner. Interestingly, no increased ROS production was observed.
Conclusion
We were able to identify, to the best of our knowledge, for the first time the expression of UCPs (UCP1-6) in hSCs. UCPs can regulate the mitochondrial activity and metabolism of hSCs. Our results suggest that UCPs dysfunction could play a central role in the crosstalk between metabolic disorders, high oxidative stress and male infertility.

DOI: 10.1530/endoabs.81.EP893

EP894

Mitochondrial uncoupling proteins (UCPs) are key regulators of human spermatozoa motility

Laís Freire-Brito[1], David F. Carrageta[1], Bruno S. Monteiro[1], Bárbara Guerra-Carvalho[1,2,3], Alberto Barros[4,5,6], Pedro F. Oliveira[3] & Marco G. Alves[1]

[1]UMIB - Unit for Multidisciplinary Research in Biomedicine, ICBAS - School of Medicine and Biomedical Sciences, University of Porto, Porto, Portugal; [2]Department of Life Sciences, University of Coimbra, Coimbra, Portugal; [3]QOPNA & LAQV, Department of Chemistry, University of Aveiro, Aveiro, Portugal; [4]Genetics of Reproduction Center, Porto, Portugal; [5]Department of Genetics, Faculty of Medicine, University of Porto, Porto, Portugal; [6]i3S - Instituto de Investigação e Inovação em Saúde, University of Porto, Porto, Portugal

Introduction

Mitochondrial uncoupling proteins (UCPs) are mitochondrial transmembrane channels belonging to the anion carrier family. Six UCP homologues (UCP1-6) had been identified with a ubiquitous distribution throughout the body and many different physiological functions. UCPs are important regulators of several biological processes, including thermogenesis, oxidative phosphorylation, ROS production, as well as cellular metabolism. However, the knowledge concerning the molecular action mechanisms is limited. UCPs' (dys)function is pivotal to the onset of metabolic diseases and consequent increased oxidative stress. Although the molecular mechanisms are poorly understood, there is an interconnection between oxidative stress, male infertility, and metabolic disorders, such as obesity and diabetes mellitus. In addition, the expression and function of UCPs in the human spermatozoa remains to be explored.

Aim of the study

This study aimed to evaluate the expression of UCPs homologues (UCP1-6) in human spermatozoa. In addition, the influence of UCPs in spermatozoa viability, total and progressive motility, mitochondrial activity, and ROS production was evaluated through its inhibition by genipin, a selective UCP inhibitor.

Matherials and methods

Highly motile and viable spermatozoa were isolated from seminal samples of normozoospermic men ($n=10$) by density gradient centrifugation. The mRNA expression of UCPs homologues (UCP1-6) was evaluated by RT-PCR and the protein expression (UCP1-3) by immunofluorescence. Samples were incubated in BWW media supplemented with genipin (0, 0.5, 5, and 50 μM) at 37°C. After 3 h, total motility and viability were analyzed. The mitochondrial activity and total ROS production were accessed by JC-1 dye and CM-H2DCFDA probe, respectively. The culture media were collected and evaluated by 1H-NMR. To further study the observed loss of motility and its reversibility, total and progressive motility were evaluated each 15 min up to a total of 105 min.

Results

We were able to identify the mRNA expression of all UCPs homologues (UCP1-6) in human spermatozoa. Inhibition of UCPs by the highest concentration of genipin (50 μM) led to the irreversible loss of motility. Mitochondrial membrane potential was also found diminished, although no alterations in human spermatozoa viability, metabolic profile, or ROS production were observed.

Conclusion

UCPs are major regulators of human spermatozoa's mitochondrial activity and motility. Our data suggests that the dysfunction of human spermatozoa UCPs is not only potentially interconnected to metabolic diseases, oxidative stress, and male infertility but also a potential novel target for the development of male contraceptives.

DOI: 10.1530/endoabs.81.EP894

EP895

Sperm medium supplementation with hyperoside as a potential strategy to counteract spermatozoa dysfunction associated with oxidative stress

Mafalda V. Moreira[1], Sara C. Pereira[1], Soraia Pinto[2], Alberto Barros[2,3,4], Branca M. Silva[5], Marco G. Alves[1] & Pedro F. Oliveira[6]

[1]Institute of Biomedical Sciences Abel Salazar (ICBAS) - School of Medicine and Biomedical Sciences, University of Porto, Department of Anatomy and Unit for Multidisciplinary Research in Biomedicine (UMIB), Porto, Portugal; [2]Centre for Reproductive Genetics Professor Alberto Barros, Porto, Portugal; [3]Faculty of Medicine, University of Porto, Department of Genetics, Porto, Portugal; [4]i3S – Instituto de Investigação e Inovação em Saúde, Porto, Portugal; [5]University of Beira Interior, Covilhã, Portugal; [6]QOPNA & LAQV, University of Aveiro, Department of Chemistry, Aveiro, Portugal

Infertility is a global health problem that affects about 15% of couples and approximately half of infertility cases are associated with male factors. Oxidative Stress (OS) is reported as one of the major causes of male infertility, mainly due to spermatozoa's vulnerability to the attack of reactive oxygen species (ROS). Infertile couples often recur to assisted reproductive technology (ART) to achieve a successful pregnancy. However, ART protocols also increase the exposure of gametes to OS conditions. A strategy often used to overcome this problem is the supplementation of media with antioxidants. Hyperoside (quercetin 3-*O*-galactoside) is a flavonol glycoside that has been shown to possess prominent antioxidant properties, preventing oxidative damage in several cellular systems. Thus, we proposed to investigate the impact of hyperoside supplementation on the protection of sperm against oxidative damage. For this purpose, sperm samples of normozoospermic patients ($n=20$) were supplemented with HYP (100 and 500 μM), for 1 h, in the presence and absence of hydrogen peroxide (300 μM). As a positive control, spermatozoa were supplemented with the well-known antioxidant, vitamin C (VC). After treatment, sperm quality parameters (motility and vitality) were evaluated, according to WHO guidelines. The total antioxidant capacity (TAC) of sperm medium was measured by ferric reducing antioxidant power (FRAP) and OS biomarkers expression was assessed by slot blot technique. Further, DNA fragmentation was measured by TUNEL assay. Our results demonstrated that supplementation with HYP did not induce any deleterious effects to the physiology of the spermatozoa, after 1-h of treatment. Further, under an H_2O_2-induced OS condition, HYP was able to preserve sperm motility and decrease DNA fragmentation. Furthermore, HYP also appears to prevent the increase in lipid peroxidation under OS conditions. Overall, our findings lead us to suggest that sperm medium HYP supplementation can contribute to the improvement of sperm maintenance during ART protocols

DOI: 10.1530/endoabs.81.EP895

EP896

Vascular erectile dysfunction as a mirror of general health: focus on patients comorbidities

Barbara Rossi[1,2], Marilina Romeo[1, 2], Antonio Raffaele Michele Granata[1], Vincenzo Rochira[1, 2], Manuela Simoni[1, 2], Giorgia Spaggiari[1] & Daniele Santi[1,2]

[1]Unit of Endocrinology, Department of Medical Specialties, Azienda Ospedaliero-Universitaria of Modena, Modena, Italy.; [2]Unit of Endocrinology, Department of Biomedical, Metabolic and Neural Sciences, University of Modena and Reggio Emilia, Modena, Italy

Background

Erectile dysfunction (ED) represents the most frequent sexual dysfunction. Among several possible ED aetiologies, vascular ED (vED) presents the greatest implications for global individual health, resulting an early hallmark of cardiovascular diseases. Indeed, vED was demonstrated associated with a 1.25 times greater risk of developing major cardiovascular diseases. Alongside cardiovascular aspect, the evaluation of patients health, measured by the comorbidities number, in relation to the ED aetiology has never been investigated so far.

Aim of the study

To explore the potential relationship between the number of comorbidities and ED aetiology and severity.

Material and methods

A large database including all patients longitudinally evaluated for any andrological reason is kept the Andrology Unit of Modena (Italy). The current study is an interim analysis including ED patients evaluated from 2008 to 2010. For each patient, medical history, physical examination, ED characteristics, blood examination for hormonal assays and treatment choice were collected. The ED was graded using the International Index of Erectile Function (IIEF)-15 score and the number of comorbidities with Chronic Disease Score (CDS). Patients were grouped according to the ED aetiology, i.e. psychological, vascular, hormonal and neurological. CDS was compared among groups of patients generated on ED characteristics considering baseline and follow-up visits.

Results

418 men (mean age 43.4 ± 12.8 years) with ED were followed for 10.2 ± 6.5 years. 368 patients (87.6%) showed a psychological aetiology, 29 (6.9%) vED, 14 (3.3%) hormonal genesis and seven (1.7%) a neurological ED. Although CDS did not differ among ED groups ($P=0.226$), it was directly related to patients age (Rho: 0.449, $P<0.001$) and inversely to ED domain at IIEF-15 (Rho: -0.319, $P=0.005$). At logistic regression analysis, CDS resulted not able to predict ED diagnosis, while only smoking habit was correlated to vED (Exp: 0.211: 0.082-0.541, $P=0.001$). As expected, CDS significantly increased during follow-up

with the highest score collected at the last visit compared to baseline (1.8±2.7 vs 1.2±2.1, $P<0.001$). At follow-up visits, CDS was significantly higher in vascular ED (4.2±3.4) compared to psychological (2.2±3.0), hormonal (1.7±3.4) and neurological (1.0±1.1) forms ($P<0.001$).
Conclusions
Here, we demonstrate that the anamnestic evaluation of the comorbidities number is not useful in clinical practice to predict ED aetiology. However, the increase in CDS observed during follow-up resulted particularly evident in vED, confirming the vED role as a mirror of general health.

DOI: 10.1530/endoabs.81.EP896

EP897

Lean Polycystic Ovarian Syndrome - An evaluation of diagnostic and clinical outcome differences in relation to obese PCOS in patients attending a tertiary care institute in Colombo

Ishara Ranathunga, T G Athukorala, Manilka Sumanatilleke & Noel Somasundaram
National Hospital of Sri Lanka, Sri Lanka

Background and Objectives
Polycystic ovary syndrome (PCOS) is a common female reproductive endocrine disorder with a prevalence of 15-20%. Although a majority of patients diagnosed with PCOS are overweight/obese, minority can present with normal body mass index of $\leq$25 kg/M^2 which complicate the effective diagnosis and management. We have studied the socio-demographic and clinical characteristics of lean PCOS patients in comparison to obese PCOS patients attending the Endocrinology clinic in a tertiary care institute in Sri Lanka.
Methods
A descriptive cross sectional study was conducted from September 2019 to September 2020 at the Endocrinology Unit of the National Hospital of Sri Lanka. Systematic sampling was done recruiting PCOS patients diagnosed with Rotterdam criteria. After obtaining informed written consent, the data was collected using an interviewer administered questionnaire. HOMA-IR was calculated using the fasting insulin and blood glucose level.
Results
The study enrolled sixty females. Out of that 23 (38.3%) patients were diagnosed to have lean PCOS while the rest (37, 61.6%) had overweight/obesity. The mean age was 25.1 years (range 18-37). The mean weight was 55.0 (SD=6.7) kg and BMI was 22.2 (SD=1.8) kg/m^{-2}. Twenty (83.0%) had irregular menstrual cycles while 11 (47.8%) patients had clinical or biochemical evidence of hyperandrogenism. Only 9 (39.1%) patients had polycystic ovaries on trans-abdominal ultrasound scan. According to the body fat percentage assessed by the whole body DEXA scan 90.9% patents had their body fat in the overweight and obese category in contrast to the BMI category. HOMA-IR detected 37.5% to have high insulin resistance. There was significant difference in the presence of acanthosis nigricans, hirsutism, polycystic ovaries on USS and non-alcoholic fatty liver disease (NAFLD) in the obese PCOS patients while acne was more prevalent in the lean PCOS females ($P<0.05$).
Conclusions
The minority of patents affected with PCOS are falling under the category of lean PCOS. The diagnosis and the therapeutic approach poses a significant clinical challenge due to the absence of typical clinical features such as acanthosis nigricans, hirsutism, and polycystic ovaries on USS in this group of patients. Use of body fat estimation is more sensitive in detecting overweight/obesity in this group rather than using conventional BMI measurement. Nevertheless, the suspicion and awareness among clinicians of the possibility of lean PCOS in this group of females can improve the diagnosis and patient outcomes.

DOI: 10.1530/endoabs.81.EP897

EP898

PCOS SEVa: High prevalence anxiety and body dysmorphia in women with PCOS attending specialist care in the UK and India

Meghnaa Hebbar[1], Salomi Shaikh[2], Nawal Zia[1], Jameela Sheikh[1], Saskia Wicks[3], Sindoora Jayaprakash[4], Alisha Narendran[5], Halimah Khalil[1], Helena Gleeson[6], Lynne Robinson[7], Justin J. Ch[7], Tejal Lathia[8], Chitra Selvan[9], Wiebke Arlt[6, 10] & Punith Kempegowda[6,10]
[1]College of Medical and Dental Sciences, University of Birmingham, Birmingham, United Kingdom; [2]Padmashree D.Y, Patil School of Medicine, Navi Mumbai, Mumbai, India; [3]Barts Health NHS Trust, London, United Kingdom; [4]The Dudley Group NHS Foundation Trust, Dudley, United Kingdom; [5]King Edward VI High School for Girls, Birmingham, Birmingham, United Kingdom; [6]Department of Endocrinology, Queen Elizabeth Hospital, University Hospitals Birmingham NHS Foundation Trust, Birmingham, United Kingdom; [7]Birmingham Women's Hospital, Birmingham Women's and Children's NHS Foundation Trust, Birmingham, United Kingdom; [8]Apollo Hospitals, Navi Mumbai, Mumbai, India; [9]Department of Endocrinology, MS Ramaiah Medical College, Bengaluru, Bangalore, India; [10]Institute of Metabolism and Systems Research, University of Birmingham, Birmingham, United Kingdom

Introduction
National Institute of Health and Care Excellence (NICE) recommends screening for emotional wellbeing as part of consultations for polycystic ovary syndrome (PCOS).
Aim
We evaluated several dimensions of emotional wellbeing in people attending PCOS consultation with specialists in the UK and India.
Methods
All people attending specialist clinics in a tertiary centre in the UK from October 2020 to September 2021 and in India between March 2021 to September 2021 were invited to complete a survey before and after attending the clinic. This survey had questions on demographics, Hospital Anxiety and Depression Scale (score 8-10 borderline; score $\geq$11 cases of anxiety and depression, respectively), Body Image Concern Inventory (BICI; score $\geq$72 suggestive of body dysmorphic disorder, BDD), Beliefs About Obese Persons Scale (BAOP; higher score suggestive of weight bias), and Female Sexual Function Index (FSFI; higher score suggestive of psychosexual dysfunction).
Results
A total of 115 women (36 UK and 79 India) completed the survey. The prevalence of anxiety and depression were 56.5% (50.0% UK vs 59.5% India;Mann-Whitney U- $P=0.483$) and 16.5% (13.9% UK vs 17.7% India, $P=0.529$), respectively. Overall, 29.6% had BDD with higher prevalence in the UK women (36.1% UK vs 26.6% India; $P=0.208$). Participants had higher scores for BAOP (overall: 15.5/48 (13.0-18.0)) with higher scores for UK women (UK: 16 (13.3 - 18.9); vs India: 15 (12.5 - 17.5); $P=0.575$). The overall scores for FSFI were towards the upper end of the scale (20.4/36 (7.5-25.2)) with no significant difference between the two groups (UK: 23.1 (13.2 - 26.2); vs India: 17.7 (6.9-24.5); $P=0.413$). Post-survey results further revealed that a proportion of women felt limited information was provided about anxiety (UK: 6/19 (31.6%);vs India: 17/40 (42.5%)), depressive symptoms (UK: 5/19 (26.3%); vs India: 19/40 (47.5%)) or body image concerns UK: 3/19 (15.8%); vs India: 10/40 (25%)) during consultation.
Conclusion
There is a high prevalence of emotional ill-being associated with PCOS both in the UK and India. While it is challenging to encompass all aspects of clinical care during consultation, future work should explore alternate ways to improve screening and management of emotional wellbeing in women with PCOS.

DOI: 10.1530/endoabs.81.EP898

EP899

Perrault syndrome in a Tunsian Girl : a case report

Chayma Bel Hadj Sliman, Fatma Chaker, Anis Grassa, Nadia Khessairi, Meriem Yazidi & Melika Chihaoui
Rabta Hospital, Endocrinology Department, Tunis, Tunisia

Introduction
Perrault syndrome is a rare autosomal recessive disorder defined by the association of 46XX ovarian dysgenesis and neurosensory deafness. Other manifestations may be present, in particular cerebellar and/or peripheral neuronal degenerative disease. we report the case of Perrault syndrome in a 15-year-old Tunisian girl.
Observation
A 15-year-old girl was referred to our department for pubertal delay. She had a congenital deafness and epilepsy diagnosed at one year old and she was on sodium valproate. Physical examination showed a body weight of 45 kg (between -1 and -2SD), a body height of 1.62 m (between mean and -1 SD), Tanner scale was B1P2. Hormonal investigation showed an hypergonadotrophic hypogonadism (FSH= 153 UI/l (1-17) and LH=34 mUI/l (0,5-41,7)). Pelvic ultrasound showed an infantile uterus. Ovaries were not visible. A complementary pelvic MRI confirmed the absence of ovaries and the hypoplastic uterus. Karyotype was 46XX and the genetic study showed the absence of the GJB2 gene mutation. The diagnosis of Perrault syndrome was confirmed. The electromyography was normal and cerebral MRI showed white matter demyelination. The patient was treated with estrogen and progesterone to induce puberty.

Conclusion
We report this case because of its rarity as few cases have been reported in Tunisia so far in the literature. The prevalence of Perrault syndrome is poorly known, often under diagnosed because of the phenotypical and genetic heterogeneity of this syndrome.

DOI: 10.1530/endoabs.81.EP899

EP900

Gynecomastia: clinical, paraclinical and etiological aspects

Bel Hadj Sliman Chayma, Nadia Khessairi, Anis Grassa, Meriem Yazidi, Fatma Chaker & Melika Chihaoui
Rabta Hospital, Endocrinology, Tunis, Tunisia

Introduction
Gynecomastia is an enlargement of male breast glandular tissue caused by an imbalance of the hormones androgens and estrogens. It can be physiological at different stages of life (birth, adolescence, senescence), caused by medication or reveal a serious pathology. The aim of our study was to evaluate the characteristics of presentation, biochemical profile, and etiology of gynecomastia.
Methods
A retrospective study was conducted at the endocrinology department of the Rabta Hospital in Tunis including 100 patients who presented with gynecomastia between January 2015 and December 2020. Clinical and paraclinical data were collected from medical records.
Results
The mean age of our patients was 37.16 years with extremes ranging from 11 years to 88 years. Seven patients (7%) had a history of cryptorchidism and testicular ectopy. Impuberism and late puberty were noted in 17 patients (17%). The mean duration of Gynecomastia before seeking specialized endocrine care was 78 months with an acute onset in 19% of cases. On physical examination, 56 patients (56%) had bilateral and symmetrical gynecomastia, 19 patients (19%) had bilateral and asymmetrical and 25% unilateral gynecomastia. 15 patients had stage I, 33 patients had stage II and 52 patients had stage III gynecomastia. Testosteronemia was measured in 43 patients and was low in 26 patients (26%). Gynecomastia was considered physiological in 25 patients (25%). The etiology of gynecomastia was considered to be drug-induced in 15 patients (15%), including spironolactone in six patients. The other drugs involved were chemotherapy and dopaminergic antagonists. Other causes were non-functioning pituitary adenomas, prolactinomas, isolated hypogonadotropic hypogonadism, testicular diseases, hypothyroidism and hyperthyroidism in 7%, 6%, 8%, 7%, 2% and 1% of the cases respectively. Idiopathic gynecomastia was found in 29% of cases.
Conclusion
Gynecomastia is a frequent and often benign pathology but it can be the expression of a relevant underlying endocrine disease or even tumor pathology. This highlights the importance of an adequate and complete clinical, biochemical, and imaging assessment of every patient presenting with gynecomastia.

DOI: 10.1530/endoabs.81.EP900

EP901

Therapeutic aspects of gynecomastia: about 100 cases

Anis Grassa, Bel Hadj Sliman Chayma, Nadia Khessairi, Ibtissem Oueslati & Fatma Chaker
Rabta Hospital, Endocrinology, Tunis, Tunisia

Introduction
Gynecomastia is defined as the benign proliferation of the mammary glands in males, which results from an excess of estrogens, androgen deficiency, hormone resistance, or altered ratio of estrogens to androgens. It can be unilateral or bilateral. The aim of our study was to describe the therapeutic aspects and the evolution of gynecomastia.
Methods
This is a retrospective descriptive study of 100 patients who presented with gynecomastia at the endocrinology department of the Rabta hospital between January 2015 and December 2020. Clinical and paraclinical data were collected from medical records.
Results
Our population had a mean age of 37.16 $\pm$ 21.7 years at the time of the first visit. The mean age of puberty was 13.9 $\pm$ 2.7 years. Seven patients (7%) had a past medical history of testicular ectopy and cryptorchidism. Physical examination showed the presence of glandular tissue in all patients and diagnosis was documented by ultrasound and/or mammography in 60 patients. Biological workup revealed hypogonadotropic hypogonadism in 15 patients, including 7 patients with non-functional pituitary adenoma and 8 patients with isolated hypogonadotropic hypogonadism, hyperprolactinemia with prolactinoma in 6 patients, hypothyroidism in 2 patients, and hyperthyroidism in 1 patient. Gynecomastia was secondary to testicular disease in 7 patients. In addition, 15 patients had drug-induced gynecomastia. Finally, gynecomastia was physiological in 25 patients and idiopathic in 29 others. Regarding the management of gynecomastia, 29 patients received treatment for the etiology, 11 patients received testosterone enanthate injections. Nine patients received local treatment with androstanolone and 12 patients underwent cosmetic surgery. The rest of the patients were monitored and did not receive any treatment. The evolution was marked by clinical improvement in 38% of cases.
Conclusion
Each case of gynecomastia should be subjected to a precise etiological workup including at least a testosterone and estradiol dosage. The treatment modalities of gynecomastia depend on the results of the etiological investigation.

DOI: 10.1530/endoabs.81.EP901

EP902

Polycystic ovary syndrome : clinical, paraclinical and therapeutic profile

Anis Grassa, Nadia Khessairi, Bel Hadj Sliman Chayma, Meriem Yazidi & Melika Chihaoui
Rabta Hospital, Endocrinology, Tunis, Tunisia

Introduction
Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders in women and its main symptoms are related to menstrual disorders and hyperandrogenism. The aim of our study was to evaluate the clinical and paraclinical profile of PCOS.
Methods
We conducted a retrospective study that included 50 women, followed at endocrinology department's consultations of Rabta Hospital in Tunis. Each patient underwent a clinical examination, hormone assays and ovarian ultrasound. The diagnosis of PCOS was made according to the Rotterdam 2003 criteria.
Results
The mean age of our patients was 26.9 $\pm$ 7.9 years [15 -45]. The family history of PCOS was found in 24% and type 2 diabetes mellitus's personal medical history in 21.7%. Eight percent of patients were smokers. The mean age of menarche was 12.1 $\pm$ 1.3 years. Sixty-two percent of patients had spaniomenorrhoea and 6% had secondary amenorrhoea. These disorders were post-pubertal in half cases. The average weight was 87.5 $\pm$ 21.9 kg [38-150] for an average body mass index of 33.3 $\pm$ 7.6 kg/m^2 [16-57]. Therefore 65% of patients were obese and 37% presented acanthosis nigricans on clinical examination. Clinical hyperandrogenism signs such as acne and hyperseborrhea were found in 22.7% while major virilizationsigns were noted in 4%. Hirsutism was classified moderate to severe in 60.8%. Biological hyperandrogenism was found in 62% of cases including mean testosterone level of 0.78 $\pm$ 0.4 ng/ml. The average LH/FSH ratio was 1.7 $\pm$ 0.9, and was higher than 2 in 29%. Ovarian ultrasound showed a polycystic aspect in 72% of cases with increased ovaries size in 56%, the rest were strictly normal. Hygienic diet was instituted in 96% associated to metformin in 18% of cases and an Oestrogen -Progestin combination therapy in 60%. An additional laser hair removal treatment was done in 28%. Clinical and biological improvement was noted in half cases.
Conclusion
The etiological investigation of hyperandrogenism with menstrual disorders should remain exhaustive to eliminate potentially serious diagnoses. PCOS remains a benign disease. However, it must be managed effectively, given its impact on the patient's quality of life.

DOI: 10.1530/endoabs.81.EP902

EP903

Clinical utility of the Anti-Mullerian Hormone testing for the prediction of PCOS

Valentina Soldat Stankovic[1, 2], Snjezana Popovic Pejicic[2], Aleksandra Grbic[1, 2], Tamara Dojcinovic[1], Gabrijela Malesevic[1, 2], Milena Brkic[2] & Djuro P. Macut[3,4]
[1]University Clinical Centre of the Republic Srpska, Internal Medicine, Banja Luka, Bosnia and Herzegovina; [2]University of Banja Luka, Faculty of Medicine, Banja Luka, Bosnia and Herzegovina; [3]Endocrinology Clinic, Beograd, Serbia; [4]University of Belgrade - Faculty of Medicine, Internal Medicine, Beograd, Serbia

Introduction
The diagnostic criteria of polycystic ovary syndrome (PCOS) are still under discussion and the hormonal parameters, including anti-Mullerian hormone range and hyperandrogenism, are not determined. Serum AMH level has been proposed as a surrogate marker for PCOM and could, therefore, be integrated in the diagnostic classifications for PCOS.. The aim of the present study was to characterize hormonal features of PCOS and to establish the most important hormonal parameters for PCOS diagnosis.
Design
A case-control study.
Methods
The study included 60 women with PCOS according to the complete Rotterdam criteria, aged 18-40 years. The control group consisted of 60 healthy women with a regular menstrual cycle of the same age. Hormonal assays, and ultrasound of the pelvic organs were performed. The diagnostic accuracy of AMH, follicle-stimulating hormone (FSH), luteinizing hormone (LH), estradiol, testosterone (T), dehydroepiandrosterone sulfate (DHEAS), sex hormone-binding globulin (SHBG) and free androgen index (FAI) in predicting PCOS was established using a logistic regression model and calculating area under the receiver operator characteristic (ROC) curve (AUC).
Results
PCOS women had higher levels of serum LH ($p < 0.01$), T ($p < 0.01$), AMH ($p < 0.01$), FAI ($p < 0.01$), DHEAS ($p < 0.01$), estradiol ($P < 0.01$), 17-OH PG ($p < 0.01$) and significantly lower SHBG level ($p < 0.01$) and FSH level ($p < 0.01$) compared to healthy women. Testosterone level > 0.41 ng/ml showed the highest sensitivity (85.0%) and specificity (96.7%) for PCOS diagnosis. The level of AMH > 4.69 ng/ml also showed high sensitivity of 75% and specificity of 75% in PCOS diagnosis in the studied sample. The diagnostic accuracy of PCOS reached 94,2% with the combined use of hormonal indexes, which was significantly higher than the use of each index separately.
Conclusions
The results of the study estimate the threshold for AMH and T which could be suggested for use in the PCOS diagnostics with a high sensitivity and specificity. Moreover, the combination of hormonal indexes improved the diagnostic accuracy for the PCOS detection.
Keywords: polycystic ovary syndrome, hyperandrogenism, testosterone, anti-Müllerian hormone, threshold

DOI: 10.1530/endoabs.81.EP903

EP904

Development of ANA antibodies induced by estrogen treatment.

Daniel Medina Rivero[1], Isabel Mateo Gavira[2] & Laura Larrán Escandón[2]
[1]Hospital San Carlos San Fernando, San Fernando, Spain; [2]Hospital Universitario Puerta del Mar, Cádiz, Spain

A 36-year-old woman in follow-up due to early ovarian failure of idiopathic origin. No family history of interest. History of menarche at 12 years of age with regular menses until 18 years of age, when it begins with amenorrheic spells lasting up to 8 months. Laboratory tests revealed hypergonadotropic hypogonadism with negative ovarian autoantibodies, normal karyotype, and gynecological ultrasound showing a normal-looking uterus with slight bilateral ovarian atrophy. Negative antiadrenal and anti-TPO antibodies. She has undergone treatment with combined contraceptives since the diagnosis, only temporarily interrupted for 9 months to start the insemination protocol with egg donation, which was not completed. After 10 years of hormone replacement therapy, she develops polyarthralgia that worsens in the first days of estrogen treatment. She associates dactylitis of the hands and feet and episodes of joint angioedema. No accompanying fever. He also does not present joint deformities, abdominal pain or edema at the easy or genital level. In the study requested by Rheumatology, the following was observed: X-rays and bone scintigraphy without significant findings, densitometric study within normal limits, and the autoimmunity study revealed positive levels of ANA antibodies with a homogeneous pattern and a titer of 1/320. Other antibodies (anti-histone, anti-dsDNA, anti-nucleosome, anti-ribosome, anti-phospholipid, ENA, anti-adrenal, anti-ovarian, anti-citrullinated peptides, ANCA-MPO, ANCA-PR3 and those associated with polyglandular syndromes autoimmune) are negative. Likewise, angioedema due to hereditary or acquired defects of proteins of the complement system is ruled out. After discontinuation of estrogen treatment, the symptoms disappear. Finally, it is classified as a picture of angioedema and ANA induced by estrogen without criteria for systemic lupus erythematosus. She is currently asymptomatic and without hormone replacement therapy.

DOI: 10.1530/endoabs.81.EP904

EP905

Unrecognized premature ovarian failure in adolescents-case report

Milena Brkic[1], Svetlana Vujovic[2] & Branka Cancarevic Djajic[3]
[1]School of Medicine, University of Banja Luka, BanjaLuka, Bosnia and Herzegovina; [2]School of Medicine, University of Belgrade, Belgrade, Serbia, Department of Endocrinology, Clinical Center of Serbia, Beograd, Serbia; [3]School of Medicine, University of Banja Luka, Department of gynecology and obstetrics University Clinical Center of the Republic of Srpska Banja Luka, BanjaLuka, Bosnia and Herzegovina

Introduction
The average age for physiological menopause is 50 years. Menopause before the age of 40 is usually defined as premature ovarian failure (POF). POF in adolescents is an extremely rare event and its occurrence raises important questions about the cause-and-effect relationship, which may signal genetic and systemic disorders.
Design
Case report
The 29-year-old first reported to an endocrinologist for secondary amenorrhea. The anamnesis revealed that the patient got menarche at the age of 10. She had regular menstrual cycles for 4 years and irregular periods for 2 years. After the age of 16 she stopped menstruating. After 6 months, the therapy was excluded and during the next period of 12.5 years until the appearance of the endocrinologist and the desire to have children, she did not take anything from the therapy. From hardship allegations; irritability, insomnia, lack of energy, loss of libido, sweating, headache and weight gain. Menopause in a mother from the age of 30. Hormonal analyses:hypergonadotropic hypogonadism (FSH 200 mIU/l, LH 29.34 mIU/l, estradiol < 7 pg/ml, AMH0.01 ng/ml). Ultrasonography of the pelvis showed a normally located and normally developed uterus with a 4.7mm thin endometrium and both ovaries of reduced dimensions. Chronic autoimmune thyroiditis with elevated antibodies to thyroid peroxidase and thyroglobulin, but euthyroid with thyroid hormones in the normal range, was detected in the patient by ultrasonography. Testing did not detect congenital and acquired trobophilia. Karyotype: 46XX. Genetic analysis of FMMR1 genes normal. Ovarian antibodies negative. Introduced replacement therapy with oral estrogen-progestogens with the addition of estradiol at a dose of 2 mg in the follicular phase of the menstrual cycle, D3 hormone, antioxidants. After 2 years of treatment : FSH 28 mIU/l, LH 19.1 mIU/l, estradiol 22.4 pg/ml). Spontaneous abortion in the 6th week of gestation after *in vitro* fertilization with donated eggs.
Conclusion
Most cases of P0F remain idiopathic with a reduced success rate of assisted reproduction and procreation. The goal of treating adolescents with POF is replacement therapy with higher doses of estrogen than menopausal women to ensure proper replacement and optimal bone health.
Keywords: premature ovarian failure, secondary amenorrhea, hypergonadotropic hypogonadism

DOI: 10.1530/endoabs.81.EP905

EP906

Primary Ovarian Insufficiency in RMND1 Mitochondrial Disease

Emese Boros[1], Farel Elilie Mawa Ongoth[2], Claudine Heinrichs[1], Anne Laure Mansbach[3], Sara Seneca[4], Alec Aeby[5], Khalid Ismaili[6] & Cécile Brachet[1]
[1]Hôpital Universitaire des Enfants Reine Fabiola, Université Libre de Bruxelles, Paediatric Endocrinology, Brussels, Belgium; [2]Hôpital Universitaire des Enfants Reine Fabiola, Paediatric Endocrinology, Brussels, Belgium; [3]Hôpital Universitaire des Enfants Reine Fabiola, Université Libre de Bruxelles, Paediatric Ear Nose and Throat Department, Brussels, Belgium; [4]Universitair Ziekenhuis Brussels, Vrije Universiteit Brussels, Center for Medical Genetics/Research Center Reproduction and Genetics,

Brussels, Belgium; [5]Hôpital Universitaire des Enfants Reine Fabiola, Université Libre de Bruxelles, Paediatric Neurology, Brussels, Belgium; [6]Hôpital Universitaire des Enfants Reine Fabiola, Université Libre de Bruxelles, Paediatric Nephrology, Brussels, Belgium

Context
The genes implicated in premature ovarian failure play a role in crucial biologic processes such as DNA repair, meiosis, germ cell recruitment, steroidogenesis and mitochondrial function. Mitochondrial disorders are varied in their onset, inheritance pattern, and clinical presentation, but they often cause dysfunction in organs with high energy demands. Frequent features include hypertrophic cardiomyopathy, heart conduction defects, myopathy, sensorineural deafness, cerebellar ataxia, epilepsy, optic and peripheral neuropathy, among others. In addition, mitochondrial disorders often present with a range of endocrine features, including diabetes mellitus, GH deficiency, hypogonadism, thyroid disease, and ovarian dysfunction. RMND1 (Required for Meiotic Nuclear Division 1 homolog) is a nuclear encoded mitochondrial protein. Biallelic variants in *RMND1* are described in patients with white matter encephalopathy, hearing loss and renal dysfunction. In addition to this phenotype, two independent families (3 patients) have been reported with ovarian failure.
Case Presentation
We report on a 17 year-old girl with *RMND1* related mitochondrial disorder including white matter encephalopathy, hearing loss and renal insufficiency who presented primary ovarian insufficiency. She is homozygous for the already described c.713 A>G (p.Asn238Ser) in *RMND1*.
Conclusions
We report the third patient with *RMND1* biallelic pathogenic variants and primary ovarian insufficiency. Given the two previous reports linking *RMND1* and ovarian insufficiency and the many reports linking mitochondrial diseases with ovarian dysfunction, we believe that the *RMND1* pathogenic variants are indeed responsible for the severe ovarian insufficiency observed in our patient.

DOI: 10.1530/endoabs.81.EP906

EP907

Associations of VDBP polymorphisms with birth neonatal anthropometry: a cohort study from Northern Greece

Spyridon Karras[1], Erdinc Dursun[2], Merve Alaylioglu[2], Duygu Gezen Ak[3], Stefan Pilz[4], Edward Jude[5] & Fatme Al Anouti[6]
[1]National Scholarschip Foundation, National Scholarschip Foundation, Thessaloniki, Greece; [2]Department of Neuroscience, Institute of Neurological Sciences, Istanbul University-Cerrahpasa, 34381 Istanbul, Turkey, Department of Neuroscience, Institute of Neurological Sciences, Istanbul University-Cerrahpasa, 34381 Istanbul, Turkey, Instanbul, Turkey; [3]Department of Neuroscience, Institute of Neurological Sciences, Istanbul University-Cerrahpasa, 34381 Istanbul, Turkey, Department of Neuroscience, Institute of Neurological Sciences, Istanbul University-Cerrahpasa, 34381 Istanbul, Turkey, Turkey; [4]Division of Endocrinology and Diabetolology, Medical University of Graz, Austria, Division of Endocrinology and Diabetolology, Medical University of Graz, Austria, Graz, Austria; [5]5Department of Endocrinology, Tameside Hospital NHS Foundation Trust, Ashton-under-Lyne UK, 5Department of Endocrinology, Tameside Hospital NHS Foundation Trust, Ashton-under-Lyne UK, London, United Kingdom; [6]Department of Health Sciences, College of Natural and Health Sciences, Zayed University, Abu Dhabi 144534, United Arab Emirates, Abu Dhabi, United Arab Emirates

Vitamin D binding protein (VDBP) has a critical role in orchestrating optimal vitamin D homeostasis and bioavailability. VDBP has been implicated in modulating the gene expression of amino-transporters within the placenta and might thus control the transfer of amino acids to neonates during *in utero* development. We hypothesize that dyshomeostasis of VDBP could lead to adverse metabolic profiles and low birth weight in neonates. VDBP genetic polymorphisms steer the unique interplay of VDBP biodynamics and pregnancy complications. The aim of this study was to investigate associations of maternal VDBP polymorphisms with neonatal anthropometric profiles at birth, according to different cut-offs of vitamin D status. We included 66 maternal-neonatal dyads recruited from Northern Greece. Serum 25(OH)D concentrations were determined using LC–MS/MS and VDBP was measured by ELISA. We classified maternal and neonatal vitamin D status at birth, according to 25-hydroxyvitamin D (25(OH)D) concentrations as follows: 25(OH)D $\leq$ 25 nmol/l (deficiency), 25–50 nmol/l (insufficiency) and 25(OH)D $\geq$ 50-75 nmol/l (sufficiency). Our results revealed that with maternal 25(OH)D $<$50 nmol/l neonatal anthropometry parameters including abdominal circumference, lower arm radial circumference and lower leg calf circumference were significantly higher in maternal VDBP genetic variants rs2298850 CG+GG and rs4588 CA+AA and rs7041 GT+TT. This relation between birth neonatal anthropometry and maternal VDBP polymorphism, was not significant for birth maternal 25(OH)D $<$ 25 nmol/l. In conclusion, these findings, emphasize a potential role of functional polymorphisms, for maternal VDBP genotypes for rs2298850, rs7041 and rs4588, in conjunction with a maternal cut-off of maternal 25(OH)D in the range of sufficiency on neonatal growth and development. Further investigations are required to decipher the exact dynamic pathways of maternal VDBP and genetic variants on pregnancy complications and offspring body anthropometry.

DOI: 10.1530/endoabs.81.EP907

EP908

Evaluation of socio-demographic and clinical characteristics of PCOS patients attending a tertiary care institute in Colombo

Ishara Ranathunga, T G Athukorala, Manilka Sumanatilleke & Noel Somasundaram
NHSL, Colombo, Sri Lanka

Background and Objectives
Polycystic ovary syndrome (PCOS) is a common endocrine disorder with heterogeneous eatiology. It is characterized by irregular menses and or oligo/anovulation, hyper-androgenism, and polycystic ovaries. The prevalence and diagnosis of PCOS changes depending on which clinical criteria are utilized to confirm the diagnosis. The prevalence can be high as 15%–20% when the Rotterdam criteria are used. However, there is significant inter-individual variation in presentation. We have studied the socio-demographic and clinical characteristics of PCOS patients attending the Endocrinology clinic in a tertiary care institute in Sri Lanka.
Methods
A descriptive cross sectional study was conducted from September 2019 to September 2020 at the Endocrinology Unit of the National Hospital of Sri Lanka. Systematic sampling was done recruiting PCOS patients diagnosed with Rotterdam criteria. After obtaining informed written consent, the data was collected using an interviewer administered questionnaire. HOMA-IR was calculated using the fasting insulin and blood glucose level.
Results
The study enrolled sixty females. The mean age was 26.7 years (range 18-44). The mean weight was 64.8 (SD=11.9) kg and BMI was 27.1 (SD=4.8) kg/m^{-2}. According to Asian BMI cut-offs, 1 (1.7%) patient was underweight and 13 (21.7%) had normal weight. Forty six (76.7%) had their weight in the overweight or obese category. Fifty four (90.0%) patients had clinical or biochemical evidence of hyperandrogenism while 24 (40.0%) females had polycystic ovaries on trans-abdominal ultrasound scan and 50 (83.3%) partipants had irregular menstrual cycles. According to the body fat percentage assessed by the whole body DEXA scan 4.1% of the study population had normal body fat, while 50.0% and 45.8% had overweight and obesity respectively. HOMA-IR detected 61.1% patients to have high insulin resistance. Out of the patients who had USS of the abdomen 27.5% had co-existent non-alcoholic fatty liver. Fifty four percent of the patients had sub/infertility.
Conclusions
The majority of the population were overweight or obese and had higher prevalence of insulin resistance and non-alcoholic fatty liver. Out of the clinical characteristics used to make the diagnosis of PCOS, the presence of clinical or biochemical evidence of hyperandrogenism and irregular menstrual cycles are more common than the detection of polycystic ovaries on trans-abdominal USS. The higher prevalence of overweight, obesity, insulin resistance and NAFLD associated with PCOS makes the diagnosis and management of the disease crucial to prevent long term consequences of the disease

DOI: 10.1530/endoabs.81.EP908

EP909

PCOS pearls - findings from the qualitative study assessing the lived experience of people with polycystic ovary syndrome

Mirna Elghobashy[1], Gar Mun Lau[1], Maureen Busby[2], Kristine Stacke[3], Pallavi Latthe[4], Helena Gleeson[5], Lynne Robinson[6], Wiebke Arlt[5, 7], Antje Lindenmeyer[8], Caroline D. T Gillett[7], Punith Kempegowda[5, 7] & PCOS Seva Working Group[7]

[1]University of Birmingham Medical School, College of Medical and Dental Sciences, United Kingdom; [2]PCOS Vitality, Belfast, United Kingdom; [3]Verity – The PCOS Self Help Group, London, United Kingdom; [4]Birmingham Women's and Children's NHS Foundation Trust, Birmingham, United Kingdom; [5]Queen Elizabeth Hospital Birmingham, Department of Endocrinology, United Kingdom; [6]Birmingham Women's Hospital, United Kingdom; [7]University of Birmingham, Institute of Metabolism and Systems Research, United Kingdom; [8]University of Birmingham, Institute of Clinical Sciences, United Kingdom

Introduction
Existing educational resources for polycystic ovary syndrome (PCOS) have limited inclusion of patient perspectives. We invited women with PCOS to share their lived experiences to understand their perception and opinion on the current standard of care.
Methodology
Women with PCOS aged 18-60 years were invited to complete an online survey in April and May 2021. The survey had open questions focused on their lived experiences with PCOS. Participants had the option to share their views either as written text or as voice note audio recording(s) on WhatsApp. The data from audio were transcribed verbatim. Responses were initially coded by two study members independently, using a thematic inductive method with NVivo 12. These codes were then reviewed by two senior study members to identify common themes.
Results
43 of 45 participants had a formal diagnosis of PCOS, the remaining two had suspected PCOS which was under investigation. Four participants opted to share their views as voice note recordings. Overall, five common themes emerged: experience of symptoms (504 references by 42 participants), patient journey (421 references by 42 participants), knowledge (197 references by 40 participants), peer-to-peer advice (162 references by 41 participants), and impact of PCOS on social aspects of life (42 references by 19 participants). Poor mental health was most commonly reported (83.3% of participants), followed by dermatological (81.0%) and menstrual issues (76.2%). Participants were generally dissatisfied with the care they received (88.1%). A lengthy diagnostic journey was reported in 35.7% of cases. 52.6% felt less feminine, particularly with regards to weight gain and infertility. Women with PCOS said that others with the condition should educate themselves and be proactive in their management. 46.3% reported that being more enlightened regarding their condition improved their health outcomes and enabled them to advocate for their own care.
Conclusion
PCOS has wide-ranging consequences for women living with the condition, with many feeling dissatisfied with the clinical support they currently receive. Education is important to improve their understanding of their condition and encourage a proactive approach to their own care. Therefore, we propose involving people with PCOS to co-create educational resources informed by lived experiences which will help those newly diagnosed to gain a more comprehensive and realistic understanding of the condition from fellow sufferers.

DOI: 10.1530/endoabs.81.EP909

EP910

Developmental programming by maternal androgen excess is mediated by androgen receptor pathways

Haojiang Lu[1], Congru Li[1], Yu Pei[1], Gustaw Eriksson[1], Han-Pin Pui[1], Sanjiv Risal[1], Sara Torstensson[1], Angelo Ascani[2], Eva Lindgren[1], Claes Ohlsson[3], Anna Benrick[4, 5], Elisabet Stener-Victorin[1] & Qiaolin Deng[1]
[1]Karolinska Institutet, Department of Physiology and Pharmacology, Stockholm, Sweden; [2]Medizinische Universität Graz, Graz, Austria; [3]University of Gothenburg, Department of Internal Medicine and Clinical Nutrition, Gothenburg, Sweden; [4]University of Gothenburg, Department of Physiology, Gothenburg, Sweden; [5]University of Skövde, School of Health and Education, Skövde, Sweden

Introduction
The hyperandrogenic *in utero* environment in pregnant women with polycystic ovary syndrome (PCOS) can affect embryo development and impair offspring health at adult age. Moreover, long term hyperandrogenic exposure also leads to unfavored changes to the mothers' reproductive physiology, leading to miscarriage, preterm delivery, and perinatal mortality. The underlying mechanism(s) of pregnancy complications associated with PCOS and the consequence of hyperandrogenic intrauterine environment on the offspring is not well known.
Method
We used a PCOS-like mouse model induced by continuous exposure of dihydrotestosterone from prepuberty that develops obesity, anovulation and dysfunctional ovarian morphology, to study the effects of maternal hyperandrogenism during pregnancy. In addition, slight modifications are applied to the prepubertal PCOS-like mouse model to investigate critical periods in peripubertal life that projects to adverse pregnancy outcomes. To explore molecular mechanisms that contribute to the developmental defects, whole genome bisulfite and RNA sequencing of primordial germ cells and placenta were performed.
Results
Lower pregnancy rate and impaired placenta and embryonic development were found in the androgenised group, which was partially prevented by co-treatment with flutamide, an androgen receptor blocker. Moreover, germ cell specification was greatly compromised at embryonic day 10.5 and 13.5. The results of whole genome bisulfite sequencing and RNA sequencing of the primordial germ cells and placentas are currently under analysis. Furthermore, androgen exposure before the onset of vaginal opening may alter the physiology of uterus and vagina causing difficulty in labour.
Conclusion
Our results so far suggest that hyperandrogenism greatly compromise the PCOS-pregnancy and embryo development due to placenta dysfunction. Such effects are mainly mediated by the androgen receptor pathway as administration of flutamide partially prevents the compromised placenta and fetal development.

DOI: 10.1530/endoabs.81.EP910

EP911

The role of level and density of PSA in screening of prostate cancer

Shakhzod Shamsiev & Azamat Umarov
Tashkent Medical Academy, Department of Endocrinology, Tashkent, Uzbekistan

Introduction
It is known from world experience that the common screening method for diagnosing prostate cancer is the level and density of prostate-specific antigen (PSA), but the high sensitivity and low specificity of PSA testing have not been evaluated in Uzbek clinical practice. There are no proper guidelines to investigate suspected prostate cancer in Uzbekistan.
Methods
A total of 101 men were included in our investigation who were examined in the Republican specialized center of urology. All the patients underwent a complete examination, including laboratory(PSA level), ultrasound, transrectal ultrasonography, and prostate biopsy The patients were divided into subgroups by PSA level and PSA density, PSA density was calculated as total PSA (ng/ml) divided by prostate volume (ml).
Results
In patients with lower PSA levels less than 4 ng/ml detected benign processes compared to patients who had higher values of more than 50 nglml. Only two cases that had less than 4 ng/mg were suspicion of malignancy. When the PSA value was more than 100 ng/ml, almost all the cases were malignant. Between PSA values of 4-100 ng/ml, the probability of cancer diagnosis was 54% (54 cancers out of 101 in this range). Limitation of PSA testing has the risk of overdiagnosis and the resultant negative biopsies owing to poor specificity. Whereas the limit for cancer diagnosis remains 4 ng/ml from our study, most of the patients can be assured of benign lesion below this level, and thus morbidity associated with the biopsy can be prevented. PSA density was associated with the risk of finding PCa both with and without adjusting for the additional clinical information age, family history, previous biopsies, total PSA, and free/total PSA.
Conclusion
The PSA level plays important role in diagnosing prostate cancer and can reassure and educate the patients towards the diagnosis of cancer of the prostate in Uzbekistan. It is recommended prostatic biopsy if the level is below 4 ng/ml and a level of 100 ng/ml can be very unfavorable for the patients. Regarding the PSA-density might inform biopsy decisions, and spare some men from the morbidity associated with a prostate biopsy and diagnosis of low-grade prostate cancer.

DOI: 10.1530/endoabs.81.EP911

EP912

Gonadal dysgenesis with mayer-rokitansky in 46, XX female; case report

Heba Moustafa, Hemmat ELhaddad, Rokia Abdel Aziz, Randa Salam, Elham Mohamed, Iman Tohamy & Amira Nashat
Cairo University, Internal Medicine, Endocrinology, Cairo, Egypt

Introduction
The normal development of the female reproductive tract depends on the interaction between genetic, hormonal and environmental factors for the differentiation of the Müller Wolff ducts, and the urogenital sinus
Case report
16-year-old female, single, school student presented to our endocrine department complaining of delayed puberty. The patient was delivered by normal vaginal delivery, no history of anosmia or hearing defects There is no history of headache or blurring of vision or other neurological symptoms No history of chronic diseases, excessive exercise, medications, anorexia, clinical hypothyroidism or hyperandrogenism Family history revealed positive consanguinity Physical examination: Weight: 60 kg Height: 172 cm, BMI: 20 No facial dimorphism, no features suggestive of Turner syndrome Female phenotype, Tanner classification: breasts (3) axillary hair (2), pubic hair (2). Normal external genitalia Laboratory work up showed follicle-stimulating hormone: 98 mIU/ml (N: 0.7-11.1) Luteinizing hormone: 26 mIU/ml (N: 0.8-7.6), Estradiol 10 pg/ml (12.5-166), prolactin 4.4 ng/ml pelvi -abdominal ultrasonography, MRI pelvis : Infantile hypo plastic uterus (body 20 mm, cervix 12 mm) Non visualized both ovaries Normal female karyotyping46, XX Hormonal substitution by estrogen and progesterone was then undertaken.
Conclusion
The Mayer-Rokitansky-Kuster-Hauser Syndrome is a specific type of mullerian duct malformation characterized by congenital absence or hypoplasia of uterus and upper two thirds of the vagina in both phenotypically and karyotypically normal females with functional ovaries. The association of gonadal dysgenesis and Mayer-Rokitansky-Kuster-Hauser syndrome is very rare, hormone substitution therapy remains the only therapeutic option, to trigger the development of secondary sexual characters and prevent osteoporosis.

DOI: 10.1530/endoabs.81.EP912

EP913

Color-doppler ultrasound predicts hypothalamic-pituitary-testicular axis function in infertile patients

Giuseppe Grande[1], Pierfrancesco Palego[2], Andrea Canossa[2], Nicola Caretta[2], Andrea Di Nisio[2], Giovanni Corona[3], Alberto Ferlin[2], Carlo Foresta[2] & Andrea Garolla[2]
[1]'San Valentino' Hospital, Endocrinology Unit, Montebelluna, Italy; [2]University of Padova, Department of Medicine, Unit of Andrology and Reproductive Medicine, Padova, Italy; [3]Azienda Usl Maggiore-Bellaria, Endocrinology Unit, Medical Department, Bologna, Italy

Scrotal color-doppler ultrasonography (sCDUS) and transrectal ultrasonography (trCDUS) provide crucial information about the clinical status of testes and male accessory glands. However, the US evaluation of the infertile male is still often considered as a second level diagnostic tool. To analyze the role of ultrasound in male infertility, in order to predict hypothalamic-pituitary-testicular axis function, 1120 records from infertile men were retrospectively evaluated (from January 2016 up to June 2020). Data on physical examination, semen analysis, sperm culture, sCDUS and trCDUS, as well as sex hormones were analyzed. Among them, 238 reports from oligozoospermic/azoospermic infertile patients (P) (mean $\pm$ SD years) fullfilling the inclusion criteria were considered for data analysis. Patients were subdivided into two groups according to FSH values (Pa with FSH $<$ 8 U/l and Pb with FSH $>$ 8 U/l). Sixtythree fertile volunteers (mean $\pm$ SD years) were enrolled as controls (C). Pb group had significantly lower bitesticular volume compared to Pa and to C. A higher prevalence of ultrasound abnormalities was recorded in P compared to C. Pa had a higher prevalence of trCDUS abnormalities than Pb (69.9 vs 38.4% $P<0.005$), while Pb had a higher prevalence of abnormalities at sCDUS (60.0 vs 28.3%, both $P<0.01$). A higher number of US abnormalities was associated with a more severe reduction in total sperm count. Bitesticular volume was inversely proportional to the number of altered seminal parameters and a bitesticular volume $<$17 cc was associated with a higher risk of azoospermia (odds ratio 1.799). Moreover, this parameter was able to predict gonadotropin levels. Finally, intratesticular number of vascular spots was directly correlated with sperm count and inversely correlated with gonadotropin levels. Our data confirm the pivotal role of ultrasound in the diagnostic workflow of male infertility.

DOI: 10.1530/endoabs.81.EP913

EP914

Isolated FSH deficiency. A rare cause of male infertility

Evangelia Vogiatzi[1], Stavroula Psachna[1], Dimitrios Ioannidis[1], Dimitrios Lilis[1], Maria Drakou[1], Anastasios G. marathonitis[2], George Marathonitis[3], Vasiliki Koika[4], Neoklis Georgopoulos[4] & Antonis Polymeris[1]
[1]Sismanoglio - Amalia Fleming Attica General Hospital, Department of Endocrinology, Diabetes Mellitus and Metabolism, Melissia, Attica, Greece; [2]Sismanoglio - Amalia Fleming Attica General Hospital, Department of Cardiology, Marousi, Attica, Greece; [3]Sismanoglio - Amalia Fleming Attica General Hospital, Department of Internal Medicine, Melissia, Attica, Greece; [4]University of Patras Medical School, Department of Internal Medicine, Devision of Endocrinology, Unit of Reproductive Endocrinology, Patras, Greece

Background
Follicle stimulating hormone (FSH), a dimeric glycoprotein hormone, stimulates Sertoli cell proliferation and spermatogenesis in males. Azoospermia is defined as the absence of sperm in the ejaculate. The majority of patients with non-obstructive azoospermia have high FSH levels. Isolated FSH deficiency has been reported in a few patients.
Case Presentation
A 22-yr-old, 172-cm-tall male presented with azoospermia. He was born at full term with normal delivery of non-consanguineous parents. He had normal pubertal development with normal erections and potency. Upon physical examination he had normal virilization, normal sense of smell and no gynecomastia. His testes were both palpable in the scrotum measuring 25ml. No sperm was observed in the semen analysis twice. Semen fructose levels were normal. Urine analysis for retrograde ejaculation and testicular ultrasound revealed no abnormalities. His chromosomal karyotype was 46, XY. His testosterone, luteinizing hormone (LH), inhibin B (INHB) and anti-mullerian hormone (AMH) levels were normal, whereas FSH was low. Hypothalamic-pituitary magnetic resonance imaging (MRI) demonstrated no abnormalities. FSH levels remained low after intravenous injection of 100μg of gonadotropin-releasing hormone (GnRH), whereas LH levels rose. Sequencing of the β-subunit of FSH (FSHβ) gene did not reveal any mutation.
Discussion
Reports on isolated FSH deficiency are very rare with a prevalence of 0.89% in a retrospective study. The first observations of isolated FSH deficiency in males were described in 1998. Since then ten more case reports have been published, half of which were caused by an inactivating mutation of FSHβ gene. The patients presented with azoospermia, testicular hypotrophy, but with normal levels of testosterone and virilization. It appears that in cases of no FSHβ gene mutation there is milder phenotype, with oligo-astheno-teratospermia and even normal testicular volume. In cases where testicular biopsy was performed, spermatogenesis arrest, Sertoli cell hypoplasia and Leydig cell hyperplasia were reported. Hypothalamic-pituitary MRI and karyotype were normal. Remarkably, despite low INHB and AMH levels in patients with FSHβ gene mutations, cases without the mutation exhibited normal levels. Exogenous FSH led to an increase in testicular volume, spermatogenesis and in some cases in successful pregnancies.
Conclusion
Isolated FSH deficiency represents a rare form of male infertility which may be restored and therefore carries a high diagnostic value.

DOI: 10.1530/endoabs.81.EP914

EP915

Developmental neuro toxicity and cytotoxic mechanism evaluation of endocrine-disrupting chemical butylparaben

KangMin Kim[1], Minsu Lee[1], Jimin Lee[1], YongIn Kim[1] & Eui-Bae Jeung[1]
[1]Chungbuk National University Gaesin Campus, Veterinary Medicine, Cheongju, Rep. of South Korea

Butylparaben is an endocrine disrupting chemical (EDC) which is used as antimicrobial preservative in many cosmetic products. EDCs are structurally diverse class of synthetic and natural compounds. EDCs can cause non-

communicable diseases such as obesity, type 2 diabetes, and neurodevelopmental disease. Present study investigated that whether exposure to butylparaben during maternal pregnancy could cause the offspring's neuronal development disorder. *In vitro* study butyl paraben promoted apoptosis and inhibited proliferation of Sox1-GFP cell. The mRNA expressions for ER stress were evaluated. Furthermore, *in vivo* study for developmental neuro toxicity test battery for butylparaben was carried out. Butylparaben 100 mg/kg, 50 mg/kg was treated for pregnant mouse from E10.5 to weaning period. The result of behavior test shows abnormal cognitive, social and anxiety like behavior in butyl paraben treated mice. *In vitro* study, ER stress genes was evaluated, BiP, CHOP, and AFT6 were significantly up-regulated following treatment with EDC. From these results, butylparaben is a potential neuro developmental toxicant.

Keywords: Developmental neurotoxic test; mouse embryonic stem cells; endoplasmic stress

DOI: 10.1530/endoabs.81.EP915

EP916

Swyer syndrome presenting with clinical features of cushing disease: a case report

Ameni Terzi, Meriem Yazidi, Cyrine Chehaider, Ibtissem Oueslati, Fatma Chaker & Melika Chihaoui
La Rabta University Hospital, Department of Endocrinology, Tunisia

Introduction
Swyer syndrome is a rare sex development disorder characterized by pure 46 XY gonadal dysgenesis. It is associated with aberrations in testicular determination and differentiation leading to a female morphotype with presence of external and internal female genitalia, undifferentiated fibrous gonads, a male karyotype and hypergonadotropic hypogonadism. We present the case of a 46 XY adolescent female with complete gonadal dysgenesis diagnosed following her hospitalization in the endocrinology department for a suspicion of Cushing syndrome.
Case presentation
A 18-year-old female patient with no medical history was referred to our department for suspicion of Cushing syndrome. She had primary amenorrhea and reported weight gain within 2 years. On physical examination, her body mass index was 34.5 kg/m2 with a height of 156 cm. She had round moon face, red cheeks, a buffalo neck, thin arms and legs, and abdominal purple stretch marks. She had a female morphotype, normal female-type external genitalia with secondary sexual characters rated S4, P3 and A3 according to Tanner's classification. A 4-mg dexamethasone suppression test reduced the serum cortisol level to 0,3µg/dl excluding the diagnosis of Cushing syndrome. Hormonal investigations revealed elevated pituitary gonadotropin levels with FSH at 34.9 UI/l and LH at 15.8 UI/l. The testosterone and prolactin level were normal at 0.92 nmol/l and 9 ng/ml respectively. A pelvic ultrasound confirmed the presence of 2 small non-follicular ovaries with uterine hypoplasia (25X17X8mm). The karyotype was male "46 XY". The diagnosis of pure 46 XY gonadal dysgenesis was made. A hormone replacement therapy was applied and the patient was referred to a gynecologist for bilateral prophylactic gonadectomy.
Conclusion
In light of this case, we wish to draw attention to a serious sex-reversal disorder that affects women in their identity, Swyer syndrome revealed here by an unusual circumstance of discovery. This pathology is associated with a higher risk of malignant degeneration and an elevated incidence of gonadal neoplasia mainly the gonadoblastoma and dysgerminoma highlighting thus the paramount urge of preventive adnexectomy. Similarly, a screening of the siblings with female morphotype is necessary since this disorder is related to mutations or deletions in several genes such as SRY that can be inherited genetically.

DOI: 10.1530/endoabs.81.EP916

EP917

Machine learning-based model for gestational diabetes mellitus prediction in the first trimester of pregnancy

Polina Popova[1], Aleksandra Tkachuk[2], Alexandra Klyushina[3], Lyudmila Vasilyeva[3], Elena Vasukova[2], Anna Anopova[1], Evgenii Pustozerov[2], Yana Teplova[1] & Elena Grineva[2]
[1]Almazov National Medical Research Centre, Saint Petersburg, Russia, World-Class Research Center for Personalized Medicine, Saint Petersburg, Russian Federation; [2]Almazov National Medical Research Centre, Saint Petersburg, Russia, Institute of Endocrinology, Saint Petersburg, Russian Federation; [3]Almazov National Medical Research Centre, Saint Petersburg, Russia, Institute of Molecular Biology and Genetics, Saint Petersburg, Russian Federation

Background and aim
Gestational Diabetes Mellitus (GDM) is often diagnosed at 24-28 weeks of pregnancy when the fetal phenotype is already altered. We aimed to develop a machine learning model based on clinical variables, lifestyle features and genetic markers for GDM prediction in the first trimester of pregnancy based on the 2013 World Health Organization (WHO) criteria.
Methods
Using multivariable logistic regression analysis, different models to predict GDM were developed based on clinical variables from early pregnancy (age, pre-pregnancy body mass index (BMI), arterial hypertension, a history of GDM, impaired glucose tolerance, polycystic ovary syndrome, family history of type 2 diabetes, and parity), lifestyle features (food consumption, physical activity and smoking habits assessed through questionnaires), genetic markers (number of risk alleles in rs10830963 of the MTNR1B gene) and their combination. The input data were obtained from 1050 pregnant women participating in prospective studies performed in the Almazov National Medical Research Centre (655 GDM cases and 395 controls). Receiver operating characteristic (AUC) analysis assessed the model's performance with eight-fold cross-validation.
Results
C-statistics for logistic regression models were as follows: clinical covariates alone: 0.690 (95% CI: 0.658 to 0.722) and 0.688 (95% CI: 0.647 to 0.729) for an eight-fold cross-validated assessment of the score; rs10830963 alone: 0.597 (95% CI: 0.565 to 0.629) and 0.546 (95% CI: 0.375 to 0.717) cross-validated; combination of clinical covariates and rs10830963: 0.721 (95% CI 0.690 to 0.752) and 0.715 (95% CI 0.672 to 0.759); combination of clinical covariates and lifestyle features: 0.806 (95% CI 0.779 to 0.833) and 0.802 (95% CI 0.724 to 0.881) cross-validated; combination of clinical covariates (age, pre-pregnancy BMI, a history of GDM), rs10830963 and lifestyle features (the frequency of pre-pregnancy consumption of meat, bread and alcohol): 0.823 (95% CI: 0.797-0.849) and 0.813 (95% CI: 0.734-0.892) cross-validated.
Conclusions
A first trimester machine learning-based model, which incorporates classical risk factors and novel biomarkers, has a high accuracy to predict GDM based on the 2013 WHO criteria.

DOI: 10.1530/endoabs.81.EP917

EP918

Partial androgen insensitivity syndrome revealed by a bilateral gynecomastia

Zineb Mhamdi, Imane Alilouch, Kaoutar Rifai, Hinde Iraqi & Mohamed El Hassan Gharbi
Ibn Sina University Hospital, Department of Endocrinology and Diabetology, Rabat, Morocco

Introduction
Partial androgen insensitivity syndrome is a disorder of sexual development, distinct from complete androgen insensitivity syndrome. It is characterized by the presence of abnormal genital development in an individual with a 46, XY karyotype, with normally developed testes and a partial response to androgens at normal levels for age. It is an autosomal recessive X-linked disorder related to molecular abnormalities of the androgen receptor gene.
Case report
We report the case of an 18-year-old patient with a history of hypospadias operated in childhood, who consulted for bilateral gynecomastia. The clinical examination revealed a 3.5 cm Tanner P5 micropenis with absence of facial and axillary hair. His karyotype was 46, XY. Biologically: testosteronemia : 18.84 ng/ml, FSH was normal and LH : 15.6 mIU/ml with a Testosterone/Dehydroepiandrosterone (DHT) ratio of 6. The diagnosis of partial androgen insensitivity was therefore retained. Androstanolone (Andractim* gel) was used for 6 months with therapeutic failure. The patient was referred to plastic surgery for surgical management of his gynecomastia.
Discussion and conclusion
Partial androgen insensitivity is most often diagnosed in a newborn with atypical genital development (hypospadias, cryptorchidism, micropenis, or even very feminine phenotype with clitoral hypertrophy). The diagnosis will be evoked more rarely in front of an isolated micropenis or an isolated gynecomastia as in the case of our patient, or pubertal virilization in a young girl or fertility disorders in a man. It varies according to the degree of insensitivity of the genital tract to androgens.

References
Lachiri B, Hakimi I, Boudhas A. Le syndrome d'insensibilité complète aux androgènes: à propos de deux cas et revue de la literature [Complete androgen insensitivity syndrome: report of two cases and review of literature]. *Pan Afr Med J*. 2015;20:400. Published 2015 Apr 23.
C. Bouvattier, Androgen resistance, Annals of Endocrinology, Volume 79, Issue 4, 2018, Pages 196-197.

DOI: 10.1530/endoabs.81.EP918

EP919

Complete androgen insensitivity syndrome: about 2 cases

Amal Elkhomri, Nassim Essabah Haraj, Siham El Aziz & Asma CHADLI
CHU Ibn Rochd, Endocrinology-Diabetology and Metabolic Diseases Department, Casablanca, Morocco

Introduction
Androgen insensitivities are rare genetic diseases, characterized by a more or less complete defect of tissue sensitivity to testosterone. It ranges from a more or less complete lack of masculinization to isolated infertility in a 46, XY individual. This partial or complete androgen insensitivity is linked to a defect in the function of the androgen receptor. We report the case of two patients with complete androgen resistance syndrome discovered during the exploration of primary amenorrhea
Observation 1
33-year-old patient, operated in 2016 for bilateral intra-abdominal gonadectomy, with an anatomopathological examination of an ectopic testicle on the right without signs of malignancy, and an embryonic carcinoma on the left, the patient underwent chemotherapy sessions, she presents a harmonious and feminine Morphological development, with absence of vaginal orifice, a carotype was done in favor of a 46 XY, pelvic MRI with absence of internal genitalia, and genitography with absence of vaginal orifice, the patient was put on estrogen and progestin, with good clinical evolution
Observation 2
20-year-old patient, who underwent bilateral gonadectomy in 2017 with pathological examination of hypoplastic testicular pulp with hamartomatous nodules and hypoplastic foci of Leydig cells compatible with androgen insensitivity syndrome without malignancy, with a gynecological examination presence of labia majora and labia minora not well formed with an incipient vagina. a carotype was done in favor of a 46 XY, pelvic MRI with absence of internal genitalia, and genitography with absence of vaginal orifice, the patient was put on estrogen and progestin, with good clinical evolution
Conclusion
Androgen insensitivity syndrome, a rare entity, is the most frequent etiology of the anomaly of the XY sex differentiation, gonadectomy is necessary, and hormonal substitution helps maintain female sexual characteristics and prevent osteoporosis.

DOI: 10.1530/endoabs.81.EP919

EP920

Safety and monitoring of gender affirming hormone therapy in portugal

Miguel Saraiva[1], Rafael Santos[2], Zé lia Figueiredo[3], Carolina Lemos[4] & Isabel Palma[1]
[1]Centro Hospitalar Universitário do Porto - Hospital de Santo António, Endocrinology, Diabetes and Metabolism, Portugal; [2]Instituto de Ciências Biomédicas Abel Salazar, Universidade do Porto, Portugal; [3]Hospital de Magalhães Lemos, Portugal; [4]i3S-Instituto de Investigação e Inovação em Saúde, Universidade do Porto, Portugal

Introduction
The prevalence of Transgender individuals seeking gender affirming hormone therapy (GAHT) has been increasing. It is important to closely monitor this therapy in order to minimize the risk of adverse effects.
Aim
To evaluate the safety and monitoring of the GAHT in the Portuguese adult transgender population
Methods
Cross-sectional study conducted in March 2021. Data collected through an *online* questionnaire that was delivered to adult transgender people living in Portugal who had been under GAHT for at least one year. To answer some of the items on the questionnaire, an ordinal scale ranging from 0 (worst result) to 6 (best result) was used.
Results
A total of 142 individuals answered the questionnaire: 101 under masculinizing GAHT (Group M) and 41 under feminizing GAHT (Group F), with a median age of 25.0(21.0–33.0) years. 43.3% of the individuals denied having signed an informed consent document and 11.3% denied having done blood sample analysis before starting GAHT. This happened more frequently with individuals of the Group F (24.4% *vs* 5.9%, $P=0.002$). Accordingly, this group also reported having obtained the first prescription of GAHT by an endocrinologist less frequently (58.5% *vs* 79.2%, $P=0.012$). 93.7% of the individuals had regular medical appointments because of the GAHT, although this was less common in Group F (85.4% vs 97.0%, $P=0.010$). 79.6% reported undergoing regular blood sample analysis to monitor the GAHT. Of those, 75.2% did so according to the timings recommend by WPATH. As for adverse effects, 89.7% of the individuals on Group M experienced at least one – more commonly mood swings (56,3%) and acne (52,9%) – and 96.3% of the individuals on Group F experienced at least one – more commonly decreased libido (66.7%) and mood swings (63.0%). The perceived overall safety of the GHAT was classified with a median of 5.0(4.0-6.0) points, although individuals on the Group F scored significantly lower (4.3 vs 5.0 points, $P=0.007$).
Discussion
This study highlights the importance of the involvement of specialized physicians, namely endocrinologists, in the prescription and monitoring of the GAHT. There is still plenty of room to improve Transgender health care in Portugal, mostly in transgender people undergoing feminizing GHAT - a population known to be especially vulnerable to social stigma.

DOI: 10.1530/endoabs.81.EP920

EP921

Clinical features of reproductive status in women who underwent Covid-19

Surayyo Mekhmanova[1], Khurshida Nasirova[1] & Zamira Khalimova[2]
[1]Tashkent Pediatric Medical Institute, Tashkent, Uzbekistan; [2]Republican Specialized Scientific and Practical Medical Center of Endocrinology named after Y.H. Turakulov, Neuroendocrinology, Tashkent, Uzbekistan

Keywords: Reproductive system of women who have had coronavirus, Covid-19, women.
The relevance of the problem. Currently, there are no published evidence-based recommendations for the management of women who have undergone COVID-19. According to statistics, women carry COVID-19 more easily than men, and the likely consequences of this coronavirus infection for reproductive health cannot be ignored. It is necessary not only to carefully monitor the respiratory parameters of patients with COVID-19, but also to assess the potential impact of a new infection on the organs of the reproductive system
Objective
To study the clinical conditions of women and assess their general condition.
Material and methods
100 women aged 18-45 years (average age 32 years) who underwent Covid-19 were examined. These women will be divided into 2 groups depending on the severity of the disease. they underwent a complete clinical hormonal and imaging examination and were divided into I a women with mild form, 60 women aged 18 to 44 years, I b women with severe form in the acute stage, 21 women aged 18 to 40 years, an average of 30 years At the moment, the control group will consist of 10 healthy women of the same age. A survey of complaints about the acute phase of women who had Covid-19 was conducted.
Results
The most frequent and significant changes were complaints of general weakness (p0,000), menstrual cycle changes (p0,002), headaches (p0,000), dry skin (p0,000), hair loss (p0,000), mood loss (p0,000), memory loss (p0,000), anxiety (p0,003) The least complaints were Hirsutism (p0,157), Decreased visual acuity (p0,317), Galactorrhea (p1,000)
Conclusion
In this way, the function of the reproductive system and somatic disease is aggravated in patients who have undergone Covid-19, which requires careful monitoring by an endocrinologist, gynecologist and neurologist.

DOI: 10.1530/endoabs.81.EP921

EP922

The clinical and etiological aspects of hirsutism : about 100 cases

Anis Grassa, Bel Hadj Sliman Chayma, Nadia Khessairi, Fatma Chaker & Melika Chihaoui
Rabta Hospital, Endocrinology, Tunis, Tunisia

Introduction
Hirsutism is often caused by hormonal disorders such as high levels of circulating androgens, hormonal changes related to menopause or disorders of the ovarian or adrenal gland. The aim of our study was to evaluate the clinical and etiological profile of hirsutism.
Methods
A retrospective study was conducted at the endocrinology department of Rabta Hospital in Tunis including 100 patients who presented with hirsutism between January 2009 and December 2020. Clinical and paraclinical data were collected from medical records. Hirsutism was classified according to the Ferriman Galleway score.
Results
The mean age of our patients was 29.5 years $\pm$ 10.7 [15 -73]. Family history of hirsutism, infertility and death in early childhood were found in 27%, 36% and 4% of cases respectively. The average age of menarche was 12.1 years $\pm$ 1.2. Eight women were menopausal. The onset of hirsutism was progressive in 95 cases either peripubertal or post-pubertal respectively 44% versus 56%. Hirsutism was classified as mild, moderate and severe in 32%, 57% and 11% of cases respectively. The clinical features found to be associated with hirsutism included acne (28%), virilism signs (9%) and menstrual irregularities in 60% of patients. The mean of testosterone level was 0.9 ng/ml $\pm$ 0.7 [0.15-4.08]. Additional investigations such as dosage of Dehydroepiandrosterone sulfate, 4-androstenedione, and 17-OH progesterone were done according to etiological orientation and revealed means of 900.1 µg/ml, 354 ng/ml, and 1.86 ng/ml respectively. The etiologic investigation showed ovarian tumor, adrenal tumor with androgen secretion, late-onset congenital adrenal hyperplasia, Cushing's syndrome, polycystic ovary syndrome (PCOS) and idiopathic hirsutism in 3%, 5%, 7%, 2%, 51% and 32% of cases respectively.
Conclusion
Hirsutism is a very frequent and troublesome symptom. However, it can reveal serious underlying pathology, especially in its severe form.

DOI: 10.1530/endoabs.81.EP922

EP923

Clinical and metabolic profile of hirsute women

Bel Hadj Sliman Chayma, Nadia Khessairi, Anis Grassa, Ibtissem Oueslati, Meriem Yazidi & Melika Chihaoui
Rabta Hospital, Endocrinology, Tunis, Tunisia

Introduction
Hirsutism is described as excessive development of facial and body hair in women in androgen-dependent areas. Our aim was to determine the clinical and metabolic aspects of hirsutism and its relationship with the metabolic syndrome.
Methods
We conducted a retrospective descriptive study at the endocrinology department of Rabta Hospital in Tunis. We recruited 100 women who presented with hirsutism between January 2009 and December 2020 Clinical and paraclinical data were collected from medical records. The diagnosis of metabolic syndrome was made according to the IDF 2009 criteria.
Results
The mean age of our patients was 29.5 $\pm$ 10.7 years. Our patients were smokers in 8% of cases and diabetics in 19% of cases. The onset of hirsutism was post-pubertal in 56% with menstrual disorders in half cases. Associated clinical signs were skin acne (50%), Acanthosis Nigricans (20%) and signs of virilization (9%). Our population had an average weight of 83.9 $\pm$ 20.9 kg [38-150] with an average body mass index of 32.5 $\pm$ 7.7 kg/m^2 [16-57]. Obesity was noted in 58% and described as grade 1 in 44.2%, grade 2 in 25% and morbid in 30.8% of cases. Mean testosteronemia was 0.9 $\pm$ 0.76 ng/ml. Biological investigations showed mean values for blood fasting glucose = 1.08 $\pm$ 0.44 g/l, glycated haemoglobi*n* = 7.37 $\pm$ 2.42%, total cholesterol = 1.8 $\pm$ 0.5 g/l, HDL-cholesterol = 0.45 $\pm$ 0.1 g/l and LDL-cholesterol = 1.11 $\pm$ 0.3 g/l. A metabolic syndrome was present in 54% of patients. Etiologies were dominated by polycystic ovary syndrome (51%), followed by idiopathic hirsutism (32%), adrenal pathology (15%) and ovarian tumors (3%).
Conclusion
Our results suggest that the increase of androgenic activity favors an android distribution of body fat, which is associated with an impairment of glucose and lipid metabolism.

DOI: 10.1530/endoabs.81.EP923

EP924

Recovery of hypothalamic-pituitary-gonadal function with low dose testosterone treatment in a male with idiopathic hypogonadotropic hypogonadism

Fernando Braca[1], Juan Carmelo Betancor Acosta[1], Nuria Perez Martin[1] & Mauro Boronat Cortes[1, 2]
[1]Hospital Insular, Las Palmas de Gran Canaria, Spain; [2]University of Las Palmas de Gran Canaria, University Institute for Biomedical and Health Research, Las Palmas de Gran Canaria, Spain

Idiopathic hypogonadotropic hypogonadism (IHH) is a rare congenital disease caused by deficiency or action of gonadotropin-releasing hormone. While generally considered a long-life condition, IHH can be reversible in about 20-30% of cases, but mechanisms of reversibility are unknown. We report the case of a male with IHH who began treatment with low dose (20 mg/day) transdermal testosterone to induce pubertal development at age 18. Following the start of treatment, he experienced testicular growth and his serum testosterone concentrations increased beyond the expectations in relation to the dose. Treatment was withdrawn, but this led to the reappearance of symptoms of hypogonadism and a drop in testosterone levels. Testosterone was again prescribed at the same dose and, for the subsequent years, he completed full puberty, including attainment of 20 cc testicular volume, mature secondary sexual characteristics, normal levels of testosterone and only partially arrested germinal function, as demonstrated by inhibin B levels and spermogram. Testosterone treatment was withdrawn three more times, but hypogonadism resumed on each occasion. This case suggests that low-dose testosterone treatment can induce reversal of IHH through the activation, albeit non-permanent, of the hypothalamic-pituitary-gonadal axis, and could be a therapeutic option for this condition.

DOI: 10.1530/endoabs.81.EP924

EP925

Cardiovascular risk factors among women with polycystic ovary syndrome in an urban Sri Lankan population

Kaveen Weerasinghe
Post Graduate Institute of Medicine, University of Colombo, Sri Lanka, Obstetrics and Gynaecology, Sri Lanka

Introduction
Polycystic ovary syndrome (PCOS) is an endocrine and metabolic disorder that affects 5-10% of women of reproductive age world wide. Women with PCOS are known to have a higher prevalence of metabolic syndrome and cardiovascular risk factors compared to the general population. However data on PCOS and cardiovascular risk factors amomg Sri Lankan women is limited.
Methodology
A case control study was conducted among 172 women from Colombo, Sri Lanka. 86 women aged $<$45 years diagnosed with PCOS according to Rotterdam criteria were compared to 86 age matched controls from the community with no history or evidence of PCOS. Biometric data, biochemical, and endocrine parameters were compared between groups using approprite statistical tests.
Results
Among 86 women with PCOS, 41 (47.7%) were overweignt and 28 (32.6%) were obese. Prevalence of obesity ($P=0.002$) and overweight ($P=0.01$)among women with PCOS were significantly higher compared to the control group. Acanthosis nigricans was present among 59.3% ($n=51$) of women with PCOS. Women with PCOS had significantly higher levels of fasting insulin ($P=0.001$), fasting blood glucose ($P=0.015$), and 2 h blood glucose level following 75g oral glucose load ($P=0.002$). Prevalence of type 2 diabetes mellitus among women with PCOS was 26.7% while prevalence was 12.8% in the control group. Further 24.4% of women with PCOS had prediabetes. Women with PCOS had significantly higher triglyceride levels ($P=0.01$), total cholesterol levels (0.02) and lower HDL levels ($P=0.02$) compared to control group. Systolic ($P=0.05$) and diastolic ($P=0.01$) blood pressures were significantly elevated among women with PCOS compared

to the control group. Prevalence of hypertension among women with PCOS was 11.6%. 34.9% ($n=30$) of women with PCOS fulfilled diagnostic criteria for metabolic syndrome. Women with PCOS had higher odds of obesity, insulin resistance, hyperglycemia, dyslipidemia, hypertension and metabolic syndromeare compared to age matched controlls.
Conclusion
Women with PCOS often have multiple cardiovascular risk factors including obesity, diabetes mellitus, dyslipidemia, and hypertension. Management of cardiovascular risk factors should be prioratized in the long term care of women with PCOS. Further research is required to assess implications of PCOS on longterm cardiovascular morbidity and mortality among Sri Lankan women.

DOI: 10.1530/endoabs.81.EP925

EP926

Molecular and comprehensive computational analysis revealed normal LHCGR gene among women with PCOS

Nidal Essa[1], Rashid Abdalla Rashid Abdalla[2] & Mohamed A. Hassan Mohamed Hassan[3]
[1]University of Medical Sciences and Technology, Clinical Chemistry, Sudan; [2]Pharmacy; [3] Department of Bioinformatics, Sudan

Background
Polycystic ovary syndrome (PCOS) is a common disorder, yet not fully understood. Multiple hormonal and metabolic factors influence the pathophysiology of disease; resulting in various phenotypic characteristics among PCOS population. The luteinizing hormone/choriogonadotropin receptor (*LHCGR*, OMIM: 152790) is a G protein- coupled receptor mapped on chromosome 2p16.3; its coding region comprises 10 exons separated by 10 introns which transcript to protein with 699 amino acids.
Objectives
To determine genetic mutations of *LHCGR* gene in Sudanese families affected by PCOS.
Methods
A prospective laboratory based cross-sectional study was implemented to examine genetic mutations in LHCGR that associate with PCOS in families (cases; $n = 35$ families, 90 females and controls; $n = 11$ families, 30 females) in Khartoum State, Sudan. Quantitative Enzyme Linked Immuno-Sorbent Assay (ELISA), enzymatic methods and partial selected exon 11 from in silico analysis data were analyzed by polymerase chain reaction (PCR) for polymorphism detection followed by Sanger sequencing for genotyping among selected families.
Results
From the In silico analysis, we revealed that the most (29) distributed SNPs were located through *LHCGR* coding region. Thereafter, we select exon 11 which contain the most reported SNPs and Sanger sequencing revealed normal sequence of exon 11 of *LHCGR* gene that were statistically correlated with serum LH, Testosterone and insulin levels among PCOS families and characterized by homozygous inheritance mode. The PCOS cases had significantly different biochemical parameters from the controls (LH: $P<0.001$; testosterone: $P<0.001$; fasting glucose: $P=0.02$; insulin: $P=0.01$; triglycerides: $P=0.03$; total cholesterol: $P<0.001$; high density lipoprotein (HDL): $P=0.012$; low density lipoprotein (LDL): $P<0.001$). There were no differences in follicle stimulating hormone (FSH) ($P=0.984$) or prolactin ($P=0.068$).
Conclusion
This is the first molecular family-based study in Sudan exploring the genetics of the *LHCGR* gene in women manifesting PCOS. These novel mutations give further information about the genetic inheritance and may explain some of the altered ovarian function and responses in women with PCOS.
Keywords: PCOS, Luteinizing hormone, SNPs, infertility, family studies, LHCGR

DOI: 10.1530/endoabs.81.EP926

EP927

Online education as effective medical training for young endocrinologist

Martina Jambrović[1], Anja Barac Nekic[2], Lana Sambula[3], Iva Petrak[4], Nino Matas[2] & Karin Zibar Tomšić[5]
[1]General Hospital Čakovec, Department of Internal medicine, ČAKOVEC, Croatia; [2]General Hospital Dubrovnik, Department of Internal medicine, Croatia; [3]General Hospital Dr. Tomislav Bardek Koprivnica, Department of Internal medicine, Croatia; [4]General Hospital Nova Gradiška, Department of Internal medicine, Croatia; [5]University Clinical Hospital Centre Zagreb, Department of Endocrinology and Diabetology, Zagreb, Croatia

Background
Learning through various online platforms is very common nowadays and its popularity has increased especially during the pandemic period. Nowadays, medical professionals are turning more than ever to online education through available online books, websites, and various online platforms. The aim of this study was to show that virtual training can improve the knowledge and confidence of young endocrinologists.
Methods
The Croatian Section for Young Endocrinologists organised the 2nd Regional Online Symposium for Young Endocrinologists in November 2021 for the purpose of continuing education and knowledge sharing among young endocrinologists from the region. The theme of the symposium was 'Endocrinopathies in Pregnancy.' The symposium started with an introductory test with 18 questions. At the end of the symposium, we administered the same test to see how much the participants had learned and improved their knowledge. The test also served as feedback for the organisers to see how good each presentation was and if there was room for improvement. The anonymous test consisted of 18 questions from 5 areas of endocrinology (pituitary, adrenal, diabetes and metabolism, calcium and bone metabolism, and thyroid).
Results
A total of 53 subjects participated in the introductory test and 37 subjects in the final test. There was a statistically significant difference in resolution between the introductory and final tests for 8 of the 18 questions. Baseline knowledge, based on the joint median of correct answers from a domain, was 24% in the pituitary area, 29% in the calcium and bone area, 46% in the adrenal area, 49% in the diabetes and metabolism area, and 59% in the thyroid area. There were statistically significant improvements in the final test (from greatest to least improvement) for the area of calcium and bone (all 3 questions achieved statistically significant improvement), then pituitary (2/3 questions achieved statistically significant improvement), thyroid (2/2 questions achieved statistically significant improvement), diabetes, and metabolism (1/4 question achieved statistically significant improvement), whereas there were no statistically significant differences in resolution between the introductory and final tests for the adrenal (0/4) area.
Conclusion
Online education is a very widely used and good learning model to improve and transfer the knowledge of young physicians and scientists. Different models of online learning need to be promoted and implemented in daily practise.

DOI: 10.1530/endoabs.81.EP927

EP928

Mild Androgen Insensitivity (MAIS): A challenging clinical and laboratory diagnosis

Tahir Omer[1,2] & Abaid Ur Rehman[1]
[1]Northampton General Hospital, Northampton, United Kingdom; [2]University of South Wales, Cardiff Campus, United Kingdom

Introduction
The androgen receptor (AR) as a steroid hormone receptor is crucial for the embryological male sex differentiation and the maintenance of the phenotypical male characteristics throughout life in addition to spermatogenesis. Mutations in the AR gene can disrupt its function leading to Androgen Insensitivity Syndrome (AIS). AIS has a recessive mode of inheritance and can be broadly classified into 3 phenotypical categories: complete androgen insensitivity syndrome (CAIS), partial (PAIS) and mild (MAIS). CAIS usually presents with female external genitalia and primary amenorrhoea. Karyotyping might be very helpful in these patients. Patients with PAIS syndrome typically have ambiguous genitalia, including partial labio-scrotal fusion and hypospadias. Patients with MAIS, on the other hand, have a mild presentation with subtle secondary sexual characteristics abnormalities that can remain unnoticed for long. Due to its variable presentation, MAIS can prove challenging to diagnose clinically and biochemically.
Case presentation
We describe the case of a young man in his early 20s with normal childhood growth and development. He has been to see the Cardiologist for recurrent palpitations when he was noticed to have some degree of gynaecomastia. He was then referred to our clinic for further work up. Physical examination demonstrated sparse body hair, hypoandrogenic phenotype, gynaecoid habitus, normal penile length and small scrotum. His blood test showed a confusing picture of raised FSH, raised LH, mildly raised Prolactin, high normal Testosterone, normal SHBG and raised Oestradiol. His total HCG was normal. His Karyotype was normal

46XY. U/S scrotum showed very small testes and no masses. MRI pituitary and MRI adrenal were normal. Genomic DNA sequencing of AR gene demonstrated a missense mutation indicating MAIS.
Discussion and Conclusion
Mutations affecting the *AR* gene can lead to either complete, partial or mild androgen insensitivity syndrome. The case reported here is consistent with mild androgen insensitivity. Due to its subtle presentation, this was not diagnosed until early adult life. The high gonadotrophins together with high normal Testosterone raised the possibility of pituitary gonadotroph adenoma initially. Klinefelter's and similar chromosomal disorders were also included in the differential diagnoses. The patient was also investigated for potentially secreting Adrenal and testicular tumours. Nevertheless, none would completely explain the clinical picture with small scrotum and the raised Testosterone and Oestrogen levels. Patients who present with gynaecomastia should always undergo adequate endocrine and genetic testing to reach a conclusive diagnosis.

DOI: 10.1530/endoabs.81.EP928

EP929

Genetic coincidence of hypo- and hypergonadotropic hypogonadism

Sava Petrov[1], Hristo Ivanov[2], Ekaterina Babadzhanova[1] & Maria Orbetzova[1]
[1]Medical University - Plovdiv, Endocrinology, Plovdiv, Bulgaria; [2]Medical University - Plovdiv, Department of Pediatrics and Medical Genetics, Plovdiv, Bulgaria

Congenital hypogonadotropic hypogonadism is characterized by delayed or absent puberty and infertility due to abnormally low levels of gonadotropic hormones and sex steroids. The most common reason for its development is Kallmann syndrome - a rare congenital disorder resulting from impaired migration of GnRH-secreting neurons from the olfactory epithelium to the hypothalamus. It is associated with hyposmia and anosmia. In 1942 Klinefelter described 9 men with gynecomastia, sparse facial and body hair, small testes and inability to produce sperm. In 1959 the additional X chromosome was discovered - genotype 47, XXY, characteristic of the complete and most common form of Klinefelter syndrome. The classic phenotype includes low serum testosterone, high LH and FSH levels. We present clinical cases of two adolescents at age of 18th and 19th with history for diminished pubertal spurt, treated with recombinant gonadotropic hormones by the pediatricians by the age of sixteen. 18-years boy was diagnosed with microdeletion of Y-chromosome and the 19-years boy did not have genetic diagnostic determination. Both patients presented with hormonal constellation for hypogonadotropic hypogonadism, low volumes of testicles, diminished spermatogenesis. We performed kariotipazation and found disomy X-47, XXY. Patients were referred to Sequence analysis and deletion/duplication testing of the 46 genes listed in the Genes Analyzed section for hypogonadotropic Hypogonadism Panel and found deletion of ANOS1 gene. That cases present a rare coincidence of two genetic states for both hypo- and hypergonadotropic hypogonadism.
Key words: Hypogonadotropic hypogonadism, Kallmann syndrome, Klinefelter syndrome

DOI: 10.1530/endoabs.81.EP929

EP930

Primary amenorrhea revealing testicular regression syndrome in two sisters

Wiem Saafi, Taieb Ach, Asma Ben Abdelkrim, Ghada Saad, Hamza Elfekih, Yosra Hasni, Maha Kacem, Molka Chaieb, Amel Maaroufi & Koussay Ach
Farhat Hached University Hospital, Endocrinolgy, Sousse, Tunisia

Introduction
Disorders of sex development represent a rare group of congenital disorders causing discord between the phenotypical and genotypical sex. We present the case of two female patients in whom we discovered a sex development disorder when they consulted for amenorrhea.
Case report
Two sisters of 21 and 25 years old had an endocrinological consult for primary amenorrhea. They were conceived from a consanguineous marriage and had no particular medical history. We didn't notice any intellectual retardation or dysmorphic syndrome. Physical examination found a high of 1.90 meters for both sisters and normal blood pressure. The Tanner stage was S3P2A2 with normal feminine external genital organs. No signs of hyperandrogenism were noted. Hormonal exploration revealed hypergonadotropic hypogonadism with normal testosterone levels and undetected estradiol levels in both cases. The patients had the same karyotype:46, XY, (SRY+). Pelvic MRI discovered the absence of gonads, uterus, and fallopian tubes. No adrenal or renal abnormalities were found. We retained the diagnosis of testicular regression syndrome. Hormonal replacement by estroprogestative was initiated in both sisters.
Conclusion
Embryonic testicular regression syndrome is a rare disorder of sex differentiation. The phenotype of patients with this disorder is variable with different degrees of masculinization. The phenotype depends on the extent and timing of the intrauterine accident concerning sexual development.

DOI: 10.1530/endoabs.81.EP930

EP931

Hyperprolactinaemia in postmenopausal women receiving long-term hormone replacement therapy: a case series

Tahir Omer & Adnan Adnan
Northampton General Hospital, Northampton, United Kingdom

Introduction
A few studies have examined the effect of Hormone replacement therapy (HRT) on serum Prolactin level (PRL) in postmenopausal women. It has been demonstrated that HRT can trigger a stimulatory response on PRL secretion. However, the significance of this is yet to be further evaluated given the great variation in PRL concentration during menopause which has not been fully meticulously examined.
Case reports
We present 3 cases of postmenopausal women who were found to have high PRL while being investigated for a variety of symptoms and other endocrinological conditions and presentations. The patients were on different HRT preparations for a variable length of time. We discuss the implications of high prolactin in this age group, the variability and scarcity in the available literature and the possible treatment strategies. Case 1: A lady in her early 50s with a chronic history of PMR on steroids. She was referred to our clinic to investigate the HPA axis for secondary adrenal insufficiency. Tests revealed raised Prolactin level with no clear cause. MRI pituitary and the anterior pituitary profile were normal. She was not on any other medication. Case 2: A lady in her late 50s who presented to her GP with severe symptoms of menopause and was started on HRT. The dose was gradually increased. She was found to have raised prolactin level and referred to our clinic. MRI pituitary and anterior pituitary profile were normal apart from the raised Prolactin. Case 3: a 60-year-old lady who has been on long term HRT which was only recently discontinued. She continued to suffer from hot flushes and excessive sweating. She was referred to our clinic for further investigation. Pituitary profile, urinary 5HIAA, urinary Metanephrines were normal apart from the raised prolactin. CT CAP and MRI pituitary were all normal.
Discussion and conclusion
PRL can vary significantly during menopause. The incidence of Hyperprolactinaemia decreases with age. The commonest cause for raised PRL in menopause is Macroprolactinomas. Exogenous oestrogen could play a crucial role in Prolactin secretion. High PRL is associated with obesity, dyslipidaemia and insulin resistance. Some studies have also shown adverse effect on bone density. HRT dose adjustment and Dopamine agonists are among the treatment strategies. Some studies, however, argue that as the patient is usually asymptomatic, treatment might not need to be introduced but long-term monitoring is warranted.

DOI: 10.1530/endoabs.81.EP931

EP932

Mc Cune ALBRIGHT Syndrome: A rare endocrine disorder with a challenging management: A case report

Maryame Ben Lafqih & Meryam Alahyane, Sana Rafi, Ghizlane EL Mghari, El Ansari Nawal
Mohammed VI University Hospital of Marrakesh, Department of Endocrinology, Diabetology, Metabolic Diseases and Nutrition, Marrakesh, Morocco

Introduction
McCune-Albright syndrome (MAS) is a rare, Mosaic genetic (Lethal in the homozygous state) but non-hereditary disorder. The diagnosis is most often made

in childhood, the management is multidisciplinary and includes several aspects. We report a case of Mc Cune Albright syndrome and the various difficulties encountered in its management.
Case report
A, H 22 years old, at the age of 6 months presented skin macules. At the age of 3 years he developed gait disorders, a taller stature compared withother children of the same age and gender, then signs of precocious puberty with secondary sexual characteristics at the age of 7 years. In 2015 the diagnosis of Mccune Albright syndrome was retained.
Discussion
Mc Cune Albright syndrome is initially defined by a clinical triad: precocious puberty, polyostotic fibrous dysplasia, skin hyperpigmentation. Currently this definition has been extended to include other endocrinopathies and hepatobiliary disorders. In addition to the classic triad, our patient presented a somatotropic adenoma complicated with a thyrotropic deficit, in association witha left testicular tumor with Leydig cells. The management is multidisciplinary with no approved treatment. The fibrous dysplasia could be managed medically sometimes surgically, but no current treatment stops lesional progression. The surgical management of polyostotic craniofacial fibrous dysplasia is often disappointing with high risk of postoperative regrowth. The thickening of skull induced by fibrous dysplasia and high hemorrhage risk makes the surgical treatment of acromegaly difficult, the reason justifying the choice of medical treatment for our patient.
Conclusion
McCune Albright syndrome is a rare pathology, the diagnosis is sometimes made early in childhood but the treatment is still limited an challenging. Furtherre search is needed to improve its management.
Bibliography
1- Marlous Rotman, Neveen Agnes Therese Hamdy and Natasha M. Appelman-Dijkstra, Clinical and translational pharmacological aspects of the management of fibrous dysplasia of bone, Br J Clin Pharmacol, 2019; 85: 1169–1179
2- Sylvie Salenave 1, Alison M Boyce, Michael T Collins, Philippe Chanson, Acromegaly and McCune- Albright syndrome, J Clin Endocrinol Metab, 2014;99(6):1955-69.

DOI: 10.1530/endoabs.81.EP932

EP933

Role of altered estrogen signalling in the pathogenesis of Recurrent Pregnancy Loss (RPL): A cohort based pilot study from Assam, India

Natasha Kashyap[1], Chandana Ray Das[2], Ratul Dutta[3], Anjuma Begum[4], Sujoy Bose[4] & Purabi Deka Bose[1]
[1]Cotton University, Molecular Biology and Biotechnology, Guwahati, India; [2]Gauhati Medical College and Hospital, Guwahati, India; [3]Down Town Hospitals, Guwahati, India; [4]Gauhati University, Biotechnology, Guwahati, India

Context
Recurrent Pregnancy Loss (RPL), defined as two or more consecutive pregnancy losses, is a serious reproductive problem, affecting 1–5 per cent of reproductive-age women. Although a high percentage (7.46%) of RPL cases are reported from India, scanty reports are available on the molecular mechanisms associated with RPL susceptibility in the population of the north-eastern state of Assam. Hormonal imbalances are a major cause of recurrent pregnancy loss. Recent studies indicate that estrogen plays a crucial role throughout pregnancy in fetal development, utero-placental blood flow, and implantation.
Objective
This work proposes to elucidate the role of alterations in the estrogen signalling pathway in the pathogenesis of RPL in the population of Assam. It would have therapeutic significance in atleast a sub-population of idiopathic RPL patients.
Methods
RPL patients who had undergone three or more spontaneous miscarriages ($n=21$) and medically terminated pregnancies (MTP) cases ($n=35$) were enrolled for this study. Biochemical level of estrogen in RPL patients and MTP cases was studied by ELISA. This was followed by transcript level study of differential expression of its receptors, ERα and ERβ by real time PCR method, and further validation at the protein level using immunofluorescence.
Results
The ELISA results indicated a higher level of estrogen in the RPL cases (5.03 $\pm$ 1.52 pg/ml) when compared with the MTP cases (3.6 $\pm$ 2.2 pg/ml) ($P<0.020$). The mRNA expression of the ER isoforms, ERα (0.08 $\pm$ 0.11 fold change) and ERβ (0.07 $\pm$ 0.09 fold change) was found to be downregulated in the RPL cohort compared to MTP. ERα, being the more functionally important receptor for estrogen-mediated signal transduction, its protein expression was also validated through immunofluorescence (IF). The IF results showed sporadic expression of ERα protein in both the MTP as well as RPL cases, with a sharp downregulation or even no expression of the receptors in the RPL product of conception (POC) tissues. However, correlation analysis did not show any significant correlation between these factors ($P>0.05$).
Conclusion
The results indicate the possible role of estrogen receptor expression that may be involved with RPL pathogenesis in the study population. However, the findings of this pilot study require validation in a larger sample size for therapeutic implementation.

DOI: 10.1530/endoabs.81.EP933

EP934

The evolution and therapeutic aspects of hirsutism: about 100 cases

Bel Hadj Sliman Chayma, Nadia Khessairi, Anis Grassa, Fatma Chaker & Melika Chihaoui
Rabta Hospital, Endocrinology, Tunis, Tunisia

Introduction
Hirsutism is defined as excessive hair growth in androgen-dependent areas in women, related to an increased exposure androgen action in pilosebaceous follicles. It may be isolated, or associated to cutaneous manifestations from acne to signs of virilism. The aim of our study was to describe the therapeutic and evolutionary aspects of hirsutism.
Methods
It was a retrospective study at the endocrinology department of Rabta Hospital in Tunis including 100 women who presented hirsutism with over a period of 10 years from January 2009 to December 2020. Clinical and paraclinical data were collected from medical records.
Results
The average age of our patients was 29.5 $\pm$ 10 years old. The mean age at puberty was 12.1 $\pm$ 1.2 years old. The onset of hirsutism was acute in 5% of cases. It was associated with spaniomenorhoea, secondary amenorhoea and infertility in 46%, 4% and 10% of cases respectively. Biological hyperandrogenism was present in 59% of cases with a mean testosterone level of 0.9 $\pm$ 0.7 ng/ml. Biological and radiological investigations led to the diagnosis of ovarian tumour in 3 patients, adrenal tumour in 5 patients, late-onset congenital adrenal hyperplasia in 7 women, Cushing's disease in 3 patients and polycystic ovary syndrome in 51 patients. Hirsutism was idiopathic in 32% of cases. Concerning treatment, all patients were recommended to follow hygienic and dietary rules and metformin was associated in eleven cases. Eighteen patients received etiological treatment, i.e. adrenalectomy, oophorectomy, hydrocortisone replacement therapy in 5%, 3% and 7% respectively. While Thirty-four percent were put under estrogen and progestin combination therapy, only 29% were treated with an antiandrogen. An additional treatment by laser hair removal was further done by 11 patients. Evolution was marked by clinical improvement in 46%.
Conclusion
Not only is hirsutism a source of anxiety and social embarrassment for women, but in some cases it can hide a serious illness requiring urgent treatment. That's why a rigorous etiological investigation is required before the treatment.

DOI: 10.1530/endoabs.81.EP934

EP935

Hormonal changes in women with abnormal endometrial bleeding in peri and postmenopause

Ana Kocevska, Bashkim Ismaili, Kristina Skeparovska, Dimitar Georgiev, Ana Marija Spisic & Pranvera Izairi
Skopje, Special Hospital for Gynecology and Obstetrics 'Mother Theresa' Skopje, Skopje, North Macedonia

Objectives
To determine the histopathological changes of the endometrium that occur during the period of perimenopause and postmenopause and to determine their association with the presence of obesity, diabetes, thyroid disorders and the levels of FSH, LH, estradiol, insulin and parathormone.
Material and methods
This study involved 120 patients with fractionated explorative curettage due to abnormal uterine bleeding. The control group consisted of 40 healthy women without fractionated explorative curettage. Anamnestic data were taken from from all respondents. Body height and weight were measured. This laboratory

analyses were performed: Glycemia, HbA1c, Hormonal Status (FSH, LH, Estradiol, Insulin, TSH, Thyroxine and Parathormone).
Results
The most common pathological change of the endometrium was an endometrial polyp. Patients with explorative curettage were older than healthy women and had significantly higher Body Mass Index, higher levels of serum glycemia, triglycerides, serum insulin, FSH, LH, PTH and lower estradiol levels. Patients in the experimental and control group did not differ significantly in TSH and thyroxine levels.
Conclusions
In the period of perimenopause and postmenopause, there are changes in the genital organs, but also there are endocrine disorders. According to our study, some of them are related to the occurrence of changes in the endometrium and the need for fractional explorative curettage as a diagnostic procedure.

DOI: 10.1530/endoabs.81.EP935

EP936

Vaginoplasty in the treatment of androgen resistance syndrome: about 2 cases

Amal Elkhomri[1], Nassim Essabah Haraj[1], Siham El aziz[1], Moataz Amine[2], Aboutaeib Rachid[2] & Asma CHADLI[1]
[1]CHU Ibn Rochd, Endocrinology-Diabetology and Metabolic Diseases Department, Casablanca, Morocco; [2]CHU Ibn Rochd, Urology and Andrology, Casablanca, Morocco

Introduction
Androgen insensitivities are rare genetic diseases, characterized by a more or less complete defect of tissue sensitivity to testosterone. It ranges from a more or less complete lack of masculinization to isolated infertility in a 46, XY individual. Many surgical methods of vaginoplasty have been opted with the aim of reconstructing the anatomy to allow future sexual activity as well as an improvement in the quality of life. We report the case of two patients with complete androgen resistance syndrome discovered during the exploration of primary amenorrhea
Observation 1
33-year-old patient, operated in 2016 for bilateral intra-abdominal gonadectomy, with an anatomopathological examination of an ectopic testicle on the right without signs of malignancy, and an embryonic carcinoma on the left, the patient underwent chemotherapy sessions, she presents a harmonious and feminine Morphological development, with absence of vaginal orifice, a carotype was done in favor of a 46 XY, pelvic MRI with absence of internal genitalia, and genitography with absence of vaginal orifice, the patient was put on estrogen and progestin, with good clinical evolution
Observation 2
20-year-old patient, who underwent bilateral gonadectomy in 2017 with pathological examination of hypoplastic testicular pulp with hamartomatous nodules and hypoplastic foci of Leydig cells compatible with androgen insensitivity syndrome without malignancy, with a gynecological examination presence of labia majora and labia minora not well formed with an incipient vagina. a carotype was done in favor of a 46 XY, pelvic MRI with absence of internal genitalia, and genitography with absence of vaginal orifice, the patient was put on estrogen and progestin, with good clinical evolution The first patient underwent a rectosigmodian vaginoplasty and the second a vaginal enlargement surgery. The result was excellent with the obtaining of a 6 cm deep neovagina. After six months of follow-up, the two patients keep neovaginal cavities with regular digital dilation
Conclusion
The choice of the most appropriate surgical technique is conditioned by the results of the clinical examination, ultrasound, genitography and endoscopic exploration.

DOI: 10.1530/endoabs.81.EP936

EP937

Melatonin ameliorates glucocorticoid-induced invasiveness and circadian rhythm disruption in human endometrial adenocarcinoma cells

Angeliki Karapanagioti[1,2], Narjes Nasiri-Ansari[2], Ioannis Kyrou[3,4,5,6,7], Despoina Mavrogianni[8], Peter Drakakis[8], gregory kaltsas[1], Athanasios G. Papavassiliou[2], Harpal Randeva[4, 7] & Eva Kassi[1,2]
[1]National and Kapodistrian University of Athens, Medical School, 1st Department of Propaedeutic Internal Medicine, Laiko General Hospital, Athens, Greece; [2]National and Kapodistrian University of Athens, Medical School, Department of Biological Chemistry, Athens, Greece; [3]Aston University, Aston Medical Research Institute, Aston Medical School, College of Health and Life Sciences, Birmingham, United Kingdom; [4]Coventry and Warwickshire Partnership NHS Trust, Warwickshire Institute for the Study of Diabetes, Endocrinology and Metabolism (WISDEM), Coventry, United Kingdom; [5]Agricultural University of Athens, Department of Food Science and Human Nutrition, Athens, Greece; [6]Coventry University, Centre for Sport, Exercise and Life Sciences, Research Institute for Health & Wellbeing, Coventry, United Kingdom; [7]University of Warwick, Warwick Medical School, Coventry, United Kingdom; [8]National and Kapodistrian University of Athens, Medical School, 1st Department of Obstetrics and Gynecology, Division of Human Reproduction, IVF Unit, Alexandra Hospital, Athens, Greece

Introduction
The biological rhythm pattern is synchronized through circadian oscillation of cortisol and melatonin release. Increased cortisol levels and circadian rhythm disruption act as an oncogenic factor in endometrial cancer through among others-dysregulation of cell proliferation/apoptosis and invasion.
Aim
To investigate, whether there is an oscillatory expression of the clock genes, MT1 and GR expression in human endometrial carcinoma cells. To explore whether glucocorticoids and melatonin can affect the expression of these genes and further to evaluate whether dexamethasone and melatonin affect the viability and invasiveness of Ishikawa cells.
Material and methods
Ishikawa cells were cultured and serum starved for 16h. Following starvation, cells were serum shocked and maintained in DCC-supplemented medium in the presence of dexamethasone (10^{-7}M), melatonin (10^{-7}M,10^{-8}M) and GR antagonist RU486(10^{-5}M), alone or co-incubated with dexamethasone and melatonin for 54h. Cell viability and cell invasion were evaluated by MTS and scratch assay, respectively. The mRNA levels of circadian clock genes: CLOCK, BMAL1, CRY-1, PER-2, ROR-α, REV-ERBb, glucocorticoid receptor-alpha and melatonin receptor were measured by qPCR.
Results
Dexamethasone induced cell invasiveness of Ishikawa cells was inversed by 10% in the presence of melatonin at 10^{-8}M for 54h. Co-incubation of dexamethasone-treated cells with melatonin (10^{-7}M,10^{-8}M) reduced the Ishikawa cell viability as compared to cells incubated with dexamethasone alone(10^{-7}M). For the first time, we showed that following synchronization with serum shock, Ishikawa cells expressed Bmal-1, Clock, Per-2, Cry1 in an oscillatory manner with a peak observed every approximately 36h. Interestingly, MT-1 and GRα also exhibited almost the same oscillaroty expression pattern. Incubation of Ishikawa cells with dexamethasone at concentration 10^{-7}did not affect the oscillatory pattern of Clock, Per-2, Cry, while it decreased the amplitude of Cry-1 expression at 18h of incubation. However, dexamethasone disrupted the pattern of Bmal-1 expression, mainly by increasing the frequency of oscillations; this effect was reversed by co-incubation with RU-486 implying a GR-mediated effect. Notably, melatonin at concentration of 10^{-8}M reversed the disruption of Bmal-1 expression pattern, without changing the GRα expression. Long-term incubation with melatonin alone at both concentrations did not affect significantly the oscillatory pattern, however at the highest concentration appeared to increase the amplitude of the oscillation in Bmal-1, Clock, Per-2, Cry-1 expression (approximately by 27%, 127%,83% and 73% respectively) with more robust effect at 18h of incubation (first peak).
Conclusion
Melatonin ameliorates the glucocorticoid-induced invasiveness of human endometrial cancer cells possibly through reversing the glucocorticoid-induced disruption of circadian clock system. Further studies need to confirm the causal link.

DOI: 10.1530/endoabs.81.EP937

EP938

Importance of karyotyping in the evaluation of male hypogonadism

Ei Thuzar Aung[1], Sanjana Srinivas[2], Helmine Kejem[3] & Upendram Srinivas-Shankar[3]
[1]Whiston Hospital, St Helens and Knowsley Teaching Hospitals NHS Trust, Department of Diabetes and Endocrinology, Prescot, United Kingdom; [2]Whiston Hospital, St Helens and Knowsley Teaching Hospitals NHS Trust, Prescot, United Kingdom; [3]Arrowe Park Hospital, Wirral University Teaching Hospital NHS Trust, Department of Diabetes and Endocrinology, United Kingdom

We present the case history of a 48-year-old man with anxiety and depression, who was referred for evaluation of absent libido, long standing erectile dysfunction and reduced body hair. There was no history of orchitis, pituitary problems or low impact fractures. He was always single and did not father children. Clinical examination revealed obesity (BMI 31 kg/m2), absent facial hair, reduced body, axillary and pubic hair. There was bilateral gynaecomastia. The phallus was normal, but the testes were not palpable. He appeared euthyroid and did not have features of cortisol or growth hormone excess. Visual fields were normal to confrontation. He was not diagnosed to have any congenital malformations but had an atrophic right kidney on a routine ultrasound scan of the abdomen. Biochemical profile revealed undetectable testosterone <1.5 nmol/l (nr 10 -28) and raised FSH 49.8 u/l (1.0 – 12) and LH 20.9 u/l (2.0 – 9.0) consistent with primary hypogonadism. Oestradiol, alpha-fetoprotein, beta HCG, prolactin, IGF1 and thyroid function tests were normal. Ultrasound scrotum revealed small testes in the lower inguinal canal. Karyotyping revealed 46XX disorder of sexual differentiation (DSD), SRY positive. Testosterone supplementation was initiated. He was referred to the urologist for orchidectomy given risk of malignant transformation in the undescended testis. He was also referred for genetic counselling and clinical psychologist. Patient chose to remain on testosterone and requested testicular implants. DEXA bone mineral density scan revealed osteoporosis.

Discussion

46XX DSD is a rare disorder occurring in about 1:20,000 males. These patients commonly present in adulthood with infertility and have various phenotypical presentations, ranging from severe impairment of external genitalia to cryptorchidism to a normal male phenotype. Our case history highlights the importance of external genitalia examination in those presenting with hypogonadism. Further karyotyping is important in the evaluation of such patients, especially in those with phenotypical abnormalities.

DOI: 10.1530/endoabs.81.EP938

EP939

The frequency of thyroid diseases in adolescents (boys and girls) in Djizakh and Namangan regions of the Republic of Uzbekistan.'

Utkir Mavlonov[1], Urmanova Yulduz[1], Dinara Alieva[2], Guzal Dalimova[2], Dilmar Savchenko[2] & Shokhsanam Safarova[2]

[1]Tashkent Pediatric Medical Institute, Tashkent, Uzbekistan; [2]Republican Specialized Scientific Practical Medical Center of Endocrinology of Public Health Ministry named by acad. Ya.Kh. Turakulov, department of neurendocrinology, Tashkent, Uzbekistan

The purpose of the study

Is to study the frequency of thyroid diseases in adolescents (boys and girls) in 2 regions of the Republic of Uzbekistan.

Material and methods.

We have been examined and surveyed in the framework of screening just for the period from January 1, 2021 to April 1, 2021 - 1023 boys and girls in the two regions of RUZ - 523 adolescents were examined in the Djizakh region and 500 adolescents in the Namangan region Aged from 11 to 15 years. The main contingent amounted to students of colleges and schools. All 1023 adolescents were performed by all anthropometric studies based on the international growth and weight map of Tanner-Waithause. The assessment of the puberty stage according to J. Tanner, if necessary, patients were sent to add-on-x-ray (radiograph of brush, CT/MRI of the Turkish saddle), ultrasound of genital organs, consultation of the surgeon, genetics, etc. research.

Results

In total, among 1023 adolescents, 230 (22.4%) patients with iodine deficient diseases of the thyroid gland were identified: diffuse goiter (DG) 1 ST - 135 B (13.3%), diffuse goiter 2 ST - 54 BC (5, 3%), autoimmune thyroiditis - 38 (3.7%). At the same time, in patients with DG, euthyroidism was observed in 106 adolescents (10.3%), and hypothyroidism - in 83 (8.1%). In the Namangan region, 141 (28.2%) patients with iodine deficient diseases of 500 examined, and in Jizzakh - 89 out of 523 examined (17.1%)

Conclusions

In total among 1023 adolescents, 230 (22.4%) patients with iodine deficient diseases of the thyroid gland were revealed. This in turn also indicates that iodine deficiencies are a factor in the risk of developing violations of sexual, physical and general development in adolescents

DOI: 10.1530/endoabs.81.EP939

EP940

Disorders of sex development 46XY revealed at adult age : A report of three cases and and literature review

Benabdelatif Katia, MALEK IABBASSEN, Bensalah Meriem & Ould Kablia Samia

Central Military Hospital, Algiers, Algeria

Introduction

Disorders of sex development include a large number of congenital conditions related to unusual chromosomal sex (gonosomal abnormalities), defective testicular development, or abnormal hormone secretion or receptivity, resulting in unusual external and/or internal genitalia development rare.

Patients and methods

we report 3 cases of disorders of sex development 46XY reveled at adult age. clinical, biological and radiological funding are reported in the following table.

Conclusion

Disorders of sex development are rare situations that require a rigorous assessment and early treatment. They often are congenital pathologies that have consequences in terms of self-esteem, sexuality and fertility in the future.

DOI: 10.1530/endoabs.81.EP940

Table 1

Patients	1	2	3
Age (years)	17	16	16
Assignation sex	F	F	M
Revealing signs	Primary Amenorrhea	primary Amenorrhea	*Lack of virilization*
Tanner stage	P5S2	P2S1	P4 G4 Testis V3 $<$ 4 cc.
EMS	5	5	7.5
Quigley stage	4	5	5
Sinnecker stage	4b	6	6
Biology	Hight testosterone	low testosterone AMH normal. Testo/DHT: 1.07	low testosterone
HCG Test	Positif (25 ng/ml)	Negatif (0.1 ng/ml)	Not done
Diagnostic	5-Alpha-Reductase Deficiency	leydig cell hypoplasia	Partiel androgen insensibiltity
Imaging (ultrasound/IRM)	Gonads corresponding to testis 33*11 mm in inguinal position without uterus.	Gonads corresponding to testis 20*19 mm in inguinal position without uterus	Left gonad corresponding to testis 20*25 mm in position scrotal, right gonad 23.9 mm in inguinal position without uterus.
treatment	surgery	surgery	Orchydopexia + Hypospadias correction
Anapathe	mature testicular tissue.	mature testicular tissue.	////

*EMS: external masculinization score.

EP941

Precocious puberty associated with primary adrenal insufficiency: A case report

Lina Ghram, Bchir Najla, Zouaoui Chadia, Rekaya Zeineb, Fatma Ben Zaied & Haroun Ouertani
Hôpital Militaire Principal d'Instruction de Tunis, Tunis, Tunisia

Introduction
Precocious puberty (PP) is a rare pathology involving approximatively 0.2% of girls and less than 0.05% of boys and is defined as the appearance of secondary sex characteristics before 8 years of age in girls and before 9 years of age in boys. We report an unusual case of a patient who presents a precocious puberty associated to a primary adrenal insufficiency.
Case presentation
We describe a case of a 7-year and 4 months old girl referred for a precocious puberty. In fact, her mother reports breast enlargement since the age of 5 years but she only consulted when she had her menarche 2 months ago. Her medical history was uneventful. Her mother had her own menarche at the age of 11. Physical examination displayed a girl with weight at 33 kg (< -2 [standard derivation] DS), height at 137 cm (> +3 [standard derivation] DS). Her statural age was 10 years and a half. The patient presented an elevated Areola above contour of the breast with development of the overall breast tissue (Tanner stage S4) and her pubic hair was adult in type (Tanner stage P4). Bone Age according to Greulich and Pyle atlas was 11 years. Pelvic ultrasound revealed a uterine long axis of 39 mm, thickness of the uterine endometrium of 6mm, follicular ovaries without ovarian cysts nor pelvic mass. Endocrine analysis showed high estrogen value: 25,5 pg/ml and high basal luteinizing hormone (LH) : 5,98 UI/l (> 5 UI/l), suggesting a central precocious puberty. The pituitary magnetic resonance imaging showed homogeneous hyperplasia of the anterior pituitary gland without sellar ou suprasellar tumor. The evaluation of the other pituitary axes showed a normal thyroid function test (FT4 : 11,3 pmol/l and TSH : 1,75 uUI/ml), and a low cortisol level 66 nmol/l concomitant to an ACTH level: 98 pg/ml. The patient received hydrocortisone. A treatment by GnRH agonist was started and a genetic investigation is now being undertaken.
Conclusion
Central PP is due to a premature activation of the hypothalamic-pituitary-gonadal axis. It can be attributable to cerebral congenital malformations or acquired insults, but the cause in about 90% of cases in girls is idiopathic. Rare cases of PP associated to adrenal insufficiency were reported in the literature. It seems to be related to a stop loss DAX1 variant.

DOI: 10.1530/endoabs.81.EP941

EP942

Mayer-rokitansky-küster-hauser syndrome: about two cases

Kadiri Chaimae & Lachkar Hassan
Hôpital Cheikh Zayd, Endocrinology, Rabat, Morocco

Introduction
Mayer-Rokitansky-Küster-Hauser syndrome (MRKH) is a rare malformation of the birth canal in women. It is defined as agenesis of the uterus and vagina with normal development of secondary sexual characteristics and a normal karyotype (46, XX). This is an entity with a heavy psychological impact requiring multidisciplinary care.
Observation 1
We report the case of a 16-year-old patient with a history of delayed puberty in the sister, who consulted for primary amenorrhea. Clinical examination revealed a height delay of -3 standard deviation, a weight delay of -1 standard deviation and a Tanner stage A1 S1 P1. Hormonal exploration found hypergonadotropic hypogonadism. The karyotype showed a female genetic sex (46 XX). Abdominal pelvic ultrasound and MRI revealed utero-vaginal aplasia. The impact assessment showed a bone age of 13 years compared to a chronological age of 16 years. Hormone therapy treatment is started, associated with psychological care.
Observation 2
A 15-year-old patient with no notable history consulted for delayed height and puberty. Clinical examination revealed a statural delay at -2 standard deviation and Tanner stage S1P1A1. Hormonal workup showed hypergonadotropic hypogonadism with FSH at 133.4 IU/l and LH at 28.85 IU/l with low plasma estradiol levels. The karyotype showed a female genetic sex of 46, XX in the absence of Y chromosomal material. Ultrasound and abdominal pelvic MRI revealed utero-vaginal hypoplasia. The impact assessment showed a bone age of 12 years compared to a chronological age of 15 years. The diagnosis of MRKH was made with the absence of associated malformations. Estrogen therapy was started in our patient.
Discussion and conclusion
MRKH syndrome is a rare congenital malformation characterized by hypergonadotropic hypogonadism and which should be considered in the presence of any utero-vaginal abnormality. MRI is the exam of choice for the diagnosis of this syndrome. Its management is multidisciplinary and is essentially based on hormone replacement therapy.

DOI: 10.1530/endoabs.81.EP942

EP943

Polycystic ovary syndrome: diagnosis and treatment

Nisrine Bouichrat[1], Dounia Zerrouki[2], Imane Assarrar[3], Messaoudi Najoua[1], Siham Rouf[4] & Hanane Latrech[4]
[1]Mohammed VI University Hospital, Medical School, Mohamed the First University, Department of Endocrinology-Diabetology-Nutrition, Oujda, Morocco; [2]Mohammed VI University Hospital, Medical School, Mohamed the First University, Department of Endocrinology-Diabetology-Nutrition, Oujda, Morocco; [3]Mohammed VI University Hospital, Medical School, Mohamed the First University, Department of Endocrinology-Diabetology-Nutrition, Oujda, Morocco; [4]Mohammed VI University Hospital, Medical School, Mohamed the First University, Department of Endocrinology-Diabetology-Nutrition, Laboratory of Epidemiology, Clinical Research and Public Health, Faculty of Medicine and Pharmacy of Oujda, Mohamed the First University, Oujda, Morocco

Introduction
Polycystic ovary syndrome is a real public health problem and is the most frequent cause of hyperandrogenism in women of childbearing age. The therapeutic management of PCOS depends on the patient's phenotype and associated comorbidities. The aim of our work is to study diagnosis and evolution after treatment of PCOS in our population.
Material and method
This is a retrospective descriptive study of 78 patients followed for PCOS at the Endocrinology Diabetology and Nutrition Department of the Mohammed VI University Hospital of Oujda in the eastern region of Morocco. The diagnosis of PCOS is based on the criteria of the Rotterdam Consensus of 2003. All patients underwent an interrogation, clinical examination, biological assessment and pelvic ultrasound. The collected data were analyzed by SPSS version 21 software.
Results
The average age of patients was 24 years. Hirsutism was the most frequent reason for consultation in 97.2% of cases with severe hirsutism in 12% of cases, followed by cycle disorders (84.3%), and acne in 55.7%. The average BMI was 26.1 $\pm$ 5.8 kg/ m^2 obesity was observed in 20% of patients, with abdominal obesity in half of the cases. Therapeutically, all our patients were put on dietary hygienic measures and metformin, the estrogen-progestogen contraceptive was indicated in 38% of patients and spironolactone in 26%, with a combination of these 2 treatments in 18% of cases. The evolution after at least 6 months of treatment revealed a very satisfactory improvement of the clinical signs with a decrease in the frequency of hair removal and a reduction in the density and darkness of the hairs.
Discussion-Conclusion
PCOS is a real problem in young women, which has psychological and social repercussions as well as metabolic ones. Its treatment should aim to: reduce hyperandrogenism, improve metabolic status and quality of life, and restore fertility. Our results are consistent with those reported in the literature.

DOI: 10.1530/endoabs.81.EP943

Thyroid

EP944

Tension-free thyroidectomy (TFT) may reduce the complication rate in thyroid surgery: experience of the first 120 cases

Ilya Sleptsov, Roman Chernikov, Ilya Sablin, Alexander Pushkaruk & Yuri Fedotov
Saint Petersburg State University Hospital, Endocrine Surgery, Saint Petersburg, Russian Federation

Background and aims
The safety of thyroid surgery in terms of recurrent laryngeal nerve palsy and hypoparathyroidism was increasing in the last decade. In this study, we present a

new method of tension-free thyroidectomy (TFT), which could be used to further decrease the complication rate after thyroidectomy.
Patients and Methods
TFT is based on the medial approach to the recurrent laryngeal nerve (RLN) and the parathyroid glands after the division of isthmus and successive total dissection of Berry's ligament with full mobilization of the RLN and the parathyroid glands before the thyroid is pilled out from the neck. One hundred twenty consecutive patients (163 nerves at risk) underwent "tension-free thyroidectomy" (TFT) from August to November 2021 performed by one surgeon. There were 96 females and 24 male patients (ratio 4:1) with a mean age of ninety-two 46,3 (range from 17 to 75). Lobectomy was carried out in 93 (77,5%) patients, total thyroidectomy in 35 (22,5%). In 42 cases patients additionally underwent central or/and lateral neck dissection. Indications for surgery were papillary carcinoma ($n=53$), medullary cancer ($n=2$), follicular neoplasia - Bethesda IV group after fine-needle biopsy ($n=49$), Graves disease ($n=12$), multinodular toxic goiter ($n=3$), multinodular euthyroid goiter ($n=1$). Mean thyroid nodule size was 25,4 mm (ranged 7 - 120 mm). Intraoperative neuromonitoring was used in all the cases (5 mA). Translaryngeal untrasound or direct laryngoscopy were used prior and after surgery to evaluate vocal cords mobility. Calcium and parathormone levels were measured in patients after thyroidectomy on the first, 14^{th} and 30^{th}postoperative days.
Results
No fluctuation of electric activity of laryngeal nerves during surgery was revealed. Intraoperative loss of signal (LOS) due to thermal effect of electrocautery and subsequent transient unilateral RLN palsy occurred in 4 cases (2,5% from the total number of nerves at risk). In all these patients normal vocal fold function was confirmed on the $30\text{-}45^{th}$ days after surgery. No permanent nerve palsy cases revealed. Four patients (out of 35 in the total thyroidectomy group – 11,4%) exhibited a decrease of parathyroid hormone level on the postoperative day 1 which was resolved at day 30^{th} under the substitution therapy with calcium and alfacalcidol. No cases of permanent hypoparathyroidism occurred.
Conclusion
TFT can be considered a safe and feasible operation. Larger and comparative (randomized) studies with conventional dissection technique should be performed to investigate the hypothesis that this approach can provide a lower complication rate.

DOI: 10.1530/endoabs.81.EP944

EP945

Radiofrequency ablation for benign thyroid nodules of 650 patients: long-term follow-up

Vyacheslav Solovov & Olga Ablekova
Samara Oncology Center, Interventional Radiology, Samara, Russian Federation

Purpose
The objective of this study was to evaluate the efficacy and safety of ultrasound (US)-guided radiofrequency ablation (RFA) for treating of benign thyroid nodules both autonomously functioning thyroid nodules (AFN) and symptomatic ones.
Material and Methods
The retrospective analysis included the results of treatment of 650 patients with benign tumors of the thyroid gland in the Samara Oncology Center since 2014 year. 182 (28 %) patients had autonomously functioning thyroid nodules and 468 (72 %) had symptomatic ones. The mean volume of nodule was 36.5 ml.
Results
RFA reduced nodular volume by 70.8 % after 6 months, 84.2 % after 60 months and it was an effective method for treating nodule-related clinical problems and hot nodules. 67 (10.1 %) patients with big nodule volume underwent 2-7 sessions of RFA. Cosmetic results were excellent in 96 % of patients. No serious complications such as thyroiditis, voice change, and hematomas were observed in RFA patients. Skin burned observed in 1 patient.
Conclusion
RFA was effective and safe method for outpatient treatment of benign thyroid nodules. RFA might be alternative to surgical treatment.

DOI: 10.1530/endoabs.81.EP945

EP946

Decrease the functional activity of adaptive immunity cells one month after radioiodine therapy for Graves' diseaseDecrease the functional activity of adaptive immunity cells one month after radioiodine therapy for Graves' disease

Andrey Savchenko[1], Margarita Dudina[2,3], Sergey A. Dogadin[2, 3], Alexandr Borisov[1], Daria Fomina[2] & Vasiliy Belenyuk[1]
[1]Federal Research Center «Krasnoyarsk Science Center» of the Siberian Branch of the Russian Academy of Sciences, Scientific Research Institute of medical problems of the North, The Cell and Molecular Physiology and Pathology Laboratory, Krasnoyarsk, Russian Federation; [2]Krasnoyarsk State Medical University, Internal disease, Krasnoyarsk, Russian Federation; [3]Krasnoyarsk Regional Clinical Hospital, Endocrinology, Krasnoyarsk, Russian Federation

Introduction
Radioactive iodine (RAI) for Graves' disease (GD) was reported to have specific immune effects. The ability of T and B lymphocytes to cooperatively interaction during the immune response may be impaired in GD patients eligible for RAI therapy. We aimed at investigating cellular subsets involved in functional activity of adaptive immunity cellsone month after RAI therapy in patients with GD.
Materials and methods
Thirty-six women with GD, mean age 42.13 ± 15.35, were included in this study. All patients treated with thiamazole for at 12 months (9 – 14) before RAI therapy. Thiamazole was withdrawal 14 days before RAI therapy. All patients had a fixed 400-700 MBq ^{131}I dose orally. Fifty-six healthy subjects were also studied. The study of the phenotype of T- and B-lymphocytes was carried out by flow cytometry using direct immunofluorescence of whole peripheral blood and monoclonal antibodies labeled with FITC (fluorescein isothiocyanate), PE (phycoerythrin), ECD (phycoerythrin-Texas Red-X), PC5 (phycoerythrin-cyanin 5), PC7 (phycoerythrin-cyanin 7), AA700 (alexa fluor 700) and AA750 (alexa fluor 750) in the following panels: CD8-FITC/CD127-PE/CD25-PC5/CD4-PC7/CD3-AA700/CD45-AA750 и CD5-FITC/CD23-PE/CD19-ECD/CD45-PC5/CD27-PC7. Serum measurement of TSH, fT4, fT3 and TRAb were performed by ELISA and enzyme immunoassay.
Results
The thyroid state of GD patients before RAI treatment corresponded to subclinical hyperthyroidism with a high level of serum TRAb (Me = 28,01 mU/l ($Q_{0,25}$ = 2,81; $Q_{0,75}$ = 35,71, $p<0,001$)). An increase in the percentage of $CD3^+CD25^+$ $CD3^+CD4^+$ $CD3^+CD4^+CD25^+$ and $CD3^+CD8^+CD25^+$ cells but with a decrease in the amount of $CD3^+CD8^+$ lymphocytes relative to the control was found in GD patients before RAI therapy. All patients treated with RAI were euthyroid, while the content of TRAb remained almost at the initial level. One month after RAI therapy in GD patients we observed decreased the percentage of cells with phenotypes $CD3^+CD25^+$ $CD3^+CD4^+CD25^+$ and $CD3^+CD8^+CD25^+$ and an increase number of $CD3^+CD4^+CD127^{Low}CD25$-High lymphocytes. Also, we detected changes in the phenotypic composition of blood B lymphocytes of GD patients before ^{131}I treatment: a decrease the percentage of $CD19^+$ cells and an increase the relative number of $CD19^+CD27^+CD23^+$ lymphocytes. One month after RAI therapy we revealed decreased percentage of $CD19^+CD5^+CD23^+$ lymphocytes and increased relative to the initial values the levels of $CD19^+CD27^-$ and $CD19^+CD5^-$ cells.
Conclusion
One month after RAI therapy in GD patients changes in the phenotype of T and B lymphocytes in the blood reflect a tendency towards a decrease in the functional activity of adaptive immunity cells which can also be realized in the inhibition of autoimmune processes.

DOI: 10.1530/endoabs.81.EP946

EP947

Myocardial Ischemia precipitating thyroid storm diagnosed during storm recovery through Wellen's wave: An ECG for an eye

Shinjan Patra[1], Ayan Roy[2], Anu Priya[1] & Atul Kaushik[3]
[1]All India Institute of Medical Sciences (AIIMS) Jodhpur, Endocrinology and Metabolism, Jodhpur, India; [2]All India Institute of Medical Sciences (AIIMS) Kalyani, Endocrinology and Metabolism, Kalyani, India; [3]All India Institute of Medical Sciences (AIIMS) Jodhpur, Cardiology, Jodhpur, India

Introduction
Thyroid storm is a major life-threatening condition in a patient of thyrotoxicosis which can precipitate the cardiovascular morbidity in forms of tachycardia, arrythmia and congestive heart failure. It can be precipitated by acute coronary

syndrome. Most literatures have reported acute coronary syndromes during the presentation itself but we describe an unique case where the diagnosis was possible after the resolution of the thyroid storm.
Clinical case
A 55-year-old graves' disease patient had presented with classical features of thyroid storm which was precipitated by discontinuation of the anti-thyroid drugs. His initial electrocardiogram (ECG) showed sinus tachycardia. He was promptly started on intravenous fluid, 80 mg of daily carbimazole along with lugol's iodine and intravenous dexamethasone. Within 48 h of treatment, his vitals became normal with resolution of the thyroid storm. His thyroid hormone status also showed marked improvement (free T4 falls from 90.31 ng/dl to 2.31 ng/dl) (normal range: 0.7 ng/dl-1.7 ng/dl). Due to his persistent jaw pain, mild chest discomfort and hiccough, ECG recordings were done in regular intervals. Interestingly it showed dynamic changes consisted of biphasic T waves. This ECG changes were seen after the resolution of the thyroid storm features. The cardiac enzymes were within normal limits. Wellen's syndrome was suspected. Coronary angiography revealed left anterior descending artery (LAD) obstruction and patient promptly underwent percutaneous transluminal angioplasty. Patient's angina equivalent symptoms had resolved remarkably. He recovered satisfactorily and was discharged after 5 days.
Clinical lesson
Ischemic heart disease is a well-known co-morbidity in a case of thyroid storm which can be identified at the initial presentation. But here the dynamic changes of ECG appeared after the resolution of the thyroid storm. It was classical of type A wellen's wave which is a harbinger of imminent massive anterior myocardial wall infarction due to near-complete blockage of LAD. Initial sinus tachycardia probably had masked the appearance of typical Wellen's wave in this case. But as soon as the thyroid storm resolved, typical dynamic changes appeared in the form of wellen's wave. Early suspicion due to following serial dynamic ECG changes has prevented a major catastrophe in this case. This case highlights the importance of tracking serial ECG changes in a patient of thyroid storm which can unmask any underlying ischemic cardiac disease even after apparent improvement of the clinical status. This clinical case also reports a unique association of thyroid storm and type A wellen's syndrome.

DOI: 10.1530/endoabs.81.EP947

EP948

Immune checkpoint inhibitors induced myxedema coma

Hatice Sebile Dökmetaş[1], Meriç Dökmetaş[2], Ayberk Bayramgil[2], Kübra Karaipek[2], Güneş Dorukhan Çavuşoğlu[2], Cansu Temiz[2], Cem İdrisoğlu[2], Fatih Kılıçlı[1] & Ahmet Bilici[3]
[1]Medipol Mega University Hospital, Endocrinology, Istanbul, Turkey; [2]Medipol Mega University Hospital, Internal Medicine, Istanbul, Turkey; [3]Medipol Mega University Hospital, Oncology, Istanbul, Turkey

Introduction
Myxedema coma is very rare and its mortality is quite high. It is even rarer to occur due to an immune checkpoint inhibitor.
Case
A 69-year-old patient presented with complaints of dyspnea, fatigue, edema, and hypotension. He had diabetes mellitus, hypertension, and metastatic lung cancer diagnosis. Three weeks ago, he had taken the 10th cycle of atezolizumab for lung cancer, which he had been taking for 7 months. The patient's body temperature was 35.80 °C, heart rate was 69/min, and arterial blood pressure was 100/50 mmHg. There was sleepiness, apathetic appearance, enlarged tongue, non-pitting edema, abdominal distension, and decreased bowel sounds. In the blood tests of the patient, serum glucose 100 mg/dl (70-100), sodium 115 mmol/l (136-145), TSH 218 μIU/ml (0,2-4,2), free T4 <0,03 ng/dl (0,9-1,7), and anti-thyroglobulin was 483 IU/ml (0-115). The thyroid gland was small and the parenchyma was heterogeneous in the ultrasonography. Blood gas showed hypoxia and hypercapnia. The patient was diagnosed with myxedema coma due to the PDL-1 inhibitor-atezolizumab, which he had taken. Treatment of myxedema coma, mainly intravenous levothyroxine and hydrocortisone, was initiated. After serum-free T4 level returned to the normal range with iv levothyroxine, his treatment with oral 150 mg/d levothyroxine was continued.
Conclusion
As a result of the increasing use of PD-1, PDL-1, and CTLA-4 inhibitors in recent years, also hypothyroidism is the most common endocrine side effect, but myxedema coma is very rare. When all the literature is examined, it is seen rarely that in patients who develop myxedema coma due to immune checkpoint inhibitor. It develops due to PD-1 inhibitors nivolumab and pembrolizumab and CTLA-4 inhibitor ipilimumab. In our case, myxedema coma developed due to atezolizumab, a PDL-1 inhibitor. It should be kept in mind that hypothyroidism and also rarely hypothyroid coma may develop in patients using these drugs.

DOI: 10.1530/endoabs.81.EP948

EP949

Subacute thyroiditis in patients after COVID-19 infections at the outpatient stage

Volha Shyshko[1,2], Darya Malakhava[2] & Alena Yurenia[1]
[1]Minsk City Clinical Endocrinology Center, Endocrinology, Minsk, Belarus; [2]Belarusian State Medical University, Endocrinology, Minsk, Belarus

Introduction
SARS-COV-2 is a new infection with little known consequences. As data accumulated, it became known that the thyroid gland is also affected as a result of infection. During the reconvalescence period, some patients developed severe thyrotoxicosis, which did not have the classic clinical picture of subacute thyroiditis or autoimmune.
Aim
To study the course of subacute thyroiditis in patients after infection with COVID-19.
Materials and methods
The study included 53 cases of subacute thyroiditis during 2020-2021. Group 1 - 13 patients with subacute thyroiditis and Covid-19 within 6 months, group 2 - 40 patients with subacute thyroiditis. The analysis of indicators was carried out: complaints at the first visit, hormonal status (T4, TSH), complete blood count, thyroid volume, nodes.
Results and discussion
Subacute thyroiditis is more often registered in women (69.2% (9) and 92.5% (37) in groups 1 and 2, respectively, compared with men (30.8% (4) and 7.5% (3) in groups 1 and 2, respectively), ($P<0.05$) The most common complaints in group 1: pain in the projection of the thyroid gland 30.4% (7), palpitations 13% (3), sweating 13% (3 cases); in group 2: pain in the projection of the thyroid gland 34.5% (19), fever 16.4% (9x), weakness 12.7% (7), palpitations 9.01% (5 cases), no complaints in 17.5%(7). The change in thyroid function is comparable in 2 groups: TSH in group 1 is lowered in 36.3% (4), normal in 36.3% (4), increased in 27.4% (3); in group 2: TSH decreased in 32.5% (13), normal in 40% (16), increased in 27.5% (11). fT4 in group 1: normal in 50% (3), increased in 33.3% (2), decreased in 16.7% (1); in group 2: decreased by 22.5%(9), normal in 52.5%(21), increased in 25%(10) ($P>0.05$). High ESR was significantly more often registered in group 1 (80% (8), compared with group 2 62.5% (25) ($P<0.05$) Nodular formations in the thyroid gland in group 1 were detected in 38.5% (5), in group 2 -in 100% (40).
Conclusions
1. Subacute thyroiditis is more common in women than in men in both groups. 2. Patients with COVID-19 are not characterized by fever in subacute thyroiditis. 3. The frequency of occurrence of thyroid status deviations is comparable in both groups. 4. In group 1, ESR increased more often than in the second group. 5. Nodular formations were significantly more often registered in patients without a history of COVID-19 infection.

DOI: 10.1530/endoabs.81.EP949

EP950

Therapeutic plasmapheresis to induce euthyroidism prior to thyroidectomy

Wee Mee Cheng & YC Kuan
Sarawak General Hospital, Medical, Kuching, Malaysia

Use of therapeutic plasmapheresis in hyperthyroidism is mainly described in thyroid storm when traditional measures fail. Patients with hyperthyroidism who respond poorly or suffer adverse effects to conventional antithyroid therapies, which then need to be stopped, can have persistently high levels of thyroxine and at risk of a full blown thyroid storm. Hence an alternative treatment to achieve euthyroidism followed by thyroidectomy as definitive therapy is vital. We report here a case of a lady who as a result of multiple adverse effects from conventional antithyroid therapies, underwent therapeutic plasmapheresis as a last resort to

achieve euthyroidism prior to thyroidectomy. A 35 year-old lady who was diagnosed with Grave's hyperthyroidism 2 months earlier and treated with carbimazole presented with fever, sore throat and generalized body weakness. Blood investigations revealed leucopenia (total white cell - $1.50x10^3$/uL) and neutropenia (absolute neutrophil count $0.03x10^3$/uL). A diagnosis of carbimazole-induced agranulocytosis with neutropenic sepsis was made. Carbimazole was stopped. Intravenous antibiotics, antifungal prophylaxis and granulocyte colony-stimulating factors (GCSF) were instituted. Her neutropenia was fairly resistant and needed twice daily GCSF for a week to recover. Thus, it was deemed unsafe to challenge with prophylthiouracil. Oral cholestyramine and lithium were started as alternative treatment for her thyrotoxicosis. Two weeks later she developed widespread pruritic maculopapular rash attributed to lithium which was then withheld. She also could not tolerate cholestyramine fully and often vomited on taking the drug. We opted to rechallenge her with lithium at lower doses and administer oral cholestyramine via nasogastric tube in the ward. However, her FT4 remained above 100 pmol/l (12.3-20.2) five days later (Table 1). Eventually we resorted to using therapeutic plasmapheresis one week before her scheduled operation date. She underwent 2 sessions of plasmapheresis uneventfully. Short term Lugol's iodine was started perioperatively along with steroid cover. She successfully underwent total thyroidectomy and is currently well on levothyroxine replacement. This case highlights the use of, plasmapheresis as an effective and safe alternative to achieve rapid restoration of euthyroidism prior to thyroidectomy when conventional measures fail, even before acute deterioration into thyroid storm.

DOI: 10.1530/endoabs.81.EP950

EP951

Ocular manifestations of Graves' disease

Kammoun Sonda[1], Rekik Mona[1], Affes Sofien[1], Faten Haj Kacem Akid[2], Ben Amor Saloua[1] & Trigui Amira[1]
[1]Habib Bourguiba Hospital, Tunisia; [2]Hedi Chaker Hospital, Tunisia

Introduction
Graves' ophthalmopathy, also called Graves' orbitopathy, is a potentially sight-threatening ocular disease that has puzzled physicians and scientists for nearly two centuries. Generally occurring in patients with hyperthyroidism or a history of hyperthyroidism due to Graves' disease, Graves' ophthalmopathy is also known as thyroid-associated ophthalmopathy or thyroid eye disease, because it sometimes occurs in patients with euthyroid or hypothyroid chronic autoimmune thyroiditis. We report two cases of Graves' ophthalmopathy and review clinical presentation, diagnosis and management of this condition.
Observation
Observation 1
A 52-year-old patient, with a history of hyperthyroidism since 1 year, referred for evaluation of the activity of his thyroid eye disease. Ophthalmologic examination found bilateral proptosis with right eyelid inocclusion, bilateral conjunctival hyperemia and superficial punctate keratitis. Oculomotricity and the remainder of the ophthalmological examination were without abnormalities in both eyes. The patient was successfully treated with corticosteroids.
Observation 2
A 55-year-old patient presented with complains of right proptosis and orbital pain for the past month. His medical history included diabetes treated with oral hypoglycemic agents. Examination revealed right ophthalmoplegia with exophthalmos. The remainder of the ophthalmological examination was unremarkable. The left eye was without abnormalities. A thyroid assessment carried out showed patent hyperthyroidism. Anti-TSH receptor antibodies were positive. Brain MRI showed bilateral orbital involvement due to dysthyroidism in the context of Graves' disease. The patient received corticosteroid associated with the etiological treatment. Outcome was favorable with regression of ocular symptoms after few days of treatment.
Conclusion
Graves' orbitopathy is the most frequent extrathyroid complication in Graves' disease. Natural history, described by Rundle, features an initial inflammatory or active phase in which acute episodes and spontaneous remissions alternate, then a fibrotic phase, with regression within 12–18 months. Diagnosis is based on symptoms and ocular signs. Clinical examination must therefore be rigorous; in case of doubt, the ophthalmologist's opinion is determining. Various classifications assess clinical signs: most widely used are the EUGOGO (European Group Of Graves' Orbitopathy). MRI imaging is essential to assess the degree of severity, in correlation with clinical involvement. Intravenous glucocorticoids are recommended in moderately severe and active OT. This condition affects the quality of life of patients and requires multidisciplinary care.

DOI: 10.1530/endoabs.81.EP951

EP952

Thyroid-associated orbitopathy exacerbation following COVID-19

Wiem Saafi[1], Ghada Saad[1, 2], Hamza Elfekih[1,2], Sinda Allegue[1], Amel Maaroufi[1, 2], Maha Kacem[1, 2], Molka Chadli Chaieb[1, 2], Yosra Hasni[1, 2] & Koussay Ach[1,2]
[1]Farhat-Hached University Hospital, Endocrinology-Diabetology Department, Sousse, Tunisia; [2]Faculty of Medicine Ibn El Jazzar, Sousse, Tunisia

Introduction
Thyroid-associated orbitopathy is an autoimmune disease of the retroocular tissues commonly associated with Graves' disease (GD) and rarely reported in Hashimoto's thyroiditis (HT). GD and HT are autoimmune thyroid disease which are sometimes hard to distinguish from one another and their association in one person is rarely described. Here, we report a case of an exacerbation of thyroid-associated orbitopathy in a patient with GD following a SARS-CoV-2 infection and a phase of spontaneous hypothyroidism.
Case report
A 36-year-old smoker male was hospitalized in the endocrinology department for the management of a Graves' orbitopathy. The diagnosis of GD was made two years ago in the presence of unilateral left orbitopathy, goiter, subclinical hyperthyroidism (TSH = 0.003 mUI/l and FT4 =1.36 ng/dl [0.9-1.7]) and positive anti-TSH receptor antibodies (TRAbs) = 5 IU/l (< 2 IU/l). Anti-thyroperoxidase (TPO-Ab) and anti-thyroglobulin (Tg-Ab) antibodies were negative. Thyroid scintigraphy showed intense homogenous hyper fixation of the gland. The patient received a small dose of antithyroid drugs. Euthyroidism was obtained after four months of treatment. After discontinuing medical treatment and follow-up for two years, the patient consulted for aggravation of his orbitopathy. He had a history of COVID-19 infection nine months ago and showed symptoms of hypothyroidism few months later. On examination, he had bilateral asymmetric orbitopathy without signs of activity. Laboratory exams confirmed hypothyroidism (TSH = 95 mUI/l and FT4 = 0.13 ng/dl). Antithyroid antibodies were positive: TPO-Ab = 291.4 IU/ml (< 60 IU/ml), Tg-Ab = 1055 IU/ml (< 100 IU/ml) and TRAbs = 2.37 IU/l.
Discussion
SARS-CoV-2 infection is associated with triggering of GD and HT. In our case, TPO-Ab and Tg-Ab were negative when the diagnosis of GD was first made. However, when the patient developed hypothyroidism, we found positive elevated levels of these antibodies and a concomitant decrease in TRAbs, suggesting a possible association between both diseases. Concerning the aggravation of the patient's orbitopathy, it is most likely related to smoking and the spontaneous shift to hypothyroidism.

DOI: 10.1530/endoabs.81.EP952

Table 1 Serial TFTs of the patient

Time	At diagnosis	After 2 months on carbimazole	After switching to lithium/ cholestyramine	Post 1st session plasma exchange	Post 2nd session plasma exchange	3 days post thyroidectomy
FT4 [12.3 - 20.2 pmol/l]	>100	22.7	>100	49.3	19.2	14.1
TSH [0.3 - 3.9 mIU/l]	<0.005	<0.005	<0.005	<0.005	<0.005	<0.005

EP953

Risk of malignancy of indeterminate thyroid nodules: an Italian single-center cohort study

Gianluca Cera[1], Roberto Novizio[1], Andrea Corsello[1], Esther Diana Rossi[2], Pietro Locantore[1] & Alfredo Pontecorvi[1]
[1]Fondazione Policlinico Universitario Agostino Gemelli IRCCS - Università Cattolica del Sacro Cuore, Unit of Endocrinology and Diabetes, Rome, Italy; [2]Fondazione Policlinico Universitario Agostino Gemelli IRCCS - Università Cattolica del Sacro Cuore, Division of Anatomic Pathology and Histology, Rome, Italy

Background
In 2014 a new Italian classification system of thyroid cytology divided the indeterminate TIR3 category in two groups, TIR3A and TIR3B, aiming to reduce unnecessary thyroidectomies. The reported risk of malignancy is: TIR3A: $<10\%$, suggesting follow-up and possible FNA repetition after 6 months, and TIR3B: 15-30%, recommending surgery.
Objectives
We aimed to: evaluate the histological prevalence of malignancy in TIR3A and TIR3B nodules in our center; investigate whether oxyphil cells in TIR3B samples correlated with benignity; assess whether cytological ThinPrep versus conventional smear preparation affects the cytological report; estimate the association between clinical and ultrasound (US) features with malignancy.
Methods
We performed a retrospective analysis of patients who received fine needle aspiration (FNA) from 05/2014 to 07/2017 at Fondazione Policlinico Gemelli, Rome. We included 139 TIR3A and 162 TIR3B nodules who underwent surgery, to compare cytology and histology. Samples were obtained with capillarity technique and prepared on conventional smears or ThinPrep slides. Clinical and US data reported to be associated with malignancy were collected. Differences in rates of malignancy were evaluated with Fisher's test. Logistic regression was performed to identify predictors of malignancy.
Results
Malignancy was reported in 12.2% ($n=17$) of TIR3A and 27.1% ($n=44$) of TIR3B nodules, with no significant difference with literature data. In TIR3B subgroup, 83 cytological samples showed oxyphil cells, with a malignancy rate of 10.8% ($n=9$), significantly lower than overall TIR3B ($P<0.01$). 66 TIR3A and 109 TIR3B FNA were prepared with ThinPrep technique, and 73 TIR3A and 53 TIR3B with conventional smears, with no difference in malignancy risks. Logistic analysis showed irregular margins to be predictive of malignancy in both TIR3A (OR 10.75, 95%CI 2.25-51.37) and TIR3B (OR 6.80, 95%CI 1.94-24.01). Other predictors were family history and microcalcifications for TIR3A, and vascularity, hypoechogenicity and, secondarily, microcalcifications for TIR3B ($P<0.05$). The predictive power of the logistic model increased when considering those features concurrently.
Conclusion
In a representative cohort of indeterminate nodules, malignancy rate of TIR3A and TIR3B nodules was overall comparable to the one reported in the Italian classification system. However, TIR3B with oxyphil cells had a malignancy rate comparable to TIR3A, advocating for careful search of this feature. US findings of irregular margins and, to a lesser extent, microcalcifications and hypoechogenicity, proved to be associated with malignancy. Some vascularity patterns were also associated with malignancy but they remained unreliable features because of their dubious interpretation. FNA preparation technique had no effect on malignancy risk.

DOI: 10.1530/endoabs.81.EP953

EP954

The level of neutrophil reactive oxygen species in euthyroid and relapse patients with Graves' hyperthyroidism

Margarita Dudina[1,2], Andrey Savchenko[3], Sergey A. Dogadin[1, 2] & Ivan Gvozdev[3]
[1]Krasnoyarsk State Medical University, Internal disease, Krasnoyarsk, Russian Federation; [2]Krasnoyarsk Regional Clinical Hospital, Endocrinology, Krasnoyarsk, Russian Federation; [3]Federal Research Center «Krasnoyarsk Science Center» of the Siberian Branch of the Russian Academy of Sciences, Scientific Research Institute of medical problems of the North, Laboratory of Molecular and Cell physiology and pathology, Krasnoyarsk, Russian Federation

Introduction
Graves' disease (GD) is organ-specific autoimmune-inflammatory disorder characterized by a complex pathogenesis. The inflammatory process is dominated by an imbalance of the antioxidant-oxidant mechanism, increased production of reactive oxygen species (ROS), which can potentiate the cytotoxicity of neutrophils and sustain the autoimmune process and perpetuate the disease. Aim: to study the level of ROS synthesis by peripheral blood neutrophils in patients with Graves' disease depending on hyperthyroidism compensation.
Materials and methods
One hundred and twenty-six women with Graves' disease, aged 18 to 65 years, divided in groups with compensated hyperthyroidism 93 (73.81%) and relapse of hyperthyroidism 33 (26.19%) were studied and compared concerning ROS production. All patients continuously treated with thiamazole about two months. The maintenance dose of thiamazole was 10 mg per day. The synthesis level of ROS in peripheral blood neutrophils was evaluated using a 36-channel chemiluminescence analyzer 'BLM-3607' (MedBioTech, Krasnoyarsk) and was characterized by Tmax – the rate of development of the chemiluminescent reaction, Imax – the maximum ROS synthesis and the area under the chemiluminescence curve (S – total synthesis of ROS for 90 minutes of measurement).
Results
Regardless for hyperthyroidism compensation the indicator S of spontaneous and zymosan-induced lucigenin-dependent chemiluminescence increases significantly relative to the control ($p<0{,}001$), but decreases the Tmax of zymosan-induced chemiluminescence ($p<0{,}01$). In GD relapse patients total synthesis of ROS during zymosan-induced chemiluminescence was higher up to 4,35 compared to euthyroid group ($p<0{,}05$). Antigenic stimulation of neutrophils in GD patients of both groups revealed an increase the Imax during luminol-dependent chemiluminescence ($p<0{,}01$). Samples with zymosan in GD relapse patients, also, demonstrated more than tenfold increase in the total synthesis of ROS relative to the control, but no statistically significant differences with euthyroid patients.
Conclusion
Violation of the ROS production by peripheral blood neutrophils in euthyroid patients mainly affects the production of primary ROS which is associated with hyperthyroidism compensation and the immunosuppressive effect of thiamazole. In patients with relapse of hyperthyroidism, there are more changes in the production of high-energy oxidants not only at initial oxidative reactions stage but also at the level of secondary ROS, indicating the activation of cellular response immunological mechanisms. Cytopathogenic effect of ROS neutrophils generation in patients with Graves' hyperthyroidism determine the intracellular targets of immunotropic treatment of the disease.

DOI: 10.1530/endoabs.81.EP954

EP955

Association between hyperthyroidism caused by Graves' disease and subjective sleep disorders

Kazuhisa Matsumoto[1], Shoichiro Izawa[1], Kenji Fukaya[1], Eriko Matsuda[2], Misato Fujiyama[2], Kazuhiko Matsuzawa[1], Tsuyoshi Okura[1], Masahiko Kato[3], Shin-ichi Taniguchi[4] & Kazuhiro Yamamoto[1]
[1]Tottori University Faculty of Medicine, Division of Endocrinology and Metabolism, Yonago, Japan; [2]Tottori University Faculty of Medicine, Head and Neck Surgery Division of Endocrinology and Metabolism, Yonago, Japan; [3]Tottori University Faculty of Medicine, Division of Pathobiological Science and Technology, Yonago, Japan; [4]Tottori University Faculty of Medicine, Department of Regional Medicine, Yonago, Japan

Background and objective
Sleep disorders (SDs) are classified into subjective and objective SDs, and subjective SDs are directly related to quality of life. According to previous studies, Graves' disease (GD) causes SDs, especially insomnia. However, the characteristics of subjective SDs and its clinical course after hyperthyroidism normalization remain unclear. Additionally, the factors involved in subjective SDs with hyperthyroidism in GD remain unclear. Hyperthyroidism is involved in sympathetic activity (SA). SA is likely to correlated with SDs. This study aims to evaluate the characteristics of subjective SDs and its clinical course after GD treatment, and to clarify the factors involved in subjective SDs associated with hyperthyroidism.
Methods
A prospective study with a substudy that involved cross-sectional analysis at baseline to evaluate the relationship thyroid function and the characteristics of SDs was perfomed. 72 participants (22 newly diagnosed with GD with untreated hyperthyroidism, 20 previously diagnosed with GD with normal thyroid function, and 30 normal controls) with no other underlying SD-related diseases were enrolled from November 2017 to October 2020. We compared the groups at enrollment and conducted prospective observations after 12 months of treatment on participants with newly diagnosed GD. Subjective SDs were assessed by

differences and changes in the Pittsburgh Sleep Quality Index (PSQI) global and component sleep quality scores. SA was assessed by pulse rate and urinary metanephrines.
Results
Free thyroxine (FT4) level, pulse rate and urinary metanephrines were significantly higher in untreated hyperthyroidism group compared to other group ($P < 0.05$). FT4 level was significantly positive correlated with pulse rate ($r = 0.643$, $P < 0.001$) and urinary metanephrines ($r = 0.387$, $P < 0.001$). PSQI global sleep quality scores ($P = 0.036$) and sleep disturbance scores ($P = 0.011$) were significantly different among the three groups, and were highest in the untreated hyperthyroidism group. Multiple regression analysis demonstrated that FT4 level was associated with poorer PSQI global sleep quality scores independently of other factors ($P = 0.006$). Prospective observation in 18 untreated hyperthyroidism group showed that FT4 ($P < 0.001$) and SA such as pulse rate ($P = 0.002$) and urinary metanephrines ($P < 0.001$) significantly improved by therapeutic intervention. PSQI global sleep quality scores ($P = 0.047$) and sleep disturbance scores ($P = 0.007$) significantly improved.
Conclusions
Hyperthyroidism in GD caused subjective SDs, especially sleep disturbance. SA due to hyperthyroidism may contribute to subjective SDs. Treatment for hyperthyroidism and SA may improve subjective SDs.

DOI: 10.1530/endoabs.81.EP955

EP956

Dosing study of brand vs. generic levothyroxine in well-controlled primary hypothyroidism

Elyes Kamoun[1,2], Manel Jemel[1, 2], Radhouen Gharbi[1, 2], Samir Mkaouer[1], Hajer Kandara[1, 2] & Ines Kammoun[1,2]
[1]Institut De Nutrition, Endocrinology Department, Tunis, Tunisia; [2]Faculté de Médecine de Tunis, Tunis, Tunisia

Introduction
Most brand-name drugs do not differ that much from their generic counterparts, so switching between the two is not an issue. Levothyroxine, however, is an exception. The question of generic equivalency of levothyroxine products has remained unanswered for several decades. The purpose of the present study was to learn whether there is a difference of dosage between brand-name and generic levothyroxine in patient with well controlled primary hypothyroidism
Methods
We performed a cross-sectional study in our outpatient consultation, including the patients presenting a well-controlled primary hypothyroidism. The patients were assigned into two groups, those already taking Levothyrox® (G1) and those already taking Berlthyrox® (G2). All patients were taking the same formulation during the three months preceding the study. Pregnant women were excluded. We assessed the duration of treatment, the age and weight, the cause of hypothyroidism, the levothyroxine dose, the adherence to the treatment and the TSH levels (N : 0,27 - 4,2µUI/ml).
Results
We included 46 patients, 16 patients under Levothyrox® and 30 patients under Berlthyrox®. The median age was 52 years, and the median duration of treatment was eight years. The cause of the hypothyroidism was an auto-immune hypothyroidism in 32 cases (70%), thyroidectomy in 5 cases (11%) and iodine therapy in 9 cases (19%). The levothyroxine dosage ranged from 25 to 200µg/day with a median of 100µg/day. TSH levels ranged from 0,29 to 4,27µUI/ml with a median of 2µUI/ml. The median dosage of levothyroxine in the group 1 was 75µg [25-125µg], and the median dosage of levothyroxine in the group 2 was 100µg [50-200µg]. The difference between the two groups was significant ($P = 0,039$). There wasn't a significant difference between the two groups concerning the age ($P = 0,772$), the weight ($P = 0,94$), the duration of treatment ($P = 0,224$), the cause of the hypothyroidism ($P = 0,147$), the adherence to the treatment ($P = 0,576$) and TSH levels ($P = 0,368$).
Conclusion
Generic and brand-name levothyroxine showed a comparative effectiveness to achieve normal TSH levels. But our study showed that the dosage required to obtain normal TSH levels was significantly different between the two groups. Therefore, the switch between formulations should be monitored for the risk of under or over treatment. It causes concerns in our practice with some patients taking the formulation available, as episodes of shortage have been noted for both formulations.

DOI: 10.1530/endoabs.81.EP956

EP957

Did well-controlled hypothyroid patients have necessary good compliance?

Elyes Kamoun[1,2], Manel Jemel[1, 2], Radhouen Gharbi[1, 2], Wafa Ben Hilel[1], Hajer KANDARA[1, 2] & Ines Kammoun[1,2]
[1]Institut De Nutrition, Endocrinology Department, Tunis, Tunisia; [2]Faculté de Médecine de Tunis, Tunis, Tunisia

Introduction
Treatment of primary hypothyroidism relies on a daily intake of levothyroxine, which dosage is determined first by the weight then by TSH levels monitoring. The daily dosage can vary with the cause of the hypothyroidism and the weight. The aim of our study was to determine if the adherence was a factor influencing the dosage of levothyroxine in a group of well-controlled hypothyroid patients.
Method
We performed a cross-sectional study including the patients presenting with a well-controlled primary hypothyroidism. We excluded pregnant women. We collected from their file their age, the cause of hypothyroidism, their weight, the TSH level (laboratory norms between 0.27 and 4.2µUI/ml), the duration of treatment and the current dosage of levothyroxine. We assessed for each patient the adherence to the levothyroxine with a Tunisian dialect translated version of the Girerd score. The adherence was defined as good compliance, minor noncompliance and noncompliance.
Results
We included 48 patients treated for primary hypothyroidism, with mean age of 50.4years and age varying from 19 to 37 years old. Mean duration of treatment was 10.5 years with extremes varying from two to 30years. The causes of the hypothyroidism were an auto-immune hypothyroidism in 69% of cases, thyroidectomy in 10% of cases, and iodine therapy in 21% of cases. The levothyroxine dosage ranged from 25µg to 200µg with a median of 100µg per day. TSH levels ranged from 0.29µUI/ml to 4.27µUI/ml with a median of 2µUI/ml. There was a good compliance in 19 patients (40%), a minor noncompliance in 26 patients (54,6%) and a noncompliance in 3 patients (6%). Adherence to treatment wasn't associated with age ($P = 0.731$) nor duration of treatment ($P = 0.262$). By performing an ANOVA test, adherence to treatment wasn't significantly associated with daily dosage ($P = 0,513$) nor dose per body weight ($P = 0,654$).
Conclusion
A lack of adherence to the treatment or to the time between the meal and the treatment is the first suspected cause of an elevation of TSH levels in a treated and well-titrated hypothyroid patient. Our study in a group of well-controlled patients showed that adherence isn't an influencing factor for the dosage when hypothyroidism is well-controlled but should always be advised to avoid TSH rise.

DOI: 10.1530/endoabs.81.EP957

EP958

Immunogenetic aspects of polyglandular autoimmune syndrome

Fatma Mnif[1], Siddiqa Soomauroo[1], Wafa Belabed[1], Hajer Fourati[2], Abdelmouhaymen Missaoui[1], Dhoha Ben Salah[1], Mouna Elleuch[1], Nabila Rekik[1] & Mohamed Abid[1]
[1]Hedi Chaker University Hospital, Department of Endocrinology, Sfax, Tunisia; [2]Hedi Chaker University Hospital, Department of Human Genetics, Sfax, Tunisia

Introduction
Polyglandular autoimmune syndrome (PAS) are uncommon constellations of autoimmune diseases characterized by the occurrence of two or more auto-immune endocrine diseases in the same individual.
Patients and methods
It is a case-control study about 108 cases for 120 healthy subjects recruited as the control group. We aimed to study the polymorphism of the HLA class-II genes of patients compared to that of healthy subjects so as to identify the genetic susceptibility to PAS.
Results
Among 108 patients, 2 patients had PAS type I (PAS-I), 39 patients had the type II (PAS-II) and 67 patients had the type III (PAS-III). Thirteen patients with PAS-II against 120 healthy subjects in the control group were included for the genetic testing of HLA class-II allele. DRB1*03 allele was associated with the occurrence of PAS-II whereas DRB1*13 was detected in only one patient but in 40 subjects expressing a negative association of this allele with PAS-II but remains statistically insignificant. We also found the association of DQB1*0302 in our population ($P = 0.004$). DQB1*06 is a protective allele more prevalent in healthy

subjects (22.97%) than in patients (3.8%) ($P=0.023$) but this difference becomes insignificant after Bonferroni correction. Twenty-seven patients with PAS-III were tested for HLA class-II alleles. DRB1*03 allele was found to be associated with PAS-III ($P=0.0001$) whereas no association was noted with DRB1*04 allele ($P=0.22$). DRB1*13 allele was found in 5 patients and 40 subjects in favor of the negative association of this allele in PAS-III ($P=0.11$). A significant association was also observed with DQB1*02 allele in our population ($P=0.0034$). In all, 40 patients with PAS-II/III were tested for HLA class-II alleles and demonstrated the association of PAS-II/III with DRB1*03 allele ($P=0.0021$) but a less significant association was noted with DRB1*04 ($P=0.05$). As far as protective DRB1*13 and DQB1*06 alleles are concerned, we noticed a negative association but insignificant after correction in PAS.

Discussion and Conclusion

The genetics of PAS is based essentially on the association of certain alleles of the human major histocompatibility complex. The presence of susceptibility alleles DRB1*03 and DQB1*0302 is described in literature. However, some studies showed the association of DR4-DQB1*0302 with PAS-II or III is due entirely to the presence of pancreatic auto-antibodies whereas haplotype DR3-DQB1*0201 is associated not only with type-1 diabetes mellitus but also PAS-II/III in the absence of pancreatic autoantibodies. The study of genetics have evolved considerably during the last years, especially due to molecular biology techniques.

DOI: 10.1530/endoabs.81.EP958

EP959

Graves' orbitopathy caused by alemtuzumab: a case series

Mariola Méndez Muros[1], Juan Jesús García González[1], Alberto Torres Cuadrado[1] & Antonio Manuel Garrido Hermosilla[2]
[1]Virgen Macarena University Hospital, Endocrinology and Nutrition Department, Seville, Spain; [2]Virgen Macarena University Hospital, Ophthalmology Department, Seville, Spain

Introduction

Alemtuzumab is a monoclonal antibody targeting the CD52 glycoprotein, which is expressed by most mature leucocytes. In early relapsing-remitting multiple sclerosis (MS) alentuzumab effectively decreases relapse rate and disability progression. However, nearly 50% of the pacients treated with alentuzumab develop secondary autoimmune disorders, being Graves' disease the most common. The development of thyroid eye disease is unusual.

Aims and Methods

We performed a retrospective chart review with MS and alemtuzumab-induced autoimmune hyperthyroid disease (AH-IA), who developed thyroid eye disease after alemtuzumab treatment. All patients with MS who had received at least one cycle of treatment with Alemtuzumab between 2014 and 2020 in Virgen Macarena University Hospital (Seville, Spain) were included.

Results

Our hospital is a regional referral center for MS, so approximately 121 MS patients were treated with alemtuzumab. 41 (33,9%) developed Graves' disease and 6 (14,6%) were referred for ophthalmological evaluation. Of these, only one presented as a severe case, while the other five presented a mild course. Five were non-smokers at the time of developing ocular signs and symptoms. Five had significantly raised TRAb ($>$ 10 IU/l) at presentation with eye disease—the sixth presented at a time prior to this test being routinely available. There was a 5:1 ratio of females to males. All patients initially received treatment with antithyroid drugs to control thyroid function. Four of them underwent total thyroidectomy as a definitive treatment. At diagnosis of orbitopathy, all patients had thyroid dysfunction consistent with hyperthyroidism. Four patients underwent conservative management with lubricants and selenium. One patient required treatment with oral corticosteroids. The most severe case was a 30-year-old woman who presented with constant diplopia, palpebral retraction >1.5 mm, severe soft tissue involvement, and exophthalmos. With a clinical activity score (CAS) of 3 she was started on treatment with i.v corticosteroids. Due to poor evolution, and an increase in the clinical activity score to 6, she started treatment with Tocilizumab, a humanized MAB against the interleukin (IL)-6 receptor approved as second-line treatment for moderate to severe and active glucocorticoid-resistant Graves' orbitopathy (GO). At 6 months, she presented great clinical improvement, with a CAS of 2 points (inactive GO).

Conclusions

We report the risk of developing GO in patients with MS treated with alemtuzumab who developed GD. In a novel way not described to date in the literature, we present a case of severe and active GO resistant to glucocorticoids in which Tocilizumab was successfully used.

DOI: 10.1530/endoabs.81.EP959

EP960

Euthyroid sick syndrome as a prognostic marker in patients with SARS-CoV-2 infection

Joana Estevens[1], Liliana R. Santos[1,2], Daniel Nunes[3], Carlos Lemos[1,3], Paula Soares[4] & António Pais de Lacerda[1,2]
[1]Faculdade de Medicina da Universidade de Lisboa, Lisboa, Portugal; [2]Centro Hospitalar Universitário Lisboa Norte EPE, Serviço de Medicina II, Lisboa, Portugal; [3]Centro Hospitalar Universitário Lisboa Norte EPE, Serviço de Patologia Clínica, Lisboa, Portugal; [4]IPATIMUP - Instituto de Patologia e Imunologia Molecular da Universidade do Porto, Porto, Portugal

After almost 3 years since SARS-CoV-2infection was detected for the first time, knowledge about its repercussions on the thyroid gland function in the course of acute illness or in the post-COVID-19 are still poorly understood. This gland may be particularly susceptible to SARS-CoV-2 as this coronavirus enters cells through ACE-2 receptors, which are largely expressed in the thyroid gland. Through an observational, longitudinal and retrospective study, we investigated the serum levels of TSH and fT4 in adult patients infected by SARS-CoV-2 admitted to an internal medicine ward of a tertiary hospital. We evaluated the changes in thyroid function during hospitalization of 221 patients and the correlation between these changes and the severity of the disease. In a smaller cohort (n1= 20) we evaluated thyroid function after hospital discharge. We found a high predictive value of serum TSH and fT4 values for severity of COVID-19 (OR = 2.5, p-value = 0.02). We used Pearson Chi-Square p-value and assume severe COVID-19 if PaO2/FiO2 $<$ 300. We have shown that low TSH (mean 0.18 mU/l) and fT4 (mean 0.6 pmol/l) values have a higher prognostic value for mortality (OR = 2.3, p-value = 0.05) than other commonly used input data: hypertension, obesity, diabetes, PCR and IL-6 levels, sex and smoking. In the follow up cohort, thyroid function values tend to return to normal values over time. TSH and fT4 decreased values may be in line with the Euthyroid Sick Syndrome that has been described in acute diseases and as well as in patients with COVID-19.

DOI: 10.1530/endoabs.81.EP960

EP961

Use of thyroid hormone in hypothyroid and euthyroid patients. the THESIS questionnaire survey in spain

Juan Carlos Galofré[1], Roberto Attanasio[2], Laszlo Hegedüs[3], Endre V. Nagy[4], Roberto Negro[5], Enrico Papini[6], Petros Perros[7] & Juan Jose Diez[8]
[1]Clínica Universidad de Navarra, Endocrinology, Pamplona, Spain; [2]IRCCS Orthopedic Institute Galeazzi, Endocrine Unit, Milan, Italy; [3]Odense University Hospital, Endocrinology and Metabolism, Odense, Denmark; [4]Department of Medicine, Faculty of Medicine, University of Debrecen, Division of Endocrinology, Debrecen, Hungary; [5]V. Fazzi Hospital, Division of Endocrinology, Lecce, Italy; [6]Regina Apostolorum Hospital, Department of Endocrinology and Metabolism, Rome, Italy; [7]Royal Victoria Infirmary, Department of Endocrinology, Newcastle upon Tyne, United Kingdom; [8]Hospital Universitario Puerta de Hierro, Department of Endocrinology, Madrid, Spain

Background

Hypothyroidism is one of the most frequent conditions in endocrinology. Despite of that fact, indications for treatment differ among specialists in Spain.

Aims

To identify attitudes of Spanish endocrinologists in the use of levothyroxine (LT4) therapy and the management of hypothyroidism.

Methods

The members of the *Sociedad Española de Endocrinología y Nutrición* (Spanish Society of Endocrinology and Nutrition) were requested to participate in a web-based survey. The questionnaire, conducted between September and November 2020, was adapted in accordance with the availability of thyroid hormone formulations in Spain.

Results

A total of 512 of 1956 (25.8%) members (66% female) completed the survey; 97.4% affirmed that LT4 is the initial treatment for hypothyroidism. The indications for LT4 therapy in euthyroidism were infertility in thyroid antibody positive women (48.5%) and simple goitre (21.2%). However, 44.2% of endocrinologists reported that there was no such indication for these patients. Only a minority of interviewees (2.6%) considered combining LT4 with liothyronine as the treatment of choice at diagnosis whereas 49% stated that it should never be used.

Conclusions
The standard of treatment of hypothyroidism in Spain is almost exclusively with LT4 tablets. Availability of other formulations of LT4 or combination therapy for hypothyroidism management remains to be explored specially in patients with persistent symptoms. Remarkably, non-evidence based use of LT4 is extensively practiced in Spain for euthyroid women with autoimmune thyroiditis and fertility problems.

DOI: 10.1530/endoabs.81.EP961

EP962

Substitution with combined vitamins and minerals will provide a sufficient level of iodine during pregnancy

Boyana Trifonova[1,2], Anna-Maria Borissova[3,4], Lilia Dakovska[3] & Eugenia Michaylova[5]
[1]University Hospital Sofiamed, Sofia, Bulgaria, Clinic of Endocrinology, Sofia, Bulgaria; [2]Sofia University Saint Kliment Ohridski, Sofia, Bulgaria, Faculty of Medicine, Sofia, Bulgaria; [3]University Hospital Sofiamed, Sofia, Bulgaria, Clinic of Endocrinology, Sofia, Bulgaria; [4]Sofia University Saint Kliment Ohridski, Sofia, Bulgaria, Sofia, Bulgaria; [5]Clinical Laboratory Bodimed, Sofia, Bulgaria

In 2005, the evaluation of an international expert group* placed Bulgaria among those who successfully overcame the problem of 'iodine deficiency'. The aim of the study is to assess the current iodine status in pregnant women in two main regions of Bulgaria - with a known iodine deficiency and other with sufficiency in the past.
Material
A cross-sectional multicenter population-based study was conducted in a total of 84 settlements from the two regions, at 537 pregnant women, mean age of 30.49 $\pm$ 5 years.
Methods
The UIC was determined by certified inductively coupled plasma mass spectrometry. The accepted intervals for assessment of median UIC are: low 1 - 149, normal 150 - 249, over-optimal $>$ 250 µg/l.
Results
The mUIC level for the whole pregnant group was 170 µg/l (11 - 497), (95% CI 161 - 177). The pregnant women only in three regions have a mUIC below the lower reference limit of the norm for pregnant women of 150 µg/l [Gotse Delchev - 144.5 (119 - 208), Gabrovo - 130.5 (108 - 168), Troyan - 113.5 (93 - 185)]. A comparison was made between these three regions and the other seven with normal mUIC levels. According to the questionnaire 271 (50.47%) of all pregnant women take combined vitamins with minerals (including iodine). Pregnant women who do not take any medications from Gabrovo-Troyan-Gotse Delchev are 23.1% v.s. 15.7% of pregnant women in the other seven regions ($P<0.006$).
Conclusion
During pregnancy it is important to substitute with combined vitamins and minerals to ensure sufficient intake of iodine for this period. *Van der Haar F. *Review of Progress towards Sustained Optimal Iodine Nutrition in Bulgaria, MoH, USAID, UNICEF, 2005, P 32*

DOI: 10.1530/endoabs.81.EP962

EP963

The relationship between thyroid hormones and different degrees of obesity; a case-control study

Bayar Qasim[1], Ayad Mohammed[1] & Mazyar Ahmed[2]
[1]College Of Medicine, University Of Dohuk, Medicine, Iraq; [2]Kurdistan Board For Medical Specialties, Medicine, Erbil, Iraq

Background
Obesity is a serious health problem worldwide and is caused by a wide variety of etiologies. There are several hormones which have been proved to be associated with increased body weight and has a direct effect on the fat metabolism like thyroid hormones.
Methods
This is a case control study which included 384 adult persons, they were divided into 2 groups according to the thyroid function status, the first group included 204 apparently healthy adults with normal thyroid function as a control group and the other group included 180 patients with decreased thyroid function status as a case group.
Results
The mean age of our patients was 37.12 years, females constituted 53.1%. Most individuals were overweight and obese. There was a very significant correlation between the levels of the TSH and the age, sex, and the BMI (P values 0.000, 0.05, and 0.000) respectively (table 1). Based on FT4 levels, 51.4% had normal level and 48.6% had decreased FT4 levels. The FT4 level had also a very significant correlation with the age, sex, and the BMI (P value 0.000, 0.001, and 0.000) respectively.
Conclusions
Body mass index is directly and positively correlated with both the TSH and the FT4 level. Overt cases of thyroid dysfunction are easier to be detected clinically than subclinical cases, obesity patients can be screened using the thyroid function status and treatment of patients with thyroid dysfunction must be adjusted according the weight.
References
1. Solanki, A., *et al*., Relationship of serum thyroid stimulating hormone with body mass index in healthy adults. Indian journal of endocrinology and metabolism, 2013. 17(Suppl1): p. S167.
2. Azo Najeeb H, Ahmad Qasim B, Ahmad Mohammed A (2020) Parental history of coronary artery disease among adults with hypothyroidism: case controlled study. Ann Med Surg (Lond) 60:92–101 QASIM, B.A., A.A. MOHAMMED, and M.J. AHMED, *LIPID PROFILE IN SUBCLINICAL HYPOTHYROIDISM: A TWO CENTERS EXPERIENCE.* Duhok Medical Journal, 2019. 13 (1): p. 56-65.

Table 1 table showing the relation of the TSH and different parameters including BMI.

			TSH value	
Main category	Subcategories	Normal ($n=204$)	Elevated ($n=180$)	Sig. 2-sided
Age groups	Young ages (18-45)	178(87.3%)	120(66.7%)	
	Middle aged (46-65)	23(11.3%)	45(25.0%)	0.000*
	Elderly (66 and above)	3(1.5%)	15(8.3%)	
	Male	105(51.5%)	75(41.7%)	
Sex	Female	99(48.5%)	105(58.3%)	0.05*
	Underweight	8(3.9%)	0(0.0%)	
BMI level	Normal	77(37.7%)	26(14.4%)	0.000**
	Overweight	86(42.2%)	62(34.4%)	
	Obese	33(16.2%)	92(51.1%)	

* Pearson Chi-Square test. ** Fisher's Exact test.

DOI: 10.1530/endoabs.81.EP963

EP964

Therapeutic approach to the diagnosis of Bethesda 5

Ana Barrera-Martín, Mª Rosa Alhambra Expósito, Paloma Moreno-Moreno & María Angeles Galvez Moreno
Reina Sofia Hospital, Córdoba, Spain

Introduction
Thyroid nodules are very common in the general population (20-75% ultrasound). There are clinical management criteria established by international societies and standardized cytological diagnostic criteria (Bethesda). However, there is still uncertainty in the management of category 5.
Objectives
To evaluate the clinical attitude to the cytological diagnosis of Bethesda category 5 (B5) in thyroid fine-needle aspiration cytology (FNA). And study associations between malignancy and other variables.
Material and methods
Retrospective study of thyroid nodules classified as B5 after FNA referred to our hospital between 2020 and 2021. Statistical analysis: SPSS v.22.0 (Student's t-test to compare means and Chi-square/Fisher's test for proportions).
Results
Twenty patients (70% female); mean (SD) age, 49.3 (15.6) years. Sonographic features of included nodules are shown in table 1. Of the nodules, 5% were ACR-TIRADS 3, 25% ACR-TIRADS 4 and 70% TIRADS 5. Application of the ACR TIRADS system's FNA criteria would have reduced the number of biopsies performed by 10%. Of the nodules without indication of FNA, both were papillary

Table 1 Sonographic features of included nodules

Structure/composition		Echogenicity		Shape		Margin		Echogenic foci	
	%		%		%		%		%
Cystic or almost completely cystic	0%	Anechoic	0%	Wider tan tall	85%	Smooth or defined	35%	None or large comet-tal artifacts	50%
Spongiform	0%	Hyperechoic o isoechoic	15%	Taller tan wide	15%	Lobulated or irregular	65%	Macrocalcifi-cations.	0%
Mixed	20%	Hypoechoic	85%			Extra-thyroi-dal exten-sion	0%	Periferical calcifica-tions	0%
Solid	80%	Very hypoe-choic	0%					Punctate echogenic foci	50%

thyroid microcarcinomas. All patients underwent surgery, 80% total thyroidectomy, and 20% hemithyroidectomy. Eighty (80%) lesions met the reference-standard criteria for malignancy: 10 papillary thyroid cancers, 4 papillary thyroid microcarcinoma, 2 Hürthle cells carcinoma. The rest: 10% (2) follicular adenoma, 5% (1) multinodular goiter and 5% (1) non-invasive follicular neoplasm with nuclear alterations of papillary carcinoma. The variable the presence of calcifications on the nodule were directly related to the malignancy/benignity of the nodule (p 0.025). In fact, microcalcifications is only present in malign pathology.

Conclusions

The percentage of patients with malignant processes of our series corresponds to the bibliography. Although the use of this category seems correct, the clinical attitude is erratic and surgical over-treatment occurs.

DOI: 10.1530/endoabs.81.EP964

EP965

An unusual pathology in graves' Disease

Sebnem Burhan[1], Rukiye Dilara Tekin Uzman[1], Ş eyma Aksoy[1], Fatih Mert Doğukan[2] & Esra Şüheda Hatipoğlu[1]
[1]Basaksehir Cam and Sakura City Hospital, Endocrinology and Metabolic Diseases, İstanbul, Turkey; [2]Basaksehir Cam and Sakura City Hospital, Pathology, Istanbul, Turkey

Introduction

Graves disease (GD) is an autoimmune disease in which thyrotropin receptor antibodies overactive the thyroid gland. Therefore, antithyroid drugs, radioactive iodine therapy, or surgical interventions are treatment options. In GD, pathology after thyroidectomy may include hypertrophy and hyperplasia in thyrocytes, mononuclear cell infiltration in the stroma, and increased blood supply. We presented a case with areas of necrosis and vasculitis due to GD in the pathological specimen obtained after a patient underwent a total thyroidectomy due to development of hepatotoxicity under antithyroid therapy.

Case

An 18-year-old female patient complained of palpitation, weakness, and fatigue. TSH was suppressed, fT4, fT3 and thyroid stimulating antibody were elevated. thyroid ultrasonography and scintigraphy also confirmed GD. After 2 months of methimazole she could not achieve adequate control and developed hepatotoxicity. Therefore she was switched to propylthiouracil and surgery was planned. On the histopathological examination, diffuse hyperplasia of thyroid follicular epithelial cells with nearly complete loss of colloid material was observed. The typical lobular structure was preserved, whereas the follicular pattern had been lost due to the pronounced lack of colloid. A focus of lymphocytic thyroiditis with accompanying pseudopapillary projections was present. Patchy areas of thyroid parenchyma showing coagulation necrosis were remarkable. In some small intraparenchymal venules, thrombotic vasculopathy was noticed. There was no cytological atypia and increased mitotic activity. Immunohistochemical test results (TTF-1 (+), PAX8 (+), calcitonin (-), GATA-3 (-)) were confirmatory of the thyroid follicular epithelial cell origin. There was no evidence of systemic vasculitis in his physical examination. Sedimentation, CRP, p-ANCA, c-ANCA, ANA, C3, and C4 were within normal ranges. PET CT did not show a systemic vasculitis.

Discussion

Vasculitis in the thyroid is not common. However, there have been few cases with giant cell arteritis or temporal arteritis in the thyroid artery. Antithyroid drug-associated vasculitis is generally ANCA-associated leukocytoclastic vasculitis and presents with skin manifestations. We did not find evidence of systemic manifestations in our case. Autoantibodies were negative. Due to absence of prominent nodular patterns, cytological atypia, increased mitosis, or solid growth pattern in histopathological examination; poorly differentiated thyroid carcinoma was excluded. The existing findings in the thyroidectomy material were evaluated as vasculitis localized to thyroid gland and related to GD.

DOI: 10.1530/endoabs.81.EP965

EP966

Radiofrequency thermal ablation (RFA) of Thyroid nodules: our initial experience

Mee Jung Rachele Mattarello[1], Roberto Mingardi[1], Francesca De Santi[1] & Mauro Mazzucco[2]
[1]Casa di Cura Villa Berica, Endocrinology and Diabetology Service, Vicenza, Italy; [2]Casa di Cura Villa Berica, Minimally Invasive Cancer Therapy Center, Vicenza, Italy

In recent years, US-guided thermal ablation techniques have been proposed as a therapeutic alternative to traditional surgery or to metabolic radiotherapy for thyroid nodes. RFA is one of the most used technique and experience in both ultrasound and ultrasound interventional is important for results and minimizing complications. We present our experience after 1 year of activity on the first 33 patients with thyroid nodules treated with RFA. The nodules were evaluated by ultrasound (Samsung RS85) and classified according to the TI-RADS criteria In all patients, 2 ultrasound-guided fine needle aspirations were performed at different points of the nodule according to guidelines. Thermoablation was performed under local anesthesia with Amica-Gen HS Hospital Service RF

Table 1 Characteristics of Thyroid Nodules

Volume Average (cc)	27.7 (4.5 - 80)
Right lobe	17 (51.5%)
Left lobe	16 (48.5%)
Ecostructure	isoechoic 3 (9.1%)
	hypoechoic 6 (18.2%)
	hyperechoic 18 (54.5%)
	mixed (solid-cystic) 6 (18.2%)
Vascularization	peripheral 21 (63.6%)
	peripheral + internal 12 (36.4%)
Cytology (2 FNAC)	TIR 2 + TIR 2 29 (87.9%)
	TIR 2 + TIR 3a 4 (12.1%)
	RFA
Power (Watt)	25-45
Average time	15' 48' (5' 43" - 34' 10")
Average number of shots	11 (5-18)
	RESULTS
RVR 1 week (33 pat.)	15% (0-33%)
RVR 1 month (33 pat.)	32% (16-65%)
RVR 6 months (27 pat.)	54% (33-75%)
RVR 1 year (6 pat)	67% (51-75%)
Reduction/resolution of symtoms	
(% pat.)	56%
1 week	80%
1 month	96%
6 months	

generator and 18G electrode needles with 7-10 mm exposed tip were used by moving shot method 33 patients were treated (9M; 24F); mean age 55.9 years (33-87); one session per patient. 25 cases presented compression symptoms; 3 cases progressive volumetric increase of the nodule at the controls; 5 cases cosmetic score equal to 4. Mean follow up 7.3 months (1-12) We have not seen any complications. The table lists the characteristics of the focal thyroid lesions, the sessions performed, and the preliminary results obtained (relative volume reduction, RVR, and effect on symptoms). A patient had a partial relapse of symptoms after 6 months and was referred for surgery. In our initial experience, the RF thermoablative treatment proved to be safe and effective and confirms what is reported in the literature data. The treatment must be preceded by adequate information on the modalities of the treatment session and the advantages and disadvantages of the procedure.

DOI: 10.1530/endoabs.81.EP966

EP967

Association between selected serum inflammatory parameters, low FT3 and mortality in hospitalized patients with COVID-19 - single center observation

Aleksandra Młodożeniec[1], Renata Orłowska-Florek[1,2], Adrianna Czarnożycka-Wróbel[1], Paulina Szul[1], Krzysztof Gargasz[2] & Agnieszka Gala-Bladzinska[1,2]
[1]St. Queen Jadwiga Clinical District Hospital No.2 Rzeszów, Department of Internal Medicine, Nephrology and Endocrinology, Poland; [2]Medical College of Rzeszów University, Poland

Introduction
The incidence and mortality rate for COVID-19 differ in different regions, but the risk of in-hospital death is high in all countries. It is very important to identify patients at risk of death at the beginning of hospitalization. The disease often leads to NTIS (nonthyroidal illness syndrome), which can be the result of the cytokines storm [1]. The inflammatory parameters and the level of FT3 appear to be obvious leading risk of death.
Objective
The study aimed to investigate the serum levels of thyroid hormones and selected inflammatory biomarkers in adult COVID-19 patients and to determine whether they predict the risk of death.
Methods
We retrospectively analyzed the lab results of patients hospitalized in our clinic from October 2020 to January 2021 with confirmed SARS-CoV-2 infection ($n=393$). Patients with a history of thyroid disease, patients treated with thyroid drugs and those who have recently received iodinated contrast were excluded. All of them were initially in stage II of the course of the disease [2]. The STATISTICA 13.1 statistical program was used to perform the tests and P values < 0.05 were considered statistically significant.
Results
Fifty-three (13,49%) adult patients were enrolled in the study. The median age was $72 \pm 12,2$ years, 26 patients (49%) were men. NTIS was detected in 64% of all patients and low FT3 serum levels showed strong correlation with disease severity and mortality prognosis in COVID-19. The results are shown in Table 1.
Conclusions
1. Low serum FT3 concentrations predict clinical deterioration and higher mortality in COVID-19 patients. 2. The levels of Il-6, WBC, ferritin, neutrophils are prognostic markers of in-hospital mortality in patients with COVID-19.
References
1. Llamas M *et al*. Low free-T3 serum levels and prognosis of COVID-19: systematic review and meta-analysis. Clin Chem Lab Med. 2021 Aug 10.
2. Siddiqi HK *et al*. COVID-19 illness in native and immunosuppressed states: A clinical-therapeutic staging proposal. J Heart Lung Transplant. 2020; 39: 405-407.

DOI: 10.1530/endoabs.81.EP967

EP968

Thyrotoxicosis and multisystemic inflammatory syndrome in a patient with recent history of COVID-19

Calin Cristiana[1,2], Daniela Ioana Iulia Greere[2,3], Iulia Florentina Burcea[2, 3] & Catalina Poiana[2,3]
[1]C.I. Parhon National Institute of Endocrinology, Pituitary and Neuroendocrine Disorders Department, Bucharest, Romania; [2]Carol Davila University of Medicine and Pharmacy, Pituitary and Neuroendocrine Disorders Department, Bucharest, Romania; [1]C.I. Parhon National Institute of Endocrinology, Pituitary and Neuroendocrine Disorders Department, Bucharest, Romania

Introduction
There is evidence on the association of subacute thyroiditis (SAT) and SARS-CoV-2 infection, the first case report being described in a young woman back in July 2020 (1). Multisystemic inflammatory syndrome in adults (MIS-A) is a rare complication of SARS-CoV-2, usually 2 to 12 weeks after initial infection. The development of Graves disease after SAT is rare, with approximately 31 reported cases, of which only 5 occurring in men (2). We present the case of a young patient with thyrotoxicosis following SARS-CoV-2 infection.
Case Report
A 45-year-old male patient presented to our hospital with weight loss, palpitations and irritability. The medical history revealed SARS-CoV2 infection 3 months prior to presentation and an acute cytomegalovirus hepatitis 2 years ago. The patient was tachycardic, normotensive and afebrile. The laboratory tests revealed markedly elevated acute inflammatory markers: fibrinogen - 1240 mg/dl, CPR - 25.02 mg/dl, cholestasis: GGT - 914 U/l, ALP - 325 U/l and thyrotoxicosis: TSH - 0.0013 microUI/ml, freeT4 - 40.5 pmol/l, with negative thyroid stimulating hormone receptor antibody (TRAb). Screening for obstructive cholestasis and liver infectious disease was negative. Ultrasound examination indicated a diffuse enlargement of thyroid gland with multiple hypoechoic areas in the left thyroid lobe, suggestive for subacute thyroiditis. Treatment with intravenous dexamethasone 24 mg per day for 1 week in combination with methimazole 20 mg per day was started. Within the first week, the patient's condition improved with significant decrease of freeT4 and serum cholestasis markers and normalization of inflammatory markers. The patient was discharged with methylprednisolone 16 mg every two days and methimazole 15 mg per day. At 2-weeks follow-up, the thyroid function was normal under treatment, but TRAb had a positive value.
Conclusion
Our patient's presentation was atypical for SAT with no pain in the anterior surface of the neck and no fever. Given the late positivity of TRAb, we can consider the hypothesis that thyrotoxicosis emerged due to Graves disease and the markedly elevated acute inflammatory markers were explained by a multisystem inflammatory syndrome in adults. Clinicians should be aware of the potential development of MIS-A as a sequela of COVID-19. Also, there is a rare possibility that the subacute thyroiditis triggered the development of Graves disease.
References
(1) Brancatella A *et al*, Subacute thyroiditis after Sars-COV-2 infection. *J Clin Endocrinol Metab*. 2020;105(7):2367-2370.
(2) Souad Al-Bacha *et al*, Graves' Disease Following Subacute Thyroiditis in a Chinese Man, *AACE Clinical Case Reports*, 2021.

DOI: 10.1530/endoabs.81.EP968

Table 1 Association among serum FT3, FT4, selected inflammatory biomarkers and hospital mortality in COVID-19 patients.

	Nonsurvivors ($n=14$)			Survivors ($n=39$)			
	median	Min.	Max.	median	Min.	Max.	P
FT3, [pg/ml]	1,8	1,2	2,5	2,2	1,3	3,4	$P=0,01$
FT4, [ng/ml]	1,1	0,6	1,5	1,3	0,6	1,8	$P=0,05$
Interleukin 6, [pg/ml]	41,9	4,8	620	15	2,7	559	$P=0,05$
Ferritin, [ng/ml]	221.25	22	994	570	12	16000	$P=0.01$
WBC, [10/l]	10.9	7.78	195	6.75	1.01	25.97	$P=0.002$
Neutrophils, [cells/μl]	7860	752	15050	5120	897	23770	$P=0.04$

EP969

A rare case of symptomatic amyloid goiter diagnosed by tru-cut biopsy

Erhan Hocaoglu, Ensar Aydemir, Coskun Ates, Filiz Mercan Saridas, Soner Cander, Ozen OZ GUL, Canan Ersoy & Erdinc Erturk
Uludag University Medical School, Endocrinology, Bursa, Turkey

Introduction
Amyloid goiter is a rare entity caused by massive amyloid infiltration of the thyroid gland. In some cases, differential diagnosis can be challenging. In this report, we present a patient with amyloid goiter caused by secondary amyloidosis.
Case
A 48-year-old male patient was admitted to our hospital with the complaints of neck swelling, pain, and mild dysphagia that started three weeks after the SARS-Cov-2 infection and continued for one month. The patient had a history of Crohn's disease, ankylosing spondylitis and renal amyloidosis. He was on hemodialysis for 8 years. On physical examination, the thyroid gland was bilaterally palpable and tender. Laboratory tests were as follows: C-reactive protein 55 mg/l, sedimentation 50 mm/hr, TSH 0.02 mU/l, free T4 0.76 ng/dl, free T3 2.17 ng/l. Anti-thyroid peroxidase (TPO) and TSH receptor antibody were negative. Ultrasound showed an enlarged thyroid gland with hyperechogenicity of the parenchyma and normal vascularity. Thyroid scintigraphy revealed low uptake. Subacute thyroiditis was considered in the patient. As the administration of ibuprofen did not ameliorate his symptoms, oral metilprednisolone (32 mg/day) was initiated. Afterwards, low-dose levothyroxine replacement was started for hypothyroidism. Despite using steroid (methylprednisolone at a maximum dose of 64 mg/day) for more than one month, his symptoms did not significantly relieve and the patient was hospitalized. Computed tomography scan of the neck showed diffuse enlargement of the thyroid gland and parenchymal heterogeneity. Fine-needle aspiration of the thyroid gland was performed, but the findings were non-specific. After that, tru-cut biopsy was planned for the patient. Pathological analysis revealed amyloid goiter. Positive staining with Congo red was obtained. Immunohistochemical staining patterns were consistent with amyloid AA. The patient, who was evaluated together with the general surgery department, was discharged with a total thyroidectomy planned for symptomatic amyloid goiter. After a short time, it was learned that the patient died due to myocardial infarction in another center.
Conclusion
In some cases, it can be difficult to distinguish amyloid goiter from subacute thyroiditis and other diseases. Amyloid goiter should be kept in mind in patients present with rapid thyromegaly and have a history of chronic inflammatory disease that may be associated with secondary amyloidosis. Fine-needle aspiration has a limited role in diagnosis. Either a core-needle biopsy or surgical specimen is often necessary.

DOI: 10.1530/endoabs.81.EP969

EP970

Autoimmune thyroid disorders and connective tissue disease

Raida Ben Salah[1], Faten Haj Kacem Akid[2], Siddiqa Soomauroo[2], Mohamed Abdellahi Mohamed Ahmed[2], Sarra Chouaib[2], Faten Frikha[1], Nabila Rekik[2], Mohamed Abid[2] & Zouheir Bahloul[1]
[1]Hedi Chaker University Hospital, Department of Internal Medicine, Sfax, Tunisia; [2]Hedi Chaker University Hospital, Department of Endocrinology, Sfax, Tunisia

Introduction
Mixed connective tissue disease (MCTD), also known as Sharṕs syndrome is a rare autoimmune disease (AD), characterized by the presence of high titers of a distinctive autoantibody: ribonucleoprotein auto-antibody (anti-RNP). It presents with varied overlapping symptoms of different connective tissue disorders which may appear sequentially over time. As other AD, MCTD may be associated with one or more AD, such as autoimmune thyroid disorders (AITD).
Patients and methods
It is a descriptive retrospective single institution study. We collected data from 113 patients diagnosed with an AITD associated with another AD over 18 years. This present study reports the association between AITD and MCTD.
Results
We identified one patient diagnosed with both MCTD and AITD. She was hospitalized in the department of Internal medicine for investigation of joints pain and Raynaud's phenomenon. Antibody testing showed positivity for anti-RNP. She was treated by a prescription of nonsteroidal anti-inflammatory drugs and calcium channel blockers. The evolution was marked by the occurrence of flares of arthralgias. Biochemical assays led to the fortuitous discovery of a hypothyroidism. Hashimoto's thyroiditis (HT) was diagnosed concomitant to the MCTD in the context of other autoimmune diseases associated with the MCTD. Both thyroid antibodies (thyroid peroxydase antibody and thyroglobulin antibody) were positive. The patient was treated by L-thyroxin substitution.
Discussion and Conclusion
MCTD are AD characterized by the involvement of several organs and the presence of various autoantibodies. It can be associated with other AD. The most frequent association are with the Sjogrens' syndrome, Hashimoto's thyroiditis and some authors reported cases of autoimmune hepatitis and MCTD or primary biliary cirrhosis and MCTD. The frequency of thyroid disease, particularly chronic autoimmune thyroiditis (Hashimoto's thyroiditis), may be increased in patients with MCTD and vice versa. In a study conducted by Biro *et al*. including 1517 patients bearing an AD, 159 patients were diagnosed with MCTD. Among them, 21.4% were also diagnosed with HT whereas only 2.5% were diagnosed with Graves' disease. The screening of other autoimmune disorders in the presence of an AD is necessary, especially in patients who remain unwell or who develop new non-specific symptoms despite proper treatment, so as to avoid the delay in diagnosis of other autoimmune disorders and thus avoid treatment delay.
References
BiroE, Szekanecz Z, Czirjak L, Danko K, Kiss E, Szabo NA, et al. Association of systemic and thyroid autoimmune diseases. Clin Rheumatol. 2006; 25(2):240–5.

DOI: 10.1530/endoabs.81.EP970

EP971

Hypovitaminosis D and Hashimoto's thyroiditis: effects of four-month supplementation therapy with oral cholecalciferol

Alice Villa[1], anna schiavo[1], Maria Gabriella Volpe[1], Andrea Sansone[2] & Francesco Romanelli[1]
[1]Sapienza University of Rome, Department of Experimental Medicine, Section of Medical Pathophysiology, Food Science and Endocrinology, Roma, Italy; [2]Tor Vergata University Polyclinic, Department of Systems Medicine, Endocrinology and Medical Sexology, Roma, Italy

Background
Hypovitaminosis D represents at present a worldwide public health problem. Recent studies have demonstrated the pleiotropic effects of vitamin D, in addition to its known actions on calcium-phosphorus metabolism. Among the several non-skeletal effects, a potential anti-inflammatory and immunomodulatory action has been suggested. Vitamin D deficiency has been reported in several chronic conditions associated with increased inflammation and deregulation of the immune system, such as Hashimoto's thyroiditis, and may act as a cofactor in the etiopathogenesis of these clinical conditions. On this basis, correction of hypovitaminosis D through therapeutic supplementation could have an impact on these pathologies.
Aim
to evaluate, in patients with Hashimoto's thyroiditis and hypovitaminosis D, the impact of cholecalciferol therapy on the parameters of calcium-phosphorus metabolism, antibody titer and indices of thyroid function.
Matherials and methods
a sample of 42 patients (6 men and 36 women) affected by hypovitaminosis D and Hashimoto's thyroiditis was recruited; oral cholecalciferol therapy was administered at a dosage of 100.000 IU, once a month during a meal. Before initiation (T0) and one week after the fourth dose of cholecalciferol (T1), the following parameters were evaluated: TSH, FT3, FT4, 25-OH-cholecalciferol, PTH, Calcium, Phosphorus, Creatinine, AbTg, AbTPO.
Results
a linear mixed-effects analysis was performed using R software (version 4.1.1). No significant changes in antibody titer or thyroid hormones were observed following cholecalciferol treatment. There was a statistically significant increase in serum 25-OH cholecalciferol after supplementation, with no significant changes in the other parameters. There was no significant reduction in PTH, although a downward trend was shown, after 4 months of therapy.
Conclusions
our results show that Vitamin D replacement therapy with cholecalciferol, in Hashimoto thyroiditis patients, does not affect the inflammatory nor the functional thyroid status, despite the fact that supplementation is effective in correcting hypovitaminosis D. No significant change in the antithyroid antibody titer emerged. Further studies are needed to investigate the immunoregulatory functions of vitamin D and its effects on thyroid autoimmunity.

DOI: 10.1530/endoabs.81.EP971

EP972

Unilateral graves' disease : a case report

Hager Khiari, Sabrine Mekni, Meriem Adel, Imen Rojbi, Youssef Lakhoua, Nadia Mchirgui, Ibtissem Ben Nacef & Karima Khiari
Charles Nicolle Hospital, Endocrinology, Tunis

Introduction
Graves disease is a frequent etiology of hyperthyroidism. It is defined as a diffuse hyperfunctioning of the thyroid gland caused by an autoimmune disorder. We herein present a rare case of unilateral Graves disease involving the right lobe of the thyroid.
Observation
A 44-year-old woman was referred for investigation of subclinical hyperthyroidism revealed by a routine check-up. On physical examination, she had tremor, eyelid retraction, tachycardia and the thyroid gland was no palpable. She complained of heat intolerance and nervousness for 1 year. On biological investigations, she had a serum TSH level of 0.001 mUI/l (normal range:0.35-4.94) and a serum free thyroxin (FT4) level of 1.48 ng/dl(normal range:0.7-1.48) : confirmed persistent grade 2 subclinical hyperthyroidism. She also had a serum glucose level of 0.96 g/l, a serum total cholesterol level of 1.51 g/l, a serum triglycerides level of 0.86 g/l, HDL-cholesterol level of 0.53 g/l and LDL- cholesterol level of 0.80 g/l. She had a white blood cells of 6680 elements/mm3, neutrophils of 3360/mm3 and lymphocytes of 2290/mm3. The liver and kidney function tests and c-reactive protein (CRP) were normal. The serum TSH receptor antibody level was high 17.54 UI/ml (normal range <2 UI/l) and the level of antithyroperoxidase antibody was within normal range. The bone mineral density was normal. The cervical ultrasonography showed a normal thyroid volume, normovascular gland and a nodule in the lower pole of the right lobe with a long-axis diameter of 14 mm EU-TIRADS 5. The thyroid scintigraphy revealed an increased uptake in the right thyroid lobe with an accompanying suppression in the left lobe. The fine needle aspiration biopsy of the nodule revealed benign appearance on cytological examination. The patient received antithyroid drug: methimazole and propranolol and recovered well.
Conclusion
Graves' disease usually presents with frank clinical signs of hyperthyroidism, bilateral exophthalmos, and a diffuse goiter. This case illustrates a rare case of unilateral involvement of the thyroid and a subclinical hyperthyroidism in a patient with confirmed diagnosis of graves' disease. Clinicians should be aware of this rare presentation of the disease as it affects treatment.

DOI: 10.1530/endoabs.81.EP972

EP973

Hyperthyroidism revealing thyroid heterotopia

Kadiri Chaimae & Lachkar Hassan
Hôpital Cheikh Zayd, Endocrinology and Metabolic Disease, Rabat, Morocco

Introduction
Thyroid heterotopia is an abnormal location of coexisting normal thyroid tissue with a normal organ and normal location. It is a congenital anomaly due to a defect in the maturation of the thyroid tissues, which is distinguished from ectopic thyroid and from a thyroid cancer metastasis.
Observation
We report the case of a 65-year-old patient, with no notable history, who consulted for clinical signs of thyrotoxicosis associating asthenia, tachycardia, thermophobia and unquantified weight loss. The thyroid hormone balance confirmed hyperthyroidism (TSH at 0 mIU/l and high FT4). Cervical ultrasound showed a normal thyroid appearance. Scintigraphy thyroid test with Technetium 99m revealed a nodule under the left hyper-fixing maxilla extinguishing the thyroid parenchyma. The patient received treatment with iodine 131 iodine therapy at a dose of 20 mcu. The evolution is marked by a disappearance of the clinical signs and a normalization of the thyroid profile. A control thyroid scintigraphy was performed objectifying a disappearance of the nodule under the left maxilla.
Discussion and conclusion
Sub maxillary thyroid heterotopia is rare, the clinical expression can be variable depending on function of neighboring organs, the diagnosis is essentially based on scintigraphy thyroid, which makes it possible to objectify hyper fixation and to obtain a precise etiological diagnosis in front of the discrepancy between the thyroid profile and the cervical ultrasound. Treatment by iodine therapy allows rapid healing.

DOI: 10.1530/endoabs.81.EP973

EP974

Cervicomediastinal thymic cyst mimicking thyroid : A case report

El Omri Malika, Amany Mallat & Marwa Ben Njima
University Hospital Farhat Hached Sousse, ENT, Tunisia

Introduction
Cervical thymic cysts are among the rarest congenital neck masses. Thymic migration into the superior mediastinum during organogenesis explains the topography and diversity of clinical presentations of these cysts. Due to the possibility of mediastinal extension, the management of these lesions is different than other congenital neck masses. The aim of our work is to present the clinical, radiological, and therapeutic features of cervicomediastinal thymic cysts.
Case report
A 13-year-old child was referred to our hospital for chronic cervical swelling. Clinical examination revealed a left basicervical mass. This *mass* was firm and *painless*. The rest of examination was without abnormalities. He did not have any neurological symptoms. Ultrasound and cervical Computed Tomography showed thyroid plunging from the lower pole of the left thyroid. On the surgical field, thyroid-independent cystic formation from the upper mediastinum with extension to the cervical region was found. A complete excision was performed after ligature and section of the lower cystic attachments. The anatomopathological examination diagnosed a thymic cyst with thymic parenchyma hyperplasia.
Conclusion
It's very important to recognize a cervicomediastinal thymus cyst as a differential diagnosis of pediatric neck masses, such as cervical lymphadenopathy, branchial anomalies, vascular malformations, inflammatory lesions and neoplasm. Ultrasound and CT scan can help to establish the etiological diagnosis.

DOI: 10.1530/endoabs.81.EP974

EP975

Correlation between thyroid nodules cytologies applying the Bethesda System with post-thyroidectomy histopathological diagnosis

Laura Mola Reyes[1], Lorea A. Herraiz Carrasco[2], Cristina Martin-Arriscado Arroba[3], Laura Kanaan Kanaan[2], Teresa De Grado Manchado[2], Rona H. Penso Espinoza[2], Irene Crespo Hernández[2] & Maria Elena Mendoza Sierra[2]
[1]Hospital Central de la Defensa Gómez Ulla, Madrid, Spain; [2]Hospital Central de la Defensa Gómez Ulla, Endocrinology and Nutrition, Madrid, Spain; [3]Hospital Universitario 12 de Octubre, Instituto de Investigación I+12., Madrid, Spain

Introduction
Thyroid nodules represent a common cause of specialist consultation, with a risk of malignancy of 4-15%. The most widely used cytopathological method for diagnosing thyroid cancer is fine-needle aspiration biopsy (FNAB) of thyroid nodules and the use of the Bethesda system (BS) for cytopathological reporting. We conducted the present study to report our experience using the BS, and to compare the results obtained with this system with the final histopathological results of the thyroidectomies performed.
Material and methods
Analytical study was carried out comparing the results of FNAB according to the BS, and the final result of histopathology of patients with thyroid gland lesions who consulted at the Hospital Central de la Defensa Gómez Ulla (Madrid), during the year 2020. The results were expressed as mean $\pm$ standard deviation for quantitative variables and as absolute and relative frequency for qualitative variables. The comparison between the characteristics of the sample and the BS was carried out using the chi-square test and ANOVA, adjusting for the Bonferroni host-post test. Statistical software: Stata InterCooled for Windows version 16. Significance level: 0.05.
Results
Reports of 201 cytologies corresponding to 152 patients were reviewed. Mean age 65.6 $\pm$ 15.1 years. Predominantly female sex 75.0%. Main reason for FNAB request: size of the nodule (40.5%). Mean size of biopsied thyroid nodules: 23.5 ± 10.5 mm. The highest percentage of cytologies corresponded to the Bethesda II category: 152 (75.6%), followed by Bethesda I: 26 (12.9%), III: 11 (5.5%), V: 6 (3, 0%) and IV: 3 (1.5%), VI: 3 (1.5%). 15 patients (9.9%) underwent surgery, corresponding to 25 cytologies performed (12.4%). 7 malignancies were identified. There was a final histopathological result of malignancy in 14.3% of Bethesda II, 33.3% in Bethesda III, 0% in Bethesda IV, 100% in Bethesda V, and 66.7% in Bethesda VI (p-value $= 0.013$). Overall, categories IV, V and VI had a malignant lesion in the final histopathology diagnosis in 66.7% of cases (positive predictive value, PPV). 85.7% of Bethesda II, had a benign lesion (negative predictive value, NPV). Considering only patients with satisfactory samples, the diagnostic accuracy was 73.7%.

Conclusion
The BS for the interpretation of the FNAB of thyroid nodules enhances the diagnostic certainty and assists the medical-surgical team in the therapeutic decision. In our institution, most part of cytologies were reported as benign. Regarding patients who underwent thyroidectomy, FNAB showed a high NPV, with a lower PPV.

DOI: 10.1530/endoabs.81.EP975

EP976

Anaplastic thyroid carcinoma: about 7 cases

Ezer Chebil, Jebahi Sameh, Thabet Wadie, Hassnaoui Mahdi & Mighri Khlifa
Taher Sfar University Hospital, ENT, Mahdia, Tunisia

Introduction
Anaplastic thyroid cancers are undifferentiated malignancies accounting for 2% of thyroid cancers.
Objective
To study the clinical, evolutionary and therapeutic characteristics of these carcinomas.
Materials and methods
A retrospective study covering 7 cases collected at our ENT department between 1994 and 2021.
Results
They were 6 women and one man with an average age of 50 (41-78). The reason for consultation was cervical swelling 100% of the time. Dyspnea was noted in 2 cases. The average duration of the symptomatology was 14 weeks. The tumor was plunging into the mediastinum in 2cas. In 4 cases, there was an invasion of the trachea and/or sub-hyoid muscles. Lymph node metastases were noted in all patients, bone in 2 patients and lung in 1 case. Histological confirmation of the diagnosis was made on thyroidectomy in 3 cases, and on a micro-biopsy of the thyroid gland in 4 cases. A tracheotomy was done in 3 cas. Three patients had a total thyroidectomy. The rest of the patients were inoperable. Radiation chemotherapy was indicated in all patients. Six patients died after an average delay of 11 months [8 months to 13 months]. A patient is still alive with a one-month decline.
Conclusion
Anaplastic thyroid carcinoma is a cancer with a dark prognosis. Patients in the localized disease stage can expect better survival. Therapeutic research explores targeted therapies that block the EGF receptor or inhibit neoplastic angiogenesis.

DOI: 10.1530/endoabs.81.EP976

EP977

Radiofrequency thermal ablation for a small papillary thyroid carcinoma: a case report

Mee Jung Rachele Mattarello[1], Francesca De Santi[1], Roberto Mingardi[1] & Mauro Mazzucco[2]
[1]Casa di Cura Villa Berica, Endocrinology and Diabetology Service, Vicenza, Italy; [2]Casa di cura Villa Berica, Minimally Invasive Cancer Therapy Center, Vicenza, Italy

Recently ultrasound-guide radiofrequency thermal ablation has been proposed as an effective and safe procedure for treating patients who have low risk papillary thyroid microcarcinomas or are unfit for surgery. We present the case of a 56 years old patient with a small (10 mm) thyroid nodule diagnosed as TIR 4, suspect citology for papillary carcinoma after fine needle aspiration. The nodule was also studied with CEUS (Sonovue US contrast medium) which showed increased vascularization in the arterial phase compared to the remaining parenchymna and late wash out. We proposed the possibility of radiofrequency thermal ablation to our patient. We used 1 cm active tip electrode needle (HS Amica Gen) with moving shot technique: 3 shots at 30W power for 5 minutes and 15 seconds. The Procedure was safely and effectively carried out. Follow examinations with ultrasonography and CEUS conduced after 1,3,6 months demostrated a complete necrosis with avascular area and progressive reduction of size in the treated site. Anyway we repeated the fine needle aspiration 6 month later and the sample detected only very poor cellularity inflammatory cells, amorphous material and no neoplastic cells. Our experience confirmed that the radiofrequency ablation can effectively eliminated small papillary carcinomas with a very low complication rate. We have to consider this alternative strategy for treatment of small indolent papillary thyroid carcinomas alternatively of traditional patients even without surgical contraindication.

DOI: 10.1530/endoabs.81.EP977

EP978

When sarcoidosis mimics cervical metastasis of thyroid cancer: a case report

Sara SI AMER[1], Imene Benoumechiara[1] & Nora Soumaya Fedala[1]
[1]University Hospital Center Mohamed Lamine Debaghine, Department of Endocrinology, Diabetology and Metabolic Diseases, Algiers, Algeria

Introduction
Sarcoidosis is a systemic inflammatory disease characterized by noncaseating granulomas. Its pseudo-tumor manifestation in certain organs such as the thyroid can mimic thyroid carcinoma and lead to erroneous therapeutic decisions. We report a case of sarcoidosis with cervical adenopathy initially considered as a cervical metastasis of thyroid cancer.
Observation
A 61-year-old woman, with a history of spontaneous subacute subdural hematoma operated in 2010, Followed at our level in consultation since 1991, for postoperative hypothyroidism, the patient underwent a left lobo-isthmectomy of a thyroid nodule suspect whose pathological study came back benign. She presents suddenly in consultation for a left cervical tumefaction on the bed of thyroid remnant which appeared recently and quickly in two months. It is a left basi-cervical mass of 4 cm, mobile and painless, without inflammatory or compressive signs, without palpable cervical lymphadenopathy, or signs of dysthyroidism,. The initial exploration made of a thyroid ultrasound showed a large mass occupying the suspicious left thyroid compartment with doubtful cervical lymphadenopathy, followed by a fine needle aspiration returned Bethesda IV. Not operated given the disappearance of the mass following a course of corticosteroids for an idiopathic thrombocytopenia discovered in parallel. This event made it possible to rectify the diagnosis thanks to a new exploration. Ultrasound found a free left thyroid compartment with bilateral cervical lymph node formations and a large suspect right supraclavicular lymphadenopathy, a dosage of thyroglobulin in needle aspiration biopsy fine was realized returning negative eliminating the thyroid origin and cytopuncture found granulomatous adenitis without caseous necrosis compatible with sarcoidosis. Biologically, the converting enzyme was twice normal and there was high calciuria. The CT scan shows a diffuse interstitial pneumopathy associated with cervical and mediastino-pulmonary lymphadenopathy concluding in an aspect of stage 3 sarcoidosis. The presumptive diagnosis was confirmed histologically by a bronchial biopsy.
Conclusion
The etiological diagnosis of a cervical mass or cervical lymphadenopathy, can represent a real challenge for the clinician. On a ground of thyroid pathology, the elimination of a neoplastic cause is a priority, sarcoidosis with these systemic and heterogeneous manifestations can constitute a diagnostic trap to be taken into consideration.

DOI: 10.1530/endoabs.81.EP978

EP979

Parathyroid carcinoma: about 3 cases and review of literature

Rachida Bouattay, Emna Bergaoui, Maroua Naouar, Mehdi Ferjaoui, Heyfa Belhadjmiled, Amel Elkorbi, Naourez Kolsi, Kaled Harrathi & Jamel Koubaa
Fattouma Bourguiba Hospital, ENT, Monastir, Tunisia

Introduction
Parathyroid carcinoma is a very rare tumor. The reported incidence is between 0.5 to 5% of primary hyper parathyroidy in various series. This entity does not present any clinical or biological specificity compared to the parathyroid adenoma which exposes to diagnostic difficulties.
Objective
The aim of our presentation is to study the clinical, therapeutic and evolutionary aspects of parathyroid carcinomas.
Material and methods
This is a retrospective study of 3 cases of parathyroid carcinomas treated in our department over a period of 22 years (2000-2021).

Results
There are two women and one man, with a history of recurrent renal lithiasis in one case and a parathyroidectomy 10 years ago for parathyroid adenoma in one case. The average age was 54 years old. The average consultation time was 6 months. The reason for consultation was diffuse bone pain in two cases and a compressive anterior cervical swelling in one case. Calcium and parathormone levels were elevated in all our patients. Cervical ultrasound done in all cases and cervico-thoracic scan done in one case, did not suggest malignancy in all cases. The scintigraphy showed a fixation at the lower left parathyroid gland in two cases and lower right gland in one case. The treatment consisted of Para-thyroidectomy in all cases, associated with ipsilateral central dissection in two cases and ipsilateral lobo-isthmectomy in one case. Frozen section examination evoked malignancy in two cases. Definitive histology examination confirmed the diagnosis of parathyroid carcinoma with capsular rupture and vascular emboles in two cases. The lower left parathyroid gland was the most affected. The average tumor size was 4 cm (range 2 cm to 7 cm). The evolution was good in all cases with a mean follow-up of 4 years.
Conclusion
Diagnosis of parathyroid carcinoma can be difficult and the management still remains a challenge.

DOI: 10.1530/endoabs.81.EP979

EP980

Thyroidectomy in laryngeal squamous cell cacinoma

Masmoudi Mohamed, Chaima Zitouni, Wadii Thabet, Chebil Azer, Hasnaoui Mahdi & Mighri Khalifa
Taher Sfar Hospital, Otorhinolaryngology, Mahdia, Tunisia

Introduction
Intraoperative management of thyroid gland in laryngeal cancer is controversial. In fact, there is no uniform consensus about the need for thyroid surgery in laryngeal cancer.
Objective
Determine the incidence of thyroid gland invasion in patients undergoing surgery for laryngeal squamous cell carcinoma.
Methods
A retrospective study including 62 cases of laryngeal squamous cell carcinoma who underwent a total laryngectomy. A thyroid surgery was performed in case of a subglottic extension $\geqslant$ 1 cm, an anterior extralaryngeal extension (T4a) or evidence of thyroid gland invasion on CT-scan or intraoperatively.
Results
The mean age of our patients was 59 years, predominantly males (98,4%). Eighteen patients had a subglottic extension $\geqslant$1 cm. The tumor was staged T4a in 14 cases. A loboisthmectomy was performed in 16 cases. A total thyroidectomy was done in 2 cases. On histopathological examination, thyroid extension was found in 2 cases (11.11%). No case of hypoparathyroidism nor hypothyroidism was noted among patients treated with thyroidectomy.
Conclusion
Thyroid gland involvement in laryngeal squamous cell carcinoma is rare (0-30%). Furthermore, hemithyroidectomy causes hypothyroidism in 63% of patients, and if combined with radiotherapy, the incidence goes up to 89% of patients. Therefore, thyroidectomy shouldn't be performed systematically for patients treated with total laryngectomy. It should be done in case of a locally advanced disease with thyroid cartilage transfixion, a macroscopic thyroid gland invasion and a signific subglottic extension.

DOI: 10.1530/endoabs.81.EP980

EP981

Primary mucinous carcinoma of the thyroid gland: A rare tumour

Sirine Ayedi[1], Wadii Thabet[1], Manel Mallouli[2], Imen Achour[1], Bouthaina Hammami[1] & Ilhem Charfeddine[1]
[1]Habib Bourguiba Hospital, University of Sfax, Otorhinolaryngology, Tunisia; [2]Habib Bourguiba Hospital, University of Sfax, Pathology, Tunisia

Introduction
Primary mucinous carcinoma of the thyroid gland is extremely rare. To the best of our knowledge, only nine cases have been reported in the literature. Our aim is to report a case of primary mucinous carcinoma of the thyroid gland and to describe its diagnostic and prognostic features.

Case Report
A 55-year-old man referred to our department for a 2-month history of an anterior neck mass associated with dysphagia. Physical exam showed a 4-cm and hard, right anterior neck mass, with left cervical lymph nodes (group V). Ultrasonography identified a 3-cm right thyroid nodule: EUTIRADS 5 with bilateral suspicious cervical lymph nodes. CT scan revealed a 3-cm hypodense right thyroid nodule associated with several mediastinal and cervical lymph nodes. TSH level was normal. Fine-needle aspiration (FNA) result was "nondiagnostic." The patient underwent total thyroidectomy with bilateral central (group VI) and lateral neck dissections (groups II, III and IV). The tumour invaded the strap muscles and the left thyroid lobe. Several lymph nodes were noted in the central group, lateral cervical and mediastinal regions. Intraoperative examination was in favour of a poorly differentiated thyroid carcinoma. Postoperative course was uneventful. The histologic exam (with immunohistochemical study) confirmed the diagnosis of a primitive mucinous carcinoma of the thyroid gland. Surgical margins were positive. Lymph node metastases were noted in the central and lateral neck regions. The patient died 15 days after the surgery.
Conclusion
Primary mucinous carcinoma of the thyroid gland is unusual. Differential diagnosis must be discussed with other primary typical thyroid carcinomas or adenomas, metastatic carcinoma of the lung, breast, colon and other organs. Primary mucinous carcinoma has a worse prognosis than common thyroid carcinomas: survival ranging from 1 month to 2 years.

DOI: 10.1530/endoabs.81.EP981

EP982

Association between vitamin D serum concentration and development of papillary thyroid cancer

Darko Katalinic[1], Ivan Aleric[1], Aleksandar Vcev[1], Miljenko Solter[2], Irena Ranogajec[3] & Lars Toetome[4]
[1]Faculty of Dental Medicine and Health and Faculty of Medicine, J. J. Strossmayer University, Osijek, Croatia; [2]School of Medicine, University of Zagreb, Zagreb, Croatia; [3]Clinical Hospital Sveti Duh, Zagreb, Croatia; [4]Center for Cancer Medicine, Oslo, Norway

Purpose
Papillary thyroid cancer (PTC) is the most common thyroid and endocrine malignancy worldwide. Vitamin D (calciferol or 25-hydroxyvitamin D) (25(OH) D) has been postulated as a key modulator in several cancer-related pathways, although its contribution to PTC still remain controversial. The aim of the study was to analyse the correlation between 25(OH)D serum levels and 25(OH)D insufficiency as well as the risk of development of PTC and its variants: classical type (CV-PTC), tall cell type (TCV-PTC) and follicular variant (FV-PTC).
Methods
The study included 259 patients: 112 patients diagnosed with PTC (CV-PTC, n = 78; TCV-PTC, n = 8; FV-PTC, n = 26), and 147 patients diagnosed with benign thyroid nodules, all aged 43-71 $\pm$ 7 years. Diagnosis of the PTC and its variants was confirmed with cyto/histopathological examination. The serum levels of 25(OH)D were measured by fully automated chemiluminescentmicroparticle immunoassay (CMIA). 25(OH)D insufficiency was defined as a serum 25(OH)D level $<$75 nmol/l.
Results
The prevalence of 25(OH)D insufficiency was 38.2%. Serum 25(OH)D levels and the prevalence of 25(OH)D insufficiency showed no significant differences between both group of patients (P=0.65). Among PTC patients, 25(OH)D insufficiency was not associated with any PTC subtype or other clinical manifestation (P=0.87).
Conclusions
This study shows no association of 25(OH)D insufficiency with the development of PTC, different PTC subvariants or any other clinical characteristic of PTC.

DOI: 10.1530/endoabs.81.EP982

EP983

A rare cause of metastasis to the thyroid gland: cervical carcinoma

Erhan Hocaoglu, Ensar Aydemir, Coskun Ates, Filiz Mercan Saridas, Soner Cander, Ozen OZ GUL, Canan Ersoy & Erdinc Erturk
Uludag University Medical School, Endocrinology, Bursa, Turkey

Introduction
Metastasis to the thyroid gland is a rare clinical presentation. The most common sites of primary tumors that metastasize to the thyroid gland are kidney, lung, gastrointestinal system and breast. Primary gynaecological tumors are account for only 3% of secondary thyroid malignancies. Here, we present a case of thyroid metastasis from squamous cell carcinoma (SCC) of the cervix.
Case
A 54-year-old female was consulted to our clinic with the pathology result of subtotal thyroidectomy. Five years ago, she had been diagnosed with cervical SCC treated with total abdominal hysterectomy and bilateral salpingo-oophorectomy and radiotherapy. The patient had no other known comorbidities. She had a history of lung metastasis. Two months ago, in addition to lung, pathological increased activity uptake (SUVmax 5.7) in the right thyroid lobe was reported in PET-CT. A 7.6 mm hypoechoic nodule was detected in the right thyroid lobe on ultrasound, and the result of fine needle aspiration biopsy was reported to be compatible with SCC. She was operated for lung metastasis last month, SCC was found in two regions, and adenocarcinoma in one region, respectively. Afterwards, right subtotal thyroidectomy was performed for suspected thyroid metastasis. The pathology result was reported as metastatic SCC. Tumoral tissue was 18x17x10 mm and tumor cell groups were scattered among the thyroid follicles. When the patient was consulted, thyroid function tests were normal, calcitonin was negative, thyroglobulin level was 22.4 ng/ml and anti-thyroglobulin 1.5 IU/ml. Thyroglobulin and thyroid transcription factor-1 (TTF-1) staining were requested from the pathology of the patient and negative staining was obtained. The patient was accepted as thyroid metastasis of cervical cancer. In addition to chemotherapy, the patient received radiotherapy to the neck and thorax. Six months later, a 23x20 mm soft tissue lesion was detected in the right thyroid lobe on ultrasound. Three months after that, a 45 mm mass (SUVmax 8.9) extending from the right thyroid lobe to the vertebral corpus was detected on PET-CT. Tracheostomy and gastrostomy were performed. The patient died shortly after.
Conclusion
Thyroid metastasis from cervical cancer is very rare and only a few cases have been reported. Patient who present with a thyroid nodule and has a history of a previous malignancy should be evaluated for metastatic disease.

DOI: 10.1530/endoabs.81.EP983

EP984

Thyroglobulin is a poor predictor of differentiated thyroid cancer in patients operated for thyroid nodular diseases

Shoham Rigbi[1], Lior Baraf[2, 3], Ben-Zion Joshua[3,4], Uri Yoel[2, 3] & Merav Fraenkel[2,3]
[1]Ben Gurion University of the Negev, Goldman School of Medicine, Be'er Sheva, Israel; [2]Soroka Medical Center, Endocrinology, Be'er Sheva, Israel; [3]Ben Gurion University of the Negev, Faculty of Health, Be'er Sheva, Israel; [4]Barzilai Medical Center, ENT, Ashkelon, Israel

Background
Thyroglobulin, serves as a specific tumor marker following thyroidectomy in differentiated thyroid cancer (DTC) patients. However, its role as DTC predictor in patients with thyroid nodules (TN) is controversial.
Aim
We aimed to assess the potential role of preoperative serum thyroglobulin concentration to predict DTC in patients who were operated for thyroid nodular disease.
Methods
This retrospective study included patients who had partial or total thyroidectomy between January 2014 and May 2019, with preoperative diagnosis of benign multinodular goiter (MNG) or a TN with indeterminate cytology (INC; Bethesda system 3/4 categories). We compared patients for demographic, clinical, imaging, and biochemical data according to their final diagnosis: DTC or benign TN disease. Further statistical analysis included odds ratios calculation and receiver-operator curves (ROC) analysis.
Results
Of 131 patients who met inclusion and exclusion criteria, the indication for surgery was benign MNG in 69, and TN with INC in 62 patients. Final diagnosis of DTC was reported in 18/69 (26%) and 30/62 (48%) of patients with preoperative diagnosis of benign MNG and INC-TN, respectively. Preoperative Median thyroglobulin was 148.5 ng/ml (IQR 67.8-1158.5) vs. 190 ng/ml (IQR 62.4-574), in malignant and benign MNG respectively ($P=$ 0.97), and 160.5 ng/ml (IQR = 82.2-536.7) vs. 205.5 ng/ml (IQR = 65.2-821.5) in malignant and benign INC-TN respectively ($p=$ 0.93). Nodule diameter, TSH level, and thyroglobulin did not differ between patients with final diagnosis of DTC versus those with benign histology.
Conclusion
Preoperative serum thyroglobulin alone is insufficient to differentiate preoperatively between malignant and benign thyroid disease.

DOI: 10.1530/endoabs.81.EP984

EP985

An unusual association between medullary thyroid carcinoma and testicular seminoma: Chemotherapy-induced complications, genetic predisposition or random relationship?

Allin Septar[1], Romeo Smarandache[2], Dan Alexandru Niculescu[1], Andrei Goldstein[1], Elena Braha[2], Andrei Muresan[2], Andra Caragheorgheopol[2], Dana Terzea[1], teodor constantin[2], Larisa Buduluca[1] & Madalina Musat[2,3]
[1]Inst. National de Endocrinologie C.I. Parhon, Bucuresti,; [2]Inst. National de Endocrinologie C.I. Parhon, Bucuresti, Romania; [3]Carol Davila University of Medicine and Pharmacy, Bucharest, Romania, Bucharest, Romania

Medullary thyroid carcinoma (MTC) is a rare malignancy arising from parafollicular C cells of the thyroid gland, sometimes due to germline mutations in the RET protooncogene. Testicular cancer is the most common malignancy in men aged 15 - 40 years with survival rates improved by the introduction of cisplatin therapy in the late 1970s. Nonetheless, platinum-based chemotherapy was shown to increase the risk of a solid second cancer with substantially increased site-specific risk of malignancies of thyroid, melanoma, kidney and bladder.
Case report
We present the case of a 42-year-old man diagnosed with MTC during oncological follow-up for testicular seminoma.18FDG PET-CT showed increased uptake in a single thyroid nodule 1 month after completion of chemotherapy (3 cycles of cisplatin, etoposide and bleomycin). The patient had left orchiectomy 8 months before. Thyroid ultrasound revealed an isoechoic nodule on the lower right lobe of 4.7/3.5/3.5 cm and suspicious bilateral lymph nodes. High serum levels of calcitonin (3820 pg/ml), carcinoembryonic antigen (12.2 ng/ml) and fine-needle aspiration citology smears were suggestive of MTC. Screening for other components of multiple endocrine neoplasia 2 syndromes was negative and no germinal mutations in the RET gene were detected either. Total thyroidectomy along with bilateral neck lymph node dissection were performed. Pathology yielded a diagnosis of MTC in the right lobe with metastasis in one ipsilateral lymph node. Immunohistochemistry revealed diffuse staining for Chromogranin A, TTF1 and CEA, weak focal staining for Calcitonin and strong SSTR2 and SSTR5 positive staining. Postoperative follow-up at 6 and 8 weeks revealed high serum calcitonin (338 pg/ml) and cervical ultrasound showed a small tissue remnant in thyroid bed and several suspicious cervical lymph nodes. No other mets were detected on 18FDG PET-CT. Second intervention surgery for neck dissection was performed with several metastatic lymph nodes excision and calcitonin reassessment was scheduled at 6 wks postop follw-up.
Discussion
The relationship between papillary and follicular thyroid cancer along with testicular germ cell tumour has been described as a consequence of cisplatin chemotherapy, however literature review showed no association of MTC and testicular seminoma so far. Screening with Next Generation Sequencing panel for 4813 Genes (TruSight^{TM}) is under consideration.
Conclusion
Association of Ret negative MTC and testicular seminoma diagnosed 8 months apart suggest synchronous association of the two cancers worth of a wider genetic screening with NGS.

DOI: 10.1530/endoabs.81.EP985

EP986

Male gender is independent factor of poor prognosis in medullary thyroid cancer

Arseny Semenov[1,2], Roman Chernikov[1], Dmitry Buzanakov[1, 2], Anna Zolotukho[2], Anna Uspenskaya[1], Nataliya Gorskaya[1], Ivan Ziborov[2], Igor Chinchuk[1], Konstantin Novokshonov[1], Yuliya Karelina[1], Fedorov Elisey[1], Viktor Makarin[1], Dina Rebrova[1], Shamil Shihmagomedov[1] & Iliya Sleptsov[1,2]
[1]Saint Petersburg State University, Saint Petersburg State University clinic, Saint-Petersburg, Russian Federation; [2]Saint Petersburg State University, Medical Faculty, Saint-Petersburg, Russian Federation

Background
*The medullary thyroid carcinomas comprise 5-7% of all thyroid carcinomas. At the same time, they are responsible for up to 13% of all deaths of thyroid cancer.*Incidence of sporadic medullary thyroid cancer in population 5-6 time higher in women, probably partially because women are likely to have thyroid nodules and undergo medical examination.
Objective
The aim of the study is to determine how gender affects prognosis in patients with medullary thyroid carcinoma
Materials and methods
A continuous retrospective cohort study of patients who underwent primary surgery for medullary thyroid carcinoma in 2010-2020 at the N.I. Pirogov Clinic for Advanced Medical Technologies, Saint Petersburg University, was conducted. Preoperative ultrasound data, basal serum calcitonin levels preoperatively and postoperatively on the 1st day after surgery, as well as histological examination data of surgical specimens were evaluated. Postoperative observation data for a period of at least 1 year were obtained for 347 patients. Patients were distributed by age to 6 age groups. Data analysis was performed using Tibco Statistica 14
Results
Patients were divided by percentage or by age and compared with each other. Male patients had a larger tumor size and basal calcitonin levels in all groups except over 70 years of age. The difference was significant and did not depend on the RET status of heritability. It is noted that with increasing age, the odds ratio of an aggressive course increased from 3.2 in all patients under 50 years to 9.25 from 50 to 60 years and 49.9 from 60 to 70 years. In the group over 70 years of age, OR is not significant due to the small number of patients and the death of most male patients with aggressive forms at an earlier age. Mostly medullary thyroid cancer even metastatic is indolent and found occasionally so difference caused by higher rate of symptomatic disease in men was found insignificant. The male sex significantly correlated with the risk of invasion into the surrounding tissues 0.715503, necrosis 0.547170, perineural growth 0.550827, the number of affected lymph nodes in the central and lateral tissues of the neck 0.465853 and 0.406780 respectively, with a probability of repeated interventions 0.485560 and a shorter recurrence period 0.444950. With a weak correlation with the node size of 0.255830.
Conclusion
the male gender is associated with a greater risk of aggressive course of medullary thyroid carcinoma, less effective surgical treatment, and greater need for target therapy.

DOI: 10.1530/endoabs.81.EP986

EP987

Thyroid Carcinoma in patients with Graves' Disease: about 7 cases

Rachida Bouattay, Maroua Naouar, Emna Bergaoui, Heyfa Belhadjmiled, Mehdi Ferjaoui, Amel Elkorbi, Kaled Harrathi, Naourez Kolsi & Jamel Koubaa
[1]Fattouma Bourguiba Hospital, ENT and Head and Neck Surgery Department, Monastir, Tunisia

Introduction
Graves' disease (GD) is an autoimmune disorder characterized by diffuse hyperplasia and excessive production of thyroid hormone. The association between thyroid carcinoma and GD is controversial. Thyroid nodular lesions in patients with GD should raise a high suspicion of carcinoma. The aim of this study is to focus on the possibility of an association between hyperthyroidism and thyroid Carcinoma.
Materials and Methods
This is a retrospective study about 7 cases of differentiated thyroid cancer out of 52 patients operated for Graves' disease in ENT department of Fattouma Bourguiba Hospital of Monastir during a 20-year period (2000-2020).
Results
All patients were female. The average age was 50 years [17-68]. Preoperative thyroid ultrasound revealed a nodular goiter in all cases, suspicious nodules in 4 cases. Indications for surgery included the following: resistance to medical treatment in 2 cases and nodular goiter with suspicious nodules in 4 cases. Frozen histological examination disclosed the presence of carcinoma in 5 cases. These patients underwent a total thyroidectomy, associated to bilateral central neck lymph node dissection. The histology concluded to the diagnosis of a papillary carcinoma in all cases. Among them, there were 2 cases of microcarcinoma. None of the cases showed lymph node metastasis. Surgical treatment was followed by radioactive iodine therapy in all cases. With a mean follow-up of 4 years, there was no distant metastasis or cancer recurrence.
Conclusion
Thyroid nodular lesions in patients with GD are not uncommon. Thus, careful evaluation of all thyroid nodules in GD patients is essential. It seems reasonable to check GD patients for the development of possible thyroid carcinoma, even if they are nodule free.

DOI: 10.1530/endoabs.81.EP987

EP988

Prevalence of differentiated thyroid carcinoma on hyperfunctioning or toxic thyroid nodules

Sandra Amuedo Domínguez[1], Irene De Lara Rodríguez[1], Ana R. Romero Lluch[1], Suset Dueñ as Disotuar[1], Juan L. Tirado Hospital[2] & Elena Navarro[1]
[1]Virgen del Rocío University Hospital, Department of Endocrinology and Nutrition, Seville, Spain; [2]Virgen del Rocío University Hospital, Department of Nuclear Medicine, Seville, Spain

Background
Autonomic hyperfunctioning thyroid nodules account for approximately 5% to 10% of all thyroid nodules. Compared with non-toxic nodules, hot nodules are traditionally believed to have an exceptionally low malignancy rate, and this has led to recommendations not to perform fine-needle aspiration (FNA) on these lesions, regardless of their size. However, recent studies have questioned the presumed low risk of malignancy in hot nodules, suggesting that the incidence of cancer has been underestimated and the need for further studies to provide more evidence in this regard.
Aims
1) To assess the prevalence of differentiated thyroid carcinoma (DTC) in the definitive histological examination in patients who underwent total thyroidectomy or hemithyroidectomy due to unique toxic nodules in a tertiary hospital. 2) To verify the existence of ultrasound predictors of malignancy on toxic nodules.
Methods
Retrospective descriptive study. Inclusion criteria: gammagraphically unique hot nodules from 2006 to 2021. Exclusion criteria: toxic multinodular goiters. Demographic data, performance or not of FNA, ultrasound characteristics of the nodules and thyroid function record at diagnosis were analyzed.
Results
The ultrasound classification by ACR TI-RADS of the remaining 68 benign nodules was: 1.5% TR1, 20.6% TR2, 20.6% TR3, 28% TR4, 1.5% TR5 and 28% unknown.
Conclusions
The prevalence of malignancy on the operated nodules was 4.2% (slightly lower than that described in the literature for non-toxic nodules). Higher scores in the malignancy risk scales on solitary toxic nodules could suggest the need to perform FNA on them.

Table 1 Baseline Demographic Characteristics

Toxic nodules (n)	172
Age (years)	64.4 ± 12.7
Gender (women), % (n)	74.4 (131)
Mena nodule size(mm)	28 ± 7.8
Underwent surgery,% (n)	41.3 (71)
Benign histology % (n)	95.7 (68)
Malignancy histology % (n)	4.2 (3)

Table 2 Sonographic characteristics of malignant interventional toxic nodules

Histologically confirmed DTC (3)	Risk ACR TI-RADS	Risk ATA
Papillary Carcinoma	4	Intermediate
Papillary Carcinoma	5	High
Follicular Carcinoma	3	Low

DOI: 10.1530/endoabs.81.EP988

EP989

King of the CASTLE? Immunohistochemistry in diagnosing rare thyroid carcinomas: a case report

Mihaela Stanciu[1,2] & Ruxandra Paula Ristea[2]
[1]"Lucian Blaga" University of Sibiu, Faculty of Medicine, Endocrinology, Sibiu, Romania; [2]Academic Emergency Hospital of Sibiu, Endocrinology, Sibiu, Romania

Introduction
Carcinoma showing thymus-like differentiation (CASTLE) is a rare, low-grade thyroid carcinoma, with indolent clinical course and usually a favorable prognosis. The clinical and imagistic features are not specific for CASTLE but similar to other malignant lesions of the thyroid, making diagnosis difficult and reliant on immunohistochemical examination. The conclusive diagnosis requires pathological examination and positive cluster of differentiation 5 (CD5) immunoreactivity
Case Report
Hence, the present paper aims to present a rare case of CASTLE compressing the trachea in a 50 year-old female patient, after being misdiagnosed in another center with undifferentiated thyroid carcinoma, for which she underwent an unsuccessful surgical procedure followed by postoperative radiotherapy and chemotherapy. The patient sought out a second opinion, for the investigation of an 18 months history of persistent dyspnea, dry cough, weight loss, loss of appetite, and fatigue, associated with dysphagia and dysphonia. The patient underwent a challenging radical surgery, total thyroidectomy and cervical lymphadenectomy being performed. Histopathological analysis of the specimen showed large areas of fibrosis, large, round vesicular nuclei with small nucleoli, low cytoplasm and peritumoral lymphoplasmacytic infiltration. Immunostaining for CD5 was positive. Postoperatively, no adjunctive radiotherapy was recommended, no acute complications were reported, replacement therapy with Levothyroxine was initiated, metastatic follow-up was negative and there was no evidence of loco-regional recurrence after 6 months of follow-up.
Conclusion
The diagnosis of CASTLE is difficult and requires a rigorous histological analysis and positive CD5 immunoreactivity. The improvement of long-term survival is based on the level of tumoral invasion in the adjacent structures, absence of metastasis and successful resection of the tumor and neck dissection. The particularity of this case consists in emphasizing the importance of establishing the accurate diagnosis for obtaining optimized management, with the purpose of reducing unnecesessary procedures.

DOI: 10.1530/endoabs.81.EP989

EP990

Thyroid storm in a patient with severe leptospirosis managed with veno-venous extracorporeal membrane oxygenation

Roy Christopher Ang & Yasmin Laura Marie Zuñiga
National Kidney and Transplant Institute, Division of Internal Medicine, Quezon City, Philippines

Background
Leptospirosis is an endemic zoonosis in the Philippines, with complications including jaundice from liver injury and acute kidney injury requiring renal replacement therapy. On the other hand, thyroid storm, most commonly in the setting of Graves's disease, is a rare complication of hyperthyroidism. To date, thyroid storm has not been documented in patients with severe leptospirosis.
Case Presentation
Herein, we present the case of a 52-year-old man, with no known thyroid disease and with prior wading in flood waters, who presented with fever, conjunctival suffusion, icterisia, and oliguria. He arrived on the 7th day of illness with hypotension and atrial fibrillation. Workups revealed low thyroid stimulating hormone (TSH), elevated free T4 (FT4), and elevated free T3 (FT3). There was also elevated serum creatinine, leukocytosis, and thrombocytopenia. He was diagnosed with severe leptospirosis, started on ceftriaxone intravenously, and underwent hemodialysis. He subsequently developed hemoptysis, prompting intubation and veno-venous extracorporeal membrane oxygenation (V-V ECMO) . Thyroid storm was suspected when he had persistent fever in the background of hyperthyroidism and atrial fibrillation. After starting propylthiouracil, super-saturated potassium iodide, and intravenous hydrocortisone, there was lysis of fever and improvement in hemodynamic status. On the 3rd day of V-V ECMO, significant improvement in oxygenation and resolution of pulmonary hemorrhage allowed weaning and decannulation. There was, however, eventual development of ventilator associated pneumonia and agranulocytosis, prompting the discontinuation of propylthiouracil. Despite the addition of broad-spectrum antibiotics, intractable metabolic acidosis and hypotension ensued, which led to the patient's demise. TSH receptor antibody was eventually revealed to be undetectable, while thyroid ultrasound was unremarkable.
Discussion
Overlap of symptoms between thyroid storm and severe leptospirosis, such as fever and jaundice, may delay early diagnosis and management of thyroid storm. Furthermore, the full therapeutic regimen was not maximized due to hypotension and development of agranulocytosis. While there is documented success on the use of V-V ECMO in severe leptospirosis, the utility of ECMO in thyroid storm is limited to Veno-Arterial ECMO for thyrotoxicosis-induced cardiomyopathy. To date, there have been no published reports of leptospirosis occurring simultaneously with thyroid storm.The absence of thyroid nodules or a diffusely enlarged thyroid gland, together with an undetectable thyroid receptor antibody, should prompt consideration of destructive thyroiditis from severe leptospirosis.
Conclusion
The case highlights diagnostic and management challenges in a rare case of thyroid storm in the setting of severe leptospirosis.
Keywords: ECMO, leptospirosis, thyroid storm, Weil's

DOI: 10.1530/endoabs.81.EP990

EP991

Thyroid abscess as a complication of post-COVID-19 subacute thyroiditis: a case report

Loubna Guissi, Ikram Amira, Kaoutar Rifai, Hind Iraqi & Mohamed Elhassan Gharbi
Ibn Sina University Hospital, Endocrinology, Rabat, Morocco

Introduction
Thyroid abscess is a rare pathology, with the incidence of less than 1% of all thyroid diseases. We describe a unique case of thyroid abscess complicating post-covid-19 thyroiditis, which is the first case reported in Morocco to our knowledge.
Case presentation
A 39-year-old man who had recently recovered from a mild episode of COVID-19 infection, consulted for weight loss, palpitations and neck pain. Examination of the neck revealed enlarged, firm, and tender thyroid gland. His electrocardiography revealed sinus tachycardia. Laboratory tests showed elevated erythrocyte sedimentation rate at 40 mm/h and c-reactive protein at 75 mg/l. TSH was low ($<$ 0.05 mU/l), T4 and T3 levels were elevated at 7.72 ng/dl (reference 0.77-2.02) and 11.23 pg/ml (reference 2.2-4.6), respectively. Thyroid peroxidase antibody and TSH-receptor antibody were negative. Ultrasound of the neck showed heterogeneous goiter with areas of thyroiditis, and reduced blood flow on Doppler study. The diagnosis of subacute thyroiditis was made, and the patient was discharged home on oral prednisone (60 mg) and atenolol (40 mg) daily. During the follow-up, the prednisone was gradually tapered off over 7 weeks, and atenolol was discontinued. The thyroid function tests returned to normal at 9 weeks follow up, however the patient developed a cervical swelling with pus discharge. Ultrasonography was consistent with Thyroid abscess. A retroviral screening for Human Immunodeficiency Virus was negative. Culture of the pus from the abscess obtained during the fine needle aspiration grew Staphylococcus aureus. The patient was successfully treated with percutaneous drainage and oral amoxicillin clavulanate.
Discussion
Thyroid abscess is a less seen diagnosis, mostly so as the gland is inherently protected. The encapsulation, rich blood and lymphatic supply, and iodine content inside offer the gland protection from being seeded. Thyroid abscess usually occurs in patients who are immuno-compromised, those with pre-existent thyroid pathologies or anatomic gland anomalies. Some authors have related thyroid abscess to neoplastic causes, thyroid nodule, subacute thyroiditis, Hashimoto's thyroiditis or traumatic causes. In our case, when no immunosuppression or anatomical factors are present, there was sufficient clinical and biological evidence within reasonable limits that failed to yield any other risk factor for thyroid abscess other than subacute thyroiditis that the patient developed after SARS-COV-2 infection.
Conclusion
Thyroid abscess is an unusual complication of post-COVID-19 subacute thyroiditis and can lead to significant morbidity. Therefore, clinicians must be aware of the presenting features and therapeutic options.

DOI: 10.1530/endoabs.81.EP991

EP992

Ectopic lingual thyroid presenting as massive bleeding in a high-risk surgical patient treated with radioactive iodine

Joaquin De Carlos, Jose Javier Pineda, Emma Anda, Marta Toni, Maria Dolores Ollero, Patricia Munarriz, Ana Irigaray, Ander Ernaga & Nerea Esparza
Hospital Universitario de Navarra, Pamplona, Spain

Introduction
Lingual thyroid ectopia is a rare congenital abnormality affecting embryogenesis of the gland descent from foregut through pre-tracheal region in the neck. Most cases have an asymptomatic course but may occasionally produce local obstructive symptoms. Diagnostic methods are ^{99m}Tc, ^{131}I or ^{123}I radionuclide scan, computed tomography scan, magnetic resonance, and ultrasound. Surgery is the elective treatment for cases presenting complaints or complications. Radioactive iodine ablation is an alternative for patients who refuse surgical intervention or unfit for anesthesia. We report 49-year-old women with an ectopic lingual thyroid presented as oral hemoptysis with high surgical risk, successfully treated with ^{131}I.
Materials and methods
A case report description conducted with the consent of the patient and with provisions of the Declaration of Helsinki.
Results
49-year women with relevant medical history such as primary hypothyroidism under thyroid hormone replacement, well controlled type 2 diabetes, HTA and morbid obesity (BMI 58). Presented to Emergency department with a 12-h history of upper gastrointestinal bleeding, mild dysphagia, and no respiratory symptoms. Gastroscopic examination demonstrates a jet arterial bleed above the epiglottis at the base of the tongue. Intubation was performed with surgical hemostasis by means of pharyngeal packing containing and resolving the hemorrhage. CT of the neck confirmed a well-defined rounded occupational image at the base of the tongue and floor of the mouth, in the midline, with intense and homogeneous enhancement, measuring 35x37x39mm, compatible with ectopic lingual thyroid that imprints on the oropharyngeal lumen. Thyroid ^{99m}Tc combined with single-photon emission computed tomography/computed tomography confirmed an increased radiotracer homogeneous activity on at this location. Hospitalization was complicated with bilateral pneumonia and bilateral acute pulmonary embolism (PESI 59, class I). Surgical option was denied because of patients' comorbidities and associated complications due to this conventional tongue surgery. She was treated with 16.5 mCi of ^{131}I remaining asymptomatic.
Conclusion
Lingual thyroid ectopia is a rare congenital anomality in population, that warrants treatment when it produces obstructive or compressive symptoms or complication arrives. Scintigraphy methods plays a major role in establishing the diagnosis, even though US and TC or RM may also be helpful in the process of differential diagnosis with other cervical masses. Surgery has been the conventional approach to remove ectopic thyroid gland. However, other strategies such as RAI are safe and efficient strategy for high risk surgical and comorbid patients, remaining them asymptomatic.

DOI: 10.1530/endoabs.81.EP992

EP993

Methimazole-induced cholestatic jaundice

Soltani Chayma[1], Rym Belaid[1], Abid Naourez[1], Hamzaoui Lamine[2] & Amri Raja[1]
[1]Mohamed Tahar's Maamouri Hospital, Internal Medicine Department, Nabeul, Tunisia; [2]Mohamed Tahar's Maamouri Hospital, Gastro-Enterology Department, Nabeul, Tunisia

Introduction
Methimazole is a widely prescribed antithyroid drug for the treatment of hyperthyroidism with a few adverse effects generally well-tolerated. However, methimazole-induced cholestatic jaundice (CJ) is a rare but serious adverse reaction. Herein we report a rare case of methimazole-induced CJ in a woman with hyperthyroidism.
Case report
A 57-years-old women presented to our endocrinology department with a 2-week history of asthenia, insomnia, tremulousness, and swollen eyes. On Physical examination she had a body weight of 69 kg, a body mass index of 23 kg/m^2, a blood pressure of 130/70 mm Hg and a pulse rate of 100 beats per minute. The neck examination revealed a homogenic and elastic goiter with a thrill. The eye examination showed bilateral and symmetric upper eyelid retraction, swelling and grade 1 exophtalmos. Laboratory tests showed hyperthyroidism with a low TSH of 0.006 µIU/ml and elevated freeT4 of 52.36 ng/l(9-17). The liver enzymes were normal. The ultrasound of the thyroid revealed a diffuse micronodular and hypervascular thyroid gland. Thyroid scintigraphy showed homogenous increased uptake of the thyroid gland. She was started on methimazole 30 mg a day and propranolol 10 mg three times a day. Six weeks later, she returned with severe jaundice, pruritus, dark urine and light-colored stool. The clinical findings showed a severe icterus. Physical examination of the abdomen, heart, liver, and spleen were unremarkable. She had neither fever nor signs of chronic liver disease. Initial tests were consistent with a CJ: elevated alanine aminotransferase 168 U/l (10-45), aspartate aminotransferase 213 U/l (10-40), gamma glutamyl transferase 129 u/l (7-50) and significantly elevated alkaline phosphatase 952 U/l (35-104), total bilirubin 321 mg/dl (5-17), conjugated bilirubin 319 mg/dl (2-5). The prothrombin time was normal. The hepatobiliary ultrasonography excluded biliary obstruction. The viral hepatitis, autoimmune hepatitis and primary biliary cirrhosis were also ruled out. Cholestatic jaundice due to methimazole was very likely. The medication was discontinued immediately. The patient was started on prednisone 1 mg/kg/day. The recovery was slow but complete after 7 weeks of methimazole withdrawal. She was then referred for iodine radiation treatment.
Conclusion
We discuss this case to study the rare association between methimazole use and cholestatic jaundice. This drug can cause severe but reversible CJ. Thus, physicians and patients should be aware of this adverse effect so that they can discontinue methimazole therapy upon the occurrence.

DOI: 10.1530/endoabs.81.EP993

EP994

Auto-immune polyglandular syndrome type IIIa: a case report

Rym Belaid, Soltani Chayma, Garbouj Wafa, Alaya Zeineb & Amri Raja
Mohamed Tahar's Maamouri Hospital, Internal Medicine Department, Nabeul, Tunisia

Introduction
Autoimmune polyglandular syndromes (APS) are rare polyendocrinopathies characterized by the failure of several endocrine glands as well as nonendocrine organs, caused by an immune-mediated destruction of endocrine tissues. The type IIIa APS is the association of thyroid autoimmune diseases, type 1 diabetes mellitus and other autoimmune conditions excluding Addison's disease and hypoparathyroidism. Herein, we report the case of autoimmune hypothyroidism associated to type 1 diabetes, systemic lupus erythematosus (SLE) and primary biliary cirrhosis (PBC) in a young woman.
Case report
A 35 years-old woman with a medical history of type 1 diabetes treated by insulin since the age of 9 years and autoimmune hypothyroidism diagnosed at the age of 25, presented to our internal medicine department with inflammatory polyarthralgia of the hands, wrests, ankles and shoulders accentuated in the last 4 months. The physical examination showed a butterfly shaped rash of the face, red spots on exposed areas that worsen with sun exposure and oral ulcerations. The blood investigations showed an accelerated erythrocyte sedimentation rate (VS) (80 mm/h), a normal blood white count with no lymphopenia and a normal serum calcium level. The X-rays of the aching joints didn't show erosions or pinches. The immunology tests showed positive anti-nuclear antibodies (ANA) (1/400) and anti-double-stranded DNA (anti-DNA). The SLE was diagnosed according to the criteria of the SLICC with a score of 5 points, ACR with a score of 4 points, EULAR/ACR 2019 with 20 points. The patient was started on hydroxychloroquine 400 mg a day and corticosteroids 10 mg a day. Further investigations were pursued showing an immunological profile compatible with PBC that was inactive at the moment of the diagnosis. The diagnosis of APS type IIIa was made after excluding an adrenal insufficiency by a normal 250 µg synacthen test.
Conclusion
We report the case of a female with type 1 diabetes, auto-immune hypothyroidism, SLE and PBC, which is a very rare combination. We present this case as evidence for the coexistence of several different immune-mediated diseases in the clinical context of a APS type IIIa. Thus, a regular follow up of these patients is needed to detect and treat the other auto-immunes disorders at an early stage.

DOI: 10.1530/endoabs.81.EP994

EP995

Coexisting grave's disease and coeliac disease in an adolescent with down's syndrome

Anissa Ben Bouzid, Rym Belaid, Nada Ben Abdelaziz, Naourez Abid & Raja Amri
Mohamed Tahar's Maamouri Hospital, Internal Medicine Department, Nabeul, Tunisia

Introduction
Trisomy 21 is the most common chromosomal disorder. It is associated with an increased risk of endocrinopathy particularly thyroid gland disorders. This is frequently a compensated hypothyroidism. Hyperthyroidism is rare. We report the case of an adolescent with Down's syndrome and celiac disease who presented with subclinical hyperthyroidism.
Case report
It was a 15-year-old female from a non-consanguineous marriage with a history of celiac disease on a gluten-free diet. The physical examination showed a stable weight of 48 kg, a height of 146 cm and a body mass index of 22.53 kg/m^2. She had a goiter visible in extension of the neck but no exophthalmos. She had no history of excessive sweating, diarrhea or tremors. Cardiovascular examination was unremarkable. Blood investigations noted a normochromic normocytic anemia of 11.3 g/dl. The thyroid assessment done as a part of an annual biological monitoring showed a TSH of 0.005 mUI/l and a free T4 of 17.21 pmol/ml (12-22). Anti-TSH receptor antibodies were positive. Cervical ultrasound showed a diffuse enlargement of the thyroid. The diagnosis of Grave's disease was retained.
Conclusion
Down's syndrome is a breeding ground for thyroid dysfunction. Celiac disease is common in people with down's syndrome and it is associated to various endocrine autoimmunities such as thyropathies. Hyperthyroidism is extremely rare. The diagnosis is often made through a systematic assessment, hence the interest of a biological control aimed at detecting dysthyroidism early to avoid complications that are potentially serious. The particularity of our observation was the association of celiac disease and grave's disease in an adolescent discovered by an annual thyroid check-up.

DOI: 10.1530/endoabs.81.EP995

EP996

Primary thyroid lymphoma: case report

Hatice Sebile Dökmetaş[1], Kü bra Karaipek[2], Meriç Dökmetaş[2], Fatih Kılıçlı[1], Ayberk Bayramgil[2], Güneş Dorukhan Çavuşoğlu[2] & Yaşar Özdenkaya[3]
[1]Medipol Mega University Hospital, Endocrinology, Istanbul, Turkey; [2]Medipol Mega University Hospital, Internal Medicine, Istanbul, Turkey; [3]Medipol Mega University Hospital, General Surgery, Istanbul, Turkey

Introduction
Primary thyroid lymphoma is a rare malignancy. In many series, it is reported that it is seen at a rate of 0.6-5% among thyroid cancers and approximately 2% among extranodal lymphomas. It is often seen as a painless mass in the neck. Almost all of them have underlying Hashimoto's thyroiditis. In many instances, thyroid lymphoma was recognized after thyroid surgery for suspected carcinoma. The most common thyroid lymphomas are B-cell and Hodgkin lymphomas. The distinction between primary and secondary lymphoma is important because of the variables in diagnosis, treatment, and prognosis. Surgery, chemotherapy, radiotherapy, or combinations can be used in the treatment.
Case
A 69-year-old male patient underwent total thyroidectomy and central neck dissection due to a 3.5x2.5 cm nodule in the right thyroid lobe. During the operation, it was observed that the mass lesion in the right lobe had progressed to the lateral carotid and invaded the right internal jugular vein. In addition, partial right internal jugular vein excision was performed. The pathology report was determined as large B-cell lymphoma and lymphocytic thyroiditis findings were observed in the surrounding thyroid tissue. Lymphoma involvement was present in most of the lymph nodes. There was vascular and muscle invasion. In patient blood tests free T3:1.7 pg/ml (N:2.04-4.4), free T4:1.15 pg/ml (N:0.93-1.7) TSH:3.72 mIU/ml (N:0 .27-4.2), and Thyroid autoantibodies negative detected. The patient received 4 cycles of R-CHOP (Adriamycin + Cyclophosphamide + Rituximab + Vincristine) chemotherapy protocol. The before and after treatment PET-CT was reported as: The focus showing pathological 18F-FDG uptake in favor of malignant involvement in the whole body cannot be identified.
Conclusions
Thyroid lymphoma, which is rarely seen in patients presenting with a thyroid mass, should also be considered. While Hashimoto's thyroiditis is seen in most primary thyroid lymphomas, primary thyroid lymphoma develops in only 0.6% of Hashimoto's thyroiditis cases.

DOI: 10.1530/endoabs.81.EP996

EP997

Influence of the mother's history during pregnancy on the development of hyperthyroidism in children living in conditions of iodine deficiency

Shakhlo Muratova[1], Anvar Alimov[1] & Shakhnoza Azimova[2]
[1]Republican Specialized Scientific and Practical Medical Center of Endocrinology named after academician E. Kh. Turakulov of the Ministry of Health of the Republic of Uzbekistan, Thyroidology, Tashkent, Uzbekistan; [2]Republican Specialized Scientific and Practical Medical Center of Endocrinology named after academician E. Kh. Turakulov of the Ministry of Health of the Republic of Uzbekistan, Pediatric Endocrinology, Tashkent, Uzbekistan

Our goal was to determine the anamnestic characteristics of mothers during pregnancy in children with hyperthyroidism living in conditions of iodine deficiency, which possibly contribute to the development of hyperthyroidism in patients of the pediatric group.
Materials and methods of research
the analysis of the anamnesis of mothers during pregnancy of 146 children and adolescents with hyperthyroidism. The control group consisted of 97 relatively healthy children under 18 whose parents agreed to participate. Statistical processing of the results was carried out using the statistical software packages 'SPSS 23 for Windows' ('IBM Corp. Armonk', NY, USA).
Results
Analysis of the mother's anamnesis during pregnancy of children and adolescents with hyperthyroidism are presented in Table 1. The results obtained indicate that the presence of autoimmune thyroid disease in the mother increases the risk of developing hyperthyroidism in the child by 7.5-8.2 times (OR = 8.2 (95% CI 3.1-21.5), $P<0.001$), while endemic maternal goitre during pregnancy and systemic autoimmune diseases (OR = 2.6 (95%

Table 1 Anamnesis of the mother during pregnancy of the studied children

		n	%	Chi-square	p
Graves' disease	Hyperthyroidism	11	7,5	0	
	Control	0	0		
Autoimmune thyroiditis	Hyperthyroidism	45	30,8	<0,001	***
	Control	5	5,2		
Diffuse goitre endemic	Hyperthyroidism	12	8,2	0,36	
	Control	6	6,2		
Systemic autoimmune diseases	Hyperthyroidism	11	7,5	0,69	
	Control	3	3,1		
Vitiligo	Hyperthyroidism	1	0,7	0	
	Control	0	0		
Type 2 diabetes mellitus	Hyperthyroidism	3	2,1	0	
	Control	0	0		
Overweight, obesity	Hyperthyroidism	16	11	0,03	*
	Control	3	3,1		
Polycystic ovary syndrome	Hyperthyroidism	1	0,7	0	
	Control	0	0		
Anaemia	Hyperthyroidism	35	24	<0,001	***
	Control	5	5,2		

CI 0.7-9.4), $P=0.69$) is not a reliable provoking factor (OR = 1.4 (95% CI 0.5-3.8), $P=0.36$). In addition, overweight and obesity (OR = 3.9 (95% CI 1.1-13.6), $P=0.03$), as well as anemia of varying severity in pregnant women (OR = 5.8 (95% CI 2.2-15.4), $P<0.001$) may increase the risk of developing hyperthyroidism in children. At the same time, vitiligo (0.7%), type 2 diabetes mellitus (2.1%), polycystic ovary syndrome (0.7%) were diagnosed only in mothers whose children had hyperthyroidism.
Conclusion
possible factors that increase the risk of developing hyperthyroidism in children living with iodine deficiency are the following maternal anamnestic indicators during pregnancy: Graves' disease, autoimmune thyroiditis, overweight and obesity, anaemia of pregnancy, type 2 diabetes mellitus, vitiligo and polycystic ovary syndrome.

DOI: 10.1530/endoabs.81.EP997

EP998

Thyroid disease in patients with type 1 diabetes

Joaquin De Carlos, Francisco Javier Basterra, Amaya Sainz De Los Terreros, Javier Garcia, Marta Garcia, Ana Iriarte, Miguel Marti & Maria Jose Goñi
Hospital Universitario de Navarra, Pamplona, Spain

Introduction
An increased risk of thyroid disease (TD) has been described in patients with type 1 diabetes (DM1) with respect to the general population. The objective is to establish the incidence and characterize the differences in patients who develop TD in relation to the debut of DM1 (previous, concurrent or a posteriori).
Materials and methods
Retrospective study of 1126 patients followed up in Endocrinology consultations in Navarra. Three types of TD were differentiated: hyperthyroidism (HI), hypothyroidism (HO) and autoimmune thyroid disease with normo function (AT). Clinical and analytical variables were analyzed. Comparison between the medians of the groups was performed using the Mann Whitney U test. Differences between categorical variables were analyzed using the $\chi 2$ test.
Results
The study population included 669 men (59.3%) and 459 women (40.7%), with a mean age at debut of 20 years and a mean follow-up of 11.4 years (7.6 sd). A total of 300 (26.6%) developed thyroid disease. The analysis of the 32 that already had TD before the onset of DM1 (8 HI, 21 HO, 3 AT) revealed thar women, gastric autoimmunity and younger patients had a higher risk of developing TD. 87 patients presented concurrent TD (10 HI, 40 HO, 37 AT) at the onset of DM1. Female gender, debut over 45 years and positive gastric autoimmunity was also more frequent in those 181 patients that developed TD at follow up (16 HI, 102 HO, 63 AT) of the DM1.
Conclusion
In the population studied, the cumulative incidence of TD in the follow-up of patients with DM1 was high, with hypothyroidism predominating. There are different clinical and analytical variables that can predict which risk groups have a greater predisposition to develop TD before, at the onset or after the diagnosis of DM1. The factors to be taken into account that affect a different susceptibility to develop TD are gender, age at DM1 debut, thyroid autoimmunity and gastric autoimmunity. Although confirmation is required in future studies, they may be indicative for closer surveillance.

DOI: 10.1530/endoabs.81.EP998

EP999

Serum selenium status in UK Graves' disease patients with and without orbitopathy

Carla Maden, Pei Chia Eng, Dri Choa, Rochan Agha-Jaffar, Jeremy Cox, Michael Yee, Stephen Robinson & Tessa Fayers
Imperial College Healthcare NHS Trust, United Kingdom

Introduction
Selenium supplementation is recommended for all patients with mild Graves' orbitopathy (GO). The thyroid gland contains high levels of selenium, which has an anti-oxidant effect and a role in the metabolism of thyroid hormones. The study on which this recommendation is based was conducted in countries of a selenium-deficient region and did not measure subjects' selenium concentrations. There is therefore no consensus on optimum dose, duration, or safety. Environmental selenium varies extensively between countries and no published studies report measured the baseline selenium status of UK GO patients. We aimed to determine baseline selenium status in a UK population, and compare this to Graves' patients without GO.
Methods
Baseline serum selenium status was measured in UK Graves' disease patients with and without orbitopathy between January – December 2021.
Results
There were 56 patients; 25 had orbitopathy (the mean Clinical Activity Score was 1.9), (20 females and 5 males, average age 48.8yrs) and 31 did not (26 and 5; 47.5). Average serum selenium was 1.13 (range 0.5-1.93, reference range 0.76-1.46 μmol/l); 1.14 in the GO group vs. 1.12 in the non-GO group. There were 12 current or previous smokers in the GO group (48%) vs. 8 in the non-GO group (26%).
Conclusion
These results show that baseline selenium status in GO and non-GO patients is largely within the normal range. This suggests that selenium may have lesser benefit in the UK compared to regions with lower environmental selenium. Patients may also be at risk of iatrogenic overdose. A randomised control trial investigating the clinical effects of selenium supplementation in a UK GO population with concurrent measurement of selenium status is warranted.

DOI: 10.1530/endoabs.81.EP999

EP1000

Assessment of thyroid function in healthy pregnant women living in iodine deficiency regions

Anastasia Rybakova, Nadezhda Platonova, Larisa Nikankina, Natalia Malysheva & Ekaterina Troshina
Endocrinology Research Centre, Moscow, Russian Federation

Background
During pregnancy, the physiology of the thyroid gland undergoes important changes. As a result, change levels of thyroid hormones. In the latest clinical guidelines, experts have recommended to perform population-based studies to determine reference intervals for thyroid hormones.
Aim
To evaluate the reference intervals of free thyroxine in different trimesters of pregnancy in women living in regions with mild iodine deficiency.
Materials and methods
We have conducted the observational multicenter cross-sectional study included 2008 healthy pregnant women at different trimesters of pregnancy, from three regions of the Russian Federation (Moscow, Ivanovo and Smolensk). We assessed the level of free thyroxine, antibodies to thyroid peroxidase, antibodies to serum thyroglobulin (Architect, Abbot, reference range 9-20 pmol/l), the level of iodine concentration in the morning portion of urine (cerium arsenic method) and we have conducted a questionnaire (date birth and gestational age). Women with elevated titers of anti-TPO and/or anti-TG antibodies were excluded from the study (245 women).
Results
We have determined the median iodine concentration: Moscow 111 μg/l, Ivanovo 125 μg/l, Smolensk 133 μg/l, which confirms the presence of mild iodine deficiency in the regions areas (median iodine concentration less than 150 μg/l in pregnant women corresponds to mild iodine deficiency). Reference intervals for free thyroxine are presented using the median, 2.5 and 97.5 percentiles with 95% confidence interval (Me [2.5;97.5] CI+-95%). We obtained the following results: 1st trimester ($n=386$): Me 11.7 [9.03;16.1] CI+1.96; -1.74; 2nd trimester ($n=478$): Me 10.7 [8.35; 13.8] CI+1.43; -1.28; 3rd trimester ($n=899$): Me 9.9 [7.73; 13.0] CI+1.41; -1.30.
Conclusions
Based on the results of our study, we determined the reference intervals of free thyroxine in healthy pregnant women without anti-TPO/TG antibodies living in mild iodine deficiency regions. We revealed a decrease in the level of free thyroxine by the third trimester, which can be physiological isolated hypothyroxinemia.

DOI: 10.1530/endoabs.81.EP1000

EP1001

Impact of age on hypothalamic-pituitary-thyroid axis

Snjezana Popovic Pejicic[1, 2] & Nina Pejicic[2]
[1]Medical Faculty, University of Banja Luka, Banja Luka, Bosnia and Herzegovina; [2]University Clinical Center of the Republic of Srpska, Banja Luka, Bosnia and Herzegovina

Background/Aim
Impact of age on hypothalamic –pituitary –thyroid axis, interesting from theoretical and practical aspects, have been studied. Our aim was to find out: correlation between T3 (triiodothyronine) and T4 (thyroxine) hormone level and old age, so as of other, for thyroid function relevant parameters: TSH (thyroid stimulate hormone), TRH (thyreothropin releasing hormone) test, thyroid ultrasonography, thyroid gland scintigraphy with ^{131} J, ^{131}J fixation test, thyroid antibodies and thyroglobulin.
Methods
Study included 125 subjects, divided in four groups, according to the age: control group (from 20 to 40 years); group A (from 41 to 50 years); group B (from 51 to 60 years) and group C (from 61 to 70 years), as well as into subgroups according to the sex. All patients were established total and free hormones T3, T4, TSH and test with TRH; thyroid gland scintigraphy with ^{131} J, ^{131} J fixation tests, thyroid antibodies and thyroglobulin. All hormone analyses, thyroglobulin and thyroid antibodies were determined by radioimmunoassay (RIA). Thyroid scinitgraphy was done with ^{131} J and ^{131} J fixation test was monitored 4, 24 and 48 h after 1.85 MBq test dose applied perorally.
Results
There was a significant decrase in levels with aging of both total and free T4, and, somewhat, minor fall of both total and free T3 in men, in contrast to mild level rise of total T4 and T3 in women, but within the range of eutyroidisam, with no alternations in free hormone levels. A significant fall of thyroglobulin antibodies with aging was observed in the group of males and a considerable increase of thyroglobulin was shown in the group of females. Old age and sex dont' have impact on radio jodine fixation persentage in thyroid gland, thyroid scintigraphy and throid gland echostructure.
Conclusion
Hypothalamic-pituitary –thyroid axis is presereved with aging. The determination of the values of the free T4 should be basic test at older persons. Evident drop in thyroid hormone levels with aging can be considered as adaptation of the organism to reduce requrements for energy, thys representing a significant metabolic parameter of biologic aging process. A normal range of thyroid hormone values shoud be modified for the persons older than 70. These physiological variation should be standardised in the interpretation of the tests of the thyroid function.

DOI: 10.1530/endoabs.81.EP1001

EP1002

Hypothyroidism associated with treatment with immunotherapy: case series

Maria Zhao Montero Benítez, Paloma González Lázaro, Cristina Montalban Mendez, Antonio Moreno Tirado, Pedro Jimenez Torrecilla, Florentino Del Val Zaballos, Amparo Lomas Meneses, Francisco Javier Gó mez Alfonso, Maria Lopez Iglesias & Inés Gómez García
Alcázar de San Juan, Endocrinology Department, La Mancha Centro Hospital Centre, Alcázar de San Juan, Spain

Introduction
The development of immunotherapy has opened up a new approach in the management of different types of tumors that previously had not treatment, and its use is becoming increasingly widespread. Immunotherapy is based on blocking immune checkpoints involved in activating the immune response to malignant neoplasms. Since its introduction into clinical practice, several adverse effects related to the immune system have been reported. Among the endocrinological adverse effects, hypophysitis and thyroid dysfunction are the most frequent. Adrenal insufficiency, DM1 and hypoparathyroidism have also been documented.
Case Series
We present the cases of 5 patients who developed hypothyroidism during immunotherapy treatment at the General La Mancha Centro Hospital and General Hospital in Tomelloso (Ciudad Real, Spain). All patients were male, aged between 56-72 years, and none of them had thyroid disorders prior to the use of immunotherapy. After the diagnosis of advanced oncological disease (melanoma, lung cancer, kidney cancer, and multiple myeloma), it was decided to start immunotherapy treatment, 3 patients with nivolumab (anti PD-1), 1 patient with durvalumab (anti PD-L1), and 1 patient with velcade (proteosomal inhibitor) plus daratumumab (AcMo anti CD38). Several months after starting treatment, patients were diagnosed with hypothyroidism (3 subclinical and 2 central), with asthenia being the main symptom. Antithyroid antibodies were present in 2 patients. In those patients with suspected hypophysitis, an MRI was performed to rule out this pathology, and no cases were observed. After ruling out adrenal insufficiency, which was only documented in the patient treated with velcade plus daratumumab, replacement therapy was initiated, without requiring suspension of immunotherapy in any case.
Discussion
Endocrine disorders related to immunotherapy are increasingly recognized as one of the most common adverse effects. Its diagnosis is sometimes complicated, as symptoms are nonspecific and may overlap with symptoms due to tumor progression. In most cases, the management of these endocrinopathies does not require discontinuation of immunotherapy, although they are usually irreversible and require long-term treatment.
Conclusion
Thyroid dysfunction is a relatively common adverse effect in patients treated with immunotherapy. The risk of developing endocrinopathy is greater at the beginning of treatment, hence the need to monitor thyroid function both at the beginning and during treatment with immunotherapy, in order to carry out an early diagnosis and treatment.

DOI: 10.1530/endoabs.81.EP1002

EP1003

Hyperthyroidism and pregnancy: About 70 patients

Amal Elkhomri, Bensbaa Salma, Nassim Essabah Haraj, Siham El Aziz & Asma Chadli
CHU Ibn Rochd, Endocrinology-Diabetology and Metabolic Diseases Department, Casablanca, Morocco

Introduction
During pregnancy, the thyroid balance of women is altered due to certain hormonal and metabolic changes. It can be all the classic causes of hyperthyroidism, very often in the first trimester it is transient gestational hyperthyroidism.
Objective of the study
The objective of this study is to evaluate the prevalence of hyperthyroidism during pregnancy and the different methods of management.
Materials and methods
Prospective study conducted in the endocrinology and diabetology department, including 70 patients with hyperthyroidism during pregnancy
Results
The results had objectified a mean age of 29 years, with a mean gestational age of 11 SA, with a history of personal thyreopathy in 4 patients, the predominant clinical reason is vomiting in pregnancy, which was present in 98% of patients. On thyroid checkups: The Mean TSHus was 0.05 mIU/l, with mean T4L at 23 ng/l and mean T3L at 7 ng/l, a basedow disease was objectified in 4 patients, and a multi-heteronodular goiter in 5 patients. Therapeutically, 57% of the patients were put on synthetic antithyroid drugs with a betablocker, while for the other patients a simple monitoring was initiated The evolution was marked by the disappearance of the signs of hyperthyroidism in 87% of the patients, with normalization of the thyroid balance after the first trimester.
Conclusion
Hyperthyroidism during pregnancy is a frequent reason for consultation, most often revealed by vomiting during pregnancy, which should not be neglected, requiring adequate management to avoid maternal-fetal complications.

DOI: 10.1530/endoabs.81.EP1003

EP1004

Thyrotoxic hepatitis during pregnancy: about 42 cases

Amal Elkhomri, Bensbaa Salma, Nassim Essabah Haraj, Siham El aziz & Asma Chadli
CHU Ibn Rochd, Endocrinology-Diabetology and Metabolic Diseases Department, Casablanca, Morocco

Introduction
Hyperthyroidism in pregnancy is a common condition representing two different conditions: transient hyperthyroidism of pregnancy and true hyperthyroidism. It is

accompanied by liver enzyme disturbances without any other obvious cause.
Objective of the study
To evaluate the prevalence of acute hepatitis associated with hyperthyroidism.
Matherials and methods
Prospective study conducted at the endocrinology and diabetology department of the CHU Casablanca including 42 patients with hyperthyroidism and acute pancreatitis complicated by hyperperemesis gravidarum
Results
The results showed a mean age of 26 years, with a mean gestational age of 11 days after birth, with no personal history of thyroid disease, the predominant clinical reason was vomiting in pregnancy, which was present in all patients. Biologically: The mean TSHus was 0.05 mIU/l, with a mean T4L of 26 ng/l and a mean T3l of 8 ng/l, with a hepatic cytolysis with an average ASAT of 111 IU/l and ALAT of 173 IU/l, a mean lipasemia of 208 IU/l, the abdominal ultrasound was without any particularities and negative hepatic serologies. Therapeutically, the patients were put on synthetic antithyroid drugs with a betablocker and digestive rest with parenteral nutrition. A normalization of the hepatic balance was observed in 87% of the patients after correction of the thyroid balance.
Conclusion
Thyrotoxic hepatitis is retained in front of a disturbed hepatic balance in the context of thyrotoxicosis after having eliminated any other cause in particular viral, autoimmune or drug-induced hepatitis. Hyperthyroidism, whatever its variant, remains a possible cause of hepatitis during pregnancy.

DOI: 10.1530/endoabs.81.EP1004

EP1005

Abstract Withdrawn

DOI: 10.1530/endoabs.81.EP1005

EP1006

Insulin resistance and insulin-like growth factor-1 in patients with nodular goiter

Oksana Miroshnichenko[1], Iurii Karachentsev[1, 2], Myroslava Mykytyuk[1, 3], Oksana Khyzhnyak[1, 3], Victor Dubovyk[1], Leonid Gerasymenko[1] & Maxim Sazonov[1]
[1]V. Danilevsky' Institute of Endocrine Pathology Problems, Kharkiv,; [2]Kharkiv National Medical University, Department of Endocrinology, Kharkiv,; [3]Kharkiv Medical Academy of Postgraduate Education, Department of Endocrinology, Kharkiv, Ukraine

Introduction
Publications suggesting that thyroid nodules might be associated with insulin resistance (IR) and metabolic syndrome are quite interesting. The **aim** of the work is to analyze the association between anthropometric indicators IR and insulin-like growth factor-1 (IGF-1) in patients with nodular goiter.
Methods
Examined 73 patients with euthyroid single-node ($n=34$) and multinodular goiter ($n=39$), age (51.0 ± 10.6) years; determining WC, WC/HC, BMI, WHtR, ABSI, BFD, BRI, CI, AVI, BAI, IGF-1. Thyroid volume, its structure, number, size, and location of foci were assessed by an ultrasonic complex.
Results
In the total group IGF-1 is associated with BMI ($r=$ -0.30; $P=0.016$), WC ($r=$ -0.26; $P=0.036$), WHtR ($r=$ -0.30); $P=0.020$), AVI ($r=$ -0.27; $P=0.03$), ABSI ($r=$ -0.31; $P=0.015$), BFD ($r=$ 0.27; $P=0.033$)), BRI ($r=$ 0.29; $P=0.02$) and BAI ($r=$ 0.36; $P=0.004$); thyroid volume is associated with age ($r=$ 0.35; $P=0.009$), WC/HC ($r=$ 0.43; $P=0.001$), BFD ($r=$ 0.26; $P=0.06$) and CI ($r=$ 0.31; $P=0.02$). In patients with BMI $\geq$ 35 kg/m^2 thyroid volume is associated with BMI ($r=$ 0.71; $P=0.049$). In patients with IGF-1 above the sex-age norm, thyroid volume is associated with WC/HC ($r=$ 0.71; $P=0.01$), BAI ($r=$ 0.66; $P=0.03$) and BFD ($r=$ -0.52; $P=0.01$). It has been found that BAI explains 82.37% of the variance of IGF-1 in the general group and more than 90% of the variance of its level in groups of patients with nodular goiter with high IGF-1 with/without obesity.
Conclusion
Patients with nodular goiter with IGF-1 above the sex-age norm have significantly higher values of anthropometric indicators IR compared with patients with a normal level of this indicator. In patients with obesity, thyroid volume is significantly associated with BMI. BRI ($R^2=81.14\%$) is a predictor of increased thyroid volume in patients with IGF-1 high levels and obesity.

DOI: 10.1530/endoabs.81.EP1006

EP1007

Quality of life and symptomatology in patients with hypothyroidism post-graves' disease

Miguel Pereira[1], Celestino Neves[2], Juliana Gonçalves[2], João Sé rgio Neves[2] & Davide Carvalho[2]
[1]São João University Hospital Center, Psychology, Porto, Portugal; [2] São João University Hospital Center, Endocrinology, Diabetes and Metabolism, Porto, Portugal

Introduction
Quality of life (QoL) and its related physical and psychological symptomatology is an important factor when we treat Graves' disease.
Objective
To analyze the QoL and physical and psychological symptomatology of patients with hypothyroidism after definitive treatment of Graves' disease.
Methods
We evaluated 16 patients with hypothyroidism that previously had Graves' disease. These patients were submitted to total thyroidectomy and/or radioiodine treatment to deal with Graves' disease. Our sample had a mean age of 58.7 ± 15.0 years, 81.3% were female and 68.8% were married. We assessed thyroid function tests, thyroid antibodies, the resistance to thyroid hormone indices (Thyroid Feedback Quantile-Based Index [TFQI], lipid profile, high-sensitivity C-reactive protein, B12 vitamin, folic acid and applied several questionnaires, namely: the Thyroid Dependent Quality of Life questionnaire (ThyDQoL), the Thyroid Symptom Rating Questionnaire (ThyTSQ) and the Brief Symptom Inventory (BSI). Statistical analysis was performed with the One-way ANOVA test and Pearson's correlation test. P values $\leq$ 0.05 were considered as statistically significant.
Results
In this sample we found that patients had a mean BMI of 27.5 ± 4.3 kg/m^2, TSH 1.67 ± 2.11 µUl/ml and FT4 1.21 ± 0.17 ng/dl. Patients reported a mean QoL value of -2.02 points (range from -9 to 1). In regard to the ThySRQ, 56% of patients have noticed at least moderately memory problems, 62.6% of patients reported at least being moderately tired and 68.9% showed some kind of dizziness symptoms. Nearly 80% of patients did not report any weight gain or appetite problems. In terms of correlations, we found significative correlations between TSH and lack of appetite ($r=$ 0.66; $P=0.01$), audition problems ($r=$ -0.65; $P=0.006$) and depression ($r=$ -0.56; $P=0.02$). We observed correlations between TFQI and weight ($r=$ -0.54; $P=0.03$) and depression ($r=$ -0.54; $P=0.02$). We also noticed a negative correlation between FT4 and dizziness symptoms ($r=$ -0.55; $P=0.02$). Results point out that QoL is negatively correlated with FT3 ($r=$ -0.59; $P=0.01$) and FT4 ($r=$ -0.49; $P=0.05$).
Conclusions
In this study we can observe that QoL in general manners seems to be strongly influenced by FT3 and FT4 than by TSH. Our study is in agreement with previous studies suggesting that FT4 has a good sensitivity regarding well-being evaluation. Further studies, with a more robust number of patients are needed to analyze more deeply the nuances of this kind of treatment and its contribution to the QoL.

DOI: 10.1530/endoabs.81.EP1007

EP1008

Rhabdomyolysis revealing a profound hypothyroidism

M'ballou Camara, Fatiha Ettalibi, Sana Rafi, Ghizlane EL Mghari & Nawal EL Ansari
CHU Mohammed VI, Endocrinology, Diabetes, Metabolic diseases and Nutrition, Morocco

Introducing
Hypothyroidism is the most common endocrinopathy causing rhabdomyolysis. Muscle manifestations are common in hypothyroidism, but myopathy is most often limited to discrete clinical signs such as myalgias, stiffness or cramps accompanied by a simple elevation of muscle enzymes. On the other hand, rhabdomyolysis associated with hypothyroidism is a rare diagnosis to our knowledge. We report a case of severe rhabdomyolysis in the setting of profound Hashimoto's hypothyroidism.
Observation
Mr A.I, 32 years old. Hospitalized in psychiatry for an acute psychotic attack, having as antecedent a schizophrenia since 6 years under neuroleptics in stop for 3 years. The interrogation found signs of hypothyroidism. The clinical examination showed a bradycardia, a generalized myxedema with a puffiness of the face and pre tibial myxedema, the osteotendinous reflexes sharp, a reduced mimic, the lower lips everted with a moderate bilateral ptosis, filling of the supra clavicular

hollows. Goitre homogeneous. On workup: Total CPK at 28 times normal, normokalemia, moderate renal failure, deep peripheral hypothyroidism. Thyroid ultrasonography revealed a goiter with significant vascularization, positive anti-TPO antibodies. The diagnosis of Hashimoto's thyroiditis was made. This hypothyroidism is associated with rhabdomyolysis diagnosed on a CPK level (28 times norma), in normo kalemia, as well as moderate renal failure. The patient was put on Levothyroxine with an initiation dose of 1.7 µg/kg/j.
Discussion
Muscle involvement during hypothyroidism is often frequent and early, simulating a pathology of the locomotor system. Moderate elevation of creatinine phosphokinase (CPK) during hypothyroidism is found in 80% of cases, however, cases of major CPK elevation during hypothyroid myopathy remain exceptional. Most patients with hypothyroidism who develop rhabdomyolysis have a clear precipitating factor, in which case intermittent use of neuroleptics can be suggested, although rhabdomyolysis caused by severe hypothyroidism alone has been reported in the literature. Myolysis in hypothyroidism is explained by muscle degeneration with atrophy of type II fibers and compensatory hypertrophy of type I fibers secondary to a defect in mitochondrial metabolism. Glycosaminoglycan deposition, altered contractility of actin-myosin units, and low myosin ATPase activity in skeletal muscle are also involved in the pathophysiology.
Conclusion
Rhabdomyolysis is a rare but fatal complication of hypothyroidism. Hormone replacement therapy, started gradually, allows resolution of muscle signs and normalization of muscle enzymes. A major elevation of CPK should prompt a search for hypothyroidism, although this is a rare cause, and warrants monitoring of thyroid status during any muscle lysis with elevated muscle enzymes, as recommended

DOI: 10.1530/endoabs.81.EP1008

EP1009

Subacute thyroiditis following asymptomatic COVID-19 case report

Iuliana Ilie[1], Madalina Musat[2, 3] & Luciana Oprea[2]
[1]Gral Medical Clinic, Endocrinology, Bucharest, Romania; [2]C.I. Parhon National Institute of Endocrinology, Bucharest, Romania, Endocrinology, Bucharest, Romania; [3]Carol Davila University of Medicine and Pharmacy, Bucureşti, Romania

Subacute thyroiditis (SAT) is a relatively uncommon and self-limited cause of thyrotoxicosis of viral or post-viral origin. During the COVID-19 pandemic a thyroid impact was also considered due to the potential of SARS-CoV-2 virus to cause multiorgan effects. Several SAT cases associated with SARS-CoV-2 infection or vaccination were recently reported in the literature. We present the case of a 52-year-old female who presented with neck pain, fever, asthenia, and malaise for approx. 2 weeks. On examination she had a moderately asymmetrically enlarged and tender thyroid gland, and was tachycardic, with no respiratory symptoms. From her medical history we retain no SARS-COV2 vaccine or any form of upper respiratory airways infection recently. A prior endocrinology evaluation in 2020 revealed thyroid cysts of max 12mm and a normal thyroid function. Currently she had mildly high serum free T4 and suppressed serum TSH, high ESR of 111 mm/h, mild leukocytosis with neutrophilia. Liver function tests were also abnormal-elevated ALT (138 IU/l), mildly elevated GGT and alkaline phosphatase. The patient did not have any history of liver disease or alcoholic intake. On ultrasonography, the thyroid appeared enlarged with bilateral hypoechogenic areas that had reduced vascularization on Color Doppler. The liver appeared normal on ultrasound. Thoracic X-Ray was also normal. One week prior to presentation the patient had two nasopharyngeal swabs SARS-CoV-2 RT-PCR tests, both negative. However, at SAT diagnosis SARS-CoV-2 IgG antibodies were positive. Other viral serologies that can affect hepatic function were negative, including: anti CMV, anti-Epstein-Barr antibodies, IgM anti-HAV, HBsAg, Anti-HCV antibodies. A diagnosis of SAT post asymptomatic SARS-CoV-2 infection was made and the patient was started on corticosteroids with improvement of both clinical and biological parameters. A benign, short-lived and subclinical hepatic involvement is also common in subacute thyroiditis. The association of SAT with SARS-CoV-2 virus is reported in the literature, mostly following symptomatic SARS-COV 2 infection or vaccine, although the size of the problem is still unclear. In our case, SAT in asymptomatic COVID-19 patient remains a challenge in establishing the certain trigger of thyroiditis, although in a review of 27 patients with COVID-19 related SAT, 4 cases were described after asymptomatic SARS-COV 2 infections. (1) 1. Trimboli P, Cappelli C, Croce L, Scappaticcio L, Chiovato L, Rotondi M. COVID-19 Associated Subacute Thyroiditis: Evidence-Based Data From a Systematic Review. Front Endocrinol (Lausanne). 2021;12:707726. Published 2021 Sep 29.

DOI: 10.1530/endoabs.81.EP1009

EP1010

Serum TSH level in hospitalized patients with moderate-to-severe COVID-19

Arina Mikhailova, Daria I. Lagutina, Ksenia Golovatyuk, Alena Chernikova, Anna Bystrova & Tatiana Karonova
National Medical Research Centre named after V.A. Almazov of the Ministry of Healthcare of Russia, Saint-Petersburg, Saint Petersburg, Russian Federation

Background
Recently, clinical evidence of thyroid dysfunction has been observed both in acute and post-COVID period. The aim of this study was to estimate the serum TSH level in hospitalized patients with moderate-to-severe COVID-19.
Methods
It was a single-center study conducted by the Almazov National Medical Research Centre (Russian Federation). Patients hospitalized with detected SARS-CoV-2 infection by RT-PCR test and chest computed tomography (CT) were enrolled. We did not include patients with a medical history of thyroid disease. Clinical data, laboratory tests (TSH at the 1st and at the 9th day of hospitalization; C-reactive protein, lactate dehydrogenase and ferritin levels at the 1st day of hospitalization), CT data and received systemic corticosteroid therapy were analyzed.
Results
A total of 77 patients with an average day of illness at the time of hospitalization 8 $\pm$ 1.2 days were included. The baseline abnormal TSH level ($<$0.4 mIU/l) was found in 4 patients (5.2%), while by the 9th day of hospitalization their number doubled and reached 9 (11.7%). Furthermore, we found that by the 9th day the TSH level more than 4.5 mIU/l was detected in 4 patients (4.2%). Thus, 13 out of 77 (16.9 %) patients had the abnormal serum TSH level by the 9th day. No statistically significant correlations with the TSH level of the C-reactive protein, lactate dehydrogenase and ferritin levels was detected in our study ($P>$ 0.05). Also we did not find any correlations with the TSH level of the CT degree and of the clinical severity ($P>$ 0.05). There was no any difference in average daily glucocorticoid dose among patients with abnormal TSH level and without it.
Conclusions
Abnormal TSH level could be explained by the function alterations of the hypothalamic-pituitary-thyroid axis associated with SARS-CoV-2. Future studies may clarify pathogenic aspects of thyroid dysfunction caused by COVID-19.

DOI: 10.1530/endoabs.81.EP1010

EP1011

Long-term thyroid function in women diagnosed with subclinical hypothyroidism in pregnancy

Rocío Revuelta[1], Ana Castro[1], Belen Martínez[1], Andrea Cruz[1], Maria-Piedad Picazo-Perea[2], Esther Martin-Torres[2], Aurora Lopez-Martos[2] & ALMUDENA VICENTE[1]
[1]Toledo University Hospital, Endocrinology and Nutrition, Toledo, Spain; [2]Toledo University Hospital, Biochemistry, Toledo, Spain

Introduction
Subclinical hypothyroidism (SCHT) in pregnancy has been associated with adverse obstetric and perinatal outcomes. However, few studies have investigated the evolution of postpartum thyroid function in women first diagnosed with SCHT in pregnancy (gestational SCHT).
Objective
To determine the evolution of thyroid function (TF) and the clinical and biochemical factors related to the long-term persistence of hypothyroidism (HT) in women with gestational SCHT.
Methods
Gestational SCHT was defined as the presence of TSH values above the upper limit of the specific range in our population (0.21-3.8 mcU/ml) determined in the first trimester (1T). We reviewed the medical records of women diagnosed with SCHT in our Health Area in 2016. We compared the clinical and biochemical characteristics of pregnant women diagnosed for the first time with SCHT in pregnancy, with TF data at least 6 months postpartum.

Results
Thyroid dysfunction screening was performed in 3821 women. 293 met SCHT biochemical criteria (7.66%). Of 140 women diagnosed with gestational SCHT, 106 had long-term TF data. The mean age was 31.4 ± 5 years, being 61.5% older than 30 years. The prevalence of persistent hypothyroidism (HT) at the end of the follow-up was 48.1%(n= 51), being significantly more frequent in women with positive anti-TPO antibodies (Ab) (61.4% vs 38.6%; $P<0.05$) and TSH greater than 10 in 1T (85.7% vs 45.4%; $P<0.001$).
Conclusions
1. In our study, almost half of the women with gestational HTSC present long-term persistent HT, being more frequent in those with positive anti-TPO and/or TSH higher than 10 in the 1T. 2. It would be advisable to monitor these women, especially when planning subsequent pregnancies.

DOI: 10.1530/endoabs.81.EP1011

EP1012

The interplay between TSH and geriatric syndromes: results from the Moscow centenarians study

Lubov Matchekhina, Ksenia Eruslanova, Ekaterina Dudinskaya & Olga Tkacheva
Pirogov Russian National Medical University, Russian Gerontology Research and Clinical Centre, Moscow, Russian Federation

Aim of the study
to assess the interaction between TSH and the most common geriatric syndromes in the cohort of centenarians
Materials and Methods
It was a longitudinal study, including 82 centenarians (95 years and older), who live in Moscow. Complex geriatric assessment and blood tests were performed. Complex geriatric assessment included past medical history, FRAIL, IADL-C, MNA, GDS-15 and MOCA scores. We analyzed the interactions between TSH, metabolic parameters, functional status and cognitive functions in centenarians. In one year after the investigations we contacted patients' relatives or social workers to find out about patients' status. The statistical analysis was performed using IBM SPSS Statistics Version 26. Statistically significant were differences with p< 0,05.
Results
Mean age of the patients was 98,3 (±1,9) years, while 87,8% of the cohort were women. Analyzing functional status we found out that 34,4% of the patients were frail, and the number of prefrail patients was 56,2%. Cognitive impairments of different severity were presented in 84,4% of the patients. In 59% of the patients HbA1c was below 6%, 33% had concentrations between 6 and 6,4% and only in 8% we found HbA1c higher than 6,5%. The median level of TSH was 2,26 mIU/l [1,8;3,6] with a tendency to higher normal concentrations. TSH was negatively correlated with C-reactive protein (r= -0,4, $P<0.05$) and positively correlated with albumin levels (r= 0,26 P=0,038). The interaction between the TSH and chronic pain severity measured by VAS was negative (r= -0,03, P=0,021). Cognitive status of centenarians assessed by MMSE showed a positive correlation with TSH levels (r= 0,38, P=0,011).
Conclusion
In the cohort of centenarians higher levels of TSH seem to play a protective role in maintaining cognitive functions and nutritional status; lower TSH levels seem to be linked with the higher intensity of chronic pain.

DOI: 10.1530/endoabs.81.EP1012

EP1013

A possible complication of hypothyroidism: ischemic colitis

Shielah Mauntana[1] & Mahesh Gajendran[2]
[1]Paul L. Foster School of Medicine, El Paso, United States; [2]Long School of Medicine, University of Texas Health Center at San Antonio, Division of Gastroenterology, San Antonio, United States

Background
Ischemic colitis (IC) is a disorder characterized by a decrease in blood flow of the large intestine. Many factors can contribute to decreased blood flow in the arteries supplying the large intestine, such as nonocclusive causes like hypertension and atherosclerosis and occlusive causes like embolism from myocardial infarction. With Ischemic colitis's high mortality rate and its association with many cardiovascular diseases, it's important to understand comorbidities that might lead to these events. Thyroid hormone is a hormone that affects not only metabolism and energy expenditure, but also cardiac function. Thus, thyroid dysfunction might play a role in the development of ischemic colitis. This study aims to find and assess comorbidities like thyroid dysfunction associated with admission for ischemic colitis.
Methods
We conducted a cross-sectional study of adults with IC listed as the primary ED diagnosis from 2005 to 2014 using the Nationwide Readmission Database (NRD). The characteristics of the IC-related ED visits were analyzed.
Results
The estimated number of ED visits with a primary diagnosis of IC from 2005-2014 was 541,267 people. Our results showed that the mean age of the cohort was 62 +/- 14 years, suggesting that most patients affected with ischemic colitis are elderly. 88,497 out of 541,267 ischemic colitis patients were found to have hypothyroidism, amounting to 16.35% of the ischemic colitis population.
Conclusions
The results suggest that Hypothyroidism and ischemic colitis may be associated, perhaps through thyroid hormone's effect on cardiovascular homeostasis. Thyroid hormone has a major role in cardiac contraction, angiogenesis, vascular function, structure, as well as mitochondrial function. Dysfunction of the thyroid hormone pathway can lead to cardiac impairment, hypertension, and heart failure. All these events may lead to decreased blood flow in the vasculature, hypoperfusion to the organs, and subsequently ischemic colitis.

DOI: 10.1530/endoabs.81.EP1013

EP1014

Thyroiditis as immune related adverse event to pembrolizumab plus lenvatinib therapy: a case report

Lamya Echchad & Abidi Ihssane
Sud Francilien Hospital Center, Endocrinology and Metabolism Disease Department, France

Introduction
The development of molecular biology and cancer immunology has brought drastic changes in anticancer in recent years. Recently, tyrosine kinase inhibitors (TKI) and immune checkpoint inhibitors (ICPIs) have emerged as new classes of anticancer therapies. Although generally considered less toxic than cytotoxic chemotherapy, these new drugs can cause significant side effects including thyroid dysfunction. We report the case of thyroiditis induced by Pembrolizumab (ICPIs) plus Lenvatinib (TKI) in patient with metastatic renal cell carcinoma.
Observation
A 72 years old male patient with a history of type 2 diabetes mellitus, arterial hypertension, was diagnosed with metastatic renal cell carcinoma and treated by pembrolizumab plus Lenvatinib. Two months after the start of this association, he was presented to the emergency department with a history of vertigo and tachycardia. Thyroid function tests revealed transient hyperthyroidism with negative TRAK, TPO and TG antibodies. The cervical ultrasound had showed a small thyroid with hypoechoic parenchyma, low vascularity consistent with thyroiditis. He was put on 40 mg of Carbimazole per day and 40 mg of Propanolol twice per day. His thyroid function was subsequently monitored until he was found to have overt hypothyroidism and put on under 200 µg of levothyroxine per day.
Discussion & Conclusion
In patients treated with TKIs or ICPIs, the thyroid toxicities are common and pauci-symptomatic at the beginning of their evolution but can lead to prolonged hypothyroidism that should not be ignored. The cumulative clinical experience of recent years and the basic studies have led to a better understanding of the mechanisms of thyroid dysfunction. Schematically, the iatrogenic thyroiditis of TKIs is linked to vascular damage related to their selectivity to block diverse vascular growth factor signaling pathways which may led to a rapid reduction in thyroid vascular flow and as a result the occurrence of ischemic thyroiditis. In the other hand, the iatrogenic thyroiditis of ICPIs is based on an inflammatory mechanism by autoimmune reaction that in many cases is accompanied by hormonal deficiency in the long term. As the use of these antibodies becomes more prelevent, more investigations and research are needed to identify risk factors for these side effects and possibly tailor the treatment of patients accordingly. Finally, thyroid function tests including TSH, FT4 and TPO antibodies screening should be a part of baseline of laboratory testing of all patient undergoing treatment with these drugs.

DOI: 10.1530/endoabs.81.EP1014

EP1015

What is the ideal approach for thyroidectomy in a given patient? Proposal of an algorithm

Ramesh Bangaraiahgari[1], Ramakanth Bhargav Panchangam[2], Rajesh Bangaraiahgari[1], Udaya Kumar U[1] & Sabaretnam Mayilvaganan[3]
[1]Arundathi Institute of Medical Sciences, India; [2]Bhargav Endocrine Hospitals, Vijayawada, India; [3]SGPGIMS, India

Introduction
Thyroidectomy can performed by open or wide array of endoscopic techniques. Lack of uniform consensus on specific indications for each technique leads to confusion on ideal thyroidectomy technique. In this context, we analysed our experience with specific emphasis on deducing an algorithm on ideal technique for a given patient.
Material and methods
This is a retrospective study conducted at a tertiary care endocrine surgery department in South India over a period of 10 years from July 2009 to June 2019. Data on our thyroidectomy techniques was analysed with the specific emphasis on choice of technique based on disease related, non disease related and patient choice factors. We categorized all the clinico-investigative, logistic and patient factors influencing the choice of thyroidectomy technique in to four types A, B, C and D. Type A included disease related factors; Type B included logistics related factors; Type C factors based on comorbidities; Type D based on patient and their family. Finally, an algorithm to select an ideal technique of thyroidectomy for a given patient was developed based on the results.
Results
Open thyroidectomy was performed in 1794/2075 (86.5 %) cases. Endoscopic thyroidectomy was employed in 281 subjects. Type A to C factors, bifurcated the choice of technique to OT and ET without the need for Type D factors. Type D factors primarily dictated the choice amongst the available ET techniques. Further, DI, II and VII factors converted some of the ET feasible subjects to OT. DIII, IV, V, VI factors dictated the choice of a particular ET technique.
Conclusions
1) The ideal technique of thyroidectomy for a given patient depended on logistics, expertise and patient choice rather than disease (goiter) related factors and 2) Our proposed algorithm appears to guide in making decision on the ideal choice of thyroidectomy technique.
Key words: Thyroidectomy; Endoscopy; Algorithm; Surgery; Technique)

DOI: 10.1530/endoabs.81.EP1015

EP1016

Opportunistic thyroid function screening in older medical patients in Ireland

Lok Yi Joyce Tan & Mary Jane Brassill
Tipperary University Hospital, Department of Medicine, Clonmel, Ireland

Introduction
Thyroid dysfunction is one of the commonest endocrine disorders with hypothyroidism being the most common thyroid dysfunction in the elderly population[1]. An elderly patient with thyroid dysfunction can be asymptomatic, or present with non-specific symptoms, making biochemical testing of thyroid function useful and essential. We reviewed the screening rate and prevalence of thyroid dysfunction in older medical patient patients admitted to an Irish secondary hospital.
Methods
A retrospective cross-sectional analysis was conducted on all hospitalized general medical patients over 70 years of age discharged during October 2020. This was identified using the Integrated Patient Management system. Chart review was carried out to identify those with a known diagnosis of thyroid disorders. Thyroid function test (TFTs) screened during admission and/or within the prior six months were include in the analysis. Data was inputted to a Microsoft excel spreadsheet and analysed. The thyroid stimulating hormone (TSH) level is measured using the Roche assay and its reference range is between 0.27 - 4.2 mIU/l.
Results
202 patients were included in this study with a median age of 80 years (SD 6.3). 51%($n=$ 102) were male. 85% of the entire cohort ($n=$ 171) had TFTs performed. 21%($n=$ 42) had a known thyroid disorder. TFTs were performed in 95 % of those (40/42). 33% (13/40) had abnormal TFTs requiring a medication adjustment. Of those with no known thyroid disorder, 82% (131/160) had TFTs performed. 11%($n=$ 14) had abnormal results. 8%($n=$ 10) had high TSH levels. One had overt hypothyroidism and the remaining 9 had subclinical hypothyroidism, providing a prevalence of 0.8% and 6.9% respectively. The mean age of the patients with subclinical hypothyroidism was 79.9 years (SD 8.1). 3.1% (4/14) had subclinical hyperthyroidism, providing a prevalence of 3.1% with mean age of 83.5 years (SD 3.7).
Discussion
We observed a high prevalence of abnormal TFTs in those with known thyroid disorders, leading to medication adjustment. Screening those without known thyroid disease also yielded abnormal results in 11%. Subclinical hypothyroidism was the most prevalent thyroid disorder among the elderly population in our study. These findings indicate that routine, opportunistic testing of TFTs in medical patients over 70 is beneficial, with medication adjustment required in 33% of those with known thyroid disorder, and 11% of the remainder having abnormal TFTs.
References
1. Faggiano A, Del Prete M, Marciello F, Marotta V, Ramundo V, Colao A. Thyroid diseases in elderly. Minerva Endocrinol. 2011 Sep 1;36(3):211-31.

DOI: 10.1530/endoabs.81.EP1016

EP1017

Prevalence of thyroid disease among women receiving antenatal care at a tertiary care centre in Sri Lanka

Kaveen Weerasinghe
Post Graduate Institute of Medicine, University of Colombo, Obstetrics and Gynaecology, Colombo, Sri Lanka

Introduction
Sri Lanka is endemic for goiters and recent studies show a high prevalence of thyroid dysfucntion among the population. However, data on thyroid dysfuntion among the general population and pregnant women in Sri Lanka is limited. Thyroid dysfunction is associated with adverse pregnancy outcomes. Furthermore, pregnancy related physiological changes increase the risk of thyroid dysfucntion. However, women in Sri Lanka are not routinely screened during pregnancy for thyroid dysfunction.
Methods
A descriptive cross sectional study was conducted among 872 women who received antenatal care and underwent universal first trimester or early second trimester thyroid status screening at a tertiary care centre in Sri Lanka over a period of one year. Pregnancy records were analyzed to extract data on past medical history, thyroid status, and pregnancy outcomes.
Results
872 women underwent screening with TSH at the booking visit. Pregnancy specific reference ranges were used (0.1-2.5 mIU/ml for first trimester and 0.2-0.3 mIU/ml for second trimester). Among them, 91.4%($n=$ 797) were euthyroid. Two women had been diagnosed with Graves disease prior to pregnancy and were on treatment with with oral antithyroid medications. Remaining 8.6%($n=$ 73) of the population were found to be hypothyroid. Among women with hypothyroidism, 21.9%($n=$ 16) had been diagnosed prior to pregnancy while remaing 80.1%($n=$ 57) were newly diagnosed during antenatal screening. Prevalaence of subclical hypothyroidism among the population was 5.4%($n=$ 47) and prevalence of overt hypotyroidism was 3%($n=$ 26). 57.5%($n=$ 42) of women with hypothyroidism were positive for TPO antibodies. One woman had undergone thyroidectomy due to papillary thyroid carcinoma while 2 women who had undergone thyroidectomy for goiters prior to pregnancy. Prevalence of goiters among the population was 6%($n=$ 52). Women with overt hypothyroidism had a higher risk of foetal graowth restriction ($P=0.04$), and neonatal intensive care admission ($P=0.02$). There were no statistically significant differences between pregnancy outcomes of women with euthyroid status and subclinical hypothyroidism.
Conclusion
Thyroid disease has a high prevalence among the study population which was comparable to findings of previous studies. Overt hypothyroidism was associated with adverse pregnancy outcomes. Further studies are required to assess thyroid status among Sri Lankan women, implications of thyroid status on pregnancy outcomes, plan strategies for screening, and interventions.

DOI: 10.1530/endoabs.81.EP1017

EP1018

Carbimazole-induced hepatocellular injury in patient with Graves' disease - avoid rechallenging

Hassan Ibrahim, Maria Comia, Mustapha Abubakar, Richard Ip & Taofeek Ojewuyi

Southend University Hospital, Mid and South Essex NHS Foundation Trust, Southend-on-Sea, United Kingdom

Grave's disease is an auto-immune disorder which responds well to medication and up to half of the patients who take anti-thyroid drugs go into remission. We present a patient with Graves' disease, who developed acute hepatitis associated with Carbimazole and, re-challenged with Carbimazole when she represented with in fast atrial fibrillation (AF) with relapse of hepatitis. A 75 year-old lady admitted with palpitation and chest tightness. She had a background of paroxysmal AF. She was found to be in AF with fast ventricular response and blood tests done during her admission showed abnormal thyroid function tests (TFT) consistent with hyperthyroidism: TSH <0.01 mU/l (0.3-5.0), FT4: 33.5 pmol/l (7.9-16.0), FT3: 11.7 pmol/l (3.8-6.0), TSH receptor antibody 5.5 IU/l (0-0.9). Patient was started on Carbimazole 20 mg once a day and planned for follow up as outpatient with the endocrine team within 2 months. Few weeks after discharge, she presented with chest tightness and blood tests revealed deranged liver function tests (LFT); total bilirubin 29 umol/l (0-21), ALT 295 U/l (<35) and ALP 458 U/l (30-130). Carbimazole was discontinued. She has had a normal liver ultrasound as well as normal autoimmune and viral hepatitis screen. Her LFT improved after stopping Carbimazole. She was followed up by the endocrine team post-discharge and definitive treatment in the form of total thyroidectomy was planned. Patient was re-admitted three weeks post outpatient follow up due to palpitations and fast AF. Patient refused to try Propylthiouracil and hence she was restarted on low dose of carbimazole with strict weekly LFT follow up until thyroidectomy could be arranged. However, while trialed on Carbimazole, LFTs started getting deranged (ALT raised to 64 U/l from 29 U/l) and Carbimazole was again discontinued. Two weeks following discontinuation of Carbimazole LFT returned to normal: total bilirubin 8 umol/l, ALT 24 U/l and ALP 125 U/l. Patient's condition discussed with surgical team and her total thyroidectomy appointment was expedited. She was started on Lugol's iodine 10 days prior to surgery with normalization of TFT. Patient underwent total thyroidectomy which was uneventful. Hepatotoxicity is rare but serious side effect of thyrostatic medications. The drug should be withdrawn immediately and alternative therapy for thyrotoxicosis should be considered. This case strongly supports the need to avoid antithyroid drugs (ATD) rechallenge in patients who develop significant liver dysfunction following ATD use and identifies that Carbimazole may be associated with acute hepatocellular dysfunction and not just Cholestasis.

DOI: 10.1530/endoabs.81.EP1018

EP1019

The hobnail variant of papillary thyroid carcinoma: clinical/molecular characteristics of a large monocentric series and comparison with conventional histotypes

Simona Censi[1], Jacopo Manso[1], Francesco Paganin[1], Federica Vianello[2], Francesca Galuppini[3], Gianmaria Pennelli[4], Maurizio Iacobone[5], Loris Bertazza[1], Susi Barollo[1] & Caterina Mian[1]
[1]Endocrinology Unit, Department of Medicine (DIMED), University of Padua, Padua, Italy; [2]Radiotherapy Unit, Veneto Institute of Oncology IOV-IRCCS, Padua, Italy; [3]Endocrinology Unit and Surgical Pathology and Cytopathology Unit, Department of Medicine (DIMED), University of Padua, Padua, Italy; [4]Endocrinology Unit and Surgical Pathology and Cytopathology Unit, Department of Medicine (DIMED), Padua, Italy; [5]First Surgery Clinic and Endocrine Surgery Unit, Department of Surgery, Oncology, and Gastroenterology, University of Padua, Padua, Italy

Background
Hobnail variant of papillary thyroid carcinoma (HPTC) has been recently identified. Given the rarity of the variant its characteristics have been studied only in little series, limiting the quality of the data available for its better management. The aims of our retrospective study were 1) to define the clinical and molecular characteristics of a series of HPTC in a monocentric and relatively large series; 2) to define the clinical and molecular characteristics able to influence its outcome and 3) to compare them with a series of conventional PTC.
Material and methods
the clinical and molecular (*BRAF*, *TERT* promoter, *TP53*) characteristics of 74 HPTC were compared with a series of 143 conventional PTC. All patients had a total thyroidectomy and radio-iodine (RAI). The median follow-up was 27 months.
Results
HPTC had: median age at diagnosis of 49.2 years, median size of 20.5mm, a T3/T4 in 42%, lymph-node involvement in 58% (38% N1a and 20% N1b), metastatic in 5%, multifocal in 45%, extra-thyroidal invasive in 63%, angio-invasive in 97%. 13.5% had further treatments (after thyroid surgery and RAI), external radio-therapy (RTE) was administered in 7%. HPTC were mutated in *BRAF*, *TERT* promoter and *TP53* in 56%, 9% and 20% of cases, respectively. At the end of the follow-up, 16% had a biochemical/structural persistence or a HPTC-related death. The outcome was influenced by TNM, stage, *TERT*-promoter mutation, lymph node ratio (LNR), but the latter was the only independent outcome determinant (odds radio, OR = 203). A Hobnail morphology $<$ or $\geq 30\%$ was not able to influence the outcome, as well as the other variants considered. Compared to classical PTC, HPTC has a lower female predominance (65% vs 78%, $P<0.01$), larger median size (20.5mm vs 13.00mm, $P<0.0001$), more frequent lymph-node and metastatic involvement and higher stage at diagnosis (all $P<0.01$), higher LNR ($P=0.002$), more frequent further treatments ($P=0.04$), more frequent RTE ($P=0.001$) and a worse outcome (being persistence/PTC-related death:16% vs 4.9%, $P<0.01$). There was no difference in the frequency of *BRAF* (56% vs 62%) and *TERT* promoter mutations (9% vs 5%), while there was a higher frequency of *TP53* mutations in HPTC (20% vs 1%, $P<0.01$).
Conclusions
the clinical characteristics of HPTC suggest a more aggressive treatment, a prompt RAI use and stricter follow-up than in conventional PTC. The LNR revealed the more powerful association with a worse outcome in HPTC. The major limit of our study is the follow-up duration available until now.

DOI: 10.1530/endoabs.81.EP1019

EP1020

Male was not a prognostic risk factor in postoperative DTC patients treated with 131I treatment: a propensity score-matching study

Wei Zheng, Yaqian Zhou, Shen Wang, Xuan Wang & Jian Tan
Tianjin Medical University General Hospital, Nuclear Medicine, Tianjin, China

Objective
Propensity score matching (PSM) was used to study whether male patients with differentiated thyroid cancer (DTC) were the risk factors for prognosis after ^{131}I treatment.
Methods
1677 patients with DTC who underwent total thyroidectomy and received ^{131}I treatment were divided into male group ($n=546$) and female group ($n=1131$). The PSM method was adopted to process all the data to reduce the influence of data bias and confounding variables. Independent sample T test and Mann-Whitney U test were used for all continuous variables, χ^2 test was used for all classified variables. Univariate and multivariate logistic regression were used to analyze the risk factors affecting prognosis, and a receiver operating characteristic (ROC) curve was used to analyze the relationship between sTg level and poor prognosis.
Results
Before PSM, the proportion of male patients with poor prognosis was significantly higher than that of female patients (21.2%(116/546) vs 14.0%(158/1131), $\chi^2 = 17.53$, $P=0.001$). After PSM, there was no difference in the proportion of poor prognosis between male and female groups (19.9%(107/537) vs 15.6%(84/537), $\chi^2 = 5.43$, $P=0.143$). Multivariate logistic regression analysis showed that male (odds radio (OR) = 1.439 (95%CI: 1.016~2.038), $P=0.040$), high T stage (T3, T4 stage)(OR = 1.816 (95%CI: 1.273~2.590), $P=0.001$), N1b stage (OR = 1.766 (95% CI: 1.233~2.530), $P=0.002$), M1 stage (OR = 9.833 (95%CI: 3.190~30.309), $P<0.001$) and sTg level (OR = 1.035 (95%CI: 1.029~1.042), $P<0.001$) were risk factors for poor prognosis before PSM, while high T stage (T3, T4 stage)(OR = 1.870 (95%CI: 1.212~2.886), $P=0.005$), M1 stage (OR = 8.993 (95%CI: 2.434~33.225), $P=0.001$), high sTg level (OR = 1.040 (95%CI: 1.030~1.049), $P<0.001$) were still risk factors, and male (OR = 1.383 (95%CI: 0.912~2.096), $P=0.127$) were no longer risk factors for poor prognosis after PSM. ROC curve analysis showed that the cut-off value of sTg was 10.25 μg/l, with the sensitivity of 81.0%(222/274) and the specificity of 84.2%(1173/1393).
Conclusions
After reduction of selection bias by PSM, males are no longer a risk factor for prognosis after ^{131}I treatment of DTC. In addition, high T stage (T3, T4 stage), M1 stage and sTg $\geq$ 10.25 μg/l were risk factors for poor prognosis.
Key words Differentiated thyroid cancer; ^{131}I treatment; Propensity Score-Matching; Gender; Risk factors; Prognosis

DOI: 10.1530/endoabs.81.EP1020

EP1021

Clinical experience with tyrosine kinase inhibitors in radioiodine-refractory differentiated thyroid cancer

Andrea Fernández Valero, Miguel Damas-Fuentes, José Ignacio Martínez Montoro, Maria Molina Vega, Isabel Mancha Doblas, Jorge García Alemán, Arantzazu Sebastian Ochoa, Jose Manuel Trigo Pérez & Francisco José Tinahones Madueño
Hospital Universitario Virgen de la Victoria, Málaga, Spain

Introduction
Differentiated thyroid cancer (DTC) represent 85- 90 % of all thyroid cancer cases. Most of these have an excellent prognosis with standard treatment. However, between 7 and 23% will develop distant metastases and, of these, more than 65% will become radioactive iodine-refractory. In some of these patients who are considered to be radioiodine-refractory with rapidly progressive or symptomatic disease, or in patients who are not candidates for other therapies, the use of systemic therapies, such as Tyrosine kinase inhibitors (TKIs), should be considered since they have demonstrated an extension of progression-free survival.
Materials and Methods
Retrospective observational study. Data of 23 patients diagnosed with DTC who received treatment with TKIs between June 2010 and October 2019 were analyzed. Clinical response according to RECIST criteria of response to treatment, toxicities and tolerability of these therapies were evaluated at 3, 6, 12 and 18 months.
Results
There were 23 patients (11 men and 12 women). The overall mean age at diagnosis was 59,17 $\pm$ 14,59 years. 12 patients had a diagnosis of papillar thyroid cancer, 4 of follicular thyroid cancer and 7 of Hurthle cell cancer, being 70% of them stage IV. The mean time from cancer diagnosis to initiation TKIs therapy was 7.6 $\pm$ 8.7 years. Regarding the therapy: 19 were treated with Sorafenib, 3 with Lenvatinb and just 1 with Axitinib. Twelve months after the beginning of the treatment 19 patients were still undergoing TKI therapy: 12 (52.5%) had a stable disease (SD), 1 (4.3%) partial response (PR) and 6 (26.1%) progressive disease (PD). The remaining 4 patients had to withdraw: 1 due to toxicity and 3 due to death as a result of progression of the disease. A group of 15 patients completed 18 months of treatment (6 of them required a shift to second-line treatment with Lenvatinib or Axitinib) 10 had SD, 3 PR and 2 PD. A total of 7 patients (30.4%) died during this time. Adverse events occurred in 100% of the patients, being hand-foot syndrome, diarrhea and fatigue the most frequent. However, they were generally low grade (grade 1 or 2) requiring dose reductions or temporary withdrawals. There was only one definitive withdrawal due to toxicity (with Axitinb)
Conclusions
- Eighteen months after the beginning of the treatment 56.5% of the patients remained without disease progression thanks to treatment with TKIs. Despite their frequent side effects, TKIs are generally well tolerated

DOI: 10.1530/endoabs.81.EP1021

EP1022

Patterns of biological behavior of anaplastic thyroid cancer - case reports

Boyan Nonchev[1, 2], Antoaneta Argatska[1], Rosen Dimov[3, 4], Veselin Chonov[5, 6] & Elena Chobankova[2]
[1]Medical University of Plovdiv, Department of Endocrinology, Plovdiv, Bulgaria; [2]Kaspela University Hospital, Clinic of Endocrinology, Plovdiv, Bulgaria; [3]Medical University of Plovdiv, Department of Special Surgery, Plovdiv, Bulgaria; [4]Kaspela University Hospital, Clinic of Surgery, Plovdiv, Bulgaria; [5]Medical University of Plovdiv, Department of General and Clinical Pathology, Plovdiv, Bulgaria; [6]Kaspela University Hospital, Department of Pathology, Plovdiv, Bulgaria

Introduction
Anaplastic carcinoma of the thyroid (ATC) is the rarest and most aggressive thyroid gland cancer accounting for less than 5 % of all thyroid gland neoplasms. There is inconclusive evidence that ATC represents a terminal dedifferentiation of preexisting well-differentiated thyroid carcinoma or it may originate as already aggressive nondifferentiated cancer without any prior thyroid neoplasm.
Case description
Case 1
A 74-year-old woman with history of long-standing nodular goiter presented with rapidly growing, painful neck mass with compressive symptoms including hoarseness, dysphagia and vocal cord paralysis. She underwent debulking thyroid surgery in November 2021 revealing a right lobe 4/3/3 cm mass with histological features of anaplastic carcinoma and extensive infiltration of the surrounding soft tissues and muscles, esophagus, carotic artery, jugular vein, laryngeal nerve. Palliative radiotherapy was initiated together with adjuvant chemotherapy but the residual tumor showed progressive enlargement and lead to life-threatening complications.
Case 2
A 57-year-old man in whom on routine US examination in 2017 a solid hypoechoic nodule 3.6/3.3/4.5 cm with increased intranodular blood flow causing tracheal deviation and local compression was seen. The patient was referred to surgery which was not performed until April 2019 when he presented with significant enlargement of the thyroid mass. After total thyroidectomy the histological result was consistent with anaplastic carcinoma 9/8/7 cm in size with capsular and soft tissue infiltration. However, the patient refused any further treatment. On the last follow-up visit 32 months following the diagnosis the patient was euthyroid on replacement therapy with no clinically evident local recurrence or distant metastases.
Discussion and conclusion
Anaplastic thyroid carcinoma is poorly responsive to current treatment modalities with a 4-month median overall survival from the time of diagnosis. Recent study demonstrated significant improvement in survival over the last 2 decades presumably due the introduction of molecular-based personalized therapies. Among the most significant prognostic factors are considered age, size of the tumor, presence of extrathyroid invasion and distant metastases along with several new factors such as white blood cell and platelet count at presentation. The two stage IV B patients described presented with similar histological findings but completely different course of the disease. Further studies on the molecular characteristics of anaplastic cancers will probably provide valuable data on the individual risk of recurrence and progression and contribute to the improvement of the long-term prognosis.

DOI: 10.1530/endoabs.81.EP1022

EP1023

Management and prognosis of anaplastic thyroid cancer

Moncef Sellami, Wadii Thabet, Malek Mnejja, Bouthaina Hammami, Souha Kallel & Ilhem Charfeddine
Habib Bourguiba Hospital, University of Sfax, Tunisia, Otorhinolaryngology, Tunisia

Introduction
Anaplastic thyroid carcinoma (ATC) is rare. This highly aggressive malignant tumor accounts for 2 – 3 % of all thyroid gland neoplasms. ATC continues to be one of the deadliest diseases worldwide and carries a very poor prognosis. The aim of this study was to describe the treatment modalities of ATC and its prognostic features.
Methods
A retrospective study of patients with ATC treated in our department between 2004 and 2021.
Results
Nine patients were included: 4 men and 5 women. The median age was 65 years [44 years – 90 years]. All patients presented with an anterior neck mass lasting for a median duration of 2.5 months [0.5 – 9] with a recent rapid increase in size. Weight loss and compressive symptoms were reported in all cases. Physical examination showed a hard anterior neck mass in all cases, with a median size of 7.8 cm [3 – 15]. Lateral neck lymph nodes were reported in 3 cases. Vocal fold paralysis was found in 4 patients. CT scan, performed in 8 cases, revealed a thyroid lesion pushing the trachea, the esophagus internal jugular vein, and carotid in 7 cases. Fine needle aspiration was performed in 3 patients and revealed a poorly differentiated thyroid carcinoma. Six patients underwent a total thyroidectomy. Central neck dissection was performed in 3 patients and lateral neck dissection in one patient. The diagnosis was made after thyroid biopsy in 2 patients and lymph node biopsy in 1 patient. The tumor invaded the trachea ($n=$ 7), thyroid cartilage ($n=1$), cricoid cartilage ($n=$ 1) esophagus ($n=$ 1), recurrent laryngeal nerve ($n=$ 3), internal jugular vein ($n=$ 1). Three patients had pulmonary metastasis. Two patients had postoperative radiotherapy. Two patients had postoperative radio-chemotherapy. Recurrence was noted in these 4 cases. Palliative radio-chemotherapy was indicated in 1 case. The median survival duration was 4 months [2 days-13 months].
Conclusion
Anaplastic thyroid cancer is a devastating thyroid cancer with the poorest prognosis. As in our study, with conventional treatment including surgery,

radiotherapy, and conventional chemotherapy the overall survival of patients with anaplastic thyroid cancer has been less than 12 months.

DOI: 10.1530/endoabs.81.EP1023

EP1024

TSHR promoter methylation level changes as a prognostic blood-based biomarker in follicular thyroid carcinoma

Mintaute Kazokaite[1], Kristina Zukauskaite[2, 3], Raimonda Klimaitė[1,4], Aistė Kondrotienė[1,4], Dalia Daukšienė[1], Birute Zilaitiene[1, 4], Rasa Sabaliauskaite[2, 3] & Albertas Dauksa[5]
[1]Lithuanian University of Health Sciences, Institute of Endocrinology, Kaunas, Lithuania; [2]National Cancer Institute, Laboratory of Genetic Diagnostic, Vilnius, Lithuania; [3]Vilnius University Life Sciences Centre, Institute of Biosciences, Vilnius, Lithuania; [4]Hospital of Lithuanian University of Health Sciences Kaunas Clinics, Department of Endocrinology, Kaunas, Lithuania; [5]Lithuanian University of Health Sciences, Institute of Digestive Research, Kaunas, Lithuania

Introduction
Papillary thyroid carcinoma (PTC) is the most common type of differentiated thyroid cancer, accounting for about 80% of all cases of thyroid cancer. Generally, PTC is an indolent disease and shows a good prognosis in most patients. However, up to 30% of patients have local tumor renewal or systemic spread. It is crucial to identify patients with a high risk of disease progression. DNA methylation biomarkers may provide clinically valuable information and improve the early non-invasive prognosis of PTC.
Aim of the study
To evaluate DNA methylation level changes of selected genes in peripheral blood plasma samples in PTC patients before and 4-6 weeks after surgery.
Methods
The studyincluded 68 patients with a histologically confirmed diagnosis of PTC with different histological variants: classical ($n=29$), diffuse sclerosing ($n=17$), follicular ($n=18$), and tall cell carcinoma ($n=4$). Peripheral blood samples were collected before surgery and 4-6 weeks after surgery during 2020 – 2021 in Hospital of Lithuanian University of Health Sciences, Kaunas clinics. DNA methylation level changes of *TSHR* gene were analysed by quantitative methylation-sensitive polymerase chain reaction. DNA methylation levels of *TSHR* were compared before and one month after the surgery using both paired and non-paired non-parametrical tests.
Results
Significantly lower *TSHR* promoter methylation levels were found 4-6 weeks after surgery compared to samples collected before surgery ($P=0.034$) in follicular variant of PTC. Paired sample analysis showed a statistically higher *TSHR* methylation level before surgery compared to *TSHR* methylation level after surgery in follicular variant PTC ($P=0.002$).
Conclusion
TSHR promoter methylation level changes may be a promising biomarker in predicting PTC prognosis.
Funding
This study was supported by the Lithuanian Research Council (Grant No. S-SEN-20-14 "The role of epigenetic markers for early detection of papillary thyroid carcinoma and prognostic significance in long-term outcome in elderly patients").

DOI: 10.1530/endoabs.81.EP1024

EP1025

Routine molecular testing of fine needle aspiration biopsies of thyroid nodules

Vlasta Sykorova[1], Jitka Moravcova[1], Eliska Vaclavikova[1], Barbora Pekova[1], Karolina Mastnikova[1], Josef Vcelak[1], Zdenek Novak[2], Petra Pacesova[2], Tereza Grimmichova[2], Jan Jiskra[3] & Bela Bendlova[1]
[1]Institute of Endocrinology, Department of Molecular Endocrinology, Prague, Czech Republic; [2]Institute of Endocrinology, Department of Clinical Endocrinology, Prague, Czech Republic; [3]General University Hospital in Prague, Department of Endocrinology and Metabolism, 3rd Department of Medicine, Prague, Czech Republic

Objectives
Fine needle aspiration biopsy (FNAB) together with ultrasonography is a necessary tool for diagnosis and follow up of thyroid nodules. Molecular testing is increasingly used mainly for indeterminate categories of the Bethesda System for Reporting Thyroid Cytopathology revised in 2017. Our aim was to introduce a routine molecular analysis of the main genetic causes of thyroid cancer.
Methods
Since 2017 we have analyzed 1171 samples of patients with thyroid nodules. We gradually established testing procedure mainly in samples evaluated as Bethesda categories III and above. First, we analyze DNA for the most common mutation V600E in the *BRAF* gene using allele specific Real Time PCR (LC480, Roche). *BRAF*-positive samples are screened for *TERT* mutations using direct sequencing (CEQ 8000, Beckman Coulter). *BRAF*-negative samples are analyzed by next generation sequencing using the Thyro-ID panel (MiSeq, Illumina) examining other 12 genes. The samples negative in the NGS panel are subjected to detection of 23 fusion genes including *ALK*, *BRAF*, *GLIS, NTRK1*, *NTRK3*, *PPARG*, *RET* genes using Real Time PCR. In samples suspected of MTC, we search for *RET* mutations.
Results
In total, *BRAF* mutation was detected in 146 patients, *RAS* mutations in 72 patients, *RET* mutations in 4 patients, *TERT* mutations in 20 patients and fusion genes in 43 patients. In 21 patients we detected genetic variants in the other genes (*TP53*, *PTEN*, *PIK3CA*, *KIT*, *TSHR)*. From our cohort, in 390 patients post-surgical histopathological evaluation has been known. Positive predictive values of *RET*, *BRAF*, *TERT*, *KRAS*, *HRAS*, *NRAS* mutations and fusion genes were 100%, 98.4%, 93.3%, 75%, 60%, 42.1% and 97.6% respectively, if borderline tumors were not included in malignancy. In the *BRAF*-positive cohort was a case of follicular adenoma with *BRAF* K601E mutation and in the *TERT*-positive cohort one case of follicular tumor of uncertain malignant potential with *TERT* and *NRAS* mutation.
Conclusions
We established molecular testing of thyroid nodules that significantly contributed to clinical management of patients in the Czech Republic. *BRAF*, *RET* and *TERT* mutations and *RET/PTC* and *ETV6/NTRK3* fusion genes are associated with almost 100% risk of malignancy or even worse prognosis, therefore according to ETA guidelines from 2017 and recent publications their carriers are recommended for the total thyroidectomy. The risk of malignancy of *RAS* mutations is lower and rather a lobectomy is recommended. *Supported by AZV NU21-01-00448 and MH CR RVO 00023761.*

DOI: 10.1530/endoabs.81.EP1025

EP1026

Detection of rare variants in BRAF gene in thyroid nodules

Bela Bendlova[1], Vlasta Sykorova[1], Barbora Pekova[1], Eliska Vaclavikova[1], Jitka Moravcova[1], Karolina Mastnikova[1], Petr Vlček[2], Rami Katra[3], Daniela Kodetova[4], Petr Lastuvka[5], Petr Bavor[6], Jana Drozenova[7], Martin Chovanec[8] & Josef Vcelak[1]
[1]Institute of Endocrinology, Department of Molecular Endocrinology, Prague 1, Czech Republic; [2]2nd Faculty of Medicine, Charles University in Prague and Motol University Hospital, Department of Nuclear Medicine and Endocrinology, Prague 5, Czech Republic; [3]2nd Faculty of Medicine, Charles University in Prague and Motol University Hospital, Department of ETN, Prague 5, Czech Republic; [4]2nd Faculty of Medicine, Charles University in Prague and Motol University Hospital, Department of Pathology and Molecular Medicine, Prague 5, Czech Republic; [5]1st Faculty of Medicine, Charles University in Prague and Motol University Hospital, Department of Otorhinolaryngology and Head and Neck Surgery, Prague 5, Czech Republic; [6]2nd Faculty of Medicine, Charles University in Prague and Motol University Hospital, Department of Surgery, Prague 5, Czech Republic; [7]3rd Faculty of Medicine, University Hospital Kralovske Vinohrady, Department of Pathology, Prague 10, Czech Republic; [8]3rd Faculty of Medicine, University Hospital Kralovske Vinohrady, Department of Otorhinolaryngology, Prague 10, Czech Republic

Objectives
Papillary thyroid carcinoma (PTC) is the most frequent malignant endocrine disease and the most common genetic cause of the PTC is the substitution c.1799T > A (p.V600E) in the *BRAF* gene (35-70% of PTC) that represents more than 95% of *BRAF* mutations. Other rare mutations in the *BRAF* gene include other substitutions (e.g. p.K601E), small deletions or insertions close to codon 600. The aim was to analyze a large cohort of thyroid nodules for rare genetic variants in the *BRAF* gene.
Methods
A total of 1106 fresh frozen thyroid tissues collected from 2003 to 2021 were screened for exon 15 *BRAF* alterations. The cohort consisted of 851 papillary thyroid carcinomas (PTC), 33 borderline tumors, 28 oncocytic and follicular carcinomas (FTC), 6 poorly differentiated carcinoma (PDTC), 15 anaplastic

carcinomas (ATC), 15 follicular adenomas (FTA) and 122 benign tissues. The exon 15 of the *BRAF* gene was analyzed by next generation sequencing using the Nextera XT Sequencing Kit (Illumina) or Thyro-ID (4 bases). The VarSome software was used to interpret detected variants.
Results
The most common *BRAF* mutation p. V600E was detected in a total of 430 thyroid tissues - in 425 PTC, two borderline tumors (NIFTP and WDT-UMP), one PDTC and two ATC. In total, *BRAF* p.V600E was detected in 51.3% of PTC. The rare somatic *BRAF* alterations were detected in 11 from 851 patients of PTC (1.29%), in one benign thyroid tissue and one FTC. We detected eight various variants - the most common was p.K601E and V600_K601delinsE in four and three patients, respectively, followed by p.V600E + p.Q609E, p.V600_S605delinsEG, VKS600-2DFT, p.T599_V600insEAT, p.A598_T599insI and p.T599dup in one case only.
Conclusions
The rare *BRAF* variants represented 2.9% of *BRAF*-positive thyroid nodules. Except for p.K601E, other rare variants were found exclusively in PTC. However, *BRAF* fusion genes, that seem to be other genetic causes of PTC, were not analyzed in this study. *Supported by AZV NU21-01-00448 and MH CR RVO 00023761.*

DOI: 10.1530/endoabs.81.EP1026

EP1027

Is obesity linked to thyroid cancer?

Iustin-Daniel Toma[1], Raluca-Alexandra Trifănescu[1,2], Maria-Alexandra Mohora[1], Ionela Florina Baciu[1, 2], Nicoleta Baculescu[1, 2], Cristina Ana-Maria Căpăţînă[1,2], Roxana Duşceac[1,2], Simona Andreea Găloiu[1,2], Dan Alexandru Niculescu[1, 2], Marian Romeo Smărăndache[3], Dumitru Lucian Ioachim[4] & Cătălina Poiană[1,2]
[1]National Institute of Endocrinology 'C.I. Parhon', Pituitary and Neuroendocrine Disorders, Bucharest, Romania; [2]University of Medicine and Pharmacy 'Carol Davila', Endocrinology, Bucharest, Romania; [3]National Institute of Endocrinology 'C.I. Parhon', Endocrine Surgery, Bucharest, Romania; [4]National Institute of Endocrinology 'C.I. Parhon', Pathology, Bucharest, Romania

Background
During the past decades, the prevalence of both obesity and differentiated thyroid carcinoma increased worldwide. The link between obesity and thyroid cancer is controversial. Some studies found a relationship between obesity and thyroid carcinoma (especially $BRAF^{V600E}$ mutated) and between type 2 diabetes mellitus and thyroid cancer, while other did not.
Aim
To assess the relationship between papillary thyroid carcinoma and increased body mass index (BMI).
Methods
Retrospective study by analyzing the files of patients with thyroid nodules who underwent thyroid surgery within a tertiary endocrine center. 101 patients (aged 54.5 ± 14 years) with thyroid nodules were included. TSH, FT4 were measured by chemiluminescence. Preoperatively, fine needle aspiration and cytology exam were performed in suspicious nodules, according to current guidelines. Bethesda classification was used for reporting the results. After thyroidectomy, according to histology exam, 51 patients had multinodular nontoxic (MNG) and 50 had papillary thyroid carcinoma (PTC).
Results
Globally, normal BMI (18.5-24.99 kg/m^2) was found in 27% of patients, while 47%were overweight and 26% were obese. 43% of patients were residents in iodine-deficient regions without significant differences between patients with MNG and PTC. Cytology exam was performed in 57 patients: Bethesda II was described in 11 patients (19,3%), Bethesda IV in 23 (40,35%), Bethesda V in 13 (22,8%), Bethesda VI in 7(12,28%) and for two patients our results came back inconclusive (Bethesda I – 3,5%) and 1 more patient (1,75%) had cytology exam performed from ganglia which came back positive for malignancy. Age was similar in patients with MNG (55.6 ± 12.3 years) and in patients with PTC (55 ± 15.6 years, P = ns). Mean TSH levels were similar in patients with MNG (1.2 ± 0,81 mIU/l) and in patients with PTC (1.4 ± 0,78 mIU/l, P = ns). Mean diameter of the largest nodule was significantly higher in patients with multinodular goiter (31.3 ± 12.6 mm) than in patients with PTC (26.3 ± 12 mm, P = 0.02). Patients with normal BMI had similar mean diameter of the largest nodule (29.9 ± 15 mm) with overweight and obese patients (31.63 ± 11.2 mm, P = ns, t-test) and also showed a similar prevalence of PTC- 48.2% as compared with 48.6% in overweight and obese patients (P = ns, chi square). Mean TSH levels was slightly higher (1.49 ± 0,80 mIU/l) in overweight and obese patients with PTC, than in patients with normal BMI (TSH = 1.26 ± 0,75 mIU/l, P = ns).
Conclusion
In our retrospective series, there was no link between BMI and papillary thyroid cancer. Larger prospective studies are needed in order to clarify this relationship.

DOI: 10.1530/endoabs.81.EP1027

EP1028

Sub acute thyroiditis following COVID infection or vaccine: case reports

Hemmat El Haddad[1], Amr El Meligui[2], Randa Salam[1], Hesham Maged El Din[1], Ahmed Rabie[1], Samar Amin[1], Mona Youssry[1] & Noha Tarek[1]
[1]Cairo University, Internal Medicine, Endocrinology, Cairo, Egypt; [2]Cairo University, Cairo, Egypt

Introduction
The novel severe-acute-respiratory-syndrome-coronavirus-2 virus has led to the ongoing Coronavirus disease 2019 (COVID-19) disease pandemic. There are increasing reports of extra pulmonary clinical features of COVID-19, either as initial presentations or sequelae of disease ((gastrointestinal, hepatobiliary, pancreatic, cardiovascular, ocular, and neurologic) Autoimmune/inflammatory syndrome induced by adjuvants (ASIA syndrome) can be seen as a post-vaccination phenomenon that occurs after exposure to adjuvants in vaccines We report cases of subacute thyroiditis following COVID infection or vaccine
Clinical cases
1-A 47 years old female developed subclinical hypothyroidism 3 weeks after COVID 19 infection TSH was 10.1 IU/ml (0.4-4), FT4 was 0.94 ng/dl ((0.7-1.9), Ant microsomal abs: 945IU/ml (0-9), Ant thyroglobulin abs: 285IU/ml (n: < 116) Thyroid sonar: diffuse heterogeneity & increased vascularity. 2-A 45 years old female developed subclinical hypothyroidism after exposure to COVID 19 infection by one month with TSH 7.74 IU/ml, FT4 1.2 ng/dl, Ant microsomal ab 959 IU/ml, Ant thyroglobulin ab 257 IU/ml Thyroid sonar: diffuse heterogeneity 3-A 35 years old female who had local pain in the neck 2 weeks after COVID infection. Investigations revealed non-uniform echo texture of the thyroid gland in the thyroid sonar TSH: 3.06 IU/ml, FT4 1.06 ng/dl, Ant microsomal ab 33 IU/ml, Ant thyroglobulin ab 955.7 IU/ml Post vaccine cases 1-A 59 years old female under treatment for thyrotoxicosis. She went into remission for 3 months with one tab neomercazole 5 mg 10 days of the first dose of vaccine for COVID 19, the patient developed exacerbation of her thyrotoxicosis with tachycardia, pulse 115, anxiety, insomnia and tremors. Her TSH became 0.009 IU/ml & increase of the dose of Inderal & neomercazole was done. Within 2 months the patient responded in a good way & entered into remission again 2-A 65 years old female who developed hypothyroidism after vaccine TSH: 10.21 IU/ml, FT4 0.82 ng/dl, Ant microsomal ab 600 IU/ml, Ant thyroglobulin ab 206 IU/ml 3-A 36 years old female who developed subclinical hyperthyroidism after vaccine Her thyroid sonar was normal sized sonar with heterogeneity TSH 0.03 IU/ml, FT4 0.93 ng/dl After 3 months her thyroid sonar is completely normal TSH 1.210 IU/ml, FT4 0.84 ng/dl, FT3 2.94 pg/ml (2.3-4.1)
Conclusion
Clinicians must be aware of the possibility of thyroid dysfunction and subacute thyroiditis after COVID-19 infection and after the inactive SARS-CoV-2 vaccine. Early recognition and timely anti-inflammatory therapy can help in successful management of the disease.

DOI: 10.1530/endoabs.81.EP1028

EP1029

Hashimoto's thyroiditis manifested with rhabdomyolysis and cardiac effusion following SARS-CoV-2 vaccination: A case report

Rachid Smaili, Randa Ait Imrane, Ikram Raaidi & Myriem Bourkia
University Hospital of Tangier, Internal Medicine and Clinical Immunology, TANGER, Morocco

Background
Autoimmune inflammatory syndrome induced by adjuvants (ASIA syndrome), include the different conditions linked following exposure to an adjuvant. Autoimmune thyroiditis following vaccination as an auto-immune/inflammatory syndrome is rarely reported. In the era of mass vaccination against SARSCov2, there is limited information about cases of auto-immune thyroid disease as an ASIA syndrome following SARS-CoV-2 vaccination.

Case
A 19years old man, with no medical history was presented five days after second vaccination doses against SARS-CoV-2 with unusual clinical symptoms of hypothyroidism as acute rhabdomyolysis with a pericardial effusion, and a very high level of thyroid stimulating hormone, decreased free thyroxin and higher level of peroxidase and thyroglobulin thyroid autoantibody. One week after L-thyroxin treatment CK was normal and kidney function is normalized with a remarkable improvement of thyroid functions.
Conclusion
Rhabdomyolysis and pericardial effusion can occur as severe symptoms of Hashimoto thyroiditis as an ASIA syndrome after vaccination against SARS-CoV-2.
Key words:ASIA syndrome - SARS-CoV-2 vaccine - Hashimoto's thyroiditis - Acute rhabdomyolysis - pericardial effusion.

DOI: 10.1530/endoabs.81.EP1029

EP1030

Hand and foot skin changes resembling PTU-induced vasculitis in a young male with diffuse toxic goiter- a case report

Martina Tomasovic[1], Marija Sinik[1], Bojan Joksimovic[1], Milena Lackovic[1], Vladimir Samardzic[1], Marina Vujovic[1], Zoran Gluvic[1], Milan Obradovic[2], Sonja Zafirovic[2] & Esma R. Isenovic[2]
[1]Zemun University Clinical Hospital, Department of Endocrinology and Diabetes, Belgrade, Serbia; [2]"VINČA" Institute of Nuclear Sciences – National Institute of the Republic of Serbia, Department of Radiobiology and Molecular Genetics, Belgrade, Serbia

Propylthiouracil (PTU) sometimes induces autoimmune syndromes, such as PTU–induced lupus or vasculitis. Here we present hands and feet vasculitis-like skin changes observed several days after PTU introduction in a patient who suffered from serious diffuse toxic goiter. Because of segmental distribution, normal liver function test, and no signs of clinical deterioration, it was decided to continue PTU management and observe the patient. Primarily maculopapular rash became vesicular shortly after and then scaly. After two weeks, skin changes were entirely restored with no scaring. Taking into account thorough epidemiological survey, clinical course, and performed diagnostics, presented skin changes were diagnosed as Hand, Foot, and Mouth disease (HFMD). Clinicians must be aware of the side effects of used drugs, especially after their introduction. Some clinical presentations could only resemble expected or well-known side-effects, intolerance, or hypersensitivity to the used drug. Every clinical presentation associated with any drug introduction must be thoroughly evaluated. The presented case revealed that skin changes of HFMD mimicked PTU-induced vasculitis.
Keywords: Propylthiouracil, autoimmunity, Hand, Foot and Mouth Disease

DOI: 10.1530/endoabs.81.EP1030

EP1031

Frequency of thyroid ultrasound alterations in polycystic ovary syndrome

Sawsen Essayeh[1], Wassim Frikha[2], Radhouan Gharbi[1], Wiem Madhi[1], Manel Jemel[1] & Ines Kammoun[1]
[1]National Institute of Nutrition and Food Technology of Tunis, Endocrinology, Tunis, Tunisia; [2]La Rabta Hospital, Radiology, Tunis, Tunisia

Introduction
Polycystic ovary syndrome (PCOS) is a common endocrine disease in women of childbearing age. This condition combines, according to the diagnostic criteria of the Rotterdam consensus 2003, clinical and/or biochemical signs of hyperandrogenism, oligo- and/or anovulation and polycystic ovaries detected by ultrasound. Thyroid diseases are also frequent in the general population. The aim of our study was to determine the prevalence of thyroid ultrasound alterations in a group of patients with PCOS compared to a control group.
Patients and Methods
31 patients with PCOS and 30 age- and body mass index-matched healthy volunteer women were recruited into the study. Thyroid ultrasound was performed in all participants.
Results
The age and the body mass index were comparable between the two groups (29.8 ± 7 vs 29.5 ± 5.5 years, $P = 0.86$; 32 ± 6.6 vs 31.1 ± 8.9 kg/m^2 $P = 0.62$). Cervical ultrasound was more frequently pathological in the group of PCOS women (58% vs 33%, $P = 0.05$). The ultrasound feature of thyroiditis was significantly higher in the PCOS group compared to the control group (39% vs 3%, $P = 0{,}001$). The means of thyroid volume were similar in both groups (9.4 ± 5.5 vs 10 ± 7.2, $P = 1$). The percentages of goiter and thyroid nodules were comparable between the two groups ($P = 1$, $P = 0.7$ respectively).
Conclusion
Our study showed an increased prevalence of thyroiditis on cervical ultrasound in PCOS women but it did not show any difference in the occurrence of thyroid nodules or goiter.

DOI: 10.1530/endoabs.81.EP1031

EP1032

Efficacy of ethanol injection in cystic thyroid nodules

Naween Kumar[1], Rajeev Ranjan[2] & Siddharth Singh[3]
[1]Global Healthcare & Diabetes Research Centre, Diabetes, Darbhanga, India; [2]Chest Clinic, Medicine, Chapra, India; [3]IGIMS, Diabetes, Patna, India

Introduction
Thyroid cystic nodules (TCN) are generally due to degenerative changes within colloid nodules or adenomas. True thyroid cysts are uncommon. But the prevalence of malignancy among TCN is controversial since some authors consider it to be low risk while some others consider it to have the same risks as malignancy as the solid lesions of the thyroid. Percutaneous ethanol injection (PEI) is utilised for treating benign cystic thyroid nodules. It is a protected option for cystic TNs and compelling treatment for lessening strong TNs of various sizes whether or not hyperfunctioning. In this meta-analysis study, the aim is to obtain strong evidence regarding the safety and long-term efficacy of PEI.
Methods
Data reported on compressive symptoms, cosmetic concerns, and volume reduction rate were collected from different well-known databases like PubMed, Web of Science and Scopus. Data collected since 2020 were used for this study. For pooling the data, a random-effects model was also designed.
Results
From the final selected 395 papers, 19 studies that evaluated 1667 nodules were included. Volume reduction rate at 6, 12, 24, 36, 60 and 120 months were 78%, 82%, 73%, 69%, 75% and 70% respectively. Observations were made for significant reductions of cosmetic concerns and compressive symptoms. However, extremely durable inconveniences were not seen in this review.
Conclusions
In this present meta-analysis study, the PEI significantly reduced the volume of harmless cystic thyroid nodules. This reduction was seen as effective at the post-treatment of six months, and stability was seen in the effects over time.

DOI: 10.1530/endoabs.81.EP1032

EP1033

Pregnant patient with a history of methimazole-induced agranulocytosis presenting with hyperthyroidism: a case report

Abdusattar Abduraup & Jerome Barrera
Zamboanga City Medical Center, Internal Medicine, Zamboanga City, Philippines

Background
Pregnancy has a profound impact on the thyroid gland and its function. Severe thyrotoxicosis can lead to many complications and endanger the mother or fetus. Antithyroid drug (ATD), at its lowest possible dose, should be given. However, one of the complications of treatment include agranulocytosis which is a rare but serious allergic event with a prevalence of 0.1 to 0.5 percent. Thus, alternative treatment should be prescribed because a cross-reaction between ATDs was observed in 15.2% of patients in a study. Insufficient data is available regarding the use of these medications in pregnant patients with history of drug-induced adverse reactions. There are alternative treatments but are contraindicated in pregnancy.
Case
We report a 29-year old patient gravida 5 para 4 at 10 weeks age of gestation presenting with palpitations. She is a known case of Graves' disease for 7 years and maintained on Methimazole. She was admitted a year prior as a case of impending thyroid storm; methimazole-induced agranulocytosis. Initially, maintained on Lithium but shifted back to Methimazole without a physician's

advice and later on, discontinued the medication upon knowledge of pregnancy. On her first trimester, noted with palpitations and elevated free thyroxine (T4) at 71.29 pM (normal range: 11-24 pM). She was started on Propylthiouracil 50 mg/tablet 1 tablet thrice a day. On her second trimester, no reported symptoms of hyperthyroidism and/or agranulocytosis such as fever or sore throat. Thyroidectomy was offered but she strongly refused. Free T4 was then maintained at a value slightly above the upper normal limit. Propylthiouracil was shifted to methimazole 5 mg/tablet 1 tablet once daily and revised to 1 tablet every other day on her third trimester. Delivery was uneventful and the newborn was evaluated with unremarkable findings. Four weeks postpartum, no noted symptoms of hyperthyroidism and/or agranulocytosis. Free T4 was within normal at 18.84 pM. Alternative treatment was offered due to the risk of agranulocytosis.
Conclusion
Hyperthyroidism in pregnancy is associated with a variety of complications for the mother and fetus. Effective treatment options include ATD, thyroidectomy or RAI therapy. But, not all are relatively safe for pregnancy. In initiating ATD, cross-reaction between medications should be considered especially for patients with history of adverse reaction, such as agranulocytosis, which can be life-threatening. However, there are limited studies in the management of this specific case. Treating physician and patient should discuss each of the options, including the benefits and drawbacks.

DOI: 10.1530/endoabs.81.EP1033

EP1034

Place of scintigraphy in case of diagnostic doubt in Graves' disease

Severin N'Koua, Jaddi Oussama, Sana Rafi, Ghizlane EL Mghari & Nawal EL Ansari
Department of Endocrinology, Diabetology and Metabolic Diseases, CHU Mohamed VI. Marrakech., Marrakech, Morocco

Graves' disease is a rare and severe disease that most often affects older children and is predominantly female. The diagnosis is made in the presence of a clinical picture very suggestive of thyrotoxicosis, confirmed by biological and radiological tests. We present the case of an 11-year-old female patient who presented with a moderate presented of basedow with an ultrasound appearance of thyroiditis for which scintigraphy was helpful in the diagnosis. Female patient, 11 years old with no history, has been suffering from moderate weight loss for 2 months without any other signs of thyrotoxicosis. On clinical examination: bilateral exophthalmos, normocadic at 78 bpm non palpable thyroid. On clinical examination: bilateral exophthalmos, normocadic at 78 bpm non palpable thyroid. On workup: TSH $<$ 0,05 Mui/l; T4L : 20,8 (N:9-19) pmol/l; Cervical echography : aspect of a thyroiditis. diagnosis doubt and therapeutic necessity, a scintigraphy was performed showing a diffuse and homogeneous fixation. the patient had been put on carbimazol 20 mg/d. The difference between Graves' disease and thyroiditis is not always trivial in view of the clinical manifestations during the Hashi toxicosis phase and the ultrasound appearance, the interpretation of which remains operator dependent. In such conditions, the use of anti-thyroid antibodies or scintigraphy can play a decisive role. Indeed, in Graves' disease the scan image appears diffuse and homogeneous unlike in thyroiditis where the image appears white. Thyroid scintigraphy is one of the definitive diagnostic tools, especially when there is clinical and sonographic confusion between the two conditions.

DOI: 10.1530/endoabs.81.EP1034

EP1035

The effect of l-thyroxine replacement on blood pressure and heart rate in children with hypothyroidism: correlation with free thyroxine and thyrotropin levels

Ahmed Elawwa[1], Ashraf Soliman[2] & Marwa Faraj[1]
[1]Department of Pediatrics, College of Medicine, Alexandria University, Alexandria, Egypt; [2]Hamad Medical Center, Pediatrics, Doha, Qatar

Chronic administration of L thyroxine to children with hypothyroidism may affect cardiovascular dynamics.
Aim of the study
We measured the BP and heart rate (HR) of 25 randomly selected children with hypothyroidism in relation to their serum free T4, and TSH levels and thyroxine dose mg/kg.
Methods
25 randomly selected children with a mean age 9.6 +/- 4.5 years with the diagnosis of congenital or acquired hypothyroidism. They were on L thyroxine therapy to keep serum FT4 and TSH in the normal range for age. Their blood pressure (BP) and HR (average of three readings), weight, height, dose of thyroxine, and their serum level of TSH and Free T4 levels within two weeks before the clinic visit were recorded. The Z scores of the height (HtSDS), BMI (BMISDS), systolic (SBPSDS) and diastolic blood pressure (DBPSDS) were calculated (as per the 2004 guideline report on hypertension from the National Heart and Lung institute) and HR (as per the Monitoring and Diagnosis Group at Oxford (MADOX) systematic review of 2011) were calculated for age and gender.
Results
L thyroxine dose was 2.11 +/- 0.7 mg/kg. Their mean serum free thyroxine levels was 15.1 +/- 2.5 mg/l and TSH level was 3.9 +/- 2.8 mIU/ml. Their HtSDS (-0.57 +/- 1.4) and BMISDS (0.63 +/- 1.63) were within normal. All had normal diastolic blood pressure readings (within 2 standard deviations of the mean for age and sex). Two of the individuals had systolic blood pressures $>$ 2SDS above the mean for age and gender, with normal BMISDS. Both had normal FT4 and TSH levels. One patient had tachycardia (HR = 146/min (z score +3.2 for age). His FT4 and TSH levels were normal. There was a positive correlation between thyroxine dose/kg and serum level of FT4(r=0.52), heart rate (r=0.56), SBPSDS (r= 0.38), and DBPSDS (r=0.24). There was no significant correlation between the HtSDS on the one hand and FT4, TSH or thyroxine dose on the other hand. The BMISDS was negatively correlated with TSH level (r=-0.4)
Conclusion
In this study on hypothyroid children on L thyroxin therapy, 2 had high systolic blood pressure and one had tachycardia. The significant correlation between the thyroxine dose, FT4 level and BP and HR should alert the Pediatrician to monitor BP and HR closely in relation to TSH and FT4 levels these patients.

DOI: 10.1530/endoabs.81.EP1035

EP1036

Diagnosis and management of anaplastic thyroid carcinoma: about 3 cases and review of literrature

Rachida Bouattay, Emna Bergaoui, Maroua Naouar, Mehdi Ferjaoui, Heyfa Belhadjmiled, Amel Elkorbi, Kaled Harrathi, Naourez Kolsi & Jamel Koubaa
Fattouma Bourguiba Hospital, ENT, Monastir, Tunisia

Introduction
Anaplasic thyroid carcinoma is an extremely aggressive undifferentiated tumor of follicular cell origin. It is uncommon and comprising approximately 1% of all thyroid cancers.
Purpose of the presentation
The objective of this work is to determine the clinical, histological and therapeutic aspects of anaplasic thyroid carcinoma.
Methods
This is a retrospective study about 4 patients treated for an anaplasic thyroid carcinoma, in the ENT department of Fattouma Bourguiba hospital in Monastir over a period of 22 years (2000-2021).
Results
The average age was 68 years. A female predominance was noted. The average consultation time was 2 months. Patients consulted for a rapidly progressive goitre in all cases, associated with dysphagia and dyspnea in 3 cases (75%). Cervical examination showed a painful and indurated anterior cervical swelling with a medium size of 5 cm in all patients. Associated lymph nodes were found in 2 cases (50%). Indirect laryngoscopy showed laryngeal paralysis in 2patients (50%), one of which was bilateral (25%). Cervical ultrasound and cervico-thoracic scan showed a mass pushing back the trachea in three cases (75%). 3 patients (75%) had an emergency tracheostomy with thyroid biopsy. The other patient underwent a lobo-isthmectomy. Radiotherapy was indicated in all cases. The evolution was fatal in all patients with a survival of less than 6months.
Conclusion
Anaplastic thyroid cancer is a very rare case and has a poor prognosis. The important information such as clinical manifestations, physical examination and imaging are necessary to diagnose and administer the proper management.

DOI: 10.1530/endoabs.81.EP1036

EP1037

Hürthle cell tumors of the thyroid gland: diagnostic and therapeutic features

Masmoudi Mohamed, Chaima Zitouni, Wadii Thabet, Chebil Ezer, Hasnaoui Mahdi & Mighri Khalifa
Taher Sfar Hospital, Otorhinolaryngology, mahdia, Tunisia

Introduction
Oncocytic tumors can occur in the thyroid gland and other endocrine tissues, including the parathyroid, pituitary gland, adrenal cortex, pancreas, gut, and lung. Thyroid oncocytic tumors are rare: 3-10% of thyroid epithelial tumors. They are characterized by the presence of oncocytic cells called "Hürthle" cells.
Objective
Describe the clinical, pathological and therapeutic features of oncocytic tumors of the thyroid gland.
Methods
A retrospective study including 35 cases of thyroid oncocytic tumors treated in our department between 1988 and 2021.
Results
The average age of our patients was 48 years. The sex-ratio (F/M) was 10,9. The mean size of the nodules on ultrasonography was 31,3mm. The nodule was unique in 25 cases. The nodules were classified according to the EU-TIRADS classification: EUTIRADS 2 (12 cases), EUTIRADS 3 (22 cases), EUTIRADS 4 (10 cases) and EUTIRADS 5 (10 cases). A lobectomy was performed in 31 cases, a total thyroidectomy was done in 1 case, and an isthmectomy was done in 3 cases. Among our patients, 33 patients had oncocytic adenoma and 2 patients had oncocytic carcinoma. In case of oncocytic carcinoma, a totalization with central lymph node dissection and radioactive iodine therapy were done. Evolution was favorable in these 2 cases.
Conclusion
In general, oncocytic tumors do not have a specific clinical presentation or distinguished features on ultrasonography. Furthermore, distinguishing hyperplasia from neoplasia, and benign from malignant is difficult on cytology. Anatomopathological examination is often needed to make the diagnosis of these tumors. Compared to other differentiated tumors, oncocytic carcinomas tend to be more aggressive, and have less radioactive iodine intake. Overall survival in 5 years is 50-70%.

DOI: 10.1530/endoabs.81.EP1037

EP1038

Type 1 diabetes mellitus and autoimmune thyroid disorders

Faten Haj Kacem Akid[1], Raida Ben Salah[2], Siddiqa Soomauroo[1], AbdelMouhaymen MISSAOUI[1], Sarra Chouaib[1], Sameh Marzouk[2], Nadia Charfi[1], Zouheir Bahloul[2] & Mohamed Abid[1]
[1]Hedi Chaker University Hospital, Department of Endocrinology, Sfax, Tunisia; [2]Hedi Chaker University Hospital, Department of Internal Medicine, Sfax, Tunisia

Introduction
Type 1 diabetes mellitus (T1DM) is the result of the autoimmune destruction of beta-cells of the endocrine pancreas, leading to absolute insulin deficiency. The process of this autoimmune destruction occurs in genetically susceptible individuals with positive relevant autoantibodies. T1DM may be associated with other autoimmune diseases (AD) such as autoimmune thyroid disorders (AITD).
Patients and methods
It is a descriptive retrospective study. We collected data from 113 patients diagnosed with AITD associated with another AD over 18 years. The present study reports the association between T1DM and AITD.
Results
T1DM was diagnosed in 41 patients (31.53%) which consisted of 25 women and 16 men. The mean age upon discovery of the T1DM was 30.49 years. The T1DM was associated with an overt hypothyroidism in 18 patients, a subclinical hypothyroidism in 1 patient, an autoimmune thyropathy in euthyroid phase in 7 patients, an overt hyperthyroidism in 14 patients and a subclinical hyperthyroidism in 1 patient. It was affiliated with Hashimoto's disease in 26 cases (63.4% of cases) and with Graves' disease in 15 cases (36.6% of cases). The T1DM preceded the diagnosis of the thyroid disorder in 24 cases with a mean period of 69 months between and succeeded the latter in 6 cases within a mean period of 40 months. In 11 cases, both diagnoses were concomitant.
Discussion and Conclusion
T1DM is the most frequent AD associated with AITD. Their prevalence is 2 to 3 times higher in the T1DM population than that of the general population. As a matter of fact, 6.6% out of 10% of healthy adults have positive thyroid antibodies compared to 20% out of 40% of T1DM adults. According to Barker, T1DM is associated with Hashimoto's disease in 14-28% of cases. In other studies, it is associated with Graves' disease in 0.5-7% of cases. Several studies demonstrated that AITD was more frequent in diabetic women than men, which could be explained by higher prevalence of AITD in women. Serum TSH assay is recommended upon discovery of diabetes in patients with hypothyroid or hyperthyroid symptoms, then every 1-2 years as follow up. Our results consistent with that of the literature showed the high prevalence of the T1DM in patients with AITD, and thus the necessity of regular screening in these patients.
References
Barker JM. Clinical review: type 1 diabetes-associated autoimmunity: natural history, genetic associations, and screening. Journal of Clinical Endocrinology and Metabolism. 2006; 91(4): 1210–1217.

DOI: 10.1530/endoabs.81.EP1038

EP1039

Predictive factors of malignancy in thyroid nodules: value of ultrasonography

Masmoudi Mohamed, Chaima Zitouni, Wadii Thabet, Chebil Azer, Hasnaoui Mahdi & Mighri Khalifa
Taher Sfar Hospital, Otorhinolaryngology, Mahdia, Tunisia

Introduction
Ultrasound has become an indispensable diagnostic modality in the evaluation of the risk of malignancy of a thyroid nodule.
Objective
Identify the predictive factors of malignancy in thyroid nodules on ultrasound.
Methods
This is a retrospective study including 333 patients diagnosed with thyroid nodules and operated between 2010 and 2020. A significance threshold of 0.05 was adopted for the statistical analysis.
Results
The mean age of the patients was 44 years, predominantly females (88.3%). A thyroid cancer was diagnosed in 43 cases. The most common histological types were papillary carcinoma (83%) and vesicular carcinoma (14%). Predictive factors of malignancy were: solitary nodule ($P = 0,01$), cervical lymph node metastasis ($P = 0,017$), size > 4 cm ($P < 0,001$), solid nodule ($P < 0,001$), hypoechogenic nodule ($P = 0,004$), central vascularization ($P < 0,001$), central and peripheral vascularization ($P = 0,006$), microcalcifications ($P < 0,001$).
Conclusion
Although the vast majority of thyroid nodules are benign, a small proportion are cancers. Several predictive factors can evaluate the risk of malignancy of a thyroid nodule, however, predictive factors on ultrasonography are still the most important. The EU-TIRADS classification, is the most commonly used classification to stratify this risk of cancer in thyroid nodules. In the EUTIRADS classification, markedly hypoechoic, non-oval shape, irregular margins and microcalcifications are the only predictive factors included.

DOI: 10.1530/endoabs.81.EP1039

EP1040

Risk factors for central neck lymph node metastasis in patients with macro and micropapillary thyroid carcinoma

Georgios Boutzios[1], Sofia Chatzi[2], Areti Mina[2], Eleni Koukoulioti[2], Ilias Giovannopoulos[2] & Gerasimos Tsourouflis[3]
[1]School of Medicine, National and Kapodistrian University of Athens, Department of Pathophysiology, Athens, Greece; [2]School of Medicine, National and Kapodistrian University of Athens, Pathophysiology, Athens, Greece; [3]School of Medicine, National and Kapodistrian University of Athens, Second department of Propedeutic Surgery, Athens, Greece

Introduction
The prevalence of lymph node metastasis from micropapillary thyroid carcinoma (mPTC) in different studies is up to 33%. Preoperative diagnosis of central lymph node (CLN) metastasis is essential for the surgical management of those patients. Prophylactic CLN dissection for patients with mPTC is controversial. Our study aimed to assess the prevalence and the risk factors of LMN metastasis in patients mPTC

Methods
We retrospectively study the clinicopathological characteristics of 167 patients with PTC operated at the Second Department of Propaedeutic Surgery, University of Athens. Patients before surgery underwent ultrasound thyroid mapping for lymph node invasion assessment. All underwent total thyroidectomy with prophylactic central neck dissection.
Results
A total of 167 patients (73,1% females) were analyzed. The mean age was 51.08 ± 13.38 years, and the mean follow-up was 5.3 years. In 30.2% (55/161) of the patients, the lesion was located in both thyroid lobes, in 29.1% (53/161) and 26.4% (48/161) in the right and left lobe, respectively. Only 2.7% (5/161) of the patients had lesions located in the isthmus. 33% (60/162) of PTC patients had bilateral lesions, and 41.8% (76/165) had more than one lesion. The median number of lesions was 1.0 ± 3.05. 54.5% (91/167) of the patients had macro-PTC. In 34.8% of them, the lesion was located in both thyroid lobes. 45.7% % had multiple lesions. Furthermore, 49.3% had capsule penetration, 39.1% had an extrathyroidal expansion, and 32.8% had lymph node invasion. 45.5% (76/167) had micro-PTC. In 41.8% of the patients, the lesion was located in both thyroid lobes. 48.1 % had multiple lesions. In addition, 47.3% of these patients had capsule penetration, 35.9% had an extrathyroidal expansion, and 30.8% had lymph node invasion.
Conclusion
Our study found an increased risk of lymph node invasion in patients with micro-PTC, compatible with macro-PTC. Thus, an ultrasound thyroid mapping for lymph node invasion assessment before surgery is needed.

DOI: 10.1530/endoabs.81.EP1040

EP1041

Papillary thyroid cancer and its variants - genomic evidence and clinical significance

Darko Katalinic[1], Ivan Aleric[1], Aleksandar Vcev[1], Miljenko Solter[2], Irena Ranogajec[3] & Lars Toetome[4]
[1]Faculty of Dental Medicine and Health and Faculty of Medicine, J. J. Strossmayer University, Osijek, Croatia; [2]School of Medicine, University of Zagreb, Zagreb, Croatia; [3]Clinical Hospital Sveti Duh, Zagreb, Croatia; [4]Center for Cancer Medicine, Oslo, Norway

Purpose
Papillary thyroid cancer (PTC) accounts for approximately 80% of all thyroid cancers and is defined by its unique cytologic and histologic features. Mutations of the *RET and BRAF/V600* genes are found in nearly 70% of PTC cases. They are able to trigger the activation of mitogen-activated protein kinase pathways and to promote neoplastic cell proliferation. Genetic events may further lead to numerous different cell variants of PTC which may be identified via the different cyto/histopathologic features. The most common are the classical (CV), tall cell (TCV) and follicular variant (FV). The aim of the study was to perform the genomyc analysis of the *RET* and *BRAF (V600)* mutations in patients with PTC as well as to compare the obtained results with clinical findings.
Methods
The study included 112 patients diagnosed with PTC, aged 41-74 years. Mutations of the *RET* and *BRAF (V600)* genes were detected using Real-time polymerase chain reaction. Diagnosis of the PTC and its variants was confirmed with cyto/histopathological examination.
Results
The most important genomic, cyto/histopathological and prognostic elements regarding all three variants of the PTC are as follows: CV-PTC ($n = 78$): *RET* and *BRAF (V600)* mutations are common findings, with *BRAF (V600)* confirming a worse prognosis. The 65% of these patients have shown stabile disease course, with 25% with metastatic nodes; TCV-PTC ($n = 8$): Aggressive behavior has been attributed to *BRAF (V600)* mutation; FV-PTC ($n = 26$): Absence of *BRAF (V600)* mutation was the most important genetic element.
Conclusions
In most cases, PTC has an excellent prognosis, but certain variants express more aggressive clinical course. CV-PTC: *BRAF (V600)* mutation was negative prognostic element; TCV-PTC presents mostly in older patients, has agreater propensity for locoregional dissemination and has more aggressive course than CV-PTC; The prognosis of FV-PTC has been similar to that of CV-PTC. The patients with CV-PTC and FV-PTC had fovorable clinical course comparing to those with TCV-PTC. Our study suggests that PTC is etiopathogenically complex disease and requires further molecular investigations.

DOI: 10.1530/endoabs.81.EP1041

EP1042

Graves' disease associated with thyroid papillary carcinoma

Mohamed Masmoudi, Marwa Regaeig, Wadii Thabet, Azer Chebil, Mehdi Hasnaoui & Khalifa Mighri
Tahar Sfar Hospital, Mahdia, Otorhinolaryngology, Tunisia

Introduction
Thyroid carcinoma in Graves' disease is rare (1 to 2%). Papillary carcinoma is the most common histologic type. It is usually discovered incidentally after histologic exam. Our aim is to report a case of Graves' disease associated with thyroid papillary carcinoma and to describe its therapeutic and prognostic features.
Case report
A 51-year-old woman treated with anti-thyroid drugs and β blockers for Graves' disease. Cervical ultrasound found an enlarged, hypervascular thyroid gland with a 10 mm nodule classified EUTIRADS 5. Indication for surgery was: failed medical therapy after 3 years of treatment and concomitant suspicious thyroid nodule. The patient underwent total thyroidectomy. Intraoperative examination suggested a papillary thyroid carcinoma. So, a central neck dissection was performed. Histologic exam confirmed the diagnosis of papillary thyroid carcinoma associated with Graves' disease. The patient underwent ablative radioiodine therapy. After 7 years of follow-up, she had no recurrence.
Conclusion
Patients with Graves' disease had a higher risk of developing thyroid cancer than the general population. However, studies reported conflicting results about the prognosis of thyroid cancer concomitant with graves' disease.

DOI: 10.1530/endoabs.81.EP1042

EP1043

Lymph node metastasis in adults and young adults with thyroid carcinoma: an algerian observation

Nadjib Kaouache, Bilal Zouraghen, Merabet Samira, Grari Soumaya, Menacer Sami, Boulefkhad Ryma, Habi Chahinez, Azzouz Nassim, Lezzar Al Kassem & Nassim Nouri
University Hospital of Constantine, Endocrinology, Constantine, Algeria

Introduction
Thyroid cancer (TC) in adolescents and adults (AYA) is defined as thyroid cancer diagnosed among those aged between 15-39 years. It is the fifth most common cancer in AYAs, and its incidence is increasing. Compared with older adult patients, the AYA with TC has a higher prevalence of node metastasis which represents a risk factor for recurrence.
Aim
To describe the characteristics of thyroid carcinoma with confirmed nodal metastases at the time of diagnosis in an Algerian cohort of AYA patients. And to compare patient with and without lymph nodes metastases.
Methods
Medical records of patients diagnosed with differentiated thyroid carcinoma and aged 18-40 years at the moment of diagnosis followed in the endocrinology department of The University Hospital of Constantine in Algeria during the period between July 2014 and December 2018 were retrospectively reviewed. Clinical and pathological data were collected. The group with no lymph node metastases (LN0) was compared to the group with lymph node metastases (LN1) and factors associated with LN metastases were evaluated.
Results
101 patients were included, the mean age was 31 (17- 40 years) and 85.1% were females. Total thyroidectomy was done in 88.1% and lymph node dissection in 23.8% which was central in 13.9% and central and lateral in 9.9%. 90.1% of patients had papillary thyroid cancinoma, 7.9% had follicular carcinoma and 2 patients had Noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP). Following the 8th AJCC classification, 64% were T1, 12.9% T2 and 20.8% were T3. 15.8% had lymph node involvement. Multifocality, bilaterality, vascular thyroid invasion, and capsular thyroid invasion were present in 30.7%, 15.8%, 7.9%, and 17.8%. As for risk stratification according to the ATA system, the initial risk was low, intermediate, and high in 41.6%, 35.6%, and 10.9% of patients, and data were insufficient to state this risk in 11.9% of patients. Thyroid cancer LN1 group had greater tumor size (27.5mm and 17.2mm $P = 0.0.38$) and thyroid dysfunction (7.1% and 0% $P = 0.048$) at the moment of diagnosis than the LN0 group. There was no difference between thyroid cancer with LN1 and LN1concerning, mean age, sex, pathology type and variant, vascular and capsular invasion.

Conclusion
In this cohort of AYA Algerian patients with thyroid cancer, greater tumor size and thyroid dysfunctions were more important in patients with lymph node metastasis at the moment of diagnosis.

DOI: 10.1530/endoabs.81.EP1043

EP1044

Dyshormonogenic goiter: about three cases

Marwa Ben Njima[1], El Omri Malika[1], jihen haouas[2], Meherzi Abir[2], Ghammmam Monia[2], Mouna Bellakhdhar[2], nihed abdessayed[2], Kermani Wassim[2] & Abdelkefi Mohamed[2]
[1]Sousse, ENT, Sousse, Tunisia; [2]Hôpital Universitaire Farhat Hached Sousse, ENT, Sousse, Tunisia

Introduction
Dyshormonogenetic goiter (DG) is considered as a form of thyroid hyperplasia due to enzymatic defects in hormone synthesis. The architectural polymorphism and cellular atypia may mimic thyroid neoplasms and cause difficulties in differential diagnosis.
Results
We report 3 cases of DG occurring in one females and two males who were aged 20, 9, and 7 years old, respictively. All patients presented with clinically evidence of goiter. Hypothyroidism was documented before the histological diagnosis was made in all patients. The thyroid gland was enlarged and multinodular in all cases. Cervical ultrasound and thyroid scintigraphy were performed for all patients. The ultrasound showed a multinodular goiter in all patients. The scintigraphy showed a global hyperfixation of the thyroid for two patients with a right hypofixing zone for one patient. All patients underwent surgical treatment. A total thyroidectomy for two patients and a right loboishmectomy for one patient. The anatomopathological examination confirmed a DG in all cases. The evolution was favorable for all patients and without recurrence.
Conclusion
DG is a rare entity, representing one of the causes of congenital hypothyroidism. It is morphologically characterized by architectural and cellular pleomorphism that may mimic thyroid malignancy and cause difficulties in differential diagnosis that explains the delema of establishing surgical indications.

DOI: 10.1530/endoabs.81.EP1044

EP1045

Metachronous renal cell carcinoma metastasis to the thyroid

Cristina Cretu[1], Cristina Cristea[1], Ioana- Cristina Barbacariu[1], Paula Dragoman[1], Lucia Flavia Livenschi[1], Diana Nicoleta Florescu[1], Radu Danila[2, 3], Delia Ciobanu[3, 4] & Cristina Preda[1,3]
[1]Saint Spiridon County Hospital, Endocrinology, Iaşi,; [2]Saint Spiridon County Hospital, Surgery, Iaşi, Romania; [3]'Grigore T. Popa' University of Medicine and Pharmacy of Iaşi, Iaşi, Romania; [4]Saint Spiridon County Hospital, Pathology, Iaşi, Romania

Introduction
Metastatic disease into the thyroid is a rare event, despite the gland's rich vascular supply. Renal cell carcinoma (RCC) is an unusual neoplasm that not only has the potential to recur after a latent disease-free interval, but also has the potential to metastasize to rare sites like the thyroid. However, of the clinically significant secondary neoplasms of the thyroid, metastatic RCC is the culprit in most cases.
Case report
We present the case of a patient with metachronous RCC metastasis to the thyroid. A 62-year-old male with a 2-year history of non-toxic multinodular goiter was admitted to our Endocrinology Department. He had a history of multiple malignancies: 5 years earlier he had been diagnosed with clear cell RCC (ccRCC) (for which a left nephrectomy was performed) as well as basal cell carcinoma and 25 years earlier he had been diagnosed with colon cancer. Ultrasound evaluation documented a solid, very hypoechoic right thyroid nodule with significant growth, but fine needle aspiration biopsy couldnt be performed because of the nodule's posterior position. Considering the sonographic features of the lesion, the inability to perform a biopsy and the history of prior malignancies, we recommended surgical treatment. A total thyroidectomy was performed. Immunohistochemistry findings, along with the patient's history, confirmed the diagnosis of thyroid metastasis from ccRCC. The patient was subsequently referred to an oncologist for further evaluation and treatment and he received targeted therapy with Sunitinib.
Conclusions
RCC recurrence after nephrectomy is highly variable, presenting with metastasis ranging from a few months to several years after the initial diagnosis. Metastatic RCC to the thyroid should be considered in any patient presenting with a thyroid mass and a medical history of RCC.

DOI: 10.1530/endoabs.81.EP1045

EP1046

Occult papillary thyroid carcinoma with lymphatic metastasis as first presentation of the disease - A report of two cases

Adela Haxhiraj[1,2,3], Adishah Çerma[2], Violeta Hoxha[2], Dorina Ylli[2] & Agron Ylli[2]
[1]Klinika Neo Style, Tiranë, Albania; [2]Mother Teresa Hospital, Tiranë, Albania; [3]Salus Hospital, Tiranë, Albania

Introduction
Occult papillary carcinomas are small thyroid carcinomas (<1 cm) diagnosed after an initial manifestation of lymph nodes or distant metastasis. We report two cases of patients with this pattern of clinical presentation.
Case description
The first case is a 21-year-old woman, with a one-year history of a growing cervical cyst. Fine needle aspiration of the cyst showed metastasis from papillary thyroid cancer. She had no previous history for thyroid pathologies. A thyroid ultrasound was performed and the gland was described as heterogeneous, with no clear evidence of a primary carcinoma site but with too highly hypoechoic areas in the left lobe. Initial blood tests were as follow: TSH, Thyroglobulin and Calcitonin within the normal range, high levels of anti-TPO and anti-TG confirming the diagnose of Hashimoto thyroiditis. Total thyroidectomy and lymph node resection was recommended to the patient. The post-surgery biopsy confirmed multiple papillary focal lesions of papillary carcinoma with maximal diameter 1 cm. The patient received 131-iodine therapy with 100 mCi and is on regular follow up. The second patient is a 45-year-old man, with no medical history who went to the general practitioner for a neck lump. After initial examination, a biopsy of the lymph node was recommended. The result revealed lymph node metastases probable from thyroid papillary carcinoma. Blood test were within normal range. Thyroglobulin 13.54 ng/ml (3.5-77). The patient underwent total thyroidectomy and bilateral neck dissection. Histopathological exam was consistent with a papillary carcinoma of 3 mm in size. Post-surgery thyroglobulin 8.02 ng/ml. In a couple of weeks, the neck lumps reappeared. A computerised tomography was performed and bilateral neck and axillary lymph nodes were observed. The patient underwent a second surgery and later, radioactive iodine therapy with 100 mCi. The second biopsy confirmed once again metastasis from thyroid papillary cancer. Post-second surgery Thyroglobulin 0.01 ng/ml. The patient is still under strict observation because of the recidivist lymphatic disease.
Conclusion
It is important to consider the diagnosis of papillary thyroid carcinoma in every patient that seeks medical evaluation for lymph node swelling. Despite the improvement of ultrasonography, many cases of occult papillary carcinoma remain undetected, emphasizing the role of pathological examination to confirm the diagnosis. The preferred treatment approach remains total thyroidectomy with ipsilateral cervical lymph node resection, usually followed by 131-iodine therapy.
Key words: occult carcinoma, cervical lymph node, thyroglobulin, thyroidectomy, biopsy

DOI: 10.1530/endoabs.81.EP1046

EP1047

Thyroid incidental uptake at 18F-FDG PET/CT, an alert to malignancy - a case report

Inês Manique[1], Luí sa Cortez[1] & José Silva-Nunes[2]
[1]Centro Hospitalar Universitário Lisboa Central, Endocrinologia, Diabetes e Metabolismo; [2]Centro Hospitalar Universitário Lisboa Central, Endocrinologia, Diabetes e Metabolismo, Portugal

Introduction
Thyroid incidentaloma in 18F-FDG PET-CT is relatively common and the most focal uptake are benign. However, the risk of malignancy of thyroid lesions with focal uptake on 18F-FDG PET-CT is 34.8%. Metastasis to the thyroid is uncommon (less than 0.2% of thyroid fine needle aspiration – FNA - puncture

findings), with renal neoplasms being the most frequently associated (48.1%) and, more rarely, those from the breast (7.8%).
Case report
A 54-year-old female with breast adenocarcinoma (HER2+; pT3pN3M0) diagnosed in 2009, underwent neoadjuvant chemotherapy (CT), left radical mastectomy, adjuvant chemoradiation and immunotherapy. Six years later, she had a recurrence of the disease with pericardial effusion. A new CT treatment was performed, and the patient started goserelin, transtuzumab and pertuzumab (dual blockade anti-HER2). In 2020 a 18F-FDG PET-CT was performed and showed mild thyroid uptake in a left lobe's nodular lesion. At the first Endocrinologist observation she denied cervical compressive symptoms and blood tests revealed euthyroidism. The thyroid ultrasound showed in the left lobe "a nodule with 30x15x25mm, undefined contours, heterogeneous ecostructure, hyperechoic punctate foci … valuable bilateral cervical lymph node expression". Cytological evaluation of the nodule was suggestive of metastatic carcinoma. Given the absence of possible confirmatory immunohistochemistry (IHC) with FNA and this being the only secondary lesion to suggest progression of the disease, in a multidisciplinary discussion, it was decided to perform total thyroidectomy. The anatomopathological examination clarified the diagnosis, revealing "Thyroid tissue with extensive infiltration by adenocarcinoma. Lymphovascular and neural invasions are identified. The neoplasm coincides with the margin (CK7+, focal GCDFP15, ER 100%, Her2 score 3+, CK20-)". In this context, she suspended hormone therapy and double anti-HER2 blockade and started CT. She is awaiting for postoperative imaging revaluation.
Conclusion
The report of thyroid focal uptake on PET-CT with 18F-FDG in patients with breast carcinoma should raise the suspicion for metastasis. There is no consensus on the therapeutic approach in these patients, namely with respect to total thyroidectomy. In the present clinical report, histological confirmation with IHC confirmed the progression of the oncological disease and had an impact on the therapy.

DOI: 10.1530/endoabs.81.EP1047

EP1048

Papillary thyroid cancer with larger-volume lymph node metastases: evaluation of response to surgical treatment for decision making on indication of radioiodine

Hernan Tala[1], Jeannie Slater[2], Jose Ignacio Figueroa[3], Eduardo Brigando[4] & Josefina Razmilic[3]
[1]Clínica alemana de Santiago, Facultad de Medicina Clínica Alemana/Universidad del Desarrollo, Santiago, Chile, Internal Medicine (Endocrinology Unit), Santiago, Chile; [2]Clínica alemana de Santiago, Facultad de Medicina Clínica Alemana/Universidad del desarrollo, Pathology Department, La Pintana, Chile; [3]Clínica Alemana de Santiago, Facultad de Medicina Clínica Alemana/Universidad del Desarrollo, Santiago, Chile, Internal Medicine (Endocrinology Unit), Chile; [4]Clínica Alemana de Santiago, Facultad de Medicina Clínica Alemana/Universidad del Desarrollo, Santiago, Chile, Chile

Introduction
PTC patients with lymph node (LN) metastases of greater volume (in>5 LN and/or with larger metastases >5mm, hereinafter N1>5) usually receive radioiodine (RAI). Some guidelines suggest carrying out an evaluation of the response to surgical treatment (RST), recommending lower RAI dose (activity) in patients with good RST.
Objectives:
a)To evaluate the RST in patients with PTC and N1>5 b)To evaluate the disease-free-survival (DFS) in patients with PTC and N1>5 who present thyroglobulin (Tg) <1.0 ng/ml, absence of Tg-Antibodies (TgAb (-)) and non-suspicious ultrasound (US) findings in the evaluation of the RST and who are treated with low doses of RAI.
Experimental Design
Prospective Observational Cohort Study
Materials and Methods
Patients with PTC and N1>5, operated between 2016 and 2020 and who had RST evaluation by US, Tg and TgAb (using LT4) and with TSH≤2.0mIU/ml at least 6 weeks after surgery and prior to the administration of RAI were included. Patients were divided into 3 groups according to the RST (Table 2). Low-dose RAI (30-50mCi) was offered to patients who presented RST defined in this study as adequate (Tg ≤1ng/ml, TgAb (-) and non-suspicious US, Group I). In patients with metastases ≥10mm and/or ≥10 involved LN, low-dose RAI was offered when their Tg was ≤0.2ng/ml, AcTg (-) and normal US. Continuous variables are described as median and range, and categorical variables as proportions. Study was approved by local ethics committee.

Table 1 Characteristics at diagnosis

	n=97
Age	37 (14-78)
Female gender.	70%
PTC (Non-agressive histology)	91%
Agressive PTC histology	9%
TNM 8th Edition	
pT1a-pT1b-pT2	89%
pT3a-pT3b	11%
N1a	33%
N1b	67%
n>5 & <10 and size>5 & <10mm	45%
n≥10 or size ≥10mm	55%

Table 2 Post-surgical evaluation (prior to RAI)

I:Tg ≤1 ng/ml, TgAb (-) & non-suspicious US	55.7%
II:Tg >1.0 and/or TgAb (+) & US non-suspicious US	19.9%
III:suspicious US regardless TgAb & Tg levels	14.5%

Results
Of 581 patients with LN metastases, 97 met the inclusion criteria.
In 53.7% of the patients of group I low dose (30-50 mCi) of RAI was given. With a median follow-up of 24months, DFS was 96% (only 1 patient presented a tiny 3 mm suspicious adenopathy).
Conclusions
a)Approximately half of PTC patients with N1>5 have an adequate RST. b)This preliminary data suggests that in this group of patients, the administration of a low dose of RAI would be associated with a very good disease-free survival, appearing to be a safe option in them.

DOI: 10.1530/endoabs.81.EP1048

EP1049

Worsening dysphagia and dysphonia: a case report

Donatella Rausa, Silvia Irina Briganti, Giovanni Rossini, Lavinia Monte, Nicola Napoli & Silvia Manfrini
Campus Biomedico via Alvaro del Portillo 200, Unit of Endocrinology and Diabetes, Department of Medicine, Roma, Italy

Premise
multinodular goiter and compressive symptoms in the neck could not be necessarily associated.
Case-report
A 82-year-old woman diagnosed follicular lymphoma in 2017 reached to the Emergency Department in Agoust 2021 because of a progressive and worsening dysphagia and dysphonia, begun six weeks before. The patient complained a weight loss of about 8 kg due to the inability in feeding. Her medical history was relevant for thyroid goiter, known since the age of 18, undergone partial right lobectomy at the age of 30 and regular follow-up until July 2021 (also FNA with a benign response was performed in 2019). Thyroid function tests showed subclinical hyperthyroidism. Anti-Tg, anti-TPO and TSH-Receptor antibodies resulted negative. ENT consultation and laryngoscopy showed a paralysis of the left vocal. Neck ultrasound and CT were performed, confirming the presence of a substernal goiter with the whole left thyroid lobe filled-up by a multilobate nodule about 3.5 cm-sized, strongly adherent to the trachea and the internal jugular vein. No enlarged cervical lymphnodes were described. Total body CT identified a solid mass 3 cm-sized in the mediastinum at the level of D3, with no evident cleavage plane to oesophagus. Enlarged mediastinal lymphnodes and pulmonary localization were found, suspicious for metastatic localizations. Cerebral MRI described a solid tissue area 1 cm-sized in the left jugular foramen, surrounding IX, X, XI cranial nerves in the intra-foramina tract, suspicious for perineural metastatic disease. Core-biopsy of the left thyroid nodule and of the paravertebral mass was performed identifying a diffuse and aggressive B-cell lymphoma.. Bone marrow aspiration resulted negative. The patient died a few weeks after in consequence of an acute gastrointestinal bleeding.

Discussion
Secondary thyroid lymphoma can be diagnosed in presence of thyroid nodules with cytologic benign result. Metastatic thyroid tumors are very uncommon and occur as goiter, worsening dysphonia and stridor, dysphagia, tightness of the neck. It is clinically important to discriminate between primary and secondary thyroid lymphoma because therapy and prognosis are different: thyroid metastatic lymphoma has a worse prognosis than primary thyroid lymphoma and it requires an accurate clinical and radiological staging because most of the cases have a widely disseminated disease from the diagnosis and a poor prognosis.

DOI: 10.1530/endoabs.81.EP1049

EP1050

Metastatic papillary thyroid carcinoma - a multidisciplinary approach

Tiberiu Manole[1], Ionela Florina Baciu[1, 2], Anda Dumitrascu[3], Liviu Goldstein[4] & Catalina Poiana[1,2]
[1]'C I Parhon' National Institute of Endocrinology, Pituitary and Neuroendocrine Pathology, Bucharest, Romania; [2]'Carol Davila' University of Medicine and Pharmacy, Department of Endocrinology, Bucharest, Romania; [3]'C I Parhon' National Institute of Endocrinology, Radiology, Romania; [4]'C I Parhon' National Institute of Endocrinology, Nuclear Medicine, Bucharest, Romania

Introduction
Papillary thyroid carcinoma (PTC) is the most common endocrine malignancy. It represents over 80% of all follicular derived well-differentiated thyroid cancers. Despite the fact that the majority of PTCs are well differentiated and have a low rate of local invasion, recurrences, or metastases, there are complex cases which require a multidisciplinary team for a favourable result.
Methods
Clinical examination, blood tests, scintigraphy, CT scan, radioiodine therapy.
Case
We present the case of a 67-year-old woman who underwent a total thyroidectomy in 2019 for multinodular goitre with Graves' disease, which at the pathological report turned out to be papillary thyroid carcinoma in the right thyroid lobe. She received 1 dose of radioiodine therapy one month after the surgery (100 mCi ^{131}I) and did a whole-body scintigraphy which revealed iodine fixing areas in the right thyroid lodge, both lungs (pulmonary metastases), right parietal dura mater, left iliac bone and left femur (bone metastases). Four days after the iodine therapy, the patient developed a partial seizure and left hemiparesis and hypoesthesia caused by the brain metastasis. She underwent tumoral resection in the Neurosurgery Department but the neurological deficit and hypoesthesia didn't improve, while the pathological report concluded the growth was a PTC metastasis. Six months after the thyroidectomy the patient did another dose of radioiodine therapy (135 mCi) with no spontaneous TSH increase after LT4 withdrawal, so she was administered Thyrogen which secured a good uptake of radioiodine in the tumour. She then did a whole-body scintigraphy which revealed a reduction of the primary and secondary lung lesions and stable bone metastases, with no cerebral uptake. Also, the thyroglobulin (TG) decreased every time she did radioiodine therapy. Eighteen months after the thyroidectomy she underwent a third dose of radioactive iodine (100 mCi) which revealed stable lesions. The patient will therefore return for a fourth dose of radioiodine therapy two years after the thyroidectomy.
Discussions
This patient initially presented with a multinodular goitre and Graves' disease which turned out to be PTC at the pathological report. She has multiple metastases which require a multidisciplinary approach. Also, it is important to note that the TG drops every time she undergoes radioiodine therapy.
Conclusions
PTC is a common endocrine carcinoma which in rare cases can metastasise and severely affect the quality of life of the patients.
Keywords
papillary thyroid carcinoma, metastases, radioiodine therapy.

DOI: 10.1530/endoabs.81.EP1050

EP1051

Rare association of two primary carcinomas: papillary thyroid carcinoma and pulmonary adenocarcinoma (about a case)

Nezha Raki, Nassim Essabah Haraj, Siham El Aziz & Asma Chadli
Uhc Ibn Rochd, Endocrinology and Metabolic Disorders, Casablanca, Morocco

Introduction
the coexistence of pulmonary adenocarcinoma and papillary thyroid carcinoma is a rare event. We report the case of a patient followed in consultation with thyroid carcinoma who was diagnosed with pulmonary adenocarcinoma.
Observation
This is a 67-year-old patient, who had a total thyroidectomy for a multi-heteronodular goitre with dissection of a pretracheal lymph node. Histopathological examination revealed a multifocal grade 1 thyroid papillary carcinoma, 3 cm long, with reactive adenitis on the pretracheal lymph node, classified as pT2N0Mx. Radioactive iodine therapy was performed. The patient presented 2 years after the surgery an episode of pneumonia with deterioration of the general state; a chest scan revealed an 8.8 cm right lower mediastinum-pulmonary tissue process, the diagnosis of mucinous adenocarcinoma was confirmed after lung biopsy. The immunohistochemical study was carried out and showed an expression of CK7 without expression of thyroglobulin. A positron emission tomography (PET scan) performed as part of an extension assessment, objectified a hypermetabolic pulmonary process of the right lower lobe associated with a slightly hypermetabolic micronodular infiltrate perilesional with hypermetabolic microfocus of segment II of the liver.
Conclusion
The coexistence of several neoplasias is rare, and poses major diagnostic and therapeutic problems, worsening the prognosis and requiring multidisciplinary management.

DOI: 10.1530/endoabs.81.EP1051

EP1052

Rare presentation of medullary thyroid carcinoma

Viyey Kishore Doulatram Gamgaram[1,1], José Abuín Fernández[2], Araceli Pineda Cantero[3], Sergio Valdes[1] & Francisco José Sanchez Torralvo[1]
[1]Hospital Regional Universitario de Málaga, Endocrinology and Nutrition, Málaga, Spain; [2]Hospital Quirón Salud Málaga, Endocrinology and Nutrition, Málaga, Spain; [3]Hospital Regional Universitario de Málaga, Internal Medicine, Málaga, Spain

Introduction
Medullary thyroid cancer is a rare neoplasm, accounting for approximately 4% of all cases of thyroid cancer. Exceptionally, it can be associated with the hormonal production of ACTH or CRH, causing ectopic Cushing's syndrome.
Clinical Case
We present the case of a 43-year-old man who, as a history of interest, presented a T6-T8 vertebral body fracture 2 years ago and a right hip fracture 1 year ago. Bone densitometry is compatible with osteoporosis. He began daily treatment with Teriparatide 20 mg subcutaneously, calcium carbonate 2.5 g and Cholecalciferol 800 IU. He was admitted to the hospital due to worsening pain. On examination he presented facial plethora, abdominal obesity, and muscular atrophy. Given the suspicion of Cushing, a blood test was performed, highlighting ACTH 114 pg/ml, Cortisol 43.2 µg/dl, Urinary free Cortisol in 24 h 516 mg, and 1 mg Dexametasone supression test 17 µg/dl. An MRI of the spine was performed and showed multiple medullary bone infiltration of the vertebrae and posterior costal arches. A CT scan of the chest showed pathological adenopathies in the upper mediastinum and an increase in the size of the thyroid with a nodular image in the right lobe. Abdominal CT showed both enlarged adrenal glands without observing nodulations. The study was completed with cervical ultrasound, where a 4 cm nodule in the right lobe with lobulated edges, heterogeneous echogenicity, and multiple adenopathies with a pathological appearance were observed. Fine needle aspiration was performed and confirmed the result of medullary carcinoma (Bethesda V). Blood tests showed Calcitonin levels of 8202 pg/ml and urinary Metanephrines were negative. Surgical intervention was performed by means of total thyroidectomy and central and lateral lymph node dissection, with the result in the biopsy of medullary thyroid carcinoma with lymph node involvement and positive immunohistochemistry for ACTH. We arrived at the diagnosis of medullary thyroid carcinoma with bone metastases, ectopic Cushing's due to ACTH production originated in the medullary thyroid carcinoma. Treatment was started with daily Levothyroxine 150 mg on an empty stomach and Vandetanib 300 mg.
Conclusions
Medullary thyroid carcinoma is an uncommon cause of Cushing's syndrome, but it is associated with high morbidity, as described in our patient. Those affected generally have a poor prognosis due to the presence of metastatic disease at the time of diagnosis, and on many occasions they have a large primary tumor mass with little probability of successful resection.

DOI: 10.1530/endoabs.81.EP1052

EP1053

Differentiated thyroid cancer in children and adolescents: about 6 cases

Rachida Bouattay, Maroua Naouar, Emna Bergaoui, Heyfa Belhadjmiled, Mehdi Ferjaoui, Amel Elkorbi, Kaled Harrathi, Naourez Kolsi & Jamel Koubaa
Fattouma Bourguiba Hospital, ENT and Head and Neck Surgery Department, Monastir, Tunisia

Introduction
Thyroid cancer is rare in the pediatric population, but thyroid carcinomas occurring in children carry a unique set of clinical, pathologic, and molecular characteristics. In comparison to adults, children more often present with aggressive, advanced stage disease. The aim of the study is to determinate the clinical, histological and therapeutic aspects of differentiated thyroid cancer in children and adolescents.
Materials and Methods
This is a retrospective study about 6 cases of pediatric thyroid cancer collected in ENT department of Fattouma Bourguiba Hospital of Monastir during a 20-year period (2000-2020).
Results
The average age was 15 years, gender-ratio was 0,2. No personal history of radiation exposure and family history of thyroid cancer were noted. All of patients presented to our consultation for management of a thyroid nodule, associated, in one case, with middle jugular node measuring 2 cm in diameter. All of patients underwent a total thyroidectomy, associated to bilateral central neck lymph node dissection in 3 cases and ipsilateral central neck lymph node dissection in 2 cases. A lateral lymph node dissection was performed in 2 cases. Histologic examination confirmed the diagnosis of papillary carcinoma in all cases. The mean tumor size was 3 cm. In all cases, papillary thyroid carcinoma was multifocal. We noted a tumor capsular invasion in 2 cases. Lymph node metastasis were along the recurrent nerve chain in all cases and in jugular chain in 2 cases. Surgical treatment was followed by radioactive iodine therapy in all cases. There was no distant metastasis or cancer recurrence after a mean follow-up of 3 years,
Conclusion
Although children with differentiated thyroid cancer typically present with locoregional metastases and a high rate of distant metastatic disease, overall survival is very good. Treatment should be based on their increased risk for recurrence instead of overall mortality, and lifelong follow up is required because recurrence and death may not occur for decades after diagnosis.

DOI: 10.1530/endoabs.81.EP1053

EP1054

Differentiated thyroid cancer with tuberculous cervical lymphadenopathymimicking metastasis: a report of 2 cases

Rachida Bouattay, Maroua Naouar, Emna BERGAOUI, Heyfa Belhadjmiled, Mehdi Ferjaoui, Amel Elkorbi, Kaled Harrathi, Naourez Kolsi & Jamel Koubaa
Fattouma Bourguiba Hospital, ENT and Head and Neck Surgery Department, Monastir, Tunisia

Introduction
Papillary and follicular thyroid carcinoma are the most frequent endocrine malignancy. Lymphatic metastases at the time of diagnosis are common in differentiated thyroid cancer (DTC). In these patients, most authors recommend a thyroidectomy with neck dissection. However, neck dissection can lead to numerous post-operative complications. Thus, careful pre-operative evaluation of cervical lymph node metastasis may be crucial, so that patients do not undergo unnecessary neck dissection for other benign conditions The aim of the study is to determinate the clinical, histological and therapeutic aspects of the coexistence of differentiated thyroid cancer and tuberculous cervical lymphadenopathy.
Materials and Methods
We report three cases of association between differentiated thyroid cancer with tuberculous cervical lymphadenopathy collected in ENT department of Fattouma Bourguiba Hospital of Monastir over a period of 10 years.
Results
Our study investigated three women aged 47, 49 and 56 years old respectively. The first patient had a history of hypertension, diabetes mellitus and hysterectomy for endometrial stromal sarcoma while the second patient didn't have any past medical history. The third case was admitted in the Rheumatology Department for bone pain and worsening of the general state. A bone biopsy was performed during that hospitalization showing follicular thyroid carcinoma metastasis. In all cases, ultrasonography showed thyroid nodules associated to suspicious jugular node. All of patients underwent a total thyroidectomy, associated to central and lateral lymph node dissection. The histology disclosed a papillary carcinoma in two cases and follicular carcinoma in the third one. In all cases, thyroid carcinoma was associated to tuberculosis in the lateral cervical lymph node. In all cases, surgical treatment was followed by radioactive iodine therapy and antituberculosis medication. Follow-up has been negative for any recurrence or distant metastasis during the past 24 months.
Conclusion
Cervical lymphadenitis is the most common clinical presentation of extrapulmonary tuberculosis. The coincident of (DTC) and tuberculous lymphadenitis are not rare. The large lymph nodes with central necrosis recognized at uncommon site of metastasis from DTC might remind us of such coexistence. Preoperative diagnosis for tuberculous infection is important to avoid unnecessary surgical complications and secondary infections.

DOI: 10.1530/endoabs.81.EP1054

EP1055

Cushing's disease and multiple endocrine neoplasia with medullary thyroid carcinoma and bilateral pheochromocytoma : about a case

Amal Elkhomri, Nassim Essabah Haraj, Siham El Aziz & Asma CHADLI
CHU Ibn Rochd, Endocrinology-Diabetology and Metabolic Diseases Department, Casablanca, Morocco

Introduction
Multiple endocrine neoplasia (MEN) are inherited conditions of autosomal dominant transmission characterized by the occurrence of various associated endocrine lesions. We report an observation of a patient with a rare association of medullary thyroid carcinoma and bilateral pheochromocytoma with cushing's disease.
Observation
The patient was H.B, 18 years old, followed for a medullary thyroid carcinoma (MTC) since 2018 discovered at the stage of pulmonary and lymph node metastasis, having benefited from a total thyroidectomy with right lymph node curage, classified as T2N1bM1 with the presence of numerous images of emboli (6N+/12N)
Clinically
the patient presents lingual and subconjunctival neuromas, with large purple stretch marks on the flanks, the roots of the lower limbs, and the subaxillary region, associated with signs of hyper androgenism.
Para-clinical
calcitonin at 44600 pg/ml, with metanephrines at 2.53 umol/24h (0.20-1.50), with adrenal CT: two adrenal nodules, measuring 13.5 X 11.5 mm on the left, and 12.5 X 12.5 mm on the right, of spontaneous density, at 40 HU, with enhancement after injection of PDC, Cortisolemia of 8 h after a minute braking test at 14. 5 mg/d, with ACTH: 34 pg/ml (10-50), we completed by a pituitary MRI which objectified a pico adenoma of 2.9 X 2.6 mm. The genetic study did not reveal any mutations in exons 10 and 11, exons 15 and 16 were not studied. The patient underwent bilateral lymph node resection and left adrenalectomy in the first stage, with a control calcitonin level of 3360 pg/ml, a right adrenalectomy is planned.
Conclusion
NEM 2B is an autosomal dominant syndrome characterized by a variable association of pheochromocytoma, CMT, mucosal and subconjunctival neuromas, with a marfanoid and a ganglioneuromatosis, although exceptional, the association with a cushing disease is very rare.

DOI: 10.1530/endoabs.81.EP1055

EP1056

Thyroid oncocytic tumor: about 23 cases

Rachida Bouattay, Maroua Naouar, Emna Bergaoui, Heyfa Belhadjmiled, Mehdi Ferjaoui, Amel Elkorbi, Kaled Harrathi, Naourez Kolsi & Jamel Koubaa
Fattouma Bourguiba Hospital, ENT and Head and Neck Surgery Department, Monastir, Tunisia

Introduction
Oncocytic tumors (OT) are rare, representing 3 to 10% of epithelial tumors of the thyroid. It is important to individualize these tumors given the relatively high frequency of carcinomas and the aggressiveness of oncocytic carcinoma. The aim

of this study is to determinate the clinical, histological and therapeutic aspects of thyroid oncocytic tumor.
Materials and Methods
This is a retrospective study about 23 cases of oncocytic thyroid tumors collected in ENT department of Fattouma Bourguiba Hospital of Monastir during a 20-year period (2000-2020).
Results
The average age was 41 years, a female predominance was noted (19F/4M). Our study included: 20 oncocyte adenomas and 3 oncocytic carcinomas. The average consultation time was 18 months. Eighteen patients have single thyroid nodule and five patients have a multinodular goiter. The mean ultrasound size of the thyroid nodule was 4 cm. There was no cervical lymphadenopathy in all cases. Fine needle aspiration cytology from the thyroid nodule was performed in two cases showing papillary carcinoma in one case. 19 patients underwent a lobo-isthmectomy. A total thyroidectomy with node dissection were performed in 4 cases. Radioactive iodine therapy was indicated for the 3 patients with oncocytic carcinoma. There was no distant metastasis or cancer recurrence after a mean follow-up of 24 months.
Conclusion
Among well differentiated thyroid tumors, oncocytic tumors feature a distinctive set of clinical, morphologic and biologic characteristics, some of which have been a matter of controversy.

DOI: 10.1530/endoabs.81.EP1056

EP1057

Correlation between body mass index and clinico-pathological features of papillary thyroid carcinoma

Hajar Khouchaf, Nassim Essabah Haraj, Siham El Aziz & Asma Chadli
Ibn Rochd University Hospital, Endocrinology, Diabetology, Nutrition and Metabolic Diseases Department, Casablanca, Morocco

Introduction
Epidemiological studies have reported that being overweight and being obese are associated with increased incidences of numerous cancers, including thyroid cancer. In addition to cancer risk, obesity has also been demonstrated to be associated with more aggressive pathological characteristics of the tumor and worse prognosis in patients with several cancers.
Purpose of study
Demonstrate the relationships between BMI and the clinico-pathological features of papillary thyroid carcinoma.
Materials and methods
Retrospective study was conducted in the Ibn Rochd University Hospital Endocrinology and Diabetology department of Casablanca, including211 patients followed for papillary thyroid carcinoma between August 2018 and January 2022. The patients were divided into 2 groups: a group with obesity, and a control group, comparing the clinico-pathological characteristics of the two groups. Statistical analysis performed by the software SPSS 25.0
Results
According to the results, 377patients were women (90.8%), mean age was 40.4 years (12-86) and mean BMI was 28.9 kg/m^2(21-45). The mean tumor size was 28.6 mm (1-80). Statistical analysis of the prognostic factors: tumor size, multifocality, presence of vascular emboli and distant metastasis showed no significant differences in the obese group compared to the control group. Only the presence of capsular invasion ($P<0.01$) was strongly associated with obesity.
Conclusion
The association between obesity and carcinoma has been widely elucidated. Our study demonstrated that there is no relationship of BMI and clinico-pathological features of thyroid carcinoma such as multifocality, tumor size, vascular invasion and the presence of lymph node metastases apart from the presence of capsular invasion.

DOI: 10.1530/endoabs.81.EP1057

EP1058

Adenocarcinoma of the colon and papillary thyroid carcinoma: An exceptional association

Hajar Khouchaf, Nassim Essabah Haraj, Siham El Aziz & Asma Chadli
Ibn Rochd University Hospital, Endocrinology, Diabetology, Nutrition and Metabolic Diseases Department, Casablanca, Morocco

Introduction
The association of thyroid and colon cancer is rare, it can be observed in the context of Gardner's syndrome and Cowden's syndrome with a prevalence of 0.6%. We report a case of metachronous association of a differentiated thyroid cancer with a colon cancer.
Observation
45-year-old patient, followed for well-differentiated colonic adenocarcinoma without metastasis, having received eight courses of chemotherapy. One year later, the patient underwent a total thyroidectomy for multinodular goiter. Anatomopathologic examination of the surgical specimen showed a papillary carcinoma with vesicular differentiation classified as PT3. The patient received additional treatment with radioactive iodine131 at a dose of 100mci. The extension workup did not reveal any metastasis and the surveillance workup did not reveal any recurrence.
Conclusion
Multiple primary cancers are rare, but their incidence has recently increased. Common genetic and environmental risk factors seem to be involved in many cases. Multiplicity itself is not necessarily a poor prognostic factor. However, early detection will allow prompt management and increase the cure rate of the disease.

DOI: 10.1530/endoabs.81.EP1058

EP1059

Association between breast cancer and thyroid cancer : About 55 cases

Hajar Khouchaf, Nassim Essabah Haraj, Siham El Aziz & Asma Chadli
Ibn Rochd University Hospital, Endocrinology, Diabetology, Nutrition and Metabolic Diseases, Casablanca, Morocco

Background
Several studies have demonstrated the relationship between breast cancer and thyroid cancer by the presence of common genetic determinants. The aim of the study was to define the breast cancer prevalence among patients followed for thyroid carcinoma and to determine factors favoring this association.
Matherials and methods
A Cross-sectional study was conducted in the Ibn Rochd University Hospital Endocrinology and Diabetology department of Casablanca, including 55 patients followed for thyroid carcinoma between 1986- 2021 among all the thyroid differentiated carcinomas (793 patients) and presenting breast cancer. Statistical analysis performed by the software SPSS 25.0
Results
Prevalence of patients presenting breast cancer and thyroid cancer was 6.3%. Mean age was 45.5 years (36-70). Family history of neoplasia was found in 49.1% of cases. Breast cancer preceded the discovery of thyroid cancer in 51% of cases. Iratherapy was performed in 98.2% of patients. External radiotherapy was realized in 45.4% of cases for the treatment of breast cancer papillary carcinoma and invasive ductal carcinoma were the predominant histological type in 89.1% of cases. Predictor factors of this association were female patients who had the first neoplasia at a young age ($\leq$45years), family history of neoplasia and prior external radiotherapy.
Conclusion
Our study results support the hypothesis of the presence of a relationship between the breast cancer occurrence in patients followed for thyroid cancer. Close monitoring and vigilance for early detection of thyroid cancer in patients treated for breast cancer is recommended.

DOI: 10.1530/endoabs.81.EP1059

EP1060

Sorafenib for metastatic thyroid carcinoma

Diana Cuconu[1], Chiriac Iulia[2] & Corin Badiu[3]
[1]National Institute of Endocrinology, Thyroid Related Disorders, Bucharest, Romania; [2]National Institute of Endocrinology, Nuclear Medicine, Bucharest, Romania; [3]'Carol Davila' University of Medicine and Pharmacy, Endocrinology, Bucharest, Romania

Differentiated thyroid cancers include papillary, follicular carcinomas and are usually associated with a good prognosis. Up to 10% of patients develop metastatic lessions and radioiodine resistance. Tirosine kinase inhibitors (TKI) represent a strong therapeutic option for patients with advanced metastatic disease

and radioiodine resistance. Sorafenib is the only TKI approved for the treatment of locally advanced or metastatic differentiated radioiodine resistant thyroid carcinoma in Romania. Hereby we aim to evaluate the biochemical and morphological response to different doses of Sorafenib in three patients with radioiodine resistant differentiated thyroid cancer (TC). Case 1- A 54 years old woman with advanced PT3N1bM1 PTC diagnosed in october 2018. She underwent total thyroidectomy with central and lateral compartment neck dissection and radioiodine therapy with rapid onset of radioiodine resistance after a total dose of 260 mCi I131. A second surgery for local recurence was proposed and declined by the patient. She was started on Sorafenib 800 mg/day, but six months after treatment developed biochemical and morphological progression. Case 2- A 39 years old male with follicular TC pT4N1bM1 diagnosed in january 2019. After total thyroidectomy and radioiodine therapy he developed radioiodine resistance and local recurrence. A genetic testing identified TERT C228T mutation, without BRAF mutations. He received Sorafenib 800 mg/day and 6 months after treatment he presents with biochemical and morphological progression. Case 3- This is the case of a 59 years old woman, with a personal history of multinodular goiter without endocrine evaluation and FNAB citology for over a decade, diagnosed in 2013 with FVPTC and spinal metastasis. She developed pain and neurological deficits that were first managed with surgical resection of C5 metastasis followed by total thyroidectomy, then external beam radiotheraphy, multiple surgeries for locally recurent disease and radioiodine therapy with a total dose of 375 mCi. Sorafenib was initiated with an important biochemical response. Due to high blood pressure she continued with 400 mg/day and presents with biochemical and morphological stable disease.
Discussion
We used sorafenib in patients with metastatic TC with a heterogenous response from stable disease to rapid biochemical and morphological progression. Regarding treatment toxicity we observed mild to moderate adverse reactions easily manageable with antihypertensive medication or dose reduction.
Conclusion
While new TKI are being proposed for treatment of metastatic, radioiodine resistant differentiated thyroid carcinoma, there is a need to find genetic markers and histopathological factors that can predict the response to sorafenib therapy.

DOI: 10.1530/endoabs.81.EP1060

EP1061

Horner syndrome as the first manifestation of medullary thyroid cancer

Bianca Dumea[1], Carmen Sorina Martin[1, 2], Ovidiu Parfeni[1], Theodor Mustata[1], Florina Andrada Predescu[1] & Fica Simona[1,2]
[1]Elias Hospital, Endocrinology, Bucharest, Romania; [2]Carol Davila University of Medicine and Pharmacy, Endocrinology, Bucharest, Romania

Introduction
Medullary thyroid cancer is a rare neuroendocrine tumor arising from the parafollicular C cells of the thyroid gland. Calcitonin production is a characteristic feature of medullary thyroid cancer and preoperative high levels indicate an increased risk of local and distant metastatic disease. Although rare, Horner syndrome could be caused by metastatic medullary thyroid cancer. Horner syndrome usually presents with ptosis, miosis and facial anhidrosis and most of the times is aquired following a lesion anywhere along the sympathetic pathway.
Aim (s)
We report you the case of a 47 year old female reffered for sudden onset of left ptosis and vertical diplopia.
Matherials and methods
MRI of the brain and cervical spine revealed multiple left cervical lymphadenopathy suspicious for malignancy and neurologic evaluation established the diagnosis of Claude Bernard Horner syndrome due to cervical compression. Additional tests were performed and neck ultrasound revealed multiple thyroid nodules with a left dominant nodule of 3.74/2.24/2 cm with a high index of sonographic suspicion for thyroid cancer and multiple left lymphadenopathy. Lab tests revealed a hypercalcitoninemia (2000 pg/ml) and a high level of carcinoembryonic antigen (411 ng/ml) confirming the diagnosis of medullary thyroid cancer. Screening for primary hyperparathyroidism and pheocromocytoma was negative. Considering the high basal level of calcitonin and the ultrasound examination of the neck positive for ipsilateral lymph nodes, an extensive screening for regional and distant metastasis was performed. Constrast enhanced CT revealed multiple regional and distant lymphadenopathy but no distant metastasis to the brain, lungs, abdomen or pelvis region.
Results
Thus, the patient was reffered to the surgery department for total thyroidectomy and central and modified radical neck dissection.
Conclusion
Horner syndrome and medullary thyroid cancer are two rare entities and Horner syndrome is an extremely rare and unusual manifestation of the medullary thyroid cancer. It is important to emphasize the importance of multidisciplinary team approach in order to establish a correct diagnosis and treatment plan in such a challenging case.

DOI: 10.1530/endoabs.81.EP1061

EP1062

Breakfast with liquid levothyroxine (Levotirsol®): a single-center experience

Settimio D'Andrea[1], Antonella Berardicurti[2], Livia Santarelli[1] & Walter Vena[3]
[1]Ospedale SS Annunziata, Diabetology Unit and Endcorinology Service, Sulmona, Italy; [2]Università degli Studi 'Gabriele d'Annunzio' - sede di Chieti, Department of Medicine and Ageing Sciences, Chieti, Italy; [3]Humanitas Research Hospital, Endocrinology, Diabetology and Andrology Unit, Cascina Perseghetto, Italy

Introduction
Levothyroxine (LT4) tablets are the most used treatment for hypothyroidism worldwide. LT4 tablets should be taken in the morning and have a fasting state. Some patients could be unable to adhere to this recommendation resulting in poor therapy compliance and thyrotropin (TSH) concentration above the upper normal limits. A previous double-blind placebo-controlled trial showed that LT4 liquid could be ingested during breakfast without a significant difference in TSH values. Recently, a new LT4 liquid (Levotirsol®, IBSA Farmaceutici S.r.l., Lodi, Italy) was released in Italy improving therapeutic options. Our study aimed to explore the possibility to recommend LT4 liquid directly at breakfast.
Methods
We performed an observational, retrospective, and non-controlled study at the Unit of Diabetology and Endocrinology Service of Hospital "Sant'Annunziata" of Sulmona (Italy). We enrolled hypothyroid patients treated with LT4 tablets that refer poor or unsatisfied compliance to the treatment. All included participants received LT4 liquid at the same dose of LT4 tablets to ingest during breakfast. After at least 40 days, they were contacted by telephone to obtain data on TSH and fT4.
Results
We enrolled 26 hypothyroid patients in therapy with LT4 tablets that express poor compliance and/or unsatisfaction with tablets. Three patients were lost at follow-up and one patient back spontaneously to tablets treatment. Finally, we had data about 22 patients aged 54.3(IQR = 48.6-59.3) years. All selected participants were female and were affected by primary hypothyroidism. The duration of LT4 liquid treatment was 68.5 (IQR = 57.3-73.5) days. Ten enrolled subjects showed TSH serum levels before LT4 liquid above 5 mcUI/ml for poor therapy compliance, the remaining 13 subjects presents a TSH value in the normal range but referred that the tablets adherence was the difficult and impaired quality of life. We reported that TSH serum levels after LT4 liquid treatment during breakfast (3.9, IQR = 2.1-4.4) were significantly lower compared to TSH at the beginning (4.8, IQR = 3.9-6.9; $P = 0.03$). Furthermore, freeT4 serum levels after liquid therapy were higher respect to freeT4 levels before liquid therapy (1.0, IQR = 0.8-1.2 VS 0.9, IQR = 0.7-1.1; $P = 0.0002$). When only patients with TSH above the range were considered for analysis, TSH serum levels decreased significantly after LT4 liquid therapy ($P = 0.02$).
Conclusions
We showed that LT4 liquid in hypothyroid patients with poor therapy compliance improves TSH serum levels. LT4 liquid ingested during breakfast could represent an improving therapeutic choice, especially in patients with poor therapy compliance. Further longitudinal trials are needed to confirm these data and to explore the possibility to recommend LT4 liquid without a fasting state.

DOI: 10.1530/endoabs.81.EP1062

EP1063

Therapeutic plasma exchange in amiodarone induced thyrotoxicosis: a case report

Cristina Clausi, Jacopo Manso, Andrea Graziani, Simona Censi, Sofia Carducci, Yi Hang Zhu, Ilaria Piva & Caterina Mian
University of Padua, Endocrinology, Padova, Italy

A 52-year man came to Emergency Department with Atrial Fibrillation with rapid ventricular response due to amiodarone induced thyrotoxicosis (AIT). The patient was found tachi-arrhythmic (153 beats per minute), tachypnoic (27 breaths per

minute) and with intense hyperidrosis. His first blood test documented thyroid stimulating hormone (TSH) <0.01 mUI/l, free triiodothyronine (fT3) 20.0 pmol/l and free thyroxine (fT4) over 100 pmol/l. Thyroid ultrasonography revealed an enlarged hypoechoic and non-homogeneous thyroid gland, in absence of vascular signal. He was initially treated with esmolol 60 mg ev, hydration and hydrocortisone 100 mg ev. Subsequently we began therapy with prednisone 50 mg/die, methimazole 20 mg/die, propranolol 160 mg/die and digitalis 0.0625 mg/die. This first therapy did not improve his clinical condition, thus we substitute methimazole with Propylthiouracil 200 mg/die, prednisone with desametasone 8 mg/die and added potassium iodure 400 mg/die. Nevertheless, blood tests and heart rate still did not improve. We proposed therapeutic plasma exchange (TPE), whom he underwent in the next two following days, as a bridge therapy for surgery. After two runs of TPE with markedly improvement of biohumoral status, the patient underwent urgent thyroidectomy with slowly normalization of TSH and reduction of FT3 and FT4 during the post-surgery days. The man was eventually dismissed by the hospital with desametasone, propranolol, digitalis, oral anticoagulant and calcium carbonate, then introducing replacement therapy with Levothyroxine in the following days. Amiodarone is a drug frequently used in different kinds of arrhythmias. It can induce thyrotoxicosis up to 6-10 % of the patients. There are two types of AIT: AIT1 (iodine-induced in patients with underlying thyroid autonomy) treated by thyrostatic drugs and AIT2 (destructive thyroiditis, results of direct damage or apoptosis in thyrocytes) treated by corticosteroids. Thyroid storm is a rare but potentially fatal endocrinology emergency, with a mortality of 10-30 % due to cardiovascular and multisystemic involvement. AIT can be a cause of thyroid storm. Burch-Wartofsky Point Scale helps physician to determinate the gravity of the condition: a value ≥ 45 requires aggressive therapy. TPE can be used as bridge therapy to thyroidectomy in patients refractory or with contraindications to medical management of thyroid storm. TPE aims to reduce FT3 and FT4, autoantibodies and cytokines and the activity of 5'-monodeiodinasis. Those effects are usually temporary, leading to the risk of rebound-thyrotoxicosis. TPE may be considered also in other pathological endocrinological conditions, such as corticosteroid responsive encephalopathy associated with autoimmune thyroiditis.

DOI: 10.1530/endoabs.81.EP1063

EP1064

Congenital hypothyroidism due to hormone synthesis disorder : the value of early diagnosis

Kamel Farah, Mohamedou Abdouly, Manal Azriouil, Kaoutar Rifai, Hind Iraqi & Mohamed Hassan El Gharbi
Ibn Sina University Hospital, Endocrinology and Metabolic Diseases, Rabat, Morocco

Introduction
Primary congenital hypothyroidism is the most common neonatal endocrine disorder, traditionally subdivided into thyroid dysgenesis, referring to a range of abnormalities in thyroid development, and dyshormonogenesis. We report two cases of dyshormonogenesis in a brother and sister followed for congenital hypothyroidism by inactivating mutation of the TSH receptor, illustrating the good evolution in case of an adapted treatment.
Clinical cases
This is a brother and sister aged 21 and 17 years respectively, from a non-consanguineous marriage. The diagnosis of congenital hypothyroidism due to a hormone synthesis disorder was made at the age of 1 month in both of them, in view of : clinical and biological signs of peripheral hypothyroidism, the cervical ultrasound showed a thyroid gland in place, with regular contours and homogeneous echostructure, and the genetic study was in favour of an inactivating mutation of the TSH receptor. Both patients are treated with Levothyroxine, with regular intake of the treatment, and a good clinical and biological evolution with no mental retardation.
Discussion
Congenital hypothyroidism on hormone synthesis disorder is characterized by a defective molecular pathway for thyroid hormoneogenesis resulting in failure of hormone production by a structurally intact gland. Hypothyroidism secondary to TSH resistance is rare. TSH receptor abnormalities have been described first in cases of thyroid hormone resistance and then in cases of congenital hypothyroidism with an established gland in a eutopic but hypoplastic position. Delayed treatment of neonatal hypothyroidism can result in profound neurodevelopmental delay; therefore, congenital hypothyroidism is screened in developed countries to facilitate prompt diagnosis and treatment. Careful evaluation will usually reveal the etiology of congenital hypothyroidism, which can inform treatment and prognosis. Early and adequate treatment with Levothyroxine results in excellent neurodevelopmental outcomes for most patients with congenital hypothyroidism.
Conclusion
Congenital hypothyroidism is common and can result in severe neurodevelopmental morbidity. Neonatal screening is an important tool to detect congenital hypothyroidism. Prompt diagnosis and treatment are essential to optimize long-term outcomes. These two clinical cases illustrate the importance of early diagnosis and treatment for a successful outcome.

DOI: 10.1530/endoabs.81.EP1064

EP1065

Betrayed by the lab: a case of facticial thyrotoxicosis

David Veríssimo, Catarina Ivo, Vitó ria Duarte, Ana Clá udia Martins, Joao Silva, Luis Lopes, Dolores Passos, J Já come Castro & Mafalda Marcelino
Portuguese Armed Forces Hospital, Endocrinology Department, Lisboa, Portugal

Introduction
Factitious thyrotoxicosis is caused by intentional and surreptitious ingestion of thyroid hormone and can be a challenge in the differential diagnosis with other pathologies.
Case report
Female, 35 years old, referred to our department for suspected subacute thyroiditis after COVID-19. The patient had previous medical history of hysterectomy, bilateral oophorectomy, 2 galactophorectomies with right breast reconstruction, depressive syndrome and hypothyroidism medicated with levothyroxine 75 mg since 2016. In March 2021, two months after SARS-CoV-2 infection, she noticed increased cervical volume with associated pain and weight loss of 10 kg. Thyrotoxicosis was identified and thyroid scintigraphy showed diffuse low uptake, suggestive of subacute thyroiditis. Levothyroxine was suspended and she was medicated with 20 mg prednisolone. After 4 months she maintained thyrotoxicosis with no response to therapy, and a total thyroidectomy was suggested by her medical team, being referred to our department. Upon observation, she complained of tiredness and drowsiness, had no signs of thyrotoxicosis and thyroid examination was normal and painless. The patient expressed a desire to undergo surgery to control the symptoms. At that time, under prednisolone 20 mg, analytical evaluation showed: TSH <0.005 uU/ml, FT4 6.25 ng/ml (0.97-1.58), FT3 18.8 pg/ml (2.38-4.37), thyroglobulin 2.4 ng/ml, negative TRAB, TG and TPO antibodies, AST 46 IU/l (7-32), ALT 73 IU/l (7-32). Thyroid scintigraphy was repeated and showed diffuse low uptake. Due to suspected factitious thyrotoxicosis, it was decided to admit the patient and without instituting any therapy a clear improvement in thyroid function was observed after 5 days: TSH <0.008, FT4 1.11 (0.97-1.48), FT3 3.70 (1.88-3.18). When confronted with the results and after being evaluated by Psychiatry, the patient denied intentionally taking levothyroxine.
Discussion
In the presented case, the suspicion of factitious thyrotoxicosis was based on the absence of goiter, low level of thyroglobulin, low uptake on thyroid scintigraphy and persistence of thyrotoxicosis six months after the diagnosis of subacute thyroiditis. The suspicion was confirmed by the rapid decrease in the serum value of thyroid hormones (50% FT4 and 41% FT3) without any therapy.
Conclusion
This case reflects the importance of clinical suspicion and timely diagnosis of factitious thyrotoxicosis, avoiding unnecessary and potentially invasive treatments.

DOI: 10.1530/endoabs.81.EP1065

EP1066

A case of thromboembolic disease with mild hyperthyroidism

Elaine Soong[1] & Shoib Rehman[1,2]
[1]Norfolk & Norwich University Hospital, Diabetes & Endocrinology, United Kingdom; [2]University of East Anglia, United Kingdom

Background
Hyperthyroidism is a thyroid hormone excess state which usually manifests with various cardiovascular symptoms such as sinus tachycardia, tachyarrhythmia and high output cardiac failure. Pulmonary embolism is not commonly associated with thyrotoxicosis but some studies have shown an increased propensity of

thromboembolic disease with thyrotoxicosis. We report a case of an elderly lady presenting with hyperthyroidism, atrial fibrillation and associated pulmonary embolism.
Case
An 82-year-old lady presented to the emergency department as she felt faint, clammy and short of breath for one day. Her past medical history includes a multinodular goitre with subclinical hyperthyroidism, type 2 diabetes, pulmonary embolism post hernia repair, hysterectomy and gallstones. Bloods on admission showed predominantly T3 thyrotoxicosis, free T3 7.8 pmol/l (3.8-6.0) with suppressed TSH $<$0.10mu/l (0.35-4.94) and free T4 23 pmol/l (7.5-21.1). Her anti-thyroid peroxidase antibody was positive at 108.5 kU/l (0.0-34.0) but her thyroid-stimulating antibody was negative $<$0.10 iu/l ($<$0.56). On clinical examination, her heart rate was 130 bpm and she was hypotensive but responded to fluid resuscitation. ECG showed atrial fibrillation. Her D-dimer was elevated at 4230 mg/l ($<$500). Pulmonary embolism was suspected given mild derangement in thyroid functions with disproportionate hemodynamic instability and CT pulmonary angiogram reported massive bilateral pulmonary embolism with saddle embolus across the bifurcation of the main pulmonary artery with pulmonary hypertension. There was some tracheal narrowing from the multi-nodular retrosternal goitre. The patient was initiated on standard therapy with beta-blockers, antithyroid medications, anticoagulation and planned elective radioactive iodine therapy.
Discussion
Patients with hyperthyroidism have a 10-15% chance of developing atrial fibrillation. Hyperthyroidism also predisposes patients to develop venous thrombosis or pulmonary embolism as they often have endothelial dysfunction, reduced fibrinolytic activity and hypercoagulable state which form the Virchow triad. Pulmonary embolism is a potentially fatal thrombotic disease and hence it is vital to maintain a high level of suspicion even in patients with mild thyrotoxicosis but are hemodynamically unstable.
Conclusion
Hyperthyroidism is associated with an increased risk of atrial fibrillation and pulmonary embolism. These can lead to excess mortality if it is not investigated and managed promptly.

DOI: 10.1530/endoabs.81.EP1066

EP1067

A case report of hyperthyroidism which does not warrant antithyroid treatment

Eng Hui Ooi, Chin Voon Tong & Yen Nee Low
Melaka Hospital, Melaka, Malaysia

Introduction
The most common cause of hyperthyroidism in Malaysia is autoimmune cause like Grave disease, or toxic multinodular goitre. Thyroid hormone resistant syndrome is a rare genetic disease which usually presented with mild hyperthyroidism clinically and biochemically it had elevated free T4 and non suppressed TSH. Inexperienced doctor will commonly mistreat patient with antithyroid medication. This is because this genetic disease is extremely rare to encountered in practice.
Case Report
A 24 years old gentleman, he was first presented to Hospital Ipoh for left Anterior Cruciate Ligament tear after sport injury in 2019. Pre-operative assessment noted patient tachycardia. Otherwise, he did not have palpitation, tremors, weight loss, heat or cold intolerance, diarrhea, or anxiety. On the other hand, he had strong family history of hyperthyroidism which were his mother, mother's siblings and his grandmother. On examination, his blood pressure is normotensive, and heart rate was slightly tachycardic. He had no fine tremors, and goiter. Cardiovascular and respiratory system examination was unremarkable His thyroid biochemical profile showed normal thyroid stimulating hormone (TSH), 3.4 mIU/l (0.55 -4.78) with elevated free T4 (FT4), 27.9 pmol/l (11.5-22.7). In view of pendemic covid, his operation was postponed and he request his case transfer to my hospital, Hospital Melaka to continue follow up. Throughout the follow up, serial thyroid function test showed normal TSH, and elevated FT4. He was asymptomatic for hyperthyroidism other than occasionally tachycardic. His magnetic resonance imaging brain demonstrate a pituitary microadenoma. However, thyrotropin releasing hormone (TRH) stimulation test reveal normal TSH response. We presumed that he had thyroid hormone resistance syndrome, with the given history of mild hyperthyroidism features and the investigation mentioned as above. He is otherwise well without any antithyroid treatment. He had undergone left knee Anterior cruciate ligament tear repair in Jan 2022 under general anesthesia. Intraoperative and postoperative were uneventful. We had our limitation to further workup because the genetic test was not available in our country. We had rule out thyrotropin secreting tumor and primary hyperthyroidism before we come to a conclusion of thyroid hormone resistance syndrome. However, we would like to emphasis that not all hyperthyroidism warrant antithyroid treatment. Early recognition and refer to correct team is crucial to avoid unnecessary treatment.

DOI: 10.1530/endoabs.81.EP1067

EP1068

Myo-Inositol Supplementation in autoimmune thyroiditis and subclinical hypothyroidism on the background of vitamin D deficiency.

Nadiya Pasyechko & Veronika Kulchinska
Ternopil State Medical University, Internal Medicine No1, Ternopil, Ukraine

Background
In recent years, thyroid diseases have been occupying the top places in the structure of the endocrine pathology. There exists tight functional relationship between the thyroid and reproductive systems, which leads to a high probability of the development of combined disorders in one of these links of homeostasis. Vitamin D deficiency in the population remains a global problem. The purpose of the study is to investigate the effect of myoinositol on the thyroid status of women with subclinical hypothyroidism on the background of autoimmune thyroiditis and vitamin D deficiency.
Materials and methods
The study included 102 patients, aged 18-42 years, with subclinical hypothyroidism on the background of autoimmune thyroiditis. The patients were randomly subdivided into two groups. Patients of the first group ($n=$ 52) before the main treatment by levothyroxine at a dose 37,5$\pm$12,5, received the myoinositol supplementation at a dose of 2000 mg/day, and cholecalciferol at a dose of 2000 IU/day. Patients of the second group ($n=$ 50) before the main treatment received only cholecalciferol at a dose of 2000 IU/day.
Results
Vitamin D deficiency was observed in 91.68 % of women with subclinical hypothyroidism, and vitamin D insufficienty was observed in 8.32 %. A negative correlation was found between the level of 25 (OH) D and the level of ATPO ($r=$-0.194, $P<$0, 05). The myoinositol supplementation together with vitamin D led to a probable increase in the content of 25 (OH) D in the serum, as well as to a decrease in the titer of ATPO.
Conclusions
The positive effect of myoinositol drugs together with vitamin D on the functional state of the thyroid gland, on the level of antibodies to TPO in women of reproductive age with subclinical hypothyroidism on the background of autoimmune thyroiditis and vitamin D deficiency has been established.

DOI: 10.1530/endoabs.81.EP1068

EP1069

The structure of thyroid dysfunction in children with type 1 diabetes mellitus

Zhanar Nurgaliyeva, Araily Manasbayeva, Zhanerke Amangeldi & Nozima Kholmirzayeva
NJSC 'Kazakh National Medical University named after S.D. Asfendiyarov', Department of Pediatric Diseases with a Course of Neonatology, Almaty, Kazakhstan

Relevance
Type 1 diabetes mellitus (DM) is one of the most common endocrine disorders among chil-dren and accounts for 5-10% of all DM. According to scientists, in patients with type 1 diabetes, the risk of developing thyroid pathology is increased and with their combination, the course of both diseases worsens. There are different opinions among specialists regarding the clinical significance of latent thy-roid dysfunction. The study of the functional state of the thyroid gland in children with type 1 diabetes seems to be very relevant. In Kazakhstan, we have not met studies to assess the function of the thyroid gland in children with type 1 diabetes.
Materials and methods
Cohort retrospective study of data from 1140 medical records of inpatient patients with type 1 diabetes who were on inpatient treatment for the study of thyroid hormones ($n=$ 580): TSH, free T3, free T4, AT-TPO, AT-TG.

Results
For the period from 2014 to 2020, the thyroid profile was studied in 58.9% of children with type 1 diabetes: euthyroidism was detected in 41.0%, hypothyroidism - in 18.0%, hyperthyroidism - in 2.4%, other different variants of thyroid dysfunction in 38.6% of children. When analyzing the distribu-tion of primary hypothyroidism, the frequency of thyroid hypofunction was recorded in 46-52% of cases more often over the last 4 years of follow-up. The frequency of hypothyroidism among all thyroid dys-function is 30.4% of cases. Among the various thyroid dysfunctions, the following variants are regis-tered: isolated increase in free T3 - 66.0%, isolated increase in free T4 - 5.0%, increase in free T3 and free T4 with normal TSH - 13.0%, increase in TSH, free T3 with normal free T4 - 13.0%, decrease in free T3 - 3.0%.
Conclusion
In patients with type 1 diabetes, thyroid dysfunction is detected in almost 60.0%. It should be noted that primary hypothyroidism is registered in every third child with type 1 diabetes among all thyroid dysfunctions. In 39% of patients with type 1 diabetes, there were various fluctuations in the lev-els of hormones TSH, free T4, free T3, which were not included in the diagnostic criteria for thyroid pathologies and required separate study.

DOI: 10.1530/endoabs.81.EP1069

EP1070

Cardiac arrhythmias associated with subclinical primary hypothyroidism: about two cases

Henda Ben Sassi, Boubaker Fadia, Wiem Mkacher, Zohra El Mechri El Mechri, Houcem Mrabet, Alaya Wafa, Zantour Baha & Sfar Mohamed Habib
University Hospital Tahar Sfar Mahdia, Department of Endocrinology

Introduction
Thyroid hormones play an important role in the normal functioning of cardiac and vascular physiology, therefore hypothyroidism results in profound cardiovascular effects. Arrhythmia in patients with hypothyroidism seems rare and not well recognized.
Observation
Our first patient was a non-smoker 61-year-old woman, followed-up in the cardiology department for hypertension and dyslipidemia during the previous 5 years. She was treated with ACE inhibitors and a statin. Her sister had a dysthyroidism. The history was marked by the appearance of palpitations over the past 2years. Physical examination showed a palpable thyroid of normal size. The chest X-ray didn't show any anomaly. Sinus tachycardia was found on ECG. Renal and lipid balance was correct. The thyroid investigation showed a subclinical hypothyroidism with a sensitive thyroid stimulating hormone: (TSH) = 6,05 mU/l and Free T4 = 14,8 pmol/l. One year later, the patient showed symptoms of weight gain and asthenia. A check-up was done: TSH = 7,2 mU/l; FT4 = 14 pmol/l; AntiTPO antibodies were negative (= 4,9), Cholesterol = 6,5mmol, TG = 3mmol inciting to treat her with appropriate thyroxin replacement with a regular follow-up. The patient no longer reported tachycardia. Our second case was about a 57- year-old female patient, with a history of hypertension for 5 years. She was treated with ACE inhibitors. The patient was admitted to the cardiology department for junctional tachycardia and treated with beta blockers and digoxin. There was no infectious syndrome associated during her hospitalization, she was found to have subclinical primary hypothyroidism (TSH = 12.8 mU/l/FT4 = 12.5 pmol/l), her anti TPO antibodies were negative. The initial cervical ultrasound noted a 5.5 mm right lobar nodule classified as TIRADS4B (EU-Tirads5) with an ultrasound aspect of thyroiditis for the rest of the parenchyma. Three months later, the thyroid assessment was checked and was normal (TSH = 3.7 mU/l) and the control cervical ultrasound showed multiple micro cysts in both lobes Eu-TIRADS2. The cardiac rhythm disorder was resolved at that time. The ultrasound follow-up two years later showed a heterogeneous hypo echoic thyroid gland with no thyroid nodule.
Conclusion
Hypothyroidism can result in decreased cardiac output, increased systemic vascular resistance and atherosclerosis with ischemic heart disease risk. Cases of arrhythmia are rarely reported in hypothyroidism and could be due to alteration of myocyte-specific gene expression, interstitial oedema, myofibril swelling with loss of striation, endothelial dysfunction, disturbances of the sympathetic-vagal tone, increased arterial stiffness… Replacement with thyroxin could help and should be initiated cautiously.

DOI: 10.1530/endoabs.81.EP1070

EP1071

Moyamoya disease and Graves' disease in a Tunisian girl

Chayma Bel Hadj Sliman, Fatma Chaker, Anis Grassa, Nadia Khessairi, Ibtissem Oueslati & Melika Chihaoui
Rabta Hospital, Endocrinology Department, Tunis, Tunisia

Introduction
There is an association between Moyamoya syndrome and Graves' disease, described primarily in Asian populations. We report a case of Moyamoya vasculopthy with stroke and hypertension associated with graves' disease in a 15-year-old Tunisian girl.
Observation
A 15-year-old girl diagnosed with Moyamoya vasculopathy was referred to the endocrinology department for hyperthyroidism. The patient had a history of recurrent stroke and hypertension since 2 years-old. She complained of palpitations, weight loss and tremors, bilateral exophthalmia and floppy eyelid syndrome. Physical examination showed bilateral palpebral edema, bilateral exophthalmia and complete eyelid closure. Laboratory investigations showed high level free T4 = 38,8 pmol/l (12-22), low TSH < 0.05 mUI/I (0,4-4) and high level of TSH receptor antibodies: 35 UI/ml (< 5). Thyroid ultrasound revealed an hypoechoic, hypervascular goiter without nodules. Thyroid scintigraphy showed intense and homogeneous uptake. Orbital and brain MRI showed bifrontal anoxic-ischemic lesions with left wallerian degeneration associated with inflammatory myopathy of the right lower oculomotor muscle. The diagnosis of graves' disease was confirmed. The patient was treated with methimazole leading to clinical and biological euthyroidism after 8 months treatment.
Conclusion
This is the first case of Moyamoya disease coexisting with graves' diesease in a tunisian patient. The pathogenesis and the prognosis of hyperthyroidism and specially Graves' ophtalmopathy are still unknown.

DOI: 10.1530/endoabs.81.EP1071

EP1072

Impact of Ramadan fasting on patients followed for Hypothyroidism.

Amine Gueddari[1], Nassim Essabah Haraj[1], Siham El Aziz[1] & Asma Chadli[1]
[1]Uhc ibn rochd, Endocrinology and Metabolic Disorders, Casablanca, Morocco

Introduction
During Ramadan, Muslims change their eating and sleeping habits. All these changes can cause metabolic and hormonal variations. The main treatment for hypothyroidism is L-thyroxine. It is known that the absorption of L-thyroxine is optimal when taken on an empty stomach. Very few studies have been conducted to examine the best time to administer L-thyroxine during Ramadan.
Objective of the study
To evaluate the impact of Ramadan fasting on hormonal balance and to compare the use of L-thyroxine 30mn before Fotour and at Sohour.
Material and methods
Prospective study including 62 patients followed in consultation for hypothyroidism. A TSH measurement was performed before and after 6 weeks. The evaluation of the therapeutic compliance was evaluated by the MORISKY Medication Adherence Scale.
Results
We recruited 62 patients, 53 of whom were women (85.5% of cases) and 9 men (14.5% of cases). The average age was 50.4 years (29-80). Hypothyroidism of peripheral origin was present in 24 patients (38.7% of cases) while hypothyroidism secondary to total thyroidectomy was present in 38 patients which is 61.3% of cases. Twenty-nine patients preferred to take L-thyroxine at the time of Fotour (46.8% of cases), while 33 patients preferred to take it at the time of Sohour (53.2% of cases). Compliance was good in 87.1% of cases and average in 12.9% of cases. In post-Ramadan, 75.8% of patients remained euthyroid, 17.7% hypothyroid and 6.5% hyperthyroid without significant correlation between the two therapeutic schemes ($P = 0.07$).
Conclusion
Fasting during the month of Ramadan may be responsible for hormonal imbalance in patients on L-thyroxine, hence the interest of educating these patients on the use of medication and of a close follow-up after the month of fasting.

DOI: 10.1530/endoabs.81.EP1072

EP1073

A retrospective study of the medical-surgical approach of a cohort of patients with Graves' orbitopathy

Mariola Méndez Muros[1], Reyes Ravé García[1], Tomás Martín Hernández[1] & Antonio Manuel Garrido Hermosilla[2]
[1]Virgen Macarena University Hospital, Endocrinology and Nutrition Department, Seville, Spain; [2]Virgen Macarena University Hospital, Ophthalmology Department, Seville, Spain

Objective
To study the characteristics of a cohort of patients with Graves' orbitopathy (GO) as a self-audit prior to the creation of a multidisciplinary team for the global approach of these patients.
Material and Methods
Retrospective study of patients with GO treated at the Endocrinology and Ophthalmology Services of a tertiary referral hospital (Virgen Macarena University Hospital, Seville, Andalusia, Spain) between 2018 and 2021. The following variables were evaluated in a cohort of 267 patients: demographic data; date and service of diagnosis; number of visits; thyroid function at diagnosis of GO; highest severity of GO and highest level of anti-TRAb (TSI) reached during follow-up; imaging; treatments for GO and EG; smoking.
Results
The results of the 267 analyzed patients are described in Table 1. The severity of the GO was analyzed according to the EUGOGO classification: 56.93% had mild GO, 41.57% moderate to severe, and 1.50% with visual risk. Highest level of anti-TRAb (TSI) reached during follow-up was recorded in 237 patients of the total, with a mean of 15.93 IU/l $\pm$ 13.49 IU/l SD. Regarding the treatment of GD, 89.98% of the patients were treated with antithyroid drugs, 15.36% received radioactive iodine (the majority without corticosteroid prophylaxis) and 40.82% required total thyroidectomy. With regard to smoking, 41.57% were active smokers, with 81% being offered anti-smoking advice and referring 14.4% of all smokers to the Smoking Cessation Unit of the Pneumology Service.
Conclusions
After analyzing our cohort of patients with GO, we have detected some areas for improvement: A corticosteroid prophylaxis deficit has been observed in the context of radioactive iodine administration for the treatment of GD. Referral to the Smoking Cessation Unit should be performed routinely in all smokers with GD. The analysis of these results will allow us to optimize the multidisciplinary management of our patients with GO.

DOI: 10.1530/endoabs.81.EP1073

EP1074

Diagnosis of thyroid adenomas at the outpatient stage

Lubov Timofeeva[1], Elena Yanovskaya[2] & Yuriy Aleksandrov[2]
[1]FSBEI HE «I. N. Ulianov Chuvash State University», Ultrasound, Cheboksary, Russian Federation; [2]Yaroslavl State Medical University, Surgery, Yaroslavl, Russian Federation

Methods of radiation diagnostics and fine needle aspiration biopsy (FNAB) are the methods of the first stage of diagnosis of thyroid nodules, which is confirmed by a large number of international recommendations. However, these methods do not always give the right answer for thyroid adenomas. The aim of the study was to study the effectiveness of a set of methods: ultrasound, sonoelastography, scintigraphy and FNAB in the diagnosis of thyroid adenomas. The study included 86 patients with a morphologically confirmed diagnosis of thyroid adenomas. The patients underwent ultrasound (86) and FNAB (86), sonoelastography (55) and scintigraphy (37). The results of a multiparametric ultrasound examination showed that the images of the adenomas do not correspond to standard estimates. There are also no ultrasound signs that are the 'key to diagnosis'. Signs of 'border', 'contour', 'height less than width' were characteristic of most benign nodules of various structures. Signs of 'solid structure' and 'increased blood flow' have also been found in thyroid cancer. Discriminant analysis showed that the signs of 'borders', 'contours', 'halo' and the absence of 'calcification' are the 'reference' signs of thyroid adenomas. The estimate according to EU-TIRADS was: EU-TIRADS2 -20.3%, EU-TIRADS3 - 5.3%, EU-TIRADS4 - 72.5%, EU-TIRADS5 - 1.9%. The efficiency parameters of EU-TIRADS were 86.9% sensitivity, 73.5% specificity and 80.2% accuracy. Cytological examination showed results with a significant spread: TBSRTC1 - 8.5%, TBSRTC2-13.1%, TBSRTC3-15.1%, TBSRTC4 -48.5%, TBSRTC5 - 13.5%, TBSRTC6 - 1.3%. According to sonoelastography data, images of thyroid adenomas demonstrated low probability of malignant process: 1 (41.8%) and 2 patterns (54.5%). The Young's modulus index was 23.5$\pm$7.1 kPa, but in some cases the values exceeded 45 kPa. Elastography in thyroid adenomas has a sensitivity of 96.4%, specificity of 57.1% and accuracy of 88.41%. Elastography of thyroid adenomas showed better indicators than in the EU-TIRADS. However, when studying e, it was found that taking into account only e data can lead not only to the absence of thyroid cancer cases, but also to erroneous conclusions in a. In thyroid adenomas scintigraphy, sensitivity was 53.3%, specificity - 42.3%, accuracy - 44.7%. However, the possibilities of this method are mainly limited to hyperfunctional nodules, which is observed in adenomas only in half of cases. Based on the data obtained, the concept of the need for regulation (sequence) of the complex phased application of methods of radiation diagnostics and cytological examination in the examination of patients is formulated.

DOI: 10.1530/endoabs.81.EP1074

EP1075

Bioelectrical Impedance Analysis (BIA) to measure alterations on hydroelectrolytic equilibrium of peripheral cells in COVID-19 patients with nonthyroidal illness syndrome (NTIS)

Salvatore Sciacchitano[1], Carlo Capalbo[2], Valentina Salvati[3], Daniela Alampi[4], Elisa Alessandri[5], Chiara Loffredo[4], Claudia De Vitis[6], Rita Mancini[7], Flaminia Coluzzi[8] & Monica Rocco[9]
[1]Sapienza University of Rome, Department of Clinical and Molecular Medicine, Rome, Italy; [2]Sapienza University of Rome, Department of Molecular Medicine, Rome, Italy; [3]IRCCS Regina Elena National Cancer Institute, Scientific Direction, Rome, Italy; [4]Sant'Andrea University Hospital, Unit of Anesthesia and Intensive Care Medicine, Rome, Italy; [5]Sant'Andrea University Hospital, 00189, Unit of Anesthesia and Intensive Care Medicine, Rome, Italy; [6]Sapienza University of Rome, Department of Clinical and Molecular Medicine, Rome, Italy; [1]Sapienza University of Rome, Department of Clinical and Molecular Medicine, Rome, Italy; [8]Sapienza University of Rome, Department of Medical and Surgical Sciences and Biotechnologies, Latina, Italy; [9]Sapienza University, Sant'Andrea Hospital, Department of Clinical and Surgical Translational Medicine, Rome, Italy

In COVID-19 patients the occurrence of low T3 serum values is associated with disease severity and death, but hormonal substitutive replacement is still debated. Clinical trials reported so far failed to demonstrate clear beneficial effects of T3, T4 or both treatments. With the aim to analyze the peripheral effects of the acute deficiency of T3 in blood, we analyzed body fluid composition in 74 COVID-19 patients, admitted to our University Hospital during the last pandemic wave. COVID-19 patients were sub divided into those that presented low FT3 serum levels, i.e., $\leq$ 1.7 pg/ml (n. 42), 13 of which showed very low FT3 serum values, i.e., $\leq$ 1.1 pg/ml, and those that showed normal FT3 serum levels, i.e., $>$ 1.7 pg/ml (n. 32). Body fluid composition was analyzed by Bioelectrical Impedance Analysis (BIA). We demonstrated that COVID-19 patients with low FT3 serum values exhibited increased values of the Total Body Water/Free Fat Mass (TBW/FFM) ratio. Patients with the lowest FT3 serum values had also the highest level of TBW/FFM ratio, an indicator of the fraction of FFM as water and one of the best-known body-composition constants in mammals. We found an inverse

GENDER	Year of diagnosis	IMAGING				GO TREATMENT									THYROID FUNCTION AT DIAGNOSIS* (n= 266, 1 patient not evaluated)		
		Patients diagnosticated per year															
Male	2018-2021	Endocrinology	Ophthalmology	TAC	RNM	Intravenous Corticosteroids	Oral Corticosteroids	Anti-IL6	Selenium	Orbital Decompression	Eyelid Surgery	Strabismus Surgery	Radiotherapy	Other	Hyperthyroidism	Hypothyroidism	Euthyroidism
55 (20,6%)	139 (52%)	-Before 2018: 93 -2018: 26	-Before 2018: 35 -2018: 4							6%							
Female	Before 2018	-2019: 23,7	-2019: 3			18,3%	4,5%				12%	3,4%			85,7%	7,5%	6,4%
212 (79,4%)	128 (47,9%)	-2020: 28 -2021: 36	-2020: 5 -2021: 12	26,9%	18,3%			10,5%	27,34%				1,5%	1,1%			

correlation between FT3 serum values and this constant. Reduced FT3 serum values in COVID-19 patients were correlated with the increase in the total body water (TBW), the extracellular water (ECW) and the sodium/potassium exchangeable ratio (Na_e:K_e), and with the reduction of the intracellular water (ICW). Since the Na+/K+ pump is a well-known T3 target, we measured the mRNA expression levels of the two genes coding for the two major isoforms of this pump. We demonstrated that COVID-19 patients with NTIS had lower levels of mRNA of both genes in the peripheral blood mononuclear cells (PBMC)s obtained from our patients during the acute phase of the disease. In conclusion, we demonstrated that the acute T3 deficit in our COVID-19 patients has marked effects on the hydroelectrolytic equilibrium of their peripheral blood mononuclear cells. The Na+/K+ pump is a possible target of T3 action, involved in the pathogenesis of the anasarcatic condition observed in these patients. Measurement of BIA parameters is a useful method to analyze water and salt retention in COVID-19 patients hospitalized in ICU that develop NTIS and may represent a novel reliable outcome to evaluate the benefit of T3 treatment in future clinical interventional trials.

DOI: 10.1530/endoabs.81.EP1075

EP1076

Autoimmune thyroiditis after 2 years covid pandemic: prevalence, clinical features, significance. Study on 450 patients in a medical center of Bucharest-Romania

Dan Peretianu[1], Mihaela Stanciu[2] & Oprea Cristina Dana[1]
[1]Medical Center Povernei, Endocrinology and Applied Immunology, Bucharest, Romania; [2]Faculty of Medicine, V. Papilian, Endocrinology, Sibiu, Romania

Material-Method
We registered from February 26, 2020 until January 23, 2022 (almost 2 years) patients with chronic autoimmune thyroiditis Hashimoto. Usual parameters for this disease were investigated: age, sex, ATPO, FT4, TSH, ultrasound pattern, antibody evolution, immune associations, lost pregnancies, other clinical associations (alergies, breast cancer). Patients were divided into 2 groups: those who had covid-19 (C-19) vs. those who did not have viral disease (NOC). Statistical analysi: Fisher z test (percentage comparisons), X^2 (discrete data comparisons), T (continuous data comparisons).
Results
I. We registered 456 patients. Of these, 84 had covid-19 (18,24%). The prevalence was extremely high compared to the declared prevalence of covid-19 in Romania: 10,95% (https://worldpopulationreview.com/countries/romania/population, https://www.worldometers.info/coronavirus/country/romania). Z = 5,43, $P << 0{,}0001$. II. No differences between patient groups: **A**. Gender: Female: C-19 = 90,13%, NOC = 89,52%; **B.** Age of onset (mean, years): C-19 = 50,39 years, NOC = 50,94. **C.** Current age: C-19 = 55,86, NOC = 55,6. **D.** ATPO level: C-19 = 749,67 IU/ml, NOC = 837,67. **E.** ATPO evolution: predominantly undulating, 46% vs 67%, X^2 = 2,88, P= 0,24. **F**. Thyroid function at onset: C-19: normothyroidism = 41,7%, hypothyroidism = 44%, hyperthyroidism = 14,3%. NOC = normothyroidism = 41,3%, hypothyroidism = 48,95%, hyper = 9,91%. **G.** Current thyroid function: C-19: normal = 670,8%, hypo = 26,19%, hyper = 3,57%, NOC: normothyroidism = 67,2%, hypothyroidism = 29,84%, hyperthyroidism = 2,96%. **H.** Pregnancy losses: C-19 = 7,69%, NOC = 13,21%. I. Immune associations: C-19 = 45,23%, NOC = 37,09%, P= 0,16. III. Clinical forms of covid-19. Asymptomatic = 4, oligosymptomatic = 4, mild = 27, moderate = 34, severe = 8, very severe = 5, death = 2. Comparison with the evolution of the Romanian general covid population (Pantea-Stoian *et al*, 2020, Sci. Rep, 21613) is NOT different, but seemingly lighter. For example, the lethality in our group was only 2,38%, while in the general population it was 2,95%.
Conclusions
Either 1. Derived from the increased prevalence of immune associations - The genetic structure of the mucosal cells of patients with Hashimoto's thyroiditis allows the attachment of S protein much faster and to lower viral loads (research to be solved for future generations), Either 2. Derived from the lack of difference between groups and set mathematical analysis - the prevalence of covid-19 in Romanian society **was** not 10,95%, **but** 18,24%, as it appears in our group of patients with chronic autoimmune thyroiditis Hashimoto.

DOI: 10.1530/endoabs.81.EP1076

EP1077

Clinical and paraclinical features of ectopic thyroid gland in adult patients.

Anis Grassa, Ibtissem Oueslati, Hajer Yezza, Meriem Yazidi & Melika Chihaoui
La Rabta University Hospital, Department of Endocrinology, Tunis, Tunisia

Introduction
Ectopic thyroid gland is a rare pathology due to an abnormality in the embryological development and/or migration of the gland. The aim of this study was to assess clinical and paraclinical characteristics of adult patients with ectopic thyroid gland.
Methods
This was a retrospective study including adult patients with ectopic thyroid gland. Clinical, biological, hormonal, radiological and therapeutic data were collected.
Results
Five patients (four women and a man) were enrolled in this study. Their median age was 40 years [extremes: 17-61]. Their past medical history included intellectual disability, stature retardation, and type 2 diabetes mellitus in two cases respectively and vitiligo in one case. All patients were referred to our department for management of hypothyroidism. On physical examination, all patients had non-palpable thyroid gland. The mean TSH level at baseline was 48.7 mIU/l [extremes: 7.6 -100]. Three patients had overt hypothyroidism and two patients had subclinical hypothyroidism. Two patients had a cervical ultrasound showing an empty thyroid compartment. Two other had cervical CT scan, showing sublingual mass in one case and retropharyngeal mass in the other. Thyroid scintigraphy was performed to all patients, showing two sublingual thyroids, one left paramedian, one sub-hyoid and one retropharyngeal. All patients were put on replacement therapy. The doses of levothyroxine to achieve euthyroidism varied from 75 µg to 200 µg/day.
Conclusion:
The diagnosis of ectopic thyroid gland should be suspected in patients with hypothyroidism associated to a non-palpable thyroid gland in normal position even in adults. Its confirmation is radiological based on the scintigraphy.

DOI: 10.1530/endoabs.81.EP1077

EP1078

The relationship between type 2 diabetes mellitus with metabolic syndrome and clinical hypothyroidism

Rim Rachdi, Berriche Olfa, Olfa Lajili, Eya Safi, Nadia Ben Amor, Rym Ben Othman, Ramla Mizouri, Faten Mahjoub & Jamoussi Henda
The National Institute of Nutrition in Tunis, Diabetology Department A, Tunisia

Introduction
Metabolic syndrome is a multifactorial disease with multiple risk factors that arises from insulin resistance accompanying abnormal adipose deposition and function, increasing the risk of type 2 diabetes, one of the most common endocrine pathologies. Abundant evidence suggests an association between TSH levels, insulin resistance and some markers of the metabolic syndrome, without foreseeing the kind of this link. The aim of our study was to search if there was a link between type 2 diabetes with metabolic syndrome and hypothyroidism, and to explore the markers that are specially correlated with thyroid status.
Materials and methods
Retrospective study including 100 patients with type 2 diabetes showing criteria of metabolic syndrome, carried within the diabetology department 'A' of the National Institute of Nutrition in Tunis.
Results
70% of patients had a normal thyroid balance (euthyroid group (G0)) and 30% presented a clinical hypothyroidism (hypothyroid group (G1)). The average age in G0 was 57,8 years compared to 60,8 years in G1 (P=NS). All G1 patients were female (100%) compared to 82% in G0 (P=0,01). Median diabetes duration was 9,78 years in G0 compared to 11,76 years in G1 (P=NS). 51,43% of patients were on insulin in G0 vs 66,66% in G1 (P=NS). The average BMI of G0 patients was 35,9 kg/m^2 compared to 36,48 kg/m^2 in G1 (P=NS). Mean fasting blood glucose was significantly higher in G1 than G0 (12,19 mmol/l vs 10,36 mmol/l; P=0,04). The hypothyroid patients had more often low levels of HDLcholesterol and high levels of triglycerides (respectively 60% vs 57,14% in G0; P=NS and 30% vs 28,57% in G0; P=NS). Hypercholesterolemia was significantly more common in G1 than G0 (63,33% vs 25,71%; P=0,0003). The occurrence of cardiovascular events was observed in 11,43% of patients in G0 compared to 6,66% in G1 (P=NS). Thyroid status didn't have any influence on blood pressure

control (mean systolic and diastolic blood pressures were 137 mmHg and 79 mmHg, respectively in both groups).
Conclusion
The prevalence of hypothyroidism among our patients with type 2 diabetes was much higher than in the common population. Our hypothyroid patients had significantly higher fasting blood glucose levels and were more likely to be treated with insulin and to have low levels of HDLcholesterol and high levels of triglycerides. The recommendation for systematic exploration of thyroid status in patients with type 2 diabetes with metabolic syndrome requires larger-scale studies.

DOI: 10.1530/endoabs.81.EP1078

EP1079

Thyroiditis revealing a congenital anomaly: about an observation

El Omri Malika, Marwa Ben Njima, Amany Mallat, Mouna Bellakhdhar, Meherzi Abir, Jihen Haouas, Ghammmam Monia, Kermani Wassim & Abdelkefi Mohamed
Hospital Farhat Hached, ENT, Sousse, Tunisia

Introduction
Remnants of the fourth branchial arch are extremely rare with less than 100 cases reported in the literature and account for 1–4% of all branchial anomalies. These anomalies typically present as recurrent neck infections and/or abscesses or acute suppurative thyroiditis. We report a case of cyst of the 4th cleft revealed by a thyroiditis treated in our department.
Case report
A 6-year-old boy presented with recurrent neck swellings. During that time, he had a history of drainages, and attempted excisions, with recurrence of signs and symptoms after every intervention. Upon presentation to our clinic, he complained of painful swelling of his neck. Clinical examination revealed swelling of the anterior left neck that was tender to palpation and was approximately 5 cm. Ultrasound showed an irregular oval mass with polylobed contours, measuring 54 x 30mm, multi-loculated, of basi-cervical left location and pushing back the homolateral carotid axis and the left lobe of the thyroid which is of heterogeneous appearance. Computerized tomography scan showed a lobulated and multi-loculated mass of lateral and basi-cervical left location measuring 54x42x57 mm which compressed anteriorly the sternocleido-mastoid muscle as well as the left lobe of the thyroid. In the operating room, direct laryngoscopy revealed a sinus tract originating from the left side of the pyriform sinus apex; surgical exploration of the neck revealed the tract to pass through the hypopharyngeal wall, consistent with a fourth branchial anomaly. All scar from previous surgery, the ipsilateral thyroid gland, and the tract were completely mobilized. Postoperatively, the patient did well, and histopathology confirmed the presence of a sinus tract. The patient had an unremarkable postoperative course and has had no further recurrences.
Conclusions
Fourth branchial arch anomalies are rare and fascinating aberrations of fetal development that may present in many different ways such as thyroiditis. Combining a proper preoperative evaluation with careful surgical planning may result in the proficient eradication of these lesions, offering the patient relief from this source of recurrent infection.

DOI: 10.1530/endoabs.81.EP1079

EP1080

Neutropenia in hyperthyroidism

Cristina Elías Ortega, Nerea Egañ a Zunzunegui, Cristina Garcia Delgado, Maria Teresa Aramburu Calafell, Jorge Rojo Alvaro, Inmaculada Venegas Nebreda, Ane Amilibia Achucarro, Ismene Bilbao Garay & Alfredo Yoldi Arrieta
Donostia Unibertsitate Ospitalea, Donostia, Spain

Introduction
Neutropenia can indicate infectious and hematological pathology but it can also be a sign of hyperthyroidism. For this reason, it has been suggested to perform a complete blood count before starting treatment with antithyroid drugs in case of new-onset hyperthyroidism. Antithyroid drugs can cause severe neutropenia, also called agranulocytosis, when the neutrophil count is less than 500/µl. Therefore, the use of these drugs should be reconsidered if it is less than <1000/µl, and, in the event of symptoms compatible with agranulocytosis, treatment should be interrupted according to the recommendations of the American Thyroid Association (ATA). Agranulocytosis is a rare adverse effect of antithyroid drugs, appearing in 0.1%-0.5% of cases. However, there is no evidence that neutropenia in patients with hyperthyroidism is associated with an increased risk of antithyroid-induced agranulocytes.
Objectives
We studied the prevalence of neutropenia in patients with hyperthyroidism and the variations in the neutrophil count with the use of antithyroid drugs.
Material and Methods
We analyzed 52 cases of hyperthyroidism due to Graves Basedow disease diagnosed between 2014-2020. 8 men and 44 women with a mean age of 46 years (range 22-74). We studied the presence of neutropenia at diagnosis and during treatment with antithyroid drugs (methimazole or carbimazole). We classify neutropenia as mild 1000-1600/µl, moderate 500-1000/µl and severe <500/µL.
Results
5 patients presented neutropenia (9.61%), 2 at diagnosis and 3 during treatment. All the neutropenias found were mild (1000/µL -1600/µL), without clinical repercussions, and resolved during follow-up. Only 1 patient continued to present neutropenia from diagnosis until the 6th month of treatment. There were no cases of agranulocytosis.
Conclusions
Knowledge of the relationship between hyperthyroidism and neutropenia is essential for a correct diagnosis and treatment. Despite the limitations of our study, the cases of neutropenia in the context of hyperthyroidism were mild and the neutropenia was resolved without the development of agranulocytosis. This reinforces the idea that antithyroid treatment is not contraindicated in patients with mild neutropenia.

DOI: 10.1530/endoabs.81.EP1080

EP1081

Thyrotoxic crisis presented as psychiatric decompensation

Mafalda Martins Ferreira, Cátia Araújo, Mariana Lavrador, Joana Reis Guiomar, Patrí cia Oliveira, Carolina Moreno & Isabel Paiva
Centro Hospitalar e Universitário de Coimbra, Endocrinologia, Diabetes e Metabolismo, Coimbra, Portugal

Introduction
Thyrotoxic crisis is a rare endocrinological emergency with high mortality and it is more frequent in Graves' disease.
Clinical case
A 66-year-old women with schizophrenia was admitted to the Emergency Department due to altered state of consciousness, fatigue, constant moaning interspersed with unusual psychomotor agitation, heteroaggressiveness, diarrhea and anorexia. Lack of compliance with her psychiatric medication, new delusional ideas or use of recreational substances or drugs were excluded. The patient presented with normal blood pressure, peripheral oxygen saturation of 100% but she was sweating, subfebrile (37.6ºC) and tachycardic (154 bpm) and had painful palpation of the left iliac fossa without peritoneal defense. She had bilateral pulmonary stasis and showed permanent restlessness. Abdominal ultrasound excluded intra-abdominal infection and chest X-ray excluded pneumonia but showed Kerley B lines. The electrocardiogram showed persistent sinus tachycardia with poor response to beta-blockers, digoxin, analgesia and antipyretic medication. She had slight elevation of hepatic cytolysis enzymes, normal bilirubinemia, slightly elevated CRP (2.25 mg/dL) without leukocytosis,

Table 1

	Control group					Neutropenia group				
	neutro	%	T4l	T3l	Dose	neutro	%	T4l	T3l	Dose
Baseline	3333	47.79	4.15	13.41		1678	34.85	4.17	15.22	
1-3 months	3753	54.49	1.23	4.77	17.3	1540	32.33	1.03	3.20	15.5
2-6 months	3552	50.93	1.13	3.55	10.9	2056	39.7	1.05	3.15	8.9

normal amylasemia and negative cardiac markers. Due to persistent sinus tachycardia, thyroid function was requested and showed TSH <0.004 uIU/ml (0.4-4.0); free-T4 >5.0 ng/dL (0.7-1.5) and free-T3 >20 pg/mL (1.8-4.2). The diagnosis of thyrotoxic crisis was assumed with Burch-Wartofsky Scale of 60 points. The patient did not have any known thyroid disease. Propitiuracil, corticosteroids, cholestyramine and propranolol were started. She was initially stabilized in an Intermediate Care Unit due to congestive heart failure requiring non-invasive mechanical ventilation. The microbiological study was negative and no precipitating factor was found. TRABS and thyroid stimulating immunoglobulin were both detected: 9.7 U/l (< 1.0) and 1.0 U/l (<0.1) respectively. Thyroid ultrasound showed multinodular goiter with 2 larger nodules measuring 4 and 2 cm. She did not have Graves' orbitopathy. The patient was discharged after clear improvement of thyroid hormones: free-T4 1.60 ng/dL (0.7-1.5); free-T3 3.6 pg/mL (1.8-4.2) and underwent total thyroidectomy a few months later.
Conclusion
Long-term, disabling schizophrenia with a predominance of negative symptoms led to the devaluation of initial complaints - interpreted as psychiatric decompensation. In fact this was the second time the patient went to the emergency department with the same symptoms of restleness and agitation without a obvious cause. The time between the onset of symptoms and diagnosis was 5 days. Fever, persistent tachycardia and the patient's objective state of discomfort in the absence of appreciable analytical or ultrasound alterations led to the diagnosis.

DOI: 10.1530/endoabs.81.EP1081

EP1082

Lipid profile during block replace treatment in Graves disease

Ana-Maria Stancu[1], Ruxandra Dobrescu[2], Stanescu Laura Semonia[3] & Corin Badiu[3]
[1]'Carol Davila' University of Medicine and Pharmacy, Thyroid Related Disorders, Bucharest, Romania; [2]'Carol Davila' University of Medicine and Pharmacy, Endocrinology, Bucharest, Romania; [3]National Institute of Endocrinology, Thyroid Related Disorders, Bucharest, Romania

Introduction
Graves' disease (GD) is an autoimmune disorder causing hyperthyroidism. Variations of functional profile as well as type and titer of thyroid specific antibodies makes the control often difficult. One treatment option is adding levothyroxine to anti-thyroid drugs (ATDs), so-called block-replace therapy (BRT).
Aim
To study the BRT impact on lipid profile, thyroid function tests (TFTs) and TSH receptor antibodies (TRAb).
Materials & Methods
A prospective, observational study which enrolled 108 patients with active Graves' disease, aged >18 years, with new diagnosis or relapse of GD who are receiving medical therapy. Pregnant women, patients treated with radiotherapy or surgery were excluded. We compare the data regarding TFTs, TRAb and lipid profile from diagnosis (visit 0) and during BRT (3 visits). Mean time between visit 1 and 2 was 137.2 days, respectively 105.3 days between visit 2 and 3. Data were analyzed with Microsoft Excel and Minitab v21. Data are presented as mean ± SD.
Results
90 women, aged 45.07 ± 13.73 years and 18 men, aged 54 ± 14.03 years were included. Out of 108 patients, only 95 had measured their lipid profile at diagnosis and 6 of them were on therapy with statin. The mean of total cholesterol at visit 0 was 161.64 mg/dl, significantly lower than during the BRT (194.51 mg/dl at visit 1; 194.61 mg/dl at visit 2 and 202.42 mg/dl at visit 3, $P<0.001$). The mean of low density lipoprotein (LDL-cholesterol) progressively raised from 92.29 mg/dl (N: <100 mg/dl) at diagnosis to 116.45 mg/dl at visit 1 and 122.01 mg/dl at visit 3. No impact was observed on the levels of triglycerides. For 102 patients, the mean of fT4 during BRT was 13.237 pmol/l (N:9-19) on a dose of 46.15 ± 17.48 µg of levothyroxine daily. Mean dose of methimazole at diagnosis was 29.73 ± 15.43 mg/day and 16.70 ± 12.93 mg/day during BRT. Mean levels of T3 decreased from 364.53 ng/dl at diagnosis to 126.86 ng/dl (visit 1). Also, TRAb decreased from a mean of 17.07 UI/l (visit 0) to 8.71 UI/l (visit 3) ($P=0.002$).
Limitations
Small number of patients, limited time for observation, heterogeneous group.
Conclusion
Controlling hyperthyroidism in a block and replace regimen normalized the thyroid function, and worsened the lipid profile. This could be explained by the previously altered lipid profile before developing thyrotoxicosis, masked at the moment of diagnosis. A dynamic risk evaluation of lipid profile is suggested while treating thyrotoxicosis.

Key words: hyperthyroidism, Graves' disease, block-replace therapy, lipid profile.

DOI: 10.1530/endoabs.81.EP1082

EP1083

Abstract Withdrawn

DOI: 10.1530/endoabs.81.EP1083

EP1084

Basedow disease and Susac syndrome: an exceptional association

Arij Ezzouhour Yahyaoui[1], Asma Kefi[1], Khaoula Ben Abdelghani[1], Syrine Sassi[1], Sami Turki[1], Mounira El Euch[1] & Ezzeddine Abderrahim[1]
[1]Charles Nicolle, Internal Medicine A, Tunis, Tunisia

Introduction
Susac syndrome is a rare endotheliopathy causing micro-ischemic damage to vessels in the brain, ears, and eyes. While the underlying aetiology of this disease remains unknown, it is widely believed that observed clinical manifestations result of an autoimmune endotheliopathy. Herein we report a case of Basedow's disease associated to a scarce condition: Susac syndrome.
Observation
Our patient is a 48-year-old woman, who was admitted for chronic holocranial headache, without blurred vision nor vomiting. Physical examination only revealed a right hemiparesis. The brain MRI highlighted temporal and periventricular oval demyelinating lesions with T2 hypersignal and T1 hyposignal. These lesions were also described in the corpus callosum. An audiogram was performed and showed a bilateral and symmetric perceptive deafness. Ophthalmologic examination described a decreased visual acuity. Retinal fluorescein angiography showed bilateral and diffuse vasculitis. Somatosensory evoked potentials had a slightly decreased amplitude. Visual and auditory evoked potentials were normal. Cerebrospinal fluid testing did not show any abnormality. Therefore, the diagnosis of Susac syndrome was made. Thrombophilia testing and antinuclear antibodies were negative. She had a biological inflammatory syndrome and low levels of TSH. The thyroid scintigraphy was compatible with a Basedow's disease. We started treatment with radioactive iodine. Treatment of Susac syndrome consisted of three boli of methylprednisolone (1g/day for 3 days). Oral corticotherapy was then prescribed, with a good clinical and biological evolution.
Conclusion
Susac syndrome is caused by a microangiopathy that gives the classic clinical triad of subacute encephalopathy, visual loss secondary to retinal branch occlusions, and sensorineural hearing loss. Given autoimmune part of Susac aetiology, association to other autoimmune condition, especially Basedow disease, must be actively sought. Early therapy may reduce sequelae and improve recovery.

DOI: 10.1530/endoabs.81.EP1084

EP1085

The diffuse sclerosing form of papillary carcinoma of the thyroid

Meherzi Abir, Marwa Ben Njima, Mouna Bellakhdhar, El Omri Malika, Jihene Houas, Kermani Wassim & Abdelkefi Mohamed
ENT Department Farhat Hached Hospital Sousse, Tunisia

Objective
Papillary thyroid carcinoma is the most common malignant tumor of the thyroid, the diffuse sclerosing variant is however very rare and represents between 0.7 and 6.7% of all papillary thyroid carcinomas. We propose through this poster to study its clinical, epidemiological, therapeutic and prognostic characteristics.
Matherials and methods
We report two cases of diffuse papillary sclerosing carcinoma of the thyroid, collected at the ENT and CCF service of the Farhat Hached University Hospital of Sousse.
Results
The 2 patients were a man aged 38 years old and a women aged 55 years old with a family history of papillary thyroid carcinoma. The reasons for consultation were

right superclavicular swelling that had been present for 5 months in the man and right jugulocarotid adenopathy that had been present for 4 months in the woman. Cervical ultrasonography revealed a 2 cm right supraclavicular adenopathy containing fine microcalcifications and multiple microcalcifications were noted in the right lobe of the thyroid which contained a 10 mm nodule fully calcified in men and a suspicious nodule classified EUtirads 5 of 33 mm in women. Both patients underwent total thyroidectomy with dissection of the bilateral central lymph node and homolateral lateral one. Extemporaneous examination revealed papillary carcinoma in the female patient, whereas it was in favor of benign in the male patient. The final histological examination showed a papillary carcinoma in its diffuse sclerosing variant with sub-millimetric microscopic foci of epithelial malignant tumor proliferation, disseminated throughout the right lobe of the thyroid in men and infiltrating both thyroid lobes and peri-thyroid fat in women, as well as multiple endolymphatic emboli and lymph node metastases in the mediastinum-recurrent, jugulocarotid and supraclavicular. The postoperative period was dominated by the appearance of transient hypoparathyroidism. Both patients received additional treatment with radio-active iodine. The evolution was good. The decline was 12 months.
Conclusion
The diffuse sclerosing variation of papillary carcinoma is an uncommon histological form distinguished by its locally aggressive nature and deceptive clinical appearance. Its therapy must be complete.

DOI: 10.1530/endoabs.81.EP1085

EP1086

Failure of rhTSH-stimulated FDG PET-CT scan to identify metastases of a papillary thyroid carcinoma

Ricardo de Leon-Durango, Alba Hernandez-Lazaro, Carmen Acosta-Calero, Agnieszka Kuzior, Claudia Arnas-Leon & Francisco Javier Martinez Martin
Hospital Universitario de Gran Canaria Dr. Negrín, Pakistan

Introduction
Recurrences of differenciated thyroid carcinoma are occasionally hard to locate; rhTSH-stimulated FDG PET-CT may offer a higher sensitivity, particularly when thyroglobulin in high, but its utility has not been clearly established.
Methods
Review of the patient's clinical record
Results
A 61 years old woman noticed a right anterior neck lump when she was 47; FNAC was suggestive of a solid papillary thyroid carcinoma and she underwent right thyroid lobectomy. The pathology diagnosis was atypical papillary trabecular carcinoma (5.5 cm maximal diameter) with oncocytic changes, with minimal extracapsular invasion but clean surgical margins. She underwent left lobectomy two months later, with normal pathology, followed by ablation with 125 mCi of 131-I one month later, and substitution therapy with levothyroxin ever since. One year afterwards, the rhTSH test was negative, and follow-up thyroglobulin, antithyroglobulin antibodies and neck ultrasonography were negative for the next 9 years. By the tenth year, thyroglobulin was detectable (1.1 ng/mL) and increased in the 11th and 12th years (2.14 and 2.75 ng/mL) but thyroid gammagraphy scans were negative, and ultrasound only revealed unspecific laterocervical adenopathies, with negative FNAC. A CT scan showed only two well-defined pulmonary nodules of 7.5 mm maximum diameter in the lingula and the apical segment of the left lobe. A new rhTSH test with peak TSH of 87.5 mcU/mL showed little response (baseline and stimulated thyroglobulin 5 and 7.5 ng/ml, respectively) with negative stimulated gammagraphy scan. An FDG PET-CT was ordered (13th year) showing only the two known pulmonary nodules, stable in size (both 7.0 mm), without metabolic criteria of malignancy (SUVmax: 1.7). In order to elucidate if the nodules could be metastatic, a new FDG PET-CT was performed (14th year) after rhTSH stimulation, thyroglobulin showed again a modest response (8.25 to 10.4 ng/mL) and the nodules showed a small increase (10 mm) and an increase in metabolic activity under stimulation (SUVmax 1.3 to 2.3). Ablation with 150 mCi of 131-I was performed, but the gammagraphy scan did not show enhancement of the pulmonary nodules. One month afterwards, the patients's thyroglobulin was not substantially decreased (8.25 to 7.80 ng/mL).
Conclusions
The use of rhTSH-stimulated FDG PET/CT reportedly changes the patients' management only in a minority of the cases. In our patient, the apparent enhancement of two pulmonary nodules with this technique seems to be a false positive, with negative result of the post-treatment gammagraphy and no change in the patient's management.

DOI: 10.1530/endoabs.81.EP1086

EP1087

Autoimmune thyrotoxicosis Post SARS CoV-2 Vaccination

Dorothy Maria Anthony Bernard, Chin Voon Tong & Yen Nee Low
Hospital Melaka, Internal Medicine and Endocrinology, Bandar Melaka, Malaysia

Introduction
Covid-19 vaccination have been introduced to reduce overall severity and mortality of COVID-19 infection. Autoimmune/inflammatory syndrome induced by adjuvants (ASIA) is a syndrome first described in 2011 that triggers autoimmune conditions after exposure to various adjuvants through various mechanisms. We report three cases of autoimmune thyrotoxicosis post mRNA type vaccine for COVID-19 possibly linked to adjuvants present in the vaccine.
Case 1
A 34-year-old patient was newly diagnosed with Grave's disease, within 1 month after her SARS-CoV-2 vaccine (Pfizer-BioNTech) when she presented with symptoms of palpitations, heat intolerance and a painless neck swelling. Physical examination revealed fine tremors with a diffuse goiter. Results of biochemical workup was as follows: TSH (Thyroid stimulating hormone): <0.008 mIU/l (low), FT4(free thyroxine): 123.1 pmol/l (elevated), FT3(free triiodothyronine): 9.10 pmol/l (elevated), anti-TPO (antithyroid peroxidase) : 9.51 IU/ml (normal), anti TG (antithyroglobulin): 11.04 IU/ml (normal), TSHrAb (anti–TSH antibody levels) : 30.03 IU/l (elevated). Ultrasound thyroid revealed increased vascularity in bilateral thyroid lobes with heterogenous appearance. She was started on oral Carbimazole and Propanolol.
Case 2
A 29-year-old healthcare worker with underlying thyrotoxicosis in remission for 7 years presented with symptoms of as heat intolerance, agitation, oligomenorrhea, mood instability, palpitations and diarrhea within 1 month after her 1st dose of SARS-CoV-2 vaccine (Pfizer-BioNTech). Physical examination revealed fine tremors with no thyroid eye signs or goiter present. Results of biochemical workup was as follows: TSH: <0.008 mIU/l (low), FT4: 29.4 pmol/l (elevated), FT3: 8.47 pmol/l (elevated), anti-TPO: 254.8 IU/ml (elevated), anti-TG: 30.13 IU/ml (normal), TSHrAb: <0.8 IU/l (normal). Thyroid ultrasound revealed increased in vascularity. She was started on oral Carbimazole and Bisoprolol.
Case 3
A 30-year-old healthcare worker with underlying thyrotoxicosis in remission for 9 years also presented with lost of weight of 6 kg, heat intolerance and fine tremors, within 1 month after her 1st dose of SARS-CoV-2 vaccine (Pfizer-BioNTech). Physical examination revealed fine tremors with a diffuse goiter present. Results of biochemical workup was as follows: TSH: <0.008 mIU/l (low), FT4: 56.6 pmol/l (elevated), anti-TPO: 375.7 IU/ml (elevated), anti-TG:1691.1 IU/ml (elevated), TSHrAb: <0.8 IU/l (normal). Thyroid ultrasound revealed heterogenicity and increase vascularity in bilateral thyroid lobes. She was started on oral Carbimazole and Propanolol.
Conclusion
This case series reports three cases of autoimmune thyrotoxicosis post vaccination with Pfizer-BioNTech against COVID-19. Any emerging symptoms of thyrotoxicosis post vaccination should prompt clinicians to screen appropriately. However, the benefits of vaccination still outweigh any risks and should be advocated for all patients unless they have other contraindications.

DOI: 10.1530/endoabs.81.EP1087

EP1088

Amiodarone-induced thyrotoxicosis refractory to medical therapy: A case report

Zineb Mhamdi, Adil El Mesmoudi, Souad El Moussaoui & Ghislaine Belmejdoub
Military Hospital Mohammed V, Department of Endocrinology and Diabetology, Rabat, Morocco

Introduction
Amiodarone is an anti-arrhythmic drug rich in iodine compounds. One 200 mg tablet corresponds to about 25 times the daily requirement of iodine. One of the major complications of taking Amiodarone is the development of dysthyroidism which is observed in 15% to 20% of cases. Hyperthyroidism occurs in 1 and 13% of these patients.
Case report
We report the case of an 34 year old female patient, followed for complete arrhythmia by atrial fibrillation under Amiodarone 200 mg/d, who presented a thyrotoxicosis with TSH at 0.005 mUI/l, FT3 at 1.5 times normal and FT4 at 2 times normal. Anti-TPO and TSH receptor antibodies were negative. Cervical ultrasound showed an enlarged thyroid. Thyroid scintigraphy was white.

Treatment with Carbimazole 40 mg/d and Prednisolone 60 mg/d was initiated without improvement. In view of the resistance to medical treatment, total thyroidectomy was indicated.
Discussion and conclusion
Amiodarone-induced hyperthyroidism can be explained by two mechanisms: thyroid hyperfunction by iodine overload in the context of a pre-existing nodular pathology (type 1) and must be treated with synthetic antithyroid drugs or thyroiditis with follicular destruction (type 2) and which responds well to glucocorticoids or the mixed form as in our patient's case. Surgery is indicated if there is resistance to medical treatment, to correct thyrotoxicosis rapidly in patients for whom discontinuation of Amiodarone is not possible.
References
Bogazzi F, Bartalena L, Martino E. Approach to the Patient with Amiodarone-Induced Thyrotoxicosis. J Clin Endocrinol Metab 2010; 95 (6): 2529-2535

DOI: 10.1530/endoabs.81.EP1088

EP1089

The role of ACTB status for early non-invasive detection of papillary thyroid carcinoma

Raimonda Klimaite[1,2,3], Mintautė Kazokaitė[2,4,5], Aistė Kondrotienė[1,2,3], Dalia Dauksiene[1], Birute Zilaitiene[1,2,3] & Albertas Dauksa[2,3,6]
[1]Institute of Endocrinology, Medical Academy, Lithuanian University of Health Sciences, Lithuania; [2]Lithuanian University of Health Sciences, Lithuania; [3]Hospital of Lithuanian University of Health Sciences, Kauno klinikos, Department of Endocrinology, Lithuania; [4]Institute of Endocrinology, Medical Academy, Lithuanian University of Health Sciences; [5]Institute of Digestive Research, Medical Academy, Lithuanian University of Health Sciences, Lithuania; [6]Hospital of Lithuanian University of Health Sciences, Kauno klinikos, Department of Surgery, Lithuania

Introduction
Papillary thyroid carcinoma (PTC) is the most common type of differentiated thyroid cancer of all cases of thyroid cancer. Fine-needle biopsy by ultrasonography is still the main diagnostic method of PTC, but there is a technical limitation. That's why, a minimally invasive diagnostic test that can accurately diagnose the onset of the disease is the subject of research.
Our objective
We aimed to explore the concentration levels of *ACTB* in PTC patients, healthy controls (HC) plasma samples and to compare with clinicopathological factors.
Methods
Studyincluded 154 patients treated at Hospital of Lithuanian University of Health Sciences, Kaunas clinics 2020 - 2021: 68 patients with a histologically confirmed diagnosis of PTC and 86 HC. The concentration of *ACTB* was measured by qPCR in plasma samples. Statistical analyses were performed using SPSS 22.0 software (SPSS Inc., Chicago, IL, USA). The results were considered statistically significant at $P < 0.05$.
Results
Average age at diagnosis was 48.19 $\pm$ 14.9 years in PTC group and 45.30 $\pm$ 12.07 years in HC ($P > 0.05$). In the PTC group, there were 8 male patients (11.8%) and 60 female patients (88.2%), while in the HC: 65 (75.6%) female and 21 (24.4 %) male patients ($P > 0.05$). The concentration of *ACTB* was significantly higher in the PTC patients compared to HC (1005.97 vs 623.12 ng/ml, $P = 0.047$). We observed that *ACTB* concentration were significantly higher in PTC with greater tumor size (> 2 cm) compared to lower (≤ 2 cm) tumor size ($P = 0.005$). The total tumor size was calculated as the sum of the diameters of all tumors in PTC multifocal cases. A weak positive correlation between the concentration of *ACTB* with the total size of PTC tumors was found ($P = 0.012$, $r = 0.304$). However, there was no correlation between lymphovascular invasion, lymph node metastasis and other clinicopathological features.
Conclusion
This analysis included comparison of the *ACTB* concentration associations between PTC patients, HC groups and clinicopathologic factors. We found that plasma concentration of *ACTB* was significantly higher in patients with greater tumor size. Our study indicated that *ACTB* concentration changes may be used as parameter in differentiating PTC patients from HC. But further studies are also warranted to expand upon our findings.

DOI: 10.1530/endoabs.81.EP1089

EP1090

Thyroid carcinoma and anti-synthetase syndrome: A rare association!

Asma Tekaya, Asma Kefi, Khaoula Ben Abdelghani, Mounira El Euch, Cyrine Sassi, Sami Turki & Ezzedine Abderrahim
Charles Nicolle Hospital, Department of Internal Medicine A, Tunis, Tunisia

Background
Anti-synthetase syndrome (ASS) is an idiopathic inflammatory myopathy (IIM). Clinical features may include myositis, interstitial lung disease (ILD), non-erosive arthritis, Raynaud's phenomenon, and mechanic's hands with the presence of anti-synthetase antibodies. Although ASS-neoplasia association has been reported, it remains scarce and debated association. Herein, we report an original case of thyroid carcinoma in a patient followed for ASS.
Case report
A 40-year-old woman, consults for myalgia and weakness of the 4 limbs since 4 months. She presented with progressive proximal muscle deficit, elevated muscle enzymes, mechanics' hands, ILD and positive anti-JO1 antibodies, thus she was diagnosed with ASS. Treatment was based on corticosteroids and Cyclophosphamide with good evolution. Initial screening for neoplasia was negative. Six years later, during a routine check-up, examination found a centimetric thyroid nodule. Thyroid function test was normal. Cervical ultrasound showed a 7mm right lobar thyroid nodule classified as EU-TIRADS 5. Fine needle aspiration found cytological atypia of undetermined significance. Total thyroidectomy was performed. Pathological examination concluded that a non-encapsulated intrathyroid papillary carcinoma. In addition to the surgical treatment, the patient received radioactive iodine with good outcome. The current follow-up is 2 year.
Discussion
We report the occurrence of thyroid neoplasia in a patient diagnosed with IIM, after 6 years of follow-up. The originality of this case is due to of the type of the IIM and the delay in the onset of the cancer in relation to its diagnosis. Compared to other IIM, ASS' association to neoplasia is still debated: in the cohort of Pinal-Fernández, with 169 ASS patients, the frequency of cancer doesn't seem higher than that of the general population. The Chinese cohort of Shi, with 124 ASS patients, found that 6.5% developed neoplasms, with a mean time of 3 years between neoplasia and SAS, of which, the majority presented with ILD. In the review carried out by Boleto, male gender, age over 60 years, and the presence of anti-SSA/Ro were predictive factors of development of cancer in ASS patients.
Conclusion
Thyroid carcinoma was discovered in our observation during regular screening for ASS-associated neoplasia. Thyroid carcinoma-ASS is an extremely rare but possible association, which will need to be detected and treated. Given the rarity of ASS, recommendations regarding the systematic screening for cancer have yet been established. In the meantime, we must remain vigilant about the possibility of the occurrence of cancer in these patients, and therefore ensure regular screening.

DOI: 10.1530/endoabs.81.EP1090

EP1091

Diarrhea as the only symptoms in hyperthyroidism- case report

Rajmonda Tare
Endocrinology, Internal Department, Regional Hospital 'Xhaferr Kongoli', Albania

Introduction
Hyperthyroidism (overactive thyroid) is a condition where thyroid makes and releases high levels of thyroid hormone (thyroxine) in the blood. This condition can speed up our body metabolism. Hyperthyroidism causes an overactivity of the sympathetic system. It also this sympathetic hyperstimulation in the gut leads to increased motility causing diarrhea, malabsorbation and consequently weight loss.
Objective
To describe a patient with hyperfunxional nodular goiter and diarrhea as the only symptoms, for which Unimazole (ATS), was found to be effective therapy for the diarrhea.
Methods
We present the clinical course of a old woman with a prolonged diarrhea which with all diagnostic procedures and medication given did not improve until it was thought to be an endocrine cause. Unimazole control of such cases of hyperthyroidism with diarrhea can be explained by the effect of this drug in reducing intestinal hypermotility as the basis of physiopathology in hyperthyroidism.

Results
A 73-year-old woman, has not previously had gastrointestinal disorders, had prolonged diarrhea, which associated with loss of 3 kg during a 1-month period. Laboratory, ultrasound images, recommended by the infectious disease doctor could not detect the cause of this prolonged diarrhea. Despite antibiotic treatment and antidiarrheal treatment, diarrhea did not stop. Other hyperthyroidism symptoms were not reported, but when hyperthyroidism was identified, the diarrhea was dominated and very well controlled by treatment with unimazole.
Conclusion
Thyroid hormone in excess, among its other possible effects in the organism, affect the gastrointestinal tract through sympathetic intestinal hyperstimulation and increased motility causing diarrhea. Antithyroid therapy act by blocking sympathetic hyperstimulation. Our case leads us to think that hyperthyroidism should be considered in the differential diagnosis of diarrhea of unknown cause.
Keywords diarrhea, unimazole, hyperthyroidism.

DOI: 10.1530/endoabs.81.EP1091

EP1092

Case Report of Hypothyroidism as a Cause of Ataxia
Farah Elgharroudi, Ismail Zahra, Nawal EL Ansari & Ghizlane EL Mghari
Chu Mohammed VI, Endocrinology, Marrakech, Morocco

We present a case of a 56-year-old male who reported to us with history of instability of gait since one year which was acute in onset and progressive, there was also history of hearing impairment and constipation since 3 years without improvement despite several symptomatic treatments. There was no history of weakness in any part of body, headache, vomiting, convulsions or alteration of sensorium. There was no history of trauma to the head, fever or drug intake. On examination, his vitals were normal. Cognitive functions were normal. Neurological examination showed gait ataxia, dysarthria and dysmetria on finger-nose and heel-to-knee tests. The gait was wide-based and there was a tendency to fall to right side. His fundus was normal. His power was normal but had hung up reflexes. Sensory system was normal. His hemogram was normal. Serum electrolytes, blood sugar, renal and liver function tests were normal. Total cholesterol: 191 mg/dl, triglycerides: 345 mg/dl, HDL cholesterol: 45 mg/dl, LDL cholesterol: 77 mg/dl. viral serologies were negative. T3:0,1 (0,3-5 pmol/dl) T4: 1.5 pmol/dl (12-22), TSH: $>$100 uIU/ml (0.27-5.5). The Serum anti-TPO antibody was not available. Cervical ultrasound showed an appearance related to thyroiditis: Reduced thyroid with heterogeneous echo structure size, alternating hypo and hyperechogenic range producing a tabby aspect of the gland and hypervascularization on Doppler. MRI brain was normal (Figures 1 and 2). Electrocardiogram and trans-thoracic ultrasound were normal with left ventricular ejection fraction below 50%.

DOI: 10.1530/endoabs.81.EP1092

EP1093

Successful treatment of Graves' disease with high dose iodine-131, without subsequent hypothyroidism: a case report
Anna Brodovskaia
Ivanovo State Medical Academy, Department of Internal Medicine, Ivanovo, Russian Federation

Background
Radioiodine is an effective treatment for Graves' hyperthyroidism. In most cases this therapy renders the patient completely hypothyroid. As a consequence they will require lifelong thyroid replacement therapy. Now it is controversial whether radioiodine should be given in a sufficient dose to induce hypothyroidism or a lower dose in an attempt to achieve a euthyroid state.
Case Report
A 71-year-old woman with a 30 years history of Graves' disease and frequent recurrences of thyrotoxicosis presented with tremulousness, palpitations, dyspnea, progressive fatigue and weight loss. Examination revealed BMI 28 kg/m^2, Ps 105 bpm, BP 150/80 mmHg. An ECG showed sinus tachycardia. Laboratory analyses showed recurrence of hyperthyroidism: TSH 0,19 mUI/l (N 0,27-4,2), FT4 1,86 ng/dl (N 0,93-1.52), positive TSH receptor antibodies (5,62 IU/l). The thyroid ultrasonography showed diffusely enlarged thyroid (total volume 54 ml). Thyroid scintigraphy showed increased 24-hour radioiodine uptake (90%) with diffuse activity on the scan image. She was treated with methimazole (30 mg/day) and anaprilin (40 mg/daily) and the patient's condition improved. According to medical history she had poor control of the disease by drugs. Surgery was risky for the elderly patient. Therefore radioactive iodine ablation was suggested. Iodine-131 was administered orally at individual dosage of 13 millicuries (based on 200 microCi/g of thyroid tissue). Previous to therapy thyroid laboratory results showed TSH 1,75 mUI/l, FT4 0,68 ng/dl. Methimazole was canceled 3 days before the procedure. The introduction of I-131 was well tolerated. Patient had normalization of thyroid function tests within 4 weeks. Hypothyroidism occured 12 weeks after radioiodine (TSH 46,4 mUI/l, FT4 0,23 ng/dl). Then thyroid replacement therapy (75 mg of levothyroxine) was initiated. However, within the 6 month after treatment the patient presented subclinical hyperthyroidism and the dose of levothyroxine was reduced and then canceled. Ultrasound showed residual thyroid tissue (total volume 18 ml). The patient is currently euthyroid (TSH 0,58 mUI/l) and under follow-up.
Conclusion
For patients with Graves' disease, a high dose of radioiodine is directly related to the cure rate and the incidence of hypothyroidism. The most preferred is to individualize the radioiodine dose based upon the size of the thyroid gland and the 24-hour radioiodine uptake. In this case, a persistent goiter suggests incomplete destruction of the gland and the possibility of persistent autonomous thyroid tissue. After radioiodine, all patients require monitoring for hypothyroidism or persistent hyperthyroidism.

DOI: 10.1530/endoabs.81.EP1093

EP1094

Papillary carcinoma of the thyroid and cervical teratoma: incidental association?
Imane Alilouch, Farah Kamel, Zineb Mhamdi, Kaoutar Rifai, Hinde Iraqi & Mohamed Elhassan Gharbi
Ibn Sina University Hospital, Endocrinology and Diabetology, Rabat, Morocco

Introduction
Teratomas are complex malformative tumors defined by the presence of tissues derived from the 3 embryonic layers. They can be mature or immature, depending on their degree of differentiation. They are most often found in the sacrococcygeal region and the gonads. Cervical location is exceptional (4%).
Observation
We report the case of a 45-year-old patient who presented with a right cervical swelling that progressively increased in volume. The patient consulted the ORL department and a cervical ultrasound scan was performed, which revealed an ETIRADS 4 nodule, a cytopuncture was done and came back in favor of signs of malignancy, the patient underwent a total thyroidectomy with left recurrent curage, the anathamopathological study showed a papillary tumor of the thyroid classified as pT3a with the presence of 5 reactionary lymph nodes associated with a cystic formation evoking a mature terartoma.
Discussion and conclusion
Cervical teratomas are rare lesions usually diagnosed at birth. Their occurrence in adults is extremely rare and, less than 40 cases have been reported in the literature**.** The association of cervical teratoma and papillary thyroid carcinoma has not been described**,** Is it a genetic link or a simple coincidence or do we need more studies to confirm a link between the two associations?
Reference
Mohd Rashid Lukman. Malignant Cervical Teratoma in an Adult Presenting with Impending Airway Obstruction, ASIAN JOURNAL OF SURGERY VOL 28. NO 3. JULY 2005.

DOI: 10.1530/endoabs.81.EP1094

EP1095

Retroplacental hematoma : a dreaded complication of hypothyroidism : An observational study
Widad Douali[1], Mennani Fatimaeezzahra[1], Rafi Sana[1], El Mghari Tabib Ghizlane[1] & El Ansari Nawal[1]
[1]Chu Mohamed VI Marrakech, Department of Endocrinology, Diabetology, Metabolic Diseases and Nutrition, Marrakech, Morocco

Introduction
Hypothyroidism is the most common endocrine dysfunction during pregnancy. In pregnancy, hypothyroidism is most often due to chronic autoimmune thyroiditis (Hashimoto's disease) The consequences of hypothyroidism vary depending on the time of onset of hypothyroidism during pregnancy and the etiology

retroplacental hematoma is a serious complication of hypothyroidism We report the case of a patient with in utero fetal death on retroplacental hematoma complicated by hypothyroidism
Observation
questioning
The patient is 35 years old. History: followed for hypothyroidism on levothyrox 150 mg/d Admitted for heavy metrorrhagia with obstetrical ultrasound has objectified: fetal death in utero with evidence of a retroplacental hematoma **On clinical examination**
Patient Conscious, pale and discolored conjunctivae Blood pressure = 130/80 mmhg; heart rate = 69bpm; Non-palpable thyroid The rest of the exam was unremarkable. On the balance sheet: Blood count: hemoglobin = 6.9; White blood cells = 9110; platelets = 300000 TSH = 77 mui/l; Cervical ultrasound: atrophic thyroid glan
d Therapeutic care
The patient was put on levothyrox: 175 mg/d A cardiovascular evaluation has been requested
Discussion
-Retroplacental hematoma is a polycausal disease with etiological factors (vascular, age, environmental) -Publications suggest that dysthyroidism and more particularly hypothyroidism may be a risk factor for Retroplacental hematoma According to a study published in 2013; RPH in hypothyroidism can be explained by several factors: thyroid hormones play a very important role in Placentation: 11-16 amenorhea week (defined as Invasion of trophoblasts into the maternal decidua and the spiral artery) In Hypothyroidism: insufficient trophoblastic invasion responsible for ischemia and placental abruption hypothyroidism is associated with thrombo-embolic and hemorrhagic phenomena which is explained by the alteration of the coagulation system – fibrinolysis the presence of anti tpo ac is more likely associated with other immune diseases and alteration of the immune system another study published in 2020 did not find a significant link between hypothyroidism and RPH
Conclusion
This observation underlines the importance of determining the place of this risk factor within the various FDRs of RPH already known and the need to set up preventive strategies, in particular when the usually effective treatment of hypothyroidism is lacking.

DOI: 10.1530/endoabs.81.EP1095

EP1096

Cholestatic Hepatitis in Graves' Disease: A case report
Meriem Adel, Sabrine Mekni, Maysam JRIDI, Imen Rojbi, Youssef Lakhoua, Nadia Mchirgui, Ibtissem Ben Nacef & Karima Khiari
Charles Nicolle Hospital, Endocrinology, Tunis, Tunisia

Introduction
Thyrotoxicosis is an uncommon cause of cholestasis. It's a diagnostic challenge considering the broad differential diagnosis. Herein we report a case of Grave's disease revealed by severe cholestatic jaundice.
Observation
A 46 old male with a history of Sickle cell disease complained of diarrhea and significant weight loss for eight months, followed the last month by palpitations, heat intolerance, anxiety, insomnia and progressive jaundice. He had no family history of autoimmune disease. He denied hepatotoxic drugs, alcohol use or high-risk sexual behavior. On physical examination his body mass was 21.23 kg/m^2, his blood pressure was 110/50 mm Hg and his heart rate was 93 beats per minute. He had jaundice of sclerae and skin with mild hepatomegaly. His thyroid was symmetrically enlarged. Biochemical findings showed: total bilirubin 183.6 µmol/l (3.4–20), direct bilirubin 135 µmol/l (< 8.6), alkaline phosphatase 143 U/l (40–129), AST 69 U/l (1–38), ALT 23 U/l (1–41), TSH 0.005 µUI/l (0.27-4.2) and FT4 61.07 pmol/l (12-22). Hepatitis A, B, and C testing were negative and autoimmune screen was unremarkable except positive hyroid-stimulating hormone receptor antibodies. Abdominal ultrasound, computed tomography and MRI revealed hydatic cystis in the VI and VII segment without biliary ductual dilatation. Thyroid ultrasound showed a symmetrically diffuse enlarged, hyper vascular, heterogeneous gland without nodules. Regarding the severity of the thyrotoxicosis, methimazol, propranolol and corticoids were administrated before radioiodine treatment with a close monitoring of liver function. By day 40 bilirubin fell by 50% (91.4).
Conclusion
This case highlights the merit of considering thyrotoxicosis as a cause of cholestasis as attaining a euthyroid state is critical for hepatic recovery.

DOI: 10.1530/endoabs.81.EP1096

EP1097

A rare localization of lymph node metastasis from papillary thyroid carcinoma
Mohamed Masmoudi, Wadii Thabet, Marwa Regaeig, Ezer Chebil, Mehdi Hasnaoui & Khalifa Mighri
Tahar Sfar Hospital, Mahdia, Otorhinolaryngology, Tunisia

Introduction
Lymph node (LN) metastases of papillary thyroid carcinoma (PTC) usually happen in the paratracheal and internal jugular chain and are unusual in the parapharyngeal space (PPS). Our aim is to emphasize on the possibility of parapharyngeal metastatic LNs in PTC and to describe the diagnosis methods, treatment options, and impact on the prognosis.
Case Report
A 62-year-old woman presented with a dysphagia lasting for 2 years. Examination revealed an anterior neck mass. On ultrasound, it was an EU-TIRADS 5 left thyroid nodule. Consequently, the patient underwent a total thyroidectomy with a bilateral central dissection and a left selective neck dissection (II-IV). Histopathologic examination of the thyroid gland confirmed the diagnosis of a PTC of the left lobe with metastasis on central and lateral LN dissections. The tumor was staged as pT2 N1b M0. Postoperatively, she had radioactive iodine ablation therapy. She received a cumulated dose of 200 mCi (2 courses). Ultrasound and thyroid scintigraphy were normal. However, because of a high thyroglobulin (TG) level, a CT scan was performed (3 months postoperatively) and showed a left 3–cm prestyloid mass. The mass was hypodense, with some irregular areas of enhancement: a parapharyngeal metastatic LN was suspected. The patient did not present any symptom related to the mass. On physical examination, there was no evidence of cervical lymphadenopathy, no palpable thyroid lesion, no cranial nerve deficits. The oropharyngeal exam was normal. A surgical resection of the mass was performed with external cervical approach: a mass measuring 3 × 2 cm was found in the left prestyloid space. On histopathologic examination, the mass was a metastatic LN of a PTC. Three months after the surgery, the patient was doing fine, with no evidence of disease.
Conclusion
PPS metastases from thyroid carcinoma are uncommon, and only few cases have been reported in the medical literature. These PPS LNs are not included during nodal dissection. If these areas are left undissected, they might be the cause of a persistent disease or a delayed recurrence. As a result, for patients with PTC, especially those who underwent neck dissection and have an unexplained increase in serum TG levels, CT or MRI should be done for surveillance rather than ultrasound to detect the presence of nodes in this compartment.

DOI: 10.1530/endoabs.81.EP1097

EP1098

Malignant non-Hodgkin lymphoma of the thyroid Gland: About 4 cases
Rachida Bouattay, Emna Bergaoui, Maroua Naouar, Mehdi Ferjaoui, Heyfa Belhadjmiled, Amel Elkorbi, Kaled Harrathi, Naourez Kolsi & Jamel Koubaa
Fattouma Bourguiba Hospital, ENT, Monastir, Tunisia

Introduction
Cervico-facial non hodgkin lymphomas are rare conditions; they represent 5% of all malignant tumors of the head and neck. Their localizations are essentially lymph nodes but all the organs can be affected.
Purpose of the presentation
The objective of this work is to determine the clinical, histological and therapeutic aspects of malignant non-Hodgkin lymphoma localized in the thyroid gland.
Methods
This is a retrospective study about 4 patients treated for a malignant non-Hodgkin lymphoma of the thyroid gland, in the ENT and hematology departments of Fattouma Bourguiba hospital in Monastir over a period of 20 years (2000-2019).
Results
The average age was 48 years. A female predominance was noted. The average consultation time was 6 months. Patients consulted for a rapidly progressive goitre in all cases, associated with dysphagia and dyspnea in 3 cases (75%). Cervical examination showed a painful, mobile and indurated anterior cervical swelling in all patients. Associated lymph nodes were found in only one case (25%). Cervical ultrasound and cervico-thoracic scan showed a mass pushing back the trachea in two cases (50%). Fine needle aspiration showed an aspect of a

large cell lymphoma of thyroid gland in 2 cases (50%). In the histological examination, it was a diffuse large B-cell lymphoma in the 4 cases. The extension assessment did not objectivize other synchronous locations. Three patients were classified at stage IA, one patient at stage IIA. The treatment consisted on chemotherapy in all patients with no tumor recurrence or relapse in all cases with an average follow-up of 24 months.
Conclusion
Malignant non-Hodgkin's lymphoma of the thyroid gland is a rare disease. The treatment often gives good results and the prognosis depends essentially on the tumor stage and the speed of treatment.

DOI: 10.1530/endoabs.81.EP1098

EP1099

COVID-19 vaccine-associated subacute thyroiditis

Pei Chia Eng[1, 2], Lien Davidson[2], Rochan Agha-Jaffar[2], Jeremy Cox[2], Michael Yee[2], Maura Moriarty[2], Stephen Robinson[2], Tannaz Vakilgilani[2] & Vassiliki Bravis[2]
[1]Imperial College London, London, United Kingdom; [2]St Mary's Hospital, London, United Kingdom

Introduction
Subactue thyroiditis (SAT) is a self-limiting inflammatory condition caused by follicular destruction of the thyroid gland, commonly precipitated by viral upper respiratory tract infection 2 weeks preceding the onset of thyroid symptoms. However, SAT following COVID-19 vaccination is rare. Herein, we report two cases of subacute thyroiditis which presented after administration of COVID-19 vaccine.
Case series
The first patient was a 42 year old man who reported rapid onset of sore throat, neck pain and symptoms of thyrotoxicosis including weight loss, sweating and heat intolerance. The onset of symptoms was two weeks following his second dose of BNT162B2 mRNA (Pfizer-BioNTech) COVID-19 vaccine. There was no significant medical history and or prior use of medications that would precipitate thyrotoxicosis. He recovered well with a course of non-steroid anti-inflammatory agent. The second patient was a 31 year old lady, with no past medical history, who presented with neck pain and fever and symptoms of thyrotoxicosis three weeks after her third dose of BNT162B2 mRNA (Pfizer-BioNTech) COVID-19 vaccine despite having had two Sputik Covid V vaccine previously. She recovered well with a course of steroids. Both patients had negative TSH-receptor antibodies and thyroid peroxidase antibodies (0.20IU/ml, 0.39IU/ml). Imaging studies were consistent with thyroiditis with no obvious uptake noted on Technectium scan.
Discussion
SAT after vaccination, may develop as a result of direct injury by vaccine attributed by molecular mimicry. Due to the similarity between SARS-CoV2 spike protein and thyroid peroxidase, the cross reaction between the coronavirus spike protein with the TPO antibodies induce an autoimmune/inflammatory response to thyroid follicular cells. As with any form of SAT, treatment is symptomatic with non-steroidal agents and corticosteroids including levothyroxine if patient devloped hypothyroidism. In all these cases, association of SAT with the administered vaccines was suggested by temporal relationship between symptom onset and vaccination. Therefore, clinicians are encouraged to be vigilant of autoimmune diseases as possible complications of COVID-19 vaccination, even in patients with mild COVID-19 infections.
Conclusion
SAT can rarely occur following COVID-19 vaccination. Early identification of the possible endocrine side effects of the COVID-19 vaccine can help treat this condition. As SAT is a mild self-limiting illness, its possible association with prior vaccination should not deter people from vaccination.

DOI: 10.1530/endoabs.81.EP1099

EP1100

Autoimmune thyroid disease and autoimmune hepatitis

Raida Ben Salah[1], Faten Haj Kacem Akid[2], Siddiqa Soomauroo[2], Cyrine Chehaider[2], Sarra Chouaib[2], Nabila Rekik[2], Faten Frikha[1], Mohamed Abid[2] & Zouheir Bahloul[1]
[1]Hedi Chaker University Hospital, Department of Internal Medicine, Sfax, Tunisia; [2]Hedi Chaker University Hospital, Department of Endocrinology, Sfax, Tunisia

Introduction
Autoimmune hepatitis (AIH) is a generally progressive and chronic liver disease that can occur both in children and adults. Although the cause of AIH is unknown, aberrant auto-reactivity is thought to have a role in its pathogenesis. The diagnosis is based on clinical presentation, biological and histological findings. Like other autoimmune diseases (AD), AIH can be associated with one or more AD either organ-specific or non-organ specific AD.
Materials and methods
It is a descriptive retrospective single institution study. We collected data from 113 patients diagnosed with autoimmune thyroid disease (AITD) associated with another AD over 18 years. This present study reports the association between AITD and AIH.
Results
We registered one case of AIH associated with an AITD. The infertility work-up of the patient revealed hypothyroidism: Hashimoto's thyroiditis (HT) discovered at the age of 43. Both thyroid peroxidase antibody and thyroglobulin antibody were positive. She was treated by L-thyroxin with a favorable course of progress. At the age of 48 years, the patient presented with a chronic hepatitic cytolysis and the investigations led to the diagnosis of AIH. Antibody testing showed positivity for the smooth muscle antibodies (SMA) and histological findings from the liver biopsy were compatible with AIH. The patient was treated with glucocorticoid therapy and immunosuppressant drugs such as azathioprine.
Discussion and Conclusion
AIH is a heterogeneous group of chronic liver disease characterized by particular lesions on liver histopathology, elevated serum immunoglobulin, liver autoantibodies: SMA, soluble liver antigen autoantibody, Liver Kidney Microsome autoantibody, elevated serum transaminases and negative serology for viral hepatitis. AIH may affect adults of both sexes but affect mainly young women. Different studies estimated the frequency of the association: AIH and AITD around 10%. In our study, it was found to be around 1% which could be explained by the relatively small pool of patients. In 75% of cases, the AITD was HT. The cross reactions between the thyroid auto-antibodies and the presence of auto-reactive T cells or similar epithelial antigens found in the liver and the thyroid could explain the basis of the physiopathological mechanism behind this frequent association. We need to distinguish AIH from other forms of autoimmune liver diseases as it generally responds to anti-inflammatory and/or immunosuppressive treatment. Appropriate management can prolong survival and subsequently improve quality of life.

DOI: 10.1530/endoabs.81.EP1100

EP1101

Thionamides induced hypoglycemia

Nirit Aviran Barak
Maccabi Health Services, Endocrinology, Netanya, Israel

A 22-year-old female Ashkenazy Jewish previously healthy complaint on weakness In glucometer, her sugar level was 50 mg% and she felt better after ingestion of a small amount of sugar. 3 weeks ago while traveling in Peru, she developed thyrotoxicosis and was started mercaptizol 30 mg a day and deralin. She didn't drink iodine (iodinated preparations for water purification) while traveling and had no pain or fever. In physical examination there where no goiter or exophthalmos While I saw her she was already euthyroid and felt quite good except for tiredness. In literature, we found few case reports of mercaptizol and PTU-induced insulin autoantibodies which cause symptomatic hypoglycaemia. Most cases were described in the Asian population (especially Japanese people) and resolved a few weeks after stopping the drug. In our patient, the hypoglycemia resolved after only one episode and discontinuation of mertcaptizole. We don't have antibodies titer yet. insulin levels (C -peptide) were relatively high My conclusion is that physicians should be aware of Mercaptizol and PTU induced hypoglycemia which can be life-threatening

DOI: 10.1530/endoabs.81.EP1101

EP1102

Differential diagnosis between overt and transient hyperthyroidism in triplet pregnancy

Nino Abesadze
TSU, PhD Candidate, Tbilisi, Georgia

Introduction
Thyroid health in pregnancy is highly important. Best way to evaluate thyroid in pregnancy, is thyroid function assessment via blood tests. But we always have to focus also on clinical manifestations, thyroid ultrasound and other factors, that may influence test results. As we know high HCG can suppress TSH and twin pregnancy may induce subclinical hyperthyroidism. There are many reports of twin pregnancies, but very few about triplet pregnancy. Therefore we decided to report this rare case.
Case report:
34 y/o women presented with triplet pregnancy on 12 weeks of gestation. Routine thyroid tests showed laboratory picture of overt hyperthyroidism: TSH- <0.005 (0.3-2.5); FT3-3.98 (2-4.4); FT4- 1.89 (0.93-1.7). On clinical evaluation she had no signs of GO. HR-98, BP-120/80, BMI-18.6. Patient had hyperemesis gravidatum. She lost 6 kg during pregnancy. In previous 2 pregnancies she had normal thyroid functions. Positive family history of AIT. We ordered Anti-TSHR- N, thyroid ultrasound- N. Considering additional tests and mild clinical symptoms, we choose watchful waiting, to distinguish between overt thyrotoxicosis and transient hyperthyroidism of early pregnancy. After 3 weeks laboratory tests came already normal. TSH-0.22; FT4-0.93. We ordered TSH every month thereafter and it stayed in normal trimester-specific range on every occasion. Patient gave birth on 39 weeks of gestation with 3 healthy babies.
Conclusion
Because of potential harm and evidence of fetal risks, we have to be very careful with initiating of Anti-thyroid medications and avoid overusing them, if we don't have clear diagnosis. As we see in 2-3 weeks thyroid functions may improve by themselves. Also many criteria can help clinicians to distinguish very carefully between real thyrotoxicosis and transient state. Multiple pregnancy is one sign, we must take into account.

DOI: 10.1530/endoabs.81.EP1102

EP1103

Clinical profile and body composition of patients newly diagnosed with hypothyroidism

Olfa Lajili, Zouaoui Chadia, Bchir Najla, Yosra Abderrahim, Annam Benchhida & Haroun Ouertani
The Military Hospital of Tunis, Endocrinology and Nutrition Department, Tunis, Tunisia

Introduction
Patients with hypothyroidism usually gain weight, and those with hyperthyroidism lose weight. Body weight changes related with thyroid dysfunction support the idea that thyroid hormones have an effect on body weight and body composition. The aim of our study was to describe the clinical profile and body composition of Tunisian patients who were newly diagnosed with hypothyroidism.
Methods
This was a cross-sectional and descriptive study includes 25 patients: 14 who were newly diagnosed with overt hypothyroidism (Group1: G1) and 11 who were newly diagnosed with subclinical hypothyroidism (Group 2: G2). The study was conducted in the Endocrinology and Nutrition Department of the Military Hospital of Tunis during a period of 4 months (March-June 2021). Body composition was assessed by impedancemetry. Statistics were performed using SPSS 20.
Results
The mean age was 49 $\pm$ 14 years [20-80 years]. A female predominance was noted (75%). The median TSH level was 20 mUI/l [8-95 mUI/l]. Cervical ultrasound showed that 25% of patients had thyroid nodules. Anti-Thyroid Peroxydase antibodies were positive in 35% of patients. The mean Body Mass Index was 29 $\pm$ 5 kg/m^2. One third of the patients (35%) were obese. The median weight gain at time of diagnosis of the hypothyroidism was 0.6 kg [0,4-4,2 kg]; (G1: 1,5 kg vs G2: 0,5 kg; $P=0,6$). Mean percentages of fat mass (FM), lean mass (LM) and water mass (WM) in both groups were respectively (G1: 30 $\pm$9% vs G2: 35$\pm$8%; $P=0,26$), (G1: 70$\pm$9% vs G2: 65$\pm$8%; $P=0,26$) and (G1:51$\pm$7% vs G2:47$\pm$6%; $P=0,26$). The mean total cholesterol, LDL-cholesterol and triglyceride levels in both groups were respectively (G1:6$\pm$2 mmol/l vs G2: 5$\pm$1 mmol/l, $P=0,2$), (G1 3$\pm$2 mmol/l vs G2: 3 $\pm$0,7 mmol/l; $P=0,75$) and (G1: 1,7$\pm$0,7 mmol/l vs 1,7$\pm$1,1 mmol/l, $P=0,867$). Our study showed that increased TSH levels were associated with increased percentages of LM and WM (respectively $P=0,01$ and $P=0,01$) and decreased percentages of FM ($P=0,02$). However, there was no correlation between TSH level and weight gain at time of diagnosis of the hypothyroidism ($P=0,71$).
Conclusion
Our study showed that patients newly diagnosed with overt or subclinical hypothyroidism gained weight. The percentages of different body compartments were correlated with TSH level. However, there was not an association between gain weight and TSH level at time of diagnosis of the hypothyroidism.

DOI: 10.1530/endoabs.81.EP1103

EP1104

Graves' disease: Particularities in the pediatric population

Dhoha Ben Salah, Kawthar El ARBI, Asma Zargni, Mouna Elleuch, Cyrine Chehaider, Mnif Fatma, Nadia Charfi, Mouna Mnif, Nabila Rekik Majdoub, Faten Haj Kacem Akid & Mohamed Abid
Hedi Chaker Hospital, Department of Endocrinology, Sfax, Tunisia

Introduction
Graves' disease (GD) is the most common cause of hyperthyroidism in pediatric patients, up to 95% in some studies.
Observation
We report the observation of a 6-year-old female who consulted for a behavioral disorder made of agitation and lack of concentration. She had a family history of autoimmune thyroid disease. On examination, an accelerated statural growth rate of +2DS was noted. She had a significant palpebral retraction without exophthalmia. A biological check-up showed a blocked TSH level at 0.01µU/ml associated with a high T4 at 26.4 pmol/l. In addition, TSH receptor antibodies blokers (trab) were positive at 17.8 U/l for a normal value (NV) of less than 1.5. Anti-thyroperoxidase antibodies were positive at 148 U/l (NV $<$ 20U/l). The thyroid ultrasound was normal with a normal volume and homogeneous gland. The diagnosis of Graves' disease was retained and a treatment with methimazole was started at a dose of 0.5 mg/kg/d. The thyroid check-up 3 months later was normal. The treatment is in progress.
Conclusion
GD is a rare condition in children and affects mostly older children with a clear female predominance. Although rare, GD remains the most frequent cause of hyperthyroidism in children. Diagnosis is easier if exophthalmia is present, which is a very specific sign of this condition. However, palpebral disorder is the most common as exophthalmia is less frequent in children. Medical treatment is based on synthetic antithyroid drugs.

DOI: 10.1530/endoabs.81.EP1104

EP1105

Hashimoto's thyroiditis associated with primary biliary cholangitis: a case report

Hind Ouakrim, Charlene Ludwine Bifoume Ndong, Sana Rafi, Ghizlane EL Mghari & Nawal EL Ansari
Chu med 6, Endocrinologue, Marrakech, Morocco

Introduction
The association of multi-organ autoimmune disorders is described. We report a case of Hashimoto's thyroiditis (HT) and primary biliary cholangitis (PBC), both are a chronic autoimmune inflammation, with lymphocytic infiltration and destruction of thyroid cells for (HT) and progressive destruction of intrahepatic bile ducts leading to cirrhosis for (PBC)
Case report
54-year-old female patient, followed for (PBC) at cirrhosis stage admitted for evacuation of refractory ascites. Interrogatory: signs of hypothyroidism: asthenia, constipation, chilliness and hair loss, Physical examination of the patient revealed bradycardia at 55bpm, palpable thyroid, end signs of hepatocellular insufficiency: subicterus and stellate angioma. Blood tests revealed a hypothyroidism (TSH: 26.6µUI/ml; T4: 5.2 pmol/l), end anti-Thyroperoxidase and anti-mitochondria type 2 antibodies are positive.
Discussion
PBC is frequently associated with other autoimmune diseases, the most common of which are Hashimoto's thyroiditis, Gougerot Sjögren's disease, celiac disease, and scleroderma, their screening must be systematic in order to initiate early and adequate treatment. As soon as an autoimmune disease is diagnosed, the search

for other organ damage is necessary in order to initiate treatment in the early stages, which improves the patient's overall prognosis.

DOI: 10.1530/endoabs.81.EP1105

EP1106

Nephrotic lupus revealing a profound hypothyroidism

Severin N'Koua, Sana Rafi, Ghizlane EL Mghari & Nawal EL ANSARI
Department of Endocrinology, Diabetology and Metabolic Diseases, CHU Mohamed VI, Marrakech, Morocco

Abstract
Systemic lupus erythematosus is a serious autoimmune disease characterised by the production of antinuclear antibodies directed particularly against native DNA. Its presence increases the susceptibility to develop other autoimmune diseases including autoimmune dysthyroidism. We present the case of a patient who presented with profound hypothyroidism as part of the work-up for lupus nephropathy. Female patient, 40 years old, reports physical asthenia for 2 months. On clinical examination: normal BMI, discrete bilateral IMO, homogeneous goitre; erythematous lupus lesions on the face. Thyroid assessment: TSH elevated: 100 IU/l; T4l: 1.9 IU/l; T3l: 1, cervical echo: aspect of thyroiditis. Renal check-up: GFR: 20ml/24h; 24h proteinuria: 2.64g/24h; albumin: 30g/l; protein: 69g/l, Immunological check-up: anti TPO + and anti-nuclear and anti-DNA positive; renal biopsy in favour of a membrano-proliferative glomerulonephritis (GNMP). Cardiovascular work-up: normal ECG and TTE without any particularity with LVEF recommended at 65%, normal lipid profile. The patient had been put on levothyrox 25 µg/d with a progressive increase and a corticotherapie for her lupus nephropathy. Most of the studies presented in the literature show a high prevalence and incidence of new cases of hypothyroidism and autoimmune thyroiditis (AIT) in patients with systemic lupus erythematosus (SLE), globally in women. In the presence of lupus, it is advisable to look for thyroid disorders that need to be treated. In the absence of thyroid disorders, long-term monitoring for thyroid disorders is important as thyroid dysfunction has a high probability of occurring later not only because of the autoimmune terrain but also because of glomerulopathy which can be complicated by a nephrotic syndrome with leakage of thyroid hormones.

DOI: 10.1530/endoabs.81.EP1106

EP1107

Diarrhea as the only symptoms in hyperthyroidism-case report

Rajmonda Tare
Endocrinology, Internal Department, Regional Hospital 'Xhaferr Kongoli', Albania

Introduction
Hyperthyroidism (overactive thyroid) is a condition where thyroid makes and releases high levels of thyroid hormone (thyroxine) in the blood. This condition can speed up our body metabolism. Hyperthyroidism causes an overactivity of the sympathetic system. It also this sympathetic hyperstimulation in the gut leads to increased motility causing diarrhea, malabsorbation and consequently weight loss.
Objective
To describe a patient with hyperfunxional nodular goiter and diarrhea as the only symptoms, for which Unimazole (ATS), was found to be effective therapy for the diarrhea.
Methods
We present the clinical course of a old woman with a prolonged diarrhea which with all diagnostic procedures and medication given did not improve until it was thought to be an endocrine cause. Unimazole control of such cases of hyperthyroidism with diarrhea can be explained by the effect of this drug in reducing intestinal hypermotility as the basis of physiopathology in hyperthyroidism.
Results
A 73-year-old woman, has not previously had gastrointestinal disorders, had prolonged diarrhea, which associated with loss of 3 kg during a 1-month period. Laboratory, ultrasound images, recommended by the infectious disease doctor could not detect the cause of this prolonged diarrhea. Despite antibiotic treatment and antidiarrheal treatment, diarrhea did not stop. Other hyperthyroidism symptoms were not reported, but when hyperthyroidism was identified, the diarrhea was dominated and very well controlled by treatment with unimazole.
Conclusion
Thyroid hormone in excess, among its other possible effects in the organism, affect the gastrointestinal tract through sympathetic intestinal hyperstimulation and increased motility causing diarrhea. Antithyroid therapy act by blocking sympathetic hyperstimulation. Our case leads us to think that hyperthyroidism should be considered in the differential diagnosis of diarrhea of unknown cause.
Keywords diarrhea, unimazole, hyperthyroidism.

DOI: 10.1530/endoabs.81.EP1107

EP1108

Autoimmune thyroiditis and anemic syndrome

Farida Saidova[1], Leyli Akhmedova[2], Jale Aslanova[1], Oruc Shahsuvarov[1] & Nizami Muradov[3]
[1]Scientific Center of Surgery after M.A.Topchubashov, Endocrine Surgery, Baku, Azerbaijan; [2]Azerbaijan State Advanced Training Institute for Doctors after A.Aliyev, Central Scientific Research Laborator, Baku, Azerbaijan; [3]Scientific Center of Surgery after M.A.Topchubashov, Anaestethiology and Reanimatology, Baku, Azerbaijan

The purpose was to identify the frequency of occurrence of various morphological types and different degrees of severity of anemia in patients with autoimmune thyroiditis (AIT).
Material and methods
Were analyzed 97 case histories of patients operated for AIT in 2012. When assessing hematological parameters, two groups were identified: group 1 – patients with AIT with mild anemia ($n=$ 72), age 45.7 $\pm$ 1.6, men - 5 (6.9%), women - 67 (93, 1%); group 2 - patients with AIT with moderate anemia ($n=$ 25), age 40.0 $\pm$ 2.3, men - 1 (4%), women - 24 (96%). In the clinical analysis of blood, hemoglobin, hematocrit, the number of erythrocytes and erythrocyte indexes of MCV, MCH, MCHC were determined.
Results
In patients with AIT with a mild degree of anemia, microcytic anemia was determined in 55 (76.4%), normocytic - in 17 (23.6%) patients. In moderate anemia, microcytic anemia was detected in 21 (84%) patients, normocytic anemia - in 4 (16%) patients. hypochromic type of anemia in the group 'all patients' was noted in 79 (81.4%), normochromic type in 17 (17.5%) and hyperchromic in 1 (1%) patient. By morphological type in patients with AIT with mild anemia, the hypochromic type was observed in 56 (77.8%) patients, normochromic - in 16 (22.2%) patients. In moderate anemia, this tendency was more pronounced: hypochromic type of anemia was detected in 23 (92%) patients, normochromic type - in 1 (4%) and hyperchromic in 1 (4%). Thus, in patients with AIT, mild anemia was more often determined (in 72.4%), then moderate anemia (in 25.7%). With moderate severity of anemia, microcytic (84%) and hypochromic (92%) types of anemia were more often observed. With mild anemia, the same types of anemias were observed, but with a lower frequency (76.4% and 77.8%, respectively).
Conclusion
The hemogram in patients with AIT was characterized by a more frequent development of mild anemia (72.4%). With mild anemia, hematological disorders were characterized by microcytic (76.4%) and hypochromic (77.8%) types of anemia. Similar, but more pronounced disorders were observed in moderate anemia: microcytic 84% and hypochromic 92%, which is characteristic for iron deficiency anemia.

DOI: 10.1530/endoabs.81.EP1108

EP1109

Subacute thyroiditis associated with COVID-19

Yuriy Aleksandrov[1] & Vasiliy Semikov[2]
[1]Yaroslavl State Medical University, Surgery, Yaroslavl, Russian Federation; [2]I.M. Sechenov First Moscow State Medical University, Surgery, Moscow, Russian Federation

COVID-19 is a serious problem of modern medicine. The disease has many manifestations, as it affects almost all organs and systems. One of the target organs of the endocrine system is the thyroid gland. The aim of the study was to identify the patterns of development and course of subacute thyroiditis in patients who underwent COVID-19. The study included 9 clinical cases. In all cases, these

were women aged 32 to 54 years. All patients were sick with COVID-19 (4 of them were treated at home, 5 - in a specialized hospital). In two patients, the first symptoms of the disease appeared even with a positive PCR test, in 2 patients, symptoms appeared 2 weeks after receiving an already negative PCR test, in 5 - in the interval of 1.5 - 2 months after receiving a negative PCR test. All patients have subfebrility, deterioration of general well-being, sharp weakness. 5 patients complained of an unexpressed headache with irradiation in the neck. This was regarded by all patients as a consequence of the ongoing or recent COVID-19. 4 patients noted discomfort with head movements and swallowing. The examination revealed moderate leukocytosis ($11,9 \pm 4.7 \times 10^9$/l), elevated ESR (36 ± 11 mm/h). There were no other symptoms indicating the nature of the disease, except for soreness during palpation in the projection of the thyroid gland in all patients. In this regard, all of them underwent ultrasound of the neck organs, in which heterogeneous hypoechoic darkening was detected, occupying from 14 to 85% of the volume of the thyroid gland, an increase in the lymph nodes of the neck was detected in 6 patients. From the moment of the first symptoms to the diagnosis and the start of treatment, it took from 2 to 4 weeks. At that time, 4 patients were treated for COVID-19, and 5 were undergoing rehabilitation treatment. The difficulty of making a correct diagnosis was due to asthenization and nonspecific symptoms of viral infection, as well as the fact that the development of subacute thyroiditis was preceded by the use of antiviral and antibacterial drugs, as well as glucocorticoids. Sonography was the key diagnostic method for all patients.

DOI: 10.1530/endoabs.81.EP1109

EP1110

A case of graves' orbitopathy in a patient sero-negative for TSH receptor autoantibody

Chayma Besrour, Rojbi Imen, Mekni Sabrine, Meriem Adel, Mchirgui Nadia, Ben Nacef Ibtissem & Khiari Karima
Hospital Charles Nicolle, Endocrinology, Tunis, Tunisia

Introduction
The orbit represents the second target after the thyroid gland in autoimmune dysthyroidism. In 80% of cases, endocrine orbitopathy occurs as a result of hyperthyroidism, especially Grave's disease (GD). Males are rarely affected but the damage is more serious.
Observation
We report the case of a 52-year-old patient, an active smoker (35 Pack-Year), transferred from the neurology department for treatment of bilateral malignant exophthalmos with subclinical hyperthyroidism. The examination showed a palpable normal sized thyroid with no vascularity. Orbital MRI showed bilateral grade 2 proptosis with oculomotor muscle hypertrophy consistent with Grave's orbitopathy (GO). The biology showed a subclinical hyperthyroidism, but the assay of the anti-TSH receptor antibodies came back negative twice. A thyroid scintigraphy was performed and it confirmed the Grave's disease. The patient was treated with corticosteroid therapy for his GO and showed a slight improvement. As for his subclinical hyperthyroidism, he was put on a low dose of an anti-thyroid drug, and developed euthyroidism.
Discussion
GO concerns 50% of patients with GD, among them only 3-5% develop severe forms. The responsible pathophysiological mechanism is linked to the presence of TRAKs. But these antibodies are only present in 95% of cases; suggesting are there other mechanisms to this GO?

DOI: 10.1530/endoabs.81.EP1110

EP1111

Graves' disease refractory to a cumulative dose of 72 mci of iodine 131

Kadiri Chaimae & Lachkar Hassan
Hôpital Cheikh Zayd, Endocrinology, Rabat, Morocco

Introduction
Graves' disease is the most common cause of hyperthyroidism. There are three main therapeutic weapons: synthetic antithyroid drugs, surgery and radioactive iodine. The latter represents an effective treatment without noticeable side effects. We report a case of Graves' disease refractory to iratherapy.
Observation
This is a 38-year-old patient, with no notable history, who consulted for Graves' disease diagnosed with clinical signs of thyrotoxicosis and a biological profile of primary hyperthyroidism (TSH = 0.00 mUi/ml; T3 = 4.23 pg/ml; T4 = 22.13 pg/ml) with positive TRAKs. The morphological assessment objectified a goiter hyper fixing to the thyroid scintigraphy. Iodine-131 treatment is given at an initial dose of 25 mci. The course is marked by a persistence of a suppressed TSH (0.05 mIU/ml) after 6 months leading to the administration of an additional dose of 25 mci. Laboratory evaluation after 6 months objected to hyperthyroidism with TSH low at 0.08 mIU/ml. The patient received an additional 25 mci dose with the onset of hypothyroidism for which the patient was put on hormone replacement therapy with LT4 with good clinical and biological progress.
Discussion and conclusion
Graves' disease is a frequent endocrinopathy with potentially serious complications which can sometimes pose a difficulty in choosing a treatment. Iodine-131 iratherapy is a low-cost, simple treatment that is currently considered the treatment of choice for Graves' disease. However, the course can sometimes be marred by an absence of response to the radioactive treatment requiring a repeat of the doses in order to obtain a clinical and biological resolution as is the case for our patient.

DOI: 10.1530/endoabs.81.EP1111

EP1112

Thyroid tuberculosis: a case report

Kadiri Chaimae & lachkar hassan
Hôpital Cheikh Zayd, Endocrinology, Rabat, Morocco

Introduction
Thyroid tuberculosis is a rare localization that can pose problems of differential diagnosis with thyroid nodules. Its rarity is explained by the good oxygenation of the thyroid parenchyma and the bacteriostatic role of thyroid hormones. The definitive diagnosis is based on the pathological examination of the surgical specimen or after cytopathology or bacteriological examination of the transparietal puncture in complicated cases of collection.
Observation
This is a 30-year-old patient with no notable history who presents with multiherenodular goiter with the presence of satellite lymphadenopathy confirmed by cervical ultrasound without associated general signs. The thyroid workup is normal. A total thyroidectomy is performed with simple operative consequences. Pathological examination revealed a hyperplastic thyroid parenchyma with the presence of epitheliogigantocellular granulomas with local caseous necrosis. Anti-tuberculosis treatment is started for six months as well as LT4 supplementation with a favorable clinical course and normal TSH.
Discussion and conclusion
Thyroid tuberculosis remains a rare condition. It poses a diagnostic problem and sometimes induces inappropriate treatment. Fine-needle aspiration makes it possible to make the diagnosis by looking for an epithelio-gigantocellular granuloma with caseous necrosis and/or a Koch's bacillus and to initiate the anti-tuberculosis treatment which consists of multiple antibiotic therapy. Excisions are exceptional except in cases of diagnostic doubt as is the case for our patient. The prognosis is very favorable.

DOI: 10.1530/endoabs.81.EP1112

EP1113

Coexistence of two different thyroid malignancies: an exceptional phenomenon

Mehdi Ferjaoui, Emna BERGAOUI, Maroua Naouar, Rachida Bouattay, Amel Elkorbi, Naourez Kolsi, Kaled Harrathi & Jamel Koubaa
Fattouma Bourguiba Hospital, ENT, Monastir, Tunisia

Introduction
Simultaneous papillary thyroid carcinoma (PTC) and follicular thyroid carcinoma (FTC) of the same thyroid lobe is a very rare pathology.
Purpose of the presentation
The objective of this work is to determine the clinical, histological and therapeutic aspects of an association of papillary thyroid carcinoma (PTC) and follicular thyroid carcinoma (FTC) on the same thyroid lobe.
Methods
We report 2 cases of PTC and FTC on the same thyroid lobe, treated in the ENT department of Fattouma Bourguiba hospital in Monastir over a period of 21 years (2000-2020).

Case1
A 22-year-old woman was referred to our department due to nodules in the right thyroid lobe detected on ultrasonography during a routine health check-up. the thyroid function tests were normal. Ultra sound showed multiples nodules in the right lobe, the biggest one was 20mm and classified as EUTIRADS IV. The patient underwent a right lobo-isthmectomy with an extemporaneous examination that suggest the benignity. Postoperative pathology revealed that the nodule with a size of about 18 mm in the right lobe was a follicular thyroid carcinoma with angio-invasionassociated with another nodule in the same lobe that was a micro papillary carcinoma (6mm) developed on a lymphocytic thyroiditis. The patient underwent a totalisation with central ipsilateral lymph-node dissection 1month later. She was initiated with thyroid hormone replacement therapy and a radioactive iodine treatment. The evolution was judged good, no recurrence or metastasis, with a follow-up of 20 months.
Case2
A 54-year-old women was evaluated at our hospital for a quick installation of a paraplegia. X-ray-imaging revealed a spinal compression. Vertebral biopsy was suggestive of a bone metastasis of a follicular thyroid carcinoma. Cervical ultrasonography showed a 29mm nodule in the right lobe that was suspected of malignancy. The patient underwent a total thyroidectomy with bilateral central lymph node dissection. There were no postoperative complications. Final histological examination revealed the coexistence of a large invasive follicular carcinoma associated with a micro papillary carcinoma in the right lobe of the thyroid. She was initiated on suppressive doses of thyroid hormone replacement therapy, a radioactive iodine treatment and vertebral radiotherapy. During its monitoring, the patient developed skull, femoral and spinal dorsal metastases with the indication of external radiotherapy.
Conclusion
Pathologists and surgeons should be aware of the possibility of the simultaneous presence of PTC and FTC tumours to avoid possible misdiagnoses.

DOI: 10.1530/endoabs.81.EP1113

EP1114

Differentiated thyroid carcinoma in Basedow disease : a series of five cases

Kamel Farah, Khaoula Gorgi, Kaoutar Rifai, Hinde Iraqi & Mohamed Hassan El Gharbi
Ibn Sina University Hospital, Endocrinology and Metabolic Diseases, Rabat, Morocco

Introduction
The occurrence of thyroid cancer in Basedow disease is rare. We report a series of five cases of patients with Basedow disease who were operated on and whose pathological examination showed an association with differentiated thyroid cancer.
Clinical cases
We report a series of five patients with a mean age of 39 years. The diagnosis of Basedow disease was made on the basis of clinical, biological and scintigraphic evidence. Cervical ultrasound showed a benign multiheteronodular goitre in four patients, while thyroiditis with a nodule classified as EU-TIRADS V was present in one patient. All patients underwent total thyroidectomy after medical preparation with synthetic antithyroid drugs. However, one patient underwent central lymph node dissection. Histology was consistent with papillary thyroid carcinoma in four patients and vesicular carcinoma in one patient. Four patients classified as low-risk received 100 mci isotope totalization and TSH- suppressive Levothyroxine therapy, while one patient classified as very low-risk received TSH- suppressive Levothyroxine therapy alone. All clinical cases were in remission.
Discussion
The association of thyroid carcinoma with Basedow disease, once considered antinomian, is now a proven but rare occurrence. The incidence of differentiated thyroid carcinoma in Basedow disease is usually between 2 and 10%. Papillary carcinoma is the most frequently found. Nodularity should suggest Basedow disease -associated carcinomas. The pathogenesis of this association remains poorly understood. Studies have shown that anti-TSH receptor antibodies can stimulate adenyl cyclase activity and induce the formation and growth of thyroid cancer. In addition, the influence of synthetic antithyroid drugs can normalise the level of TSH that is inhibited in hyperthyroidism, with the risk of growth of a previously occult tumour. The most frequent situation is juxtaposed hyperthyroidism, resulting from healthy thyroid tissue adjacent to the cancer. These observations underline the importance of a careful search for malignancy in nodules associated with Basedow disease.
Conclusion
The diagnosis of Basedow disease does not eliminate the possibility of associated thyroid cancer. Thus, the appearance of a nodule within the goitre should raise suspicion of malignancy and indicate radical surgical treatment. Our results suggest a good prognosis for differentiated carcinomas on Basedow disease with isotopic totalisation.

DOI: 10.1530/endoabs.81.EP1114

EP1115

Coexistence of chronic lymphocytic thyroiditis with papillary thyroid carcinoma: about 13 cases

Rachida Bouattay, Maroua Naouar, Emna BERGAOUI, Heyfa Belhadjmiled, Mehdi Ferjaoui, Elkorbi Amel, Harrathi Khaled, Kolsi Naourez & Jamel Koubaa
Fattouma Bourguiba University Hospital, ENT and Head and Neck Surgery Department, Monastir, Tunisia

Introduction
The association between chronic lymphocytic thyroiditis (CLT) and papillary thyroid carcinoma (PTC) has been investigated for several years from different perspectives. In spite of that, there were only few attempts to design a common frame of references to understand the complex mutual interactions between the various pathways of inflammatory response and of thyroid tumor induction and progression. The aim of this study is to investigate the clinical characteristics and outcome of the association between chronic lymphocytic thyroiditis and papillary thyroid carcinoma.
Materials and Methods
Our study was retrospective, realized on 13 cases of simultaneous chronic lymphocytic thyroiditis and papillary thyroid carcinoma collected in ENT department of Fattouma Bourguiba Hospital of Monastir a 20-year period (2000-2020).
Results
Among the 13 patients, there were 2 men and 11 women. Mean age was 41 years [20-56]. 4 patients were under hormone replacement therapy for hypothyroidism. Patients presented to our consultation for management of anterior neck swelling in 10 cases, associated to compression symptoms in one case. We noted 2 cases of an incidental finding of thyroid nodule during an ultrasound (US) examination of neck. Thyroid nodules were highly suspicious for malignancy on US in 4 cases. The mean size of nodule was 4 cm. We noted the presence of antithyroidal antibodies in 2 cases. All of patients underwent a total thyroidectomy, associated to bilateral central neck lymph node dissection in 10 cases. Histologic examination confirmed the diagnosis of papillary carcinoma in all cases. Surgical treatment was followed by radioactive iodine therapy except in one case which was a papillary microcarcinoma measuring 4 mm. In all cases, Thyroglobulin level was undetectable after withdrawal of T4 treatment with an average follow-up of 3 years.
Conclusion
The association between chronic lymphocytic thyroiditis and papillary thyroid carcinoma is not a rare entity. Patients with CLT were younger and predominantly female. The presence of CLT in patients with PTC has been associated with better prognostic outcome, lower recurrence rate and less aggressive disease, which are the most important and well-known prognostic variables for thyroid cancer mortality.

DOI: 10.1530/endoabs.81.EP1115

EP1116

Distant metastases from thyroid cancers: About 4 cases

Marwa Ben Njima, El Omri Malika, Mouna Bellakhdhar, Jihen Haouas, Ghammmam Monia, Meherzi Abir, Nihed Abdessayed, Kermani Wassim & Abdelkefi Mohamed
Hospital Farhat Hached, Sousse, Tunisia

Introduction
Metastases of thyroid tumors are rare. Metastatic sites are in order of frequency : pulmonary, bone and brain. Facial bones metastases are exceptional. These metastases are more frequent in vesicular than papillary carcinoma histological.

The aim of our work is to describe the clinical and radiological aspects as well as the therapeutic modalities.
Observation 1 and 2
A 38-year-old woman and 13-year-old boy consulted for a chronic cough with thyroid nodules on examination. The chest X-ray showed a micronodular miliary. The diagnosis of distant metastases was confirmed on an adenectomy specimen for the boy and on a lung biopsy for the woman. A total thyroidectomy with bilateral central and functional lymph node dissection was underwent and radio-iodine ablation for both cases.
Observation 3
A 55-year-old woman consulted for low back pain with neurological deficit due to lumbosacralosteolysis. A bone biopsy showed a metastases of a vesicular carcinoma of the thyroid. Further imaging showed 2 left nodules. The patient underwent decompressive radiotherapy followed by a total thyroidectomy and bilateral central lymph node dissection.
Observation 4
A 43 year old woman consulted for chronic nasal obstruction and decreased visual acuity. Clinical examination showed a median basicervical swelling that measured 9 cm and a tumoral mass filling the right nasal cavity that bleeded on contact. The ophthalmological examination showed the presence of a compressive optic neuropathy. Imaging showed a large tissue mass in the right pterygopalatine fossa extending to the right nasal cavity, the right maxillary sinus, the sphenoidal sinus, the sella turcica and the endocraniumassociatedwith a right thyroid mass with endothoracic extension and secondary pulmonary lesions. Biopsy of these lesions confirmed a poorly differentiated thyroid carcinoma. The therapeutic decision was taken in a multidisciplinary consultation meeting and was palliative chemotherapy. The evolution was marked by death.
Conclusion
Distant metastases of thyroid cancer have no clinical or radiological specificity. The metastatic potential remains independent of the size of the thyroid nodule. These metastases are more common with the vesicular histological type and have more reserved prognosis.

DOI: 10.1530/endoabs.81.EP1116

EP1117

Managing thyroid storm in acute setting: a single centre experience case series

Gloria Elekwa[1, 2], Akunna Elonu[1, 2], Rebecca Volmy[1, 2], Alexanderia Williams[1, 2], Gideon Mlawa[2] & Janessa Bell[2,3]
[1]Ross University School of Medicine; [2]Queens Hospital, Romford, United Kingdom; [3]American University of the Caribbean School of Medicine, Sint Maarten (Dutch Part)

Background
Thyrotoxicosis is one of the commonest endocrine disorders and its severe form can manifest as thyroid storm in acute setting leading to organ dysfunctions including heart failure.
Cases
1: A 58-year-old female with a significant past medical history of MI, paroxysmal AF/atrial flutter, and hyperthyroidism presented with a one-week history of palpitations, plethora, diaphoresis, heat intolerance, loose stools, and a TSH < 0.01; Free T4-33. On physical exam, patient was warm and well perfused, minimal pedal edema. She was in fast AF. She was medically managed carbimazole, b-blockers and steroids 2: A 28-year-old female with past medical history of asthma and a current smoker. Patient presented with palpitations, anxiety, diarrhea, fatigue, and 2 stone weight loss in 6 months. On physical examination the patient had a smooth, painless goiter, carotid bruits and prominent exophthalmos. The patient was tachycardic (HR 163), and febrile (38.1 C) with elevated CRP 42 and T4 58 TSH<0.01 She was medically managed with Propylthiouracil 100 mg tds; Propranolol 40 mg TDS Prednisolone 30 mg OD 3. 39-year-old patient with known hyperthyroidism presents with palpitations, anxiety. She was found to have swollen legs and was tachycardic at 110 bpm. CXR showed bilateral shadowing suggestive of fluid overload. Blood tests: TSH <0.01, T4 >100, TSH receptor positive. 4.64-year-old lady presented with for 4 months of breathlessness. Found to be in thyrotoxicosis, atrial fibrillation (AF) as well as peripheral oedema. Blood test showed FT4 69 pmol, positive TSH – receptor antibodies. Treated with rate controlling medications, propylthiouracil, steroids and diuretics
Discussion
Thyroid storm is on the severe end of the thyrotoxicosis spectrum, and it is usually triggered by a secondary external event such as infection, myocardial infarction, trauma or surgery. The Burch Wartfosky point scale is used to diagnose thyroid storm. In this scale, the following are assessed: Temperature, cardiovascular dysfunction, central nervous system derangements, gastrointestinal symptoms and heart failure. A score greater than or equal to 45 aligns with a clinical diagnosis of thyroid storm, and scores between 25 and 44 suggest thyroid storm as a likely diagnosis. Scores below 25 points make a diagnosis of thyroid storm unlikely.
Conclusion
Thyroid storm is medical and an endocrine emergency and appropriate and timely treatment will ensure better patient care and outcome In an emergency like acute thyrotoxicosis or thyroid storm, higher doses of thionamides, beta blockers as well as glucocorticoids can be used to return the patient to a euthyroid state.

DOI: 10.1530/endoabs.81.EP1117

EP1118

Factitious thyrotoxicosis: A case report

Hajar Khouchaf, Nassim Essabah Haraj, Siham El Aziz & Asma CHADLI
Ibn Rochd University Hospital, Endocrinology, Diabetology, Nutrition and Metabolic Diseases, Casablanca, Morocco

Introduction
Although the most common cause of thyrotoxicosis is Graves' disease, identification of other causes is important to establish appropriate management. The diagnosis of factitious thyrotoxicosis often presents a difficult challengebut should not be overlooked. We report a case of a patient with treated thyroid carcinoma who presented with factitious hyperthyroidism.
Observation
50-year-old patient, followed for papillary thyroid microcarcinoma under L-Thyroxin 125µg, halted for 3 months, admitted for hyperthyroidism. The patient was then put on Carbimazol 90 mg/day + corticotherapy for 1 month. As the hyperthyroidism persisted and did not improve, he was given radioactive iodine therapy at a rate of 100mCi. All this evolved in a context of weight loss of 24 kg in 4 months. The clinical examination found a patient in general good condition, BMI: 17 kg/m^2, Burch Wartofsky score at 10, free thyroid compartment, no gynecomastia, testicles in place, not swollen, normal size. On biological test T4L: 3051 pmol/l vs 50 pmol/l (8.5-34.90), T3L: 30.43 ng/l vs 6.22 pg/ml (2-4.40), TSHus:0.05 µIU/ml, Tgus: 0.1 ng/ml, BHCG: < 5IU/l (< 5), CEA: 0.99 ng/ml (< 4.30), AFP:5.5 ng/ml (<8.8), LDH: 144 IU/l (125-220), cervical-thoracic-abdominal-pelvic CT scan objectified an anterosuperior mediastinal mass of thymic appearance with adenolymphitis of the ileo-coecal region, F-FDG PET-CT did not show a hypermetabolic processes at the thyroidectomy lodge, locoregional lymph node, or distant suspicious processes for dedifferentiated recurrence of papillary microcarcinoma. The diagnosis of factitious thyrotoxicosis was retained in view of the degression of thyroid hormones during his hospitalization with clinical improvement of the patient during the hospitalization: degression of symptoms, and weight gain of 3 kg. The diagnosis was confirmed after a psychiatric evaluation.
Conclusion
Thyrotoxicosis has a wide spectrum of etiologies. Patients with factitious thyrotoxicosis are extremely difficult to identify because they do not appear to be different from patients with thyrotoxicosis of other causes.

DOI: 10.1530/endoabs.81.EP1118

EP1119

Simultaneous occurrence of medullary and papillary thyroid carcinomas: a report of 2 cases

Mehdi Ferjaoui, Maroua Naouar, Emna BERGAOUI, Rachida Bouattay, Elkorbi Amel, Harrathi Khaled, Kolsi Naourez & Jamel Koubaa
Fattouma Bourguiba University Hospital, ENT and Head and Neck Surgery Department, Monastir, Tunisia

Introduction
Papillary thyroid carcinoma (PTC) and medullary thyroid carcinoma (MTC) are two different types of thyroid carcinoma with significant different clinical and histological findings. Synchronous occurrence of these two carcinomas is uncommon. The aim of the study is to determinate the clinical, histological and therapeutic aspects of the coexistence of medullary and papillary thyroid carcinomas.

Materials and Methods
We report two rare cases of simultaneous medullary thyroid carcinoma and papillary thyroid carcinoma collected in ENT department of Fattouma Bourguiba Hospital of Monastir over a period of 20 years.
Results
Case one was a 46-year-old woman, with no personal history of radiation exposure and family history of thyroid cancer, presented to our consultation for management of a left thyroid nodule discovered by ultrasound examination of her neck. The patient underwent a total thyroidectomy with node dissection. The histology disclosed a medullary carcinoma in left lobe and a micropapillary carcinoma in the right lobe. Three months postsurgery, the patient's calcitonin levels were less than three ng/l and there was no distant metastasis. The second case was a 49-year-old man, with no apparent family history of endocrine disorders or any previous external radiation therapy, hospitalised in our ENT department for multinodular goiter with compression symptoms. A cervical computed tomography objectified a laryngo-tracheal invasion by an endoluminal tissue lump. Fine needle aspiration cytology from the thyroid nodule was performed showing a medullary carcinoma. A total thyroidectomy and total laryngectomy with node dissection were performed. The histology results showed a medullary carcinoma occupying the majority of the thyroid associated to a papillary carcinoma in the right lobe. Surgical treatment was followed by I-131 100 mCi therapy and external radiotherapy. The extension assessment revealed synchronous renal cell carcinoma associated to bone and lymph node metastases due to MTC.
Conclusion
PTC and MTC are two different types of thyroid carcinoma with significant different histology. Synchronous occurrence of these two carcinomas is uncommon and rare. The prognosis depends essentially on MTC.

DOI: 10.1530/endoabs.81.EP1119

EP1120

Postoperative hypoparathyroidism after total thyroidectomy: prevalence and risk factors

Mehdi Ferjaoui, Maroua Naouar, Emna BERGAOUI, Rachida Bouattay, Elkorbi Amel, Harrathi Khaled, Kolsi Naourez & Jamel Koubaa
Fattouma Bourguiba University Hospital, ENT and Head and Neck Surgery Department, Monastir, Tunisia

Introduction
Total thyroidectomy is the most common surgical procedure for the treatment of thyroid diseases. Postoperative hypoparathyroidism and the resulting hypocalcemia are frequent complications after total thyroidectomy. The aim of this study was to assess the rate of postoperative hypoparathyroidism after total thyroidectomy in order to identify potential risk factors.
Methods
We designed a retrospective study including 387 patients with total thyroidectomy who were operated in our department from January 2016 to January 2019. The prevalence of hypoparathyroidism was evaluated at day 3, 1 month, 6 months and 12 months after surgery.
Results
The average age of our patients was 46.9 years old; 16.7% were males and 83.3 % were females. The total thyroidectomy was done in 210 (54.2 %) of cases for a malignant pathology. A total of 189 patients (48.83%) underwent a neck dissection. 90 (23.2 %) developed postoperative hypoparathyroidism at day 3. Most of them recover parathyroid function over time. Prevalence of hypoparathyroidism at 1 month, 6months and 12 months was 9%, 4% and 2.8 %, respectively. The risk of developing definitive hypoparathyroidism was related to the presence of parathyroid tissue at histology, concomitant central lymph node dissection and incidental para thyroidectomy without auto transplantation.
Conclusion
Although most patients with postsurgical hypoparathyroidism recover parathyroid function, intra-operative preservation of the parathyroid glands is the best prophylaxis to avoid postoperative hypoparathyroidism after total thyroidectomy.

DOI: 10.1530/endoabs.81.EP1120

EP1121

Metastatic medullary carcinoma of the thyroid

Hajar Khouchaf, Nassim Essabah Haraj, Siham El Aziz & Asma Chadli
Ibn Rochd University Hospital, Endocrinology, Diabetology, Nutrition and Metabolic Diseases, Casablanca, Morocco

Introduction
Medullary thyroid carcinoma (MTC) is a rare and silent endocrine tumor representing 5-10% of thyroid cancers. It is the most aggressive form of thyroid carcinoma, usually diagnosed at advanced stages.
Purpose of study
Study the phenotypic and genotypic profiles as well as the anatomical-histological characteristics related to the recurrence of the disease.
Matherials and methods
Descriptive cross-sectional study including patients followed for CMT in the Endocrinology and Diabetology Department of the Ibn ROCHD University Hospital of Casablanca from 2007 to 2021. The statistical analysis was performed by the software SPSS version 25.0.
Results
The study included 24 patients followed up for CMT, the mean age was 47.6 $\pm$ 14.35 years, the majority were women (70.8%), a family history of thyroid carcinoma was found in two patients, clinically the thyroid nodule was the reason for consultation in thirteen patients (54. 2%), all patients underwent total thyroidectomy, lymph node dissection was performed in eighteen patients, CMT was in the context of MEN2 in six patients (25%), the genetic study of RET proto-oncogene mutations was positive in three patients. Fourteen patients had metastatic disease (58.3%). Lymph nodes were the most frequent metastatic site. Calcitonin levels at diagnosis were $>$ 500 pg/ml in 57.1% of patients. Most of them had undergone an incomplete first thyroid surgery. In addition, the tumors were larger, multifocal ($P<0.05$) and with capsular invasion ($P<0.02$). Of these patients three received chemotherapy, radiotherapy was performed in two patients, and two patients were scheduled for treatment with Sorafenib.
Conclusion
The prognosis of CMT is more pejorative than papillary thyroid carcinoma, several factors were correlated with the development of metastasis, which requires adequate management with close monitoring of the disease.

DOI: 10.1530/endoabs.81.EP1121

EP1122

Papillary thyroid carcinoma revealed by hyperthyroidism

Messaoudi Najoua[1], Imane Assarrar[1], Nisrine Bouichrat[1], Marouan Karrou[1], Siham ROUF[2] & Hanane Latrech[3]
[1]Mohammed VI University Hospital Center, Faculty of Medecine and Pharmacy, University of Mohammed 1st, Department of Endocrinology-Diabetology and Nutrition, Oujda, Morocco; [2]Faculty of Medicine and Pharmacy of Oujda, Mohamed the First University, Department of Endocrinology-Diabetology-Nutrition, Oujda, Morocco; [3]Faculty of Medicine and Pharmacy of Oujda, Mohamed the First University, Department of Endocrinology-Diabetology-Nutrition, Laboratory of Epidemiology, Clinical Research and Public Health, Oujda, Morocco

Introduction
Papillary thyroid carcinoma is the most common histological type of differentiated thyroid malignancy. This type of tumor is rarely associated with thyroid hormone hypersecretion. We report the case of a patient with papillary thyroid carcinoma revealed by hyperthyroidism.
Case report
A 35 years old patient was admitted for the management of malignant hypercalcemia discovered incidentally on the biological workup performed preoperatively for a humerus fracture. The biological and radiological assessment revealed a primary hyperparathyroidism secondary to a parathyroid adenoma and hyperthyroidism secondary to a nodular goiter. TSH anti-receptor antibodies and calcitonin were negative. After obtaining normocalcemia and normalization of the thyroid assessment, the patient underwent a total thyroidectomy with a left parathyroid adenectomy. The anatomopathological study confirmed the presence a parathyroid adenoma without signs of malignancy, as for the thyroidectomy specimen, the histological study revealed a vesicular carcinoma with presence of a capsular effraction and vascular emboli, classified pT3aNxMx.
Conclusion
The association of thyroid cancer and hyperthyroidism is a rare event. Its pathogenesis remains poorly elucidated. Hyperthyroidism in these cases may be

secondary to the primary carcinoma, as well as due to metastases, hence the importance of a complete extensive evaluation.

DOI: 10.1530/endoabs.81.EP1122

EP1123

Two types of thyroid cancer in one patient

Emir Muzurovic[1], Sanja Borozan[2] & Snezana Vujosevic[2]
[1]Clinical Centre of Montenegro, Department of Endocrinology, Podgorica, Montenegro; [2]Clinical Centre of Montenegro, Department of Endocrinology, Podgorica, Montenegro

A 65–year-old male was referred to endocrinologist due to significantly elevated calcitonin level of 3662 pg/ml. Previously, almost 3 decades before, the patient underwent right thyroid lobectomy for papillary carcinoma. Then, 9 years afterwards, he was reoperated and total thyroidectomy with neck exploration was performed. In pathohistological finding, metastatic papillary carcinoma was proved. Radioactive iodine ablation was used as a post surgical treatment. After completing a proposed therapeutic course, a patient has not been motivated for a regular follow-up. During the hospital examination, CT scan of the neck region revealed a solitary pathological node in front of the trachea, 18 mm in diameter which was surgically removed. Pathohistological finding was suggestive for metastatic medullary thyroid carcinoma. A bone scan and nuclear magnetic resonance demonstrated a 32 mm extramedullary intraspinal solid mass in Th10 region. In further course, a Galium PET/CT scan showed an increased update in right cervical level lymph node, measuring 12x8 mm in diameter, and in left side of the spinal canal at the level of Th9-Th10, consistent with metastasis, without pathological uptake on brain images, thorax, abdomen or pelvis. One month afterwards, a solid mass in spinal region and neck dissection were removed, followed with calcitonin level normalization.

DOI: 10.1530/endoabs.81.EP1123

EP1124

Branchial cyst into the thyroid gland: an usual presentation

Sirine Ayedi[1], Chaabouni Medamin[1], Rim Hammami[1], Moncef Sellami[1], Abid Najla[2] & Ilhem Charfeddine[1]
[1]Habib Bourguiba Hospital - University of Sfax, Ent Department, Sfax, Tunisia; [2]Habib Bourguiba Hospital - University of Sfax, Pathology Department, Sfax, Tunisia

Introduction
Fourth branchial cleft cyst are commonly reported as recurrent low-neck abscesses, acute suppurative thyroiditis, and neck masses. We report an accidental finding of a fourth branchial cleft as a suspected thyroid nodule.
Case presentation
We present a case of a 47-year-old woman who consulted the Ear, Nose, and Throat department of our hospital with a 4-year history of thyroid nodule. The thyroid nodule was discovered incidentally on ultrasonography. She reported no cervical swelling, pain, dysphagia, dysphonia or dyspnea. She did not report any recent infections, neck trauma, or surgery. The patient had no palpable neck mass or *fistulous orifices*, with a strictly normal ENT examination. Several ultrasonographic examinations revealed the thyroid nodule. Its size was a 14*8*7 mm tissular nodule classified EU-Tirads 5 but didn't show a cyst, without significant modification compared to the previous ultrasonographic examinations. The patient underwent lobo-isthmectomy. The patient's postoperative course was satisfactory. Meanwhile, the pathologist confirmed the presence of a 1 cm lateral neck cyst within this thyroid lobe with no other thyroid nodules. After a mean follow-up of 5 years, no superinfection episodes or recurrence were reported.
Conclusion
Fourth branchial anomalies are very rare and can remain asymptomatic for a long time. Its localization and mode of discovery may be unusual. Clinical presentation and imagery can't always help to diagnosis. In our case, it was considered as a suspicious thyroid nodule, but the anatomopathological examination rectified the diagnosis.

DOI: 10.1530/endoabs.81.EP1124

EP1125

Thyroid nodule: an exceptional mode of revelation of extrapulmonary Tuberculosis

Arij Ezzouhour Yahyaoui, Asma Kefi, Ben Abdelghani Khaoula, El Euch Mounira, Sassi Syrine, Turki Sami & Abderrahim Ezzeddine Charles Nicolle, Internal Medicine A, Tunis, Tunisia

Introduction
The incidence of extrapulmonary forms of tuberculosis has increased. Thyroid tuberculosis is an uncommon condition even in developing countries where tuberculosis is endemic. Herein we report an original case of a 62 year-old woman in whom tuberculosis was revealed by thyroid nodule.
Observation
Our patient is a 62-year-old woman with a history of mild asthma for 7 years. She presented with a slight neck swelling and a loss of weight and appetite for three months, with no discomfort on swallowing nor tenderness. There were no specific signs suggestive of dysthyroidism. She denied any history of tuberculosis, night sweats, fever, dyspnea or cough. On examination, she had a slight thyromegaly without tenderness nor bruit. Other systemic and regional examinations did not show any abnormality. The blood routine tests were normal. The thyroid function tests disclosed normal levels of serum thyroid stimulating hormone (TSH) and free thyroxin (FT4). Blood and urine calcium levels were normal. Cervical ultrasound revealed multiple nodules of various sizes in the right lobe associated to lymph nodes in the lower internal jugular chain. Ultrasound (US)-guided fine needle aspiration biopsy of lymphadenopathies demonstrated non-caseating granulomatous lymphadenitis. A CT scan was performed and revealed apical ground glass opacities, symmetric hilar, mediastinal and abdominal adenopathies. Quantiferon test was positive. Tuberculin skin test was positive too with an 18 mm-diameter reaction. Sputum smear microscopy was negative. Bronchoalveolar lavage was normal: there was no alveolitis, CD4/CD8 ratio was normal, mycobacterium tuberculosis PCR was negative. The angiotensin-converting enzyme and beta2-microglobulin were not elevated. The patient was diagnosed with ganglionar and thyroid tuberculosis. The patient is now put on anti-tuberculosis drugs: combination of Rifampicin, Isoniazid, Ethambutol and Pyrazinamide for 2 months, which will be followed by Rifampicin and Isoniazid for 4 months. Now the patient is remaining euthyroid, neck swelling is not progressing and her appetite improved significantly. Follow-up sonography is scheduled in one month.
Conclusion
Thyroid tuberculosis is a scarce condition which should be considered in front of thyroid nodule. Fine-needle aspiration cytology may avoid unnecessary surgical intervention. Treatment options for thyroid tuberculosis are antituberculous drugs and/or surgery.

DOI: 10.1530/endoabs.81.EP1125

EP1126

Multinodular goiters: management

Meherzi Abir, Marwa Ben Njima, Mouna Khalifa, Mouna Bellakhdhar, El Omri Malika, Jihene Houas, Kermani Wassim & Abdelkefi Mohamed
ENT Department Farhat Hached Hospital Sousse, Sousse, Tunisia

Background
analysis the epidemiologic and the clinical features of this entity, then to discuss the management
Patients and methods
We report a retrospective study of 120 patients operated on for multi nodular goiter over a period of 5 years between January 2017 and December 2021.
Results
In our study a female predominance was noted with a sex ratio F/H of 8/1. The average age of the patients was 44 years with extremes from 15 to 74 years. A familial thyroid pathology was reported by 42 patients in our study (35%). On clinical examination 82 patients had a single nodule; the consistency of the GMN was firm in 88%, soft in 3% and hard in 9% of cases. 64.4% of the dominant nodules within the MNG were smaller than 4 cm. Cervical adenopathies were palpated in 13 patients (11%). Clinical signs of tracheobronchial axis compression were present in 45 patients or 37.5%. Recurrent paralysis was found at the IL in 3 patients (2.5%). A thyroid workup was performed in all patients. 96.6 of patients were euthyroid, the rest were hypothyroid. Ultrasound was performed in all patients. It revealed nodules larger than 1 cm in all patients. Cytopuncture was performed in 23 patients (19%). It concluded to a benign nodule in 19 cases (76%), a suspicious nodule in 3 cases (12%) and was non-contributory in 3 cases (12%). In 52 patients, surgical treatment consisted of total

thyroidectomy (44%) and loboisthmectomy in 68 patients (56%). The surgical treatment was complicated by 4 unilateral recurrent paralysis of which two were definitive and 5 definitive hypoparathyroidism.
Conclusion
Thyroid goiter is the most frequent endocrine disorder. Clinical testing, thyroid function testing, and imaging studies are all part of the diagnostic process. Additional FNAC testing may be necessary. Depending on the results of the diagnostic examination and related consequences, treatment options include medications, surgery, and radioiodine (I-131).

DOI: 10.1530/endoabs.81.EP1126

EP1127

Graves' disease: surgical management

Meherzi Abir, Habiba Ben Sghaier, Mouna Bellakhdhar, El Omri Malika, Jihene Houas, Kermani Wassim & Abdelkefi Mohamed
ENT Department Farhat Hached Hospital Sousse, Sousse, Tunisia

The goal of this study is to examine the role of surgery in the treatment of Graves' disease and to assess the surgical outcomes.
Methods
We present the results of a retrospective analysis of 31 Graves' disease cases operated on in the ENT and cervico-facial surgery departments of Farhat Hached Sousse Hospital during a six-year period [2015-2021]. Our group consisted of 05 males and 26 women. The average age ranged from 12 to 70 years. Between diagnosis and operation, the average period was 35.6 months [06-120 months]. A homogenous goiter (93.5%) and a thyroid of normal volume were discovered during a cervical examination (6.5 percent). TSH and FT4 levels were 14.42 pmol/l and 1.12 mU/l, respectively, at the median. When faced with: resistance to medical therapy (77.4%), existence of compression signals (9.7%), presence of thyroid nodules (6.5%), severe ophthalmopathy (3.2%), and patient desire, surgery was recommended (3.2 percent). In all of the patients, a complete thyroidectomy was performed. Following surgery, one patient experienced brief recurring paralysis. Hypocalcemia was discovered in 38.7% of the patients. In any event, it was only temporary. After surgery, no patient experienced an acute thyrotoxic crisis. A histological investigation revealed Graves' disease, but no evidence of cancer. The average period of follow-up was three years.
Conclusion
Graves' disease is a thyroid autoimmune illness. Because of the disease's evolutionary vagaries, treating it is tough. Medical therapy has been related to repeated recurrences and a variety of side effects, all of which have a negative impact on these patients' quality of life. Surgery based on total thyroidectomy represents a safe alternative with a low rate of complications.

DOI: 10.1530/endoabs.81.EP1127

EP1128

Hypoparathyroidism Post-total thyroidectomy: pathophysiology and management

Meherzi Abir, Safa Jemli, Mouna Bellakhdhar, El Omri Malika, Jihene Houas, Kermani Wassim & Abdelkefi Mohamed
ENT Department Farhat Hached Hospital Sousse, Sousse, Tunisia

Thyroid surgery is a frequent procedure that has certain risks. After a complete thyroidectomy, hypocalcemia is the most prevalent consequence. It has a variety of causes, with hypoparathyroidism being the most frequent and dangerous.
Materials and procedures
A retrospective analysis collected 27 cases of patients who had a total thyroidectomy complicated by hypocalcemia among 320 patients who underwent a total thyroidectomy throughout the study period, which spanned nine years (2010–2020). The goal of our research is to identify the characteristics that predict post-total thyroidectomy hypocalcemia, as well as the consequences and various therapy options.
Results
The average age of the participants was 40.5 years [17–78 years]. Females made up 92.6 percent of the patients. On D3, postoperatively, a systematic assessment of serum calcium was performed. In terms of clinical symptoms, 48% of individuals were asymptomatic. On D1 surgical day, 3 patients had symptomatic hypocalcaemia, and on D2 postoperative day, 11 patients had symptomatic hypocalcaemia. In addition, all of the patients' preoperative serum calcium levels were normal. Apart from surgical devascularization of the parathyroid glands, 23 individuals had postoperative hypocalcemia. The primary symptom in symptomatic individuals was paresthesias of the extremities (85.7 percent). In two of the patients, muscle cramps were noted. There were no cardiac arrhythmias or tetany crises in any of the individuals. The mean serum calcium concentration was 1.67 mmol/l (range: 1.4 to 1.9 mmol/l). In 18 individuals, intra-hospital parenteral correction with calcium gluconate was required. On discharge, all patients were given calcium supplements along with vitamin D. The average treatment time was 3.7 months [1–9 months]. In 25 cases, the result was positive (correction of hypocalcaemia). Two patients were misplaced.
Conclusion
Hypocalcemia following thyroid surgery can be severe, but it's usually reversible. The first step in prevention is to carefully dissect the parathyroid glands and preserve their circulation. Despite this, a low preoperative vitamin D level predicts the development of postoperative hypoparathyroidism, which might be asymptomatic prior to surgery. Other prospective trials are needed to clarify the interest in a possible preoperative vitamin D supplementation as well as the mode of supplementation.

DOI: 10.1530/endoabs.81.EP1128

EP1129

Management of refractory Graves' disease

Meherzi Abir[1], Habiba Ben Sghaier[1], Mouna Bellakhdhar[1], El Omri Malika[1], Jihene Houas[1], Kermani Wassim[1] & Abdelkefi Mohamed[1]
[1]ENT Department Farhat Hached Hospital Sousse, Sousse, Tunisia

The goal of this paper is to analyze the factors that cause people to flee medical treatment and to put forth management guidelines. Materials and methodes: This is a retrospective analysis of 27 instances with Graves' disease that were resistive to medical treatment after escaping from well-conducted medical treatment in the ENT and cervico-facial surgery departments at Farhat Hached Sousse Hospital over a six-year period [2015-2021]. Results: All of the patients were put on a synthetic antithyroid medication as a first line of treatment (ATS). Carbimazole (thyrozol) was the most commonly used compound in 81.5 percent of instances, followed by propylthiouracil (basdene) in 18.5 percent. In 74 percent of instances, a beta-blocker was used as an adjuvant treatment. Medical treatment lasted an average of 33.7 months. Following an escape from medical treatment, surgical treatment was advised in all of the patients: resistance to medical treatment in 24 patients, 2 of whom had tried IRAtherapy cures but were ineffectual, and the presence of a gigantic goiter with compressive indicators in 3 patients. In all patients who achieved euthyroidism, a total thyroidectomy was performed (mean follow-up of 18 months).
Conclusion
Graves' illness is the most prevalent cause of thyrotoxicosis, which has life-threatening effects. Iodine and surgery are the alternatives to euthyroidism, which must be achieved first.

DOI: 10.1530/endoabs.81.EP1129

EP1130

Graves' disease revealing primary biliary cirrhosis (a case report)

Maryame Ben Lafqih, Meryam Alahyane, Sana Rafi, Ghizlane EL Mghari & El Ansari Nawal
Mohammed VI University Hospital of Marrakesh, Department of Endocrinology, Diabetology, Metabolic Diseases and Nutrition, Marrakesh, Morocco

Introduction
Liver function abnormalities in hyperthyroidism are common, several abnormalities have been reported: hepatic cytolysis, cholestasis, insufficiency or even non-specific abnormalities. The pathophysiology of hepatic dysfunction secondary to hyperthyroidism is not yet well established. Graves' disease can be associated with various autoimmune diseases. However, association with Primary biliary cirrhosis has been described in few cases in literature. We report a case of Graves' disease revealing primary biliary cirrhosis
Case report
F, I, 47-year-old female patient, with no pathological history, consults for a syndrome of thyrotoxicosis. Physical examination showed: Bulging eyes, homogeneous diffuse goiter, with vascular thrill. Thyroid function tests revealed : low serum TSH <0.05 U/l, and high serum free T4:51.46 pmol/l and free T3: 19.6 pmol/l. An ultrasound exam showed an enlarged thyroid with increased vascularity,

compatible with thyroiditis. Meanwhile, the patient presented a cholestasis and cytolysis syndrom, serology tests for hepatitis were negative; high level of total IGGs, anti-mitochondrial antibodies not made. The abdominal ultrasound: dysmorphic liver. On fibroscann : Elasticity estimated at 11.4 (F3) The patient was put on prednisone and beta blocker, with a normalization of liver and thyroid tests. Then a total thyroidectomy was performed. The anatomopathological study confirmed the diagnosis of Graves' disease.
Discussion
Hepatic involvement in Graves' disease is uncommon, however, abnormal liver function tests are relatively common. Clinical and biological cholestasis syndromes are less common. The pathophysiology of hepatic dysfunction in hyperthyroidism is multifactorial, it may be secondary to hyperthyroidism, to antithyroid drugs, or associated with autoimmune liver disease. Various theories attempt to explain cholestasis in hyperthyroidism. Its association with hyper metabolism, increases hepatic oxygen consumption, without an increase in hepatic blood flow, and therefore a decrease in oxygen in the centrilobular areas. Our patient had a clinical and biological cholestasis syndrome, the etiological assessment was negative, the fibroscann confirmed hepatic cirrhosis. The normalization of liver tests under corticosteroids is in favor of diagnosis of primary biliary cirrhosis.
Conclusion
Primary biliary cirrhosis is another autoimmune disease that should be considered as an association with Grave's disease when other causes of cholestasis syndrome are ruled out. Early identification could help plan disease management and prognosis improvement.
Bibliography
Grave's Disease and Primary Biliary Cirrhosis—An Unusual and Challenging Association Shiran Shetty*, Senthilkumar Rajasekarany, Leela Venkatakrishnan* Journal of Clinical and Experimental Hepatology, 2014, 4(1): 66–67

DOI: 10.1530/endoabs.81.EP1130

EP1131

Coronary insufficiency during hyperthyroidism: Report of six cases

Mouna Elleuch, Cyrine Chehaider, Sawssen Ben Teber, Dhoha Ben Salah, Siddiqa Soomauroo, Nadia Charfi, Mouna Mnif, Fatma Mnif, Nabila Rekik, Faten Hadj Kacem & Mohamed Abid
Hedi Chaker Hospital, Endocrinology, Sfax, Tunisia

Introduction
Cardiothyreosis is the consequence of the effects of excess free thyroid hormones on the vascular wall and myocardium. This complication is the most serious aspect of hyperthyroidism. Rhythm disorders and heart failure are the most frequently noted. The prevalence of coronary insufficiency is lower. The aim of this study is to evaluate the characteristics of coronary insufficiency in patients with hyperthyroidism.
Method
This is a retrospective descriptive study including six patients among a hundred patients who were followed for hyperthyroidism and cardiothyreosis, during a period of 20 years, in the Endocrinology department of Hedi Chaker Hospital in Sfax. These six patients had coronary insufficiency related to cardiothyreosis.
Results
The prevalence of coronary insufficiency in cardiothyreosis was 6%. All six patients were male, with a mean age of 44.16 years [extremes: 25-61]. The majority were aged $\leq$ 35 years (4 cases). They had no personal history of cardiovascular pathology except hypertension for one patient. The etiology of hyperthyroidism was Graves' disease in 2 cases, Hashimoto's thyroiditis in 2 cases, toxic multi-nodular goiter and iodine overload. The mean TSH level was 0.054 µIU/ml [extremes: 0.01 - 0.19 µIU/ml], FT4 was 54.36 pmol/l [extremes: 31.3 - 71.43 pmol/l]. No cases of subclinical hyperthyroidism were reported. The diagnosis of hyperthyroidism was concomitant with the diagnosis of cardiothyreosis in 5 patients and delayed in one patient. Tachycardia was present in all patients with a mean heart rate of 101.2 bpm. The different forms of coronary syndrome were objectified, ranging from unstable angina to myocardial infarction with or without necrosis Q wave. Coronary angiography reports of 4 patients were obtained: they showed arterial occlusion in 2 cases and a healthy coronary network in the other 2 cases. Coronary insufficiency was always associated with one or more of the other types of cardiothyreosis. Rhythm disorders were present in 5 cases (atrial fibrillation in 4 cases and atrial extrasystoles in one case). Systolic ejection fraction was low in all patients with a mean of 35.83% [extremes: 20-55%]. 2 patients had died in major heart failure. The others had not developed new coronary events after obtaining euthyroidism.
Conclusion
The risk of coronary insufficiency during hyperthyroidism is well established. Less common than rhythm disorders and heart failure, it is usually associated with them. Early diagnosis and adequate treatment of hyperthyroidism would prevent this complication.

DOI: 10.1530/endoabs.81.EP1131

EP1132

Long-term disease recurrence in the adipose tissue and striated muscle of a mimally invasive papillary thyroid carcinoma

Antonella Carbone[1], Antonella Verrienti[2], Domenico Savio Cito[3], Marialuisa Sponziello[2], Valeria Pecce[2] & Rocco Bruno[3]
[1]Endocrine Unit, Area Medica, Pisticci, Italy; [2]Department of Translational and Precision Medicine, Sapienza University, Rome, Italy; [1]Endocrine Unit, Area Medica, Pisticci, Italy

Introduction
Differenziated thyroid carcinomas (DTC), particularly papillary thyroid carcinomas (PTCs), usually have an indolent behavior, howewer 10-20% of the patients develop recurrences, following surgery. There are several histological features associated with more frequent recurrences as the hystopathological variants of PTCs, the presence of vascular invasion or lymph node metastases and the presence of extrathyroidal extension (ETE). Case history: a 56yrs old male patient prevously treated for PTC, with excellent response to the first treatment, presented twelve years after a gradual increase of thyroglobulin (Tg) (from 0.3 to 0.76 ng/ml in 6 months) and a neck lump in the left cervical region at ultrasound imaging. Fine needle aspiration cytology of the mass and Tg measurement in the wash out liquid of the needle was 472 mg/l. Cytology revealed polymorphous epithelial cells with atypical nuclei suggesting metastasis of PTC. Surgery was then performed and pathology showed a massive metastasis in the local adipose tissue and striated muscles of the neck. Genetic analysis of the primary tumor and metastatic tissue revelead a BRAF p. V600E in both primary tumor and in metastatic tissue (37% and 48% respectively). Conclusions: Our patient's history suggests the need of a continuous and prolonged follow-up in patients with multiple features that increase the recurrence risk (minimal ETE, size $>$2 cm, BRAF V600E mutation as in our case).
References
1 B.R Haugen, E.K. Alexander, K.C. Bible *et al*. (2016) 2015 American thyroid association management guidelines for adult patients with thyroid nodules and differenziated thyroid cancer: the American thyroid association guidelines task force on thyroid nodules and differentiated thyroid cancer. Thyroid 26,1-133.
2 M. Shteinshnaider, L.M. Kalmovic, S. Koren *et al*. (2018) Reassessment of differentiated thyroid cancer patients using the eighth TNM/AJCC classification system: a comparative study. Thyroid 28(2), 201-209.
3 D.L.S. Danilovic, L.A. Castroneves, C.K. Suemoto *et al*. (2020) Is there a difference between minimal and gross extension into the strap muscles for the risk of recurrence in papillary thyroid carcinomas. Thyroid 30(7), 1008-1016.
4 T. Diker- Cohen, D. Hirsch, I. Shimon *et al*. (2018) Impact of minimal extrathyroid extension in differentiated thyroid cancer : sistematic review and meta-analysis. J Clin. Endocrinol. Metab. 103 2100-2106.
5 T. P. de Castro, R. c. C. Penha *et al*. (2020) Molecular predictors for advanced papillary thyroid carcinoma recurrence. Front. Endocrinol.10, 839.

DOI: 10.1530/endoabs.81.EP1132

EP1133

Epidemiological, clinic-pathological, evolutionary profile of noninvasive follicular thyroid neoplasm: About 27 cases

Sofia Ouhessaine, Nassim Essabah Haraj, Siham El Aziz & Asma CHADLI
Ibn Rochd University Hospital, Endocrinology, Diabetology, Nutrition and Metabolic Diseases Department, Casablanca, Morocco

Introduction
Noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP) is a newly defined entity accepted as a tumor precursor.
Objective of the study
To describ the epidemiological, clinical characteristics, and the evolutionary profile.
Methods
Retrospective study including 27 patients followed for noninvasive follicular thyroid neoplasm collected at the Endocrinology and Diabetology department of Ibn Rochd Casablanca University Hospital, spread from 2017 to 2021.

Results
The mean age of our patients was 51.3 years, with a clear predominance of women (88.8% of cases). The most frequent symptomatology was cervical swelling in 88.36%, the discovery was fortuitous in 11.63%. In our series 92% patients had multinodular goiter, 14.8% followed for dysthyroidism, 26.7% had no personal history and 2 patient had a familial history of thyroid carcinoma. All patients had clinical and biological euthyroidism except 3 patients who had hyperthyroidism. All patients underwent total thyroidectomy with noninvasive follicular tyroid neoplasm, the average size of 1.07 cm. Multifocality was objectified in 5 patients, without associated malignancy. Their was no indication for Lymph node dissection and Iratherapy ($P=0.000$), with no distant metastasis ($P=0.000$). The remission rate was objectified in 100%.
Conclusion
The diagnosis of NIFTP can only be made after complete resection of the lesion. Patients diagnosed with NIFTP without associated malignancy and without nodules detected can be spared from additional treatment and from the traditional follow-up recommended for differentiated thyroid cancer.

DOI: 10.1530/endoabs.81.EP1133

EP1134

Severe hyperthyreosis

Iva Petrak[1] & Karin Zibar Tomšić[2]
[1]Opća Bolnica Nova Gradiška, Nova Gradiska, Croatia; [2]University Hospital Centre Zagreb, Zagreb, Croatia

A 72-year-old male patient presented to the ER because of general weakness, myalgia, frequent paroxysms of atrial fibrillation, shortness of breath, and hoarseness. The symptoms persisted for two months, gradually worsening and causing him to lose weight. At some point, he noticed redness of the sclera and soreness of the eyeballs. Paroxysms of rapid atrial fibrillation have been known for more than 15 years, so he had amiodarone in therapy. His initial laboratory findings showed markedly elevated fT4 >100 pmol/l, fT3 36 pmol/l, and suppressed TSH <0.01 mIU/l. Thyroid antibodies were normal. Ultrasonography showed a diffusely altered thyroid with normal blood flow, and no nodular changes. Therapy was started with thiamazole 30 mg daily, propranolol 80 mg daily, and methilprednizolone 32 mg daily. Amiodarone was excluded from therapy. Two weeks later, fT4 was still significantly elevated, above 100 pmol/l. The thiamazole dose was increased to 60 mg per day, and two weeks after that, fT4 began to decrease, so the thiamazole dose was reduced to 30 mg per day. Two weeks after the dose reduction, he came to ER due to rapid atrial fibrillation. The fT4 level was again greater than 100 pmol/l, so the thiamazole dose was increased to 60 mg per day and lithium carbonate was added to the therapy, while the dose of methilprednosolone was gradually reduced in the meantime. Because the fT4 level was still extremely high 400 pmol/l after 1 week despite therapy, the patient was hospitalized and therapy was continued with thiamazole at a dose of 90 mg daily, lithium carbonate, parenteral corticosteroid, and supportive therapy. After 7 days, a decrease in fT4 level to 64 pmol/l is observed. As the gradual decline in thyroid hormones continued, the dose of lithium carbonate and parenteral corticosteroids was gradually reduced but continued with high doses of thiamazole of 90 mg per day. As the patienťs recovery was monitored by continued reduction of corticosteroids, lithium, and thiamazole, it was planned to perform thyroidectomy after complete physical recovery and achievement of euthyroidism. The patient was discharged for home treatment. Lithium carbonate was discontinued after 1 week, corticosteroid after 3 weeks, and thiamazole after 6 months of gradual reduction with achievement of euthyroidism. The patient recovered completely, so he refused thyroidectomy.
Conclusion
Thyroid storm due to amiodarone therapy.

DOI: 10.1530/endoabs.81.EP1134

EP1135

When unilateral exophthalmos is the only manifestation of graves' disease: diagnostic and therapeutic issues

Sara Si Amer, Imene Benoumechiara & Nora Soumaya Fedala
University Hospital Henter Mohamed Lamine Debaghine, Department of Endocrinology, Diabetology and Metabolic Diseases, Algiers, Algeria

Introduction
Basedowian exophthalmos is an inflammatory disease of the orbit of autoimmune origin, potentially threatening with severe functional and psychosocial effects. It is usually accompanied by hyperthyroidism. It constitutes a real diagnostic challenge in patients with euthyroidism, as is the case with our patient.
Observation
A 34-year-old young woman with no particular pathological personal or family history. Who initially consults, a year ago, in ophthalmology for a unilateral, right, non-painful, hardly retractile exophthalmos, estimated at 27mm, and associated with ipsilateral palpebral retraction, without other signs, in particular inflammatory. The clinical activity score was 1. Faced with the unilateral character, an orbito-cerebral CT scan was performed, ruling out a tumor cause and confirming unilateral proptosis with slight infiltration of the periorbital muscles. It is oriented at our level for further exploration. The clinical examination does not find any clinical signs of hyperthyroidism or goiter. The thyroid balance was normal, namely TSH: 0.981 mui/ml, FT4: 15.67 pg/ml, TPOAb/TgAb negative, only positive TSH anti-receptors at 3.74. Thyroid ultrasound shows the appearance of lymphocytic thyroiditis. The patient received oral corticosteroid therapy which did not allow the regression of this proptosis, a cure of silicon was prescribed.
Discussion-Conclusion
Unilateral exophthalmos may be the only clinical manifestation of Graves' disease in euthyroidism, thus posing a diagnostic challenge. And although the management of Basedowian exophthalmos is well codified, it still remains problematic in some patients.

DOI: 10.1530/endoabs.81.EP1135

EP1136

Correlation between plasmatic long pentraxin PTX3 and nodular thyroid disease: a preliminary report

Damiano Chiari[1,2], Barbara Bottazzi[3], Roberto Leone[3], Giorgia Amy Rodda[1], Barbara Pirali[2], Luciano Branchini[2] & Walter Zuliani[2]
[1]Humanitas University, Milan, Italy; [2]Humanitas Mater Domini Clincal Institute, Castellanza, Italy; [3]Humanitas Research Hospital, Milan, Italy

Introduction
The long pentraxine-3 (PTX3) is a key component of humoral innate immunity that is expressed in various cell types during stress and tissue injury. PTX3 also acts like an oncosuppressor regulating tumor-promoting inflammation and it is implicated in tissue repair and autoimmunity. Autoimmune disease, tissue remodelling and oncogenesis often coexist in the thyroid. PTX3 role in thyroid disease is still unknown. Aim of the study is to evaluate if plasmatic levels of PTX3 in patients submitted to thyroidectomy for benign or malignant nodular disease are higher than normal.
Materials and methods
After informed consent, patients over 18 years old with nodular disease of the thyroid who were eligible for thyroid surgery were enrolled in this study. All patients underwent total or hemi-thyroidectomy at Humanitas Mater Domini Clinical Institute in Castellanza (VA). A blood sample was taken on the day of surgery and another one was taken 45 days after surgery to evaluate plasmatic PTX3 level. Blood samples were centrifuged and PTX3 levels were evaluated with ELISA test. In this preliminary report, we evaluated the data of the first 53 consecutive patients enrolled in the study.
Results
We found that preoperative plasmatic PTX3 levels were significantly higher than normal in patients with thyroid disease ($P<0.05$). Plasmatic PTX3 mean value was 4.54 ng/ml (range 1.06 – 8.63 ng/ml), when normal value is considered 2 ng/ml with 1 ng/ml of standard deviation. At 45 days follow-up PTX3 mean value was reduce to 3.40 ng/ml (range 0.89 – 9.21 ng/ml); this reduction was statistically significant ($P<0.05$).
Conclusions
For the first time, at the best of our knowledge, we observed a correlation between elevated PTX3 plasmatic levels and nodular disease of the thyroid. We hope to identify if plasmatic PTX3 could be used as a marker for nodular thyroid disease.

DOI: 10.1530/endoabs.81.EP1136

EP1137

Graves' orbitopathy: clinical evaluation and therapeutic aspects

Sofien AFFES[1], Ben Amor Saloua[1], Rekik Mona[1], Nadia Ben Amar[1], Faten Hadj Kacem[2] & Trigui Amira[1]
[1]Habib Bourguiba University Hospital, Ophthalmology, Sfax, Tunisia; [2]Hedi Chaker University Hospital, Endocrinology, Sfax, Tunisia

Introduction
Graves' disease is a common autoimmune disease that can be complicated by orbital damage sometimes threatening the visual prognosis. We report the case of a patient with Graves' orbitopathy and we discuss the difficulties of clinical evaluation and therapeutic management.
Case report
A 68-year-old woman presented to our department complaining of eye protrusion and progressive vision reduction in both eyes. She has had a history of Graves' disease, treated with synthetic antithyroid drugs for 1 year, then thyroidectomy. The ophthalmological examination revealed in the right eye a visual acuity at 1/10, a proptosis, intraocular pressure (IOP) at 20 mmHg, a limitation of abduction, a dense cataract with a pale optic disc at the fundus. In the left eye, visual acuity was at 3/10; there was a proptosis, IOP at 22 mmHg, a mild cataract with optic disc hyperaemia at the fundus. We completed with an orbital MRI and a thyroid assessment. The patient was put on hypotonic eye drops and received bolus of intravenous corticosteroids. The evolution was marked by an improvement in oculomotricity and a partial regression of proptosis and IOP. Given the persistence of the threat to the visual prognosis, orbital decompression surgery was indicated.
Discussion
The diagnosis of dysthyroid orbitopathy is often obvious. The clinical evaluation must specify the evolutionary stage (clinical activity score) and the gravity or severity according to the classification of the European group EUGOGO. It is important to recognize the 3 major stages of the disease: diagnosis with an ophthalmological and thyroid evaluation, the activity phase which may or not require specific treatment, and the sequelae phase after 6 months of stability and inactivity. Initially, rapid restoration of euthyroidism, smoking cessation and simple ophthalmological symptomatic treatment are proposed. In the event of advanced and active dysthyroid orbitopathy, oral or intravenous corticosteroid therapy associated or not with orbital radiotherapy. The place of emergency decompressive surgery in cases of optic neuropathy is controversial.
Conclusion
Dysthyroid orbitopathy is a complex pathology whose management is often difficult. A multidisciplinary management is recommended in order to allow an adequate biological, clinical and radiological evaluation and to propose an adequate treatment.

DOI: 10.1530/endoabs.81.EP1137

EP1138

Autoimmune thyroiditis and hypothyroidism: a personalized medical approach

Silvia Martina Ferrari[1], Francesca Ragusa[2], Giusy Elia[2], Sabrina Rosaria Paparo[2], Valeria Mazzi[2], Eugenia Balestri[2], Chiara Botrini[2], Armando Patrizio[3], Alessandro Antonelli[2] & Poupak Fallahi[4]
[1]University of Pisa, Department of Clinical and Experimental Medicine, Italy; [2]University of Pisa, Department of Surgical, Medical and Molecular Pathology and Critical Area, Italy; [3]Azienda Ospedaliero-Universitaria Pisana, Department of Emergency Medicine, Italy; [4]University of Pisa, Department of Translational Research and New Technologies in Medicine and Surgery, Italy

Autoimmune thyroid diseases (AITD) are organ specific autoimmune disorders with a T-cell-mediated immune attack directed against the thyroid. Hashimoto's thyroiditis and Graves' disease are the two principal AITD clinical presentations, which are characterized by hypothyroidism and thyrotoxicosis, respectively. We review the available data in literature about personalized medicine in patients with autoimmune thyroiditis (AT) and hypothyroidism. The synthetic Levothyroxine (L-T4) (1.5-1.7 μg/kg) is the daily treatment for these patients. L-T4 is available in different formulations, including tablet, liquid solution, or soft gel capsule. The tablets are the most prescribed, while the liquid, or the soft gel capsules formulations, are generally administered in hypothyroid patients who have issues of malabsorption, or who are in treatment with drugs interfering with L-T4 absorption. Furthermore, the administration of myoinositol and selenomethionine in patients with subclinical hypothyroidism and AT showed promising effect; with a significant decline in TSH and antithyroid autoantibodies levels. Actually, myoinositol, which is the precursor of phosphoinositides and takes part into various cellular processes, has also a key role in thyroid autoimmunity and function. Moreover, thyroidectomy can be suggested in patients with AT, owing to a variety of reasons such as: important signs or symptoms of local compression; the presence of thyroid nodules with "suspicious" features; cosmetic reasons for a goiter. Recently, a randomized trial suggested that total thyroidectomy, but not medical therapy, can ameliorate fatigue and quality of life in these patients. Further researches involving larger population will help in the evaluation of the effect of these novel treatments on the quality of life in these patients.

DOI: 10.1530/endoabs.81.EP1138

EP1139

The study of lipidic spectrum in the females with 'subclinical hypothyroidism' living in uzbekistan

Rakhshona Mirzaeva[1] & Dilfuza Karimova[2]
[1]Tashkent Medical Academy, Department of Endocrinology, Tashkent, Uzbekistan; [2]Tashkent Medical Academy, Tashkent, Uzbekistan

Introduction
Hypothyroidism - is a clinical syndrome, which occurs owing to the constant insufficiency of thyroid gland hormones in organisms for a long period of time or as a result of reducing their biological effect as a tissue. Now, hypothyroidism occurs in 7-10 % of females and 2-3 % of men. Subclinical hypothyroidism – is characterized by a gradual aggravating chronic condition of the thyroid gland of immune pathologic character, normal level (T4) of free thyroxin, and a large amount of thyroid-stimulating hormone (TSH). It is in the leading place among all pathologies of the thyroid gland according to the prevalence in the population.
Purpose
At present, the mentioned pathology is considered to be the most important. But, nevertheless, its diagnostics and study of concomitant diseases still cause some problems. If not revealed in proper time latent hypothyroidism may produce a number of grave conditions. Our aim is concentrated on estimating the lipid and hormonal profile of women ill with latent hypothyroidism, preventing its transition to manifested hypothyroidism, and stopping the development of various diseases.
Material and methods
We divided according to the degree of the thyroid-stimulating hormone of examined women. In our examination, 100 women took part from 17 years to 66 years. We divided all patients 3 groups according to the amount of thyroid-stimulating hormone:
Result
According to our investigations, the lipid profile of patients ill with subclinical hypothyroidism have been examined. The studies showed that general cholesterol, lipoproteins with low density, triglycerides have been considerably increased in the first and second groups. It consists of 32 patients.
Conclusion
In patients with an amount of TG of more than 4 mU/l the level of general cholesterol, triglycerides, lipoproteins with low density (LLD) have been found in quantities, whereas the level of lipoproteins with high density (LHD) was considerably lower. It has been determined that in patients who haven't reached the age of 66 the risk of acquiring ischemic heart disease is high as a result of subclinical hypothyroidism.

DOI: 10.1530/endoabs.81.EP1139

EP1140

Sonographic features of autoimmune thyroiditis - a clinical perspective

Samantha Anandappa & Anand Velusamy
Guy's and St Thomas' NHS Foundation Trust, Endocrinology, London, United Kingdom

Autoimmune Hypothyroidism is a common clinical condition with a suggested prevalence of up to 12% of the population. The subsequent enlargement of the thyroid gland caused by circulating thyroid antibodies can cause neck discomfort warranting a referral to the thyroid ultrasound (USG) clinic. The USG characteristics of autoimmune hypothyroidism can be challenging to grade and the atypical appearances often makes it difficult to exclude a mitotic lesion. We have set forward few recommendations and clinical perspectives to overcome some of these challenges and minimise misdiagnosis.
Case 1
30 yrs F with established Hashimoto's on Levothyroxine and under the care of Rheumatology for suspected mixed connective tissue disease. Thyroid USG performed for neck discomfort demonstrated markedly hypoechoic 2x2x4 cm nodule with an ill-defined border containing considerable punctate microcalcifications **(U5).** Several bulky lymph nodes were also noted in levels III and IV but with normal morphology. Subsequent FNA was reported to be in keeping with **THY5** and the patient underwent total thyroidectomy. The biopsy was then

reported as benign in keeping with nodular Hashimoto's thyroiditis with oncocytic metaplasia.
Case 2
52 yrs F with previous history of thyroidectomy for Hashimoto's thyroiditis and IgG4 disease on a background of other autoimmune diseases such as Raynauds and fibromyalgia. After presenting with dysphagia underwent USG assessment which identified an incidental hypoechoic vascular lesion (7x5mm) at the left thyroidectomy bed (U3). FNA demonstrated lymphoid cell infiltrate consistent with Hashimoto thyroiditis.
Case 3
33 yrs F presented after noticing a new neck lump. USG assessment demonstrated both the thyroid lobes to be heterogeneous, slightly hypoechoic with fibrous stranding and patchy areas of increased vascularity in keeping with underlying thyroiditis. In the right lobe, 1.5 x 1.5 x 1.3 cm heterogeneous predominantly hypoechoic, ill-defined nodule with areas of macro- as well as micro-calcifications were noted. The nodule seemed to invade into the overlying strap muscle in the anterior aspect. There was profound peripheral and internal vascularity **(U5).** Suspicious looking bulky lymph nodes were noted at levels 3 and 4 with mixed vascularity. Thyroid antibodies were elevated; FNA consistent with lymphocytic thyroiditis and a reactive lymph node. These cases highlight the potential setbacks and misdiagnosis of thyroid pathology if an underlying disease process is not appropriately investigated. We would recommend a clinician's interpretation of the sonographic findings along with the routine measurement of thyroid function and thyroid antibodies and an MDM referral as appropriate.

DOI: 10.1530/endoabs.81.EP1140

EP1141

Evaluation of calcitonin measurment in fine needle aspitaion biopsy in the diagnostic of medullary thyroid carcinoma

Khelil Nour El Houda[1] & Meskine Djamila[2]
[1]Tlemcen Faculty Of Medicine, Departement of Endocrinology - Tlemcen Hospital, Tlemcen, Algeria; [2]Algiers Faculty Of Medicine, Algiers, Algeria

Medullary thyroid carcinoma (MTC) is a rare but relatively serious disease, whose prognosis depends on the stage of the tumor and the quality of the initial surgical treatment. The determination of the plasma calcitonin; cervical ultrasound, and fine needle aspiration biopsy are first line examinations; nevertheless they do not always make it possible to make a certain diagnosis in preoperative; moreover they do not define the MTC nodule in a multi nodular goiter and the metastatic lymph nodes. In this study; fine needle aspiration (FNA) and CT FNA were performed in 45 lesions. By comparing the results to histology; the sensitivity of the FNA for the diagnosis is estimated at 53.12% and the specificity at 92.30% while the sensitivity of the CT FNA is 96.87% and the specificity is 100% and this for a cut off >22.99 pg/ml. These results suggest that CT FNA; a simple; accessible and inexpensive exam; represents an interesting diagnostic approach that provides an additional argument for the positive and topographic diagnosis of MTC.

DOI: 10.1530/endoabs.81.EP1141

EP1142

Application of TI-RADS and BETHESDA classification in the diagnosis of thyroid cancer

Mohina Salimova, Said Ismailov & Zulaykho Shamansurova
Tashkent Pediatric Medical Institute, Endocrinology, Tashkent, Uzbekistan

Introduction
Malignant tumors of the thyroid gland are common in the field of endocrinology as an oncological disease. The diagnosis of thyroid cancer (TC) is based on sonographic and cytological methods. The widespread use of TI-RADS classification and the Bethesda System for Reporting Thyroid Cytopathology proposed by the American College of Radiology (ACR) and the U.S. National Cancer Institute (NCI) relatively significantly increases diagnostic accuracy. In this study diagnostic value of TI-RADS and Bethesda System for early detection of TC were assessed.
Material and methods
In 90 patients record cards who were admitted to surgery in Republican Specialized Scientific Practical Medical Centre Endocrinology ($n=$ 60) and Vitamed Clinic ($n=$ 30) with TC diagnosis during 2018-2021 years were analyzed. Patients were divided into two groups: Group 1 – TC were diagnosed by using TI-RADS and Bethesda and Group 2 - TC diagnosis performed based on traditional way. All patients underwent preoperative and postoperative follow-up, with determination of serum level of TSH, free T4, TG, Anti-TG, Anti-TPO, CEA titers. The results of US, fine needle aspiration biopsy (FNAB), express histology, and final histological examination were analyzed and compared between groups.
Results
The mean age of patients were 39.64 ± 1.4 years. TC diagnosed were in 6.5 times frequently in women than in men. The results of clinical and biochemical data of blood count did not differ in TC patients from healthy subject. In group 1, results of the study on modern classifications by the method of US and FNAB were matched in 80% of cases and TC was confirmed. However, in group 2, by traditional method TC confirmed only in 23%. In Group 1 the FNAB results in 83% were matched with after surgery histology. Whereas in group 2, the result was matched in 78.6% of cases. Moreover, In group 1, after surgery histology 100% corresponds to the final histological conclusion. While in group 2, the figure was 95%.
Conclusion
TC is mainly diagnosed in middle-aged patients. and was frequent in women than in men. Using Bethesda classification and TI-RADS were more informative and corresponds with FNAB results in 80% and 100% with after surgery histology, whereas with traditional way FNAB were matched only in 23% of cases and in 95% with final histology.

DOI: 10.1530/endoabs.81.EP1142

EP1143

Hurthle cell carcinoma of the thyroid gland: diagnostic, therapeutic and prognostic features

Mohamed Masmoudi, Wadii Thabet, Chaima Zitouni, Ezer Chebil, Mehdi Hasnaoui & Khalifa Mighri
Tahar Sfar Hospital, Mahdia, Otorhinolaryngology, Tunisia

Introduction
Oncocytic tumors of the thyroid gland are rare (3-10 %). They are usually benign. Hurthle cell (oncocytic) carcinoma is uncommon: 5 % of thyroid carcinomas. Our aim is to describe the diagnostic, therapeutic and prognostic features of Hurthle cell carcinomas.
Materials and Methods
We report 3 cases of Hurthle cell carcinoma treated in our department between 1988 and 2021.
Results
Our series included 35 cases of oncocytic tumors. Hurthle cell carcinoma was noted in 3 cases. The mean age was 50 years [35 – 67 years]. All patients consulted for anterior neck mass with compressive symptoms. Ultrasonography showed a unique thyroid nodule in all cases: EUTIRADS 4 in 2 cases and EUTIRADS 5 in one case. The mean size was 4,1 cm. Thyroid-stimulating hormone (TSH) serum level was normal in all cases. Fine needle aspiration (FNA) result was "nondiagnostic" in all cases. Surgical treatment consisted of a thyroid lobectomy in all cases. The intraoperative examination was benign in all cases. The postoperative histological examination confirmed the diagnosis of Hurthle cell carcinoma; it was associated with papillary microcarcinoma in 1 case. All patients underwent totalization of the thyroidectomy with unilateral central neck dissection. No lymph node or distant metastases were noted. A complement by radioactive iodine was indicated in all cases. The evolution was favorable in all cases after a mean follow-up of 6.5 years.
Conclusion
The benignity or malignancy of oncocytic tumors cannot be confirmed by cytology. The diagnosis of malignant oncocytic tumor is usually made on postoperative histological exam. Surgery is the mainstay of treatment of Hurthle cell carcinomas. Responses to treatment with radioactive iodine are much lower when compared to other types of thyroid carcinomas. Hurthle cell carcinomas are more aggressive.

DOI: 10.1530/endoabs.81.EP1143

EP1144

Thyroid cancer arising from thyroglossal duct cyst: What are the therapeutic strategies?

Mohamed Masmoudi, Wadii Thabet, Chaima Zitouni, Ezer Chebil, Mehdi Hasnaoui & Khalifa Mighri
Tahar Sfar Hospital, Mahdia, Otorhinolaryngology, Tunisia

Introduction
Thyroglossal duct cysts are the most common congenital cervical anomaly. Malignant transformation is very uncommon: 1-1.5%. However, therapeutic strategy is still not codified. Our aim is to describe the therapeutic features of thyroid cancer arising from thyroglossal duct cyst.
Materials and Methods
We report 3 cases of thyroid cancer arising from thyroglossal duct cyst, treated in our department between 1996 and 2021.
Results
Two men and one woman were included. The mean age was 17 years. The mean size of the cervical swelling was 36 mm. The treatment consisted of excision of the thyroglossal duct according to the Sistrunk procedure in the 3 cases. The diagnosis of malignancy was made on intraoperative examination in one case and on postoperative histologic exam in 2 cases. The histologic type was papillary carcinoma in all cases. Total thyroidectomy and radioactive Iodine were performed in all cases and bilateral central neck dissection was associated in two cases. The evolution was favorable in all 3 cases after a mean follow-up of 30 months.
Conclusion
The therapeutic management of thyroid cancer arising from thyroglossal duct cyst remains a subject of debate regarding the need for thyroidectomy and radioactive iodine. According to several authors, carcinoma can develop de novo within the thyroglossal duct, while others believe that the thyroglossal duct may be a natural route for the spread of carcinoma from the thyroid gland.

DOI: 10.1530/endoabs.81.EP1144

EP1145

Thyroid ultrasound characteristics in malignancy prediction

Valentina Velkoska Nakova
Clinical Hospital, Faculty of Medical Science, University Goce Delcev, Internal Medicine, Stip, Macedonia

Objective
To evaluate the diagnostic accuracy of thyroid ultrasound characteristics of nodules in prediction of malignancy.
Material and methods
Retrospectively were analyzed 102 patients who underwent for FNA biopsy of thyroid nodule. All patients were examined by one ultrasound examiner. Size, taller than wide, echogenicity, borders, halo, calcification, and internal vascularity were recorded in all examined nodules. The Bethesda System for Reporting Thyroid Cytology was used in all cytological diagnoses.
Results
Out of the 102 patients, 88 (86.3%) were females. The mean age was 58.7 ± 14 years. The study included 14 malignant and 88 benign nodules. Size, microcalcification and internal vascularization showed statistically significant positive associations with thyroid malignancy ($P < 0.05$). The highest OR was found for the microcalcification (22.5 95% CI 4,48-112,78). The sensitivity and specificity of ultrasound characteristics in predicting malignancy were: size 66.76% (95% CI 34.89 – 90.08%) and 70.45% (95% CI 59.78 - 79.71%); microcalcification 83.33% (95% CI 51.59 -97.91%) and 81.82 (95% CI 72.16 – 89.24%); and internal vascularization 66.67% (95% CI 34.89 – 90.08%) and 68.18 (95% CI 57.39 – 77.71%), retrospectively. Each ultrasound characteristic had negative predictive value from 93 - 97% in malignant nodules.
Conclusion
The presence of microcalcification was found the most important criteria in prediction of thyroid malignancy.

DOI: 10.1530/endoabs.81.EP1145

EP1146

Papillary carcinoma of the thyroid associated with Marine-Lenarth syndrome: about a case

Amira Bouchenna[1], Abdelghani Tibouk[2], Ghennam Brahim[3] & Ould Kablia Samia[1]
[1]Central Hospital of Army, Endocrinology, Algeria; [2]Central Hospital of Army, Anatomopathology, Algeria; [3]Central Hospital of Army, Nucleary, Algeria

Introduction
The Marine-Lenhart syndrome (MLS) is commonly defined as a combination of Graves' disease and autonomous functioning thyroid nodule (s). the risk of malignancy of these nodules is less than 1% We report a case.
Observation
27-year-old patient, hospitalized for treatment of a basal disease, cervical ultrasound found a 1.5 cm lower left lobe thyroid nodule classified eutirads 4. the sintigraphy found an aspect of diffuse hypercaptive goiter, TSI rate at 18 ui/l, confirming the SML. fine needle aspiration of the nodule is suspected of malignancy. a total thyroidectomy is performed after preparation with lugol. anatomo-pathological examination found a papillary carcinoma of the thyroid of 1.5 cm classified PT1bNxMx supplemented by iratherapy of 30mci
Discussion
MLS can affect up to 4% of Graves' disease cases. Since the reported incidence of malignancy in all cold nodules is about 1%, it's recommend to practice ultrasound and FNAC before treatments.

DOI: 10.1530/endoabs.81.EP1146

EP1147

Papillary thyroid carcinoma in its cystic form: a case report

Kamel Farah, Loubna Guissi, Kaoutar Rifai, Hinde Iraqi & Mohammed Hassane Gharbi
Ibn Sina University Hospital, Endocrinology and Metabolic Diseases, Rabat, Morocco

Introduction
The cystic nodule is an unusual presentation of papillary thyroid carcinoma (PTC), seen in less than 10% of cases. Ultrasound discovery of a thyroid cyst represents less than 5% risk of malignancy. We report the case of a patient followed for papillary thyroid carcinoma in its cystic form.
Observation
A 42-year-old patient with no specific history. The patient underwent a right isthmolobectomy for a thyroid nodule. Anatomopathological examination of the surgical specimen revealed a thyroid cyst with endocystic vegetations of papillary appearance, totally necrotic, in favour of a papillary carcinoma in its cystic variant. Then the patient underwent a left totalization with benign histology. The postoperative course was simple. This tumor is classified as PT1aNxMx with low risk of recurrence. The patient benefited from TSH- suppressive Levothyroxine therapy, with good clinical and biological evolution.
Discussion
The malignant potential of cystic thyroid nodules should never be neglected, even if it carries a low risk of malignancy. The diagnosis of PTC in its cystic form relies primarily on typical nuclear features, however, in case of histologic uncertainty, immunohistochemical stains such as HBME-1 can be used to help classify unusual presentations of PTC. Treatment and monitoring of cystic PTC follows the conventional guideline for solid PTC.
Conclusion
Papillary thyroid carcinoma in its cystic form is rare. Our case illustrates the importance of the management of cystic thyroid nodules with an adapted follow-up in order not to ignore a malignant etiology such as papillary thyroid carcinoma.

DOI: 10.1530/endoabs.81.EP1147

EP1148

Metastasis of breast cancer in the thyroid gland: Report of two cases

Mehdi Ferjaoui, Emna Bergaoui, Maroua Naouar, Amel Elkorbi, Rachida Bouattay, Kaled Harrathi, Naourez Kolsi & Jamel Koubaa
Hôpital Fattouma Bourguiba, ENT, Monastir, Tunisia

Introduction
Breast cancer is the most frequently diagnosed cancer in women. Common sites of metastatic spread are bone, lungs and liver. Metastases to the thyroid gland are exceptional.
Objectives
The aim of the study is to document two rare cases of thyroid metastasis from breast carcinoma and to specify their clinical, radiological and therapeutic particularities.
Methods
Review of 2 clinical cases of thyroid gland metastasis identified in women with no known breast carcinoma.
Case1
73-year-old patient with a history of chronic renal failure, was referred to our department for an anterior cervical tumefaction evolving for 8 months. The physical examination showed a lower anterior cervical swelling. Cervical ultrasound showed a 3 cm calcified left thyroid nodule. The patient underwent a left lobo-isthmectomy. The final pathology with immunohistochemical studies revealed an intrathyroidal metastasis from an infiltrating ductal carcinoma of the breast. The patient was therefore referred to her gynaecologist and the primary breast origin was confirmed. The evolution was good with a follow-up of 24 months.
Case2
The second case was a 70-year-old woman with no pathologic history, admitted for the management of high dyspnea and progressive dysphonia for 2 months. On examination, she presented a hard lower cervical swelling with a non-palpable lower border, without cervical adenopathy. Laryngoscopy showed a fixity of the left vocal cord. Cervical ultrasound and scan confirmed the thyroid origin of this mass by showing a plunging calcified lower left nodule. Fine needle aspiration, suggested a follicular thyroid carcinoma. The treatment was surgical. The patient underwent a total thyroidectomy with bilateral dissection of sectors VI and a tracheotomy for her dyspnea. The histological examination revealed an intrathyroidal metastasis of a poorly differentiated carcinoma of the breast. The patient was then lost sight of.
Conclusion
Intra thyroid metastases, although rare, should be considered in any patient, especially females. Rarely observed in clinical practice, they often pose a diagnostic and therapeutic challenge.

DOI: 10.1530/endoabs.81.EP1148

EP1149

A female patient with diffuse sclerosing variant of papillary thyroid cancer and background autoimmune thyroiditis

Zoi Efstathiadou[1], Athanasia Michou[1], Efstathios Divaris[1], Apostolos Gogakos[1], Athanasios Panagiotou[1], Prodromos Hytiroglou[2] & Marina Kita[1]
[1]"Hippokration" General Hospital of Thessaloniki, Department of Endocrinology, Thessaloniki,; [2]Aristotle University of Thessaloniki School of Medicine, Department of Pathology

Introduction
Diffuse sclerosing variant of papillary thyroid carcinoma (DSPC) represents a rare but rather more aggressive subtype of PTC.
Purpose
Description of a patient with DSPC and background autoimmune thyroiditis.
Case description
A 33-year-old female patient reported extensive neck swelling that had progressed over several months. The patient had been diagnosed with hypothyroidism attributed to autoimmune thyroiditis, 3 years before. At that time, goiter was also found with a reported predominant nodule in the right lobe. On examination, the patient was euthyroid, with a palpable enlargement of the right lobe and isthmus, with particularly hard texture. Ultrasound imaging revealed diffuse enlargement of the thyroid gland particularly of the right lobe, where a formation of a suspicious mass was noted. Linear hyperechogenic foci were dispersed throughout the entire thyroid surface. Hypoechogenic areas with ill-defined borders were noted centrally, possibly representing lymph nodes. A fine-needle aspiration biopsy of the right lobe was positive for papillary thyroid cancer and the patient underwent total thyroidectomy. Histopathology showed a 2.4 cm papillary carcinoma of the right lobe, with psammomatus bodies, squamous metaplasia, and background sclerosis. Vascular infiltration by the tumor cells was present. The remaining thyroid parenchyma exhibited extensive lymphocytic and plasmatocytic infiltrates with abundant lymphoblastic centers. Dispersed foci of the neoplasm were observed in all sections of the entire gland. Metastases were recognized in 3 excised central lymph nodes. A few weeks later the patient underwent a completion surgery with central and right lateral compartment exploration, with metastases found in 13/24 and 4/30 lymph nodes, respectively.
Conclusions
The imaging characteristics and the overlapping presence of Hashimoto's thyroiditis can lead to a delayed diagnosis of DSPC. Considering the more aggressive nature of this variant, raising awareness for early recognition of its particular ultrasonographic characteristics is of paramount importance for effective treatment and improved prognosis.

DOI: 10.1530/endoabs.81.EP1149

EP1150

Ectopic cushing's syndrome : a rare cause

Eirini Vourlioaki, Paraskevi Floroskoufi, Aspasia Kouloukoura, Eleftheria Argyropoulou & Aikaterini Stamataki
Venizeleio General Hospital of Heraklio, Endocrinology Department, Heraklio, Crete, Greece

Introduction
Medullary thyroid carcinoma (MTC) accounts for 1-5% of all thyroid cancers. It is a neuroendocrine tumor arising from the calcitonin-secreting parafollicular cells of the thyroid. In rare cases, the neoplastic cells additionally secrete other substances, such as histamine, serotonin, ACTH, CRF etc, leading to paraneoplastic syndromes.
Case report
An 80 year old male presented to our Department with an already diagnosed metastatic MTC. Three years ago he had undergone a total thyroidectomy together with a right cervical lymph node dissection. His pre- and post-thyroidectomy calcitonin measurements were 2900 and 400pg/ml, respectively.
Past medical history
Rheumatoid arthritis At his present visit, he was in good clinical condition. Calcitonin and CEA were measured 3640pg/ml and 123ng/ml, respectively. Whole body imaging revealed metastatic lymph nodes on the right cervical area and the upper mediastinum, as well as multiple secondary liver lesions, larger than those shown in last imaging. Because of disease progression, the patient was commenced on Vandetanib (Tyrosine Kinase Inhibitor, TKI) 300 mg/d. One month later, he presented with an itchy maculopapular, exanthema, starting from face and upper extremities and extending rapidly to almost the whole body, with local exfoliation and inflamation and was barely tolerated by the patient. Antibiotics, antihistamines and local and systematic corticosteroids were administered, with almost no improvement. Vandetanib had to be discontinued for four months, during which the exanthema subsided to a great extent, while, concomittantly, melanchrosis appeared on the upper extremities and then almost everywhere on the body. In addition, the patient complained about proximal weakness and had oedema on lower extremities. Imaging and blood tests showed disease progression. There was suspicion of hypercortisolism which was confirmed by relevant tests and led to diagnosis of ECS. The patient was then administered Metopyrone 250 mg bid and Cabozatinib 40 mg/, which is a different TKI. Six months later, the patient is in good clinical condition, with almost no symptoms. Imaging and biochemical tests show stabilization of the disease.
Conclusion
At most 0,7% of patients with MTC are reported to develop ECS. MTC represents 2,2-7,5% of all causes of ECS. ECS rises morbidity and mortality of MTC, due to consequences of hypercortisolism. TKIs are considered as the first-line therapy for ECS in the setting of unresectable or progressive MTC.

DOI: 10.1530/endoabs.81.EP1150

EP1151

Papillary thyroglossal duct carcinoma: report of two cases

Mehdi Ferjaoui, Emna Bergaoui, Maroua Naouar, Amel Elkorbi, Rachida Bouattay, Kaled Harrathi, Naourez Kolsi & Jamel Koubaa
Fattouma Bourguiba Hospital, ENT, Monastir, Tunisia

Introduction
The thyroglossal duct cyst is frequently diagnosed in front of an anterior cervical swelling. Its degeneration is possible and observed in 1% to 2% of cases. The clinical feature is not specific, and the diagnosis of malignancy is most often established on final histological examination.
Purpose of review
The purpose of this paper is to review the presentation of thyroglossal duct carcinoma and discuss the clinical and therapeutic particularities.
Methods
Two cases of papillary carcinoma developed on a thyroglossal duct were identified over a period of 12 years (2010-2021).
Results
A man and a woman with no pathological history, aged 44 and 27 years old, consulted for upper cervical swelling evolving for 5 months and 3 years. The physical examination found an add-hyoid swelling of four cm and two cm, mobile on the protraction of the tongue. Cervical ultrasound suggested the degeneration in one case. The Sistrunk operation was performed associated with total thyroidectomy at the same time in a single case where the extemporaneous examination suggested malignancy. The histological study confirmed a papillary carcinoma developed on a thyroglossal duct in both cases. The other patient therefore underwent a thyroidectomy in a second time. Both patients were put on frenetic hormone therapy. Additional Iodine radiation therapy was indicated in both cases. With a follow-up of 12 months no one showed recurrence.
Conclusion
Malignancy on thyroglossal duct cyst is a rare situation. Papillary carcinoma is the most common cancer. The treatment remains a subject of debate, even if, currently, most authors recommend associating a total thyroidectomy with the Sistrunk procedure.

DOI: 10.1530/endoabs.81.EP1151

EP1152

Cholestatic jaundice: think of thyrotoxic hepatitis

Kaoutar Rifai, Loubna Guissi, Salma Ahallat, Hind Iraqi & Mohamed Elhassan Gharbi
Ibn Sina University Hospital, Endocrinology, Rabat, Morocco

Introduction
Liver dysfunction during hyperthyroidism may be secondary to thyrotoxicosis, to an associated liver pathology, or to the medical treatment of hyperthyroidism posing a problem of etiological diagnosis. In this context, we report a demonstrative observation.
Case presentation
We report the observation of a 23-year-old female patient, followed for Basedow disease under carbimazole since 1 year, not controlled under medical treatment. During her follow-up, she presented cholestatic jaundice, associated with significant cytolysis and biological cholestasis, which persisted despite the discontinuation of synthetic antithyroid drugs. Biliary tract obstruction, viral or autoimmune hepatitis, and primary biliary cirrhosis were excluded. Liver biopsy showed lymphocytic infiltrate with discrete hepatic steatosis without stigma of autoimmune or toxic hepatitis. Our patient was treated only with Iodine 131. The post-iratherapy evolution was marked by the achievement of clinical and biological euthyroidism with normalization of the hepatic balance. This constitutes a major argument in favor of the thyrotoxic origin of this hepatopathy.
Discussion
Jaundice, during uncomplicated thyrotoxicosis, is rare and moderate (5-11%). Its exact etiopathogenesis remains poorly elucidated. An increased hepatic oxygen consumption due to hypermetabolic state not compensated by an increase in hepatic blood flow has been suggested. This imbalance leads to a decrease in oxygen tension in the centrilobular areas, which may lead to hepatocyte dysfunction with cholestasis. On anatomopathological examination, lymphocytic infiltrate in portal spaces, vacuolation and more rarely hepatic steatosis and intrahepatic cholestasis are often described, which was found in our patient.
Conclusion
Hyperthyroidism is an unusual cause of cholestatic jaundice that should be evoked in the absence of underlying liver disease.

DOI: 10.1530/endoabs.81.EP1152

EP1153

Role of plasmapheresis in the management of severe amiodarone-induced hyperthyroidism refractory to conventional medical treatment

Belén García Izquierdo[1], Macarena Contreras Angulo[2], Laura Armengod Grao[2], Carlos García Gómez[2], Álvaro García García[3], Azucena Losa Maroto[3], José Luis Bueno Cabrera[3], Miguel Juan García-Oria Serrano[4], Encarnació n Donoso[5] & Pedro Iglesias[2]
[1]Hospital Universitario Puerta de Hierro Majadahonda, Endocrinology and Nutrition, Majadahonda, Spain; [2]Hospital Universitario Puerta de Hierro Majadahonda, Endocrinology and Nutrition, Madrid, Spain; [3]Hospital Universitario Puerta de Hierro Majadahonda, Hematology, Madrid, Spain; [4]Hospital Universitario Puerta de Hierro Majadahonda, General and Digestive Surgery, Madrid, Spain; [5]Hospital Universitario Puerta de Hierro Majadahonda, Biochemistry, Madrid, Spain

Introduction
Amiodarone is an antiarrhythmic drug whose high iodine content may influence thyroid function. The first line treatment of amiodarone-induced hyperthyroidism (AIH) is mainly medical. Plasmapheresis has been used in cases of antithyroid intolerance or refractory hyperthyroidism, although clinical experience is poor.
Clinical case
We present a case of a patient with structural heart disease and severe AIH refractory to medical treatment who required a high number of plasmapheresis cycles to achieve adequate control of thyroid function before definitive treatment. A 53-year-old man, with atrial fibrillation treated with amiodarone (200 mg/day) for 3 years until 2 months prior to admission, was hospitalized due to chest pain. Echocardiography showed an atrial septal defect, with indication for non-urgent surgical closure. During admission, severe hyperthyroidism was discovered (TSH <0.01 µIU/ml, normal range (NR): 0.35-5.0; free T4 (FT4) 10.03 ng/dl, NR: 0.7-1.98; and free T3 (FT3) 9.3 pg/ml, NR: 2.3-4.2). A grade 2 diffuse goiter was palpable. Thyroid autoimmunity study was negative. Suspecting AIH, medical treatment with antithyroid drugs and corticosteroids was started. The difficulty in controlling thyroid function led to an increase in treatment up to 45 mg/day of methimazole, prednisone (90 mg/day), cholestyramine (16 g/day) and of potassium perchlorate (800 mg/day). After 3 weeks, hyperthyroidism persisted (TSH $<$ 0.01 µIU/ml, FT4 11.92 ng/dl and FT3 9.76 pg/ml), establishing the diagnosis of severe AIH refractory to medical treatment; therefore, total thyroidectomy was considered. In order to reduce the perioperative cardiovascular risk, treatment with plasmapheresis was started. As complications, he presented several episodes of skin rash, a slight tendency to anemization (hemoglobin nadir 11.2 g/dl, NR: 12.0-17.0) and asymptomatic hypocalcemia with a minimum value of 7.6 mg/dl (NR: 8.7-10.3 mg/dl). After 17 sessions of plasmapheresis, a reduction in circulating levels of thyroid hormones was achieved (TSH 0.01 µIU/ml, FT4 4.33 ng/dl and FT3 4.95 pg/ml), which allowed definitive treatment with surgery 40 days after diagnosis.
Conclusion
Plasmapheresis in association with medical treatment is a useful tool in the management of severe AIH refractory to conventional therapy with maximal doses in preparation for definitive treatment with thyroid surgery.

DOI: 10.1530/endoabs.81.EP1153

EP1154

Stop oral therapy and start later: This is a new perspective for hypothyroid patients who need lifelong intravenous levothyroxine

Zafer Pekkolay
Dicle University Faculty of Medicine, Endocrinology, Diyarbakir, Turkey

Introduction
Although the replacement route is oral in most hypothyroid patients, euthyroidism cannot be achieved with oral therapy in some patients rarely (1). Although oral levothyroxine is used above the standard dose (1.6-1.9 mg/kg/day), there is resistance to oral therapy if there are laboratory and clinical signs of hypothyroidism (2). Crushing the drug and using it with vitamin C increases the absorption of levothyroxine (3). Rarely, some patients require lifelong intravenous levothyroxine.
Case report
Total thyroidectomy was performed in a 60-year-old female patient in 2014, after thyroid nodule FNAB result was found to have AUS. Its pathology was reported as medullary thyroid cancer. Despite increasing oral doses of levothyroxine after surgery, the patient with severe hypothyroidism had a negative pseudomalabsorption test, a negative celiac panel, and a negative Helicobacter pylori antigen. Although the patient was given high doses of levothyroxine and lioiodotroin, his hypothyroidism did not improve. Combining levothyroxine with vitamin C/acid

drinks and crushing the levothyroxine tablet did not ameliorate hypothyroidism. Euthyroidism was achieved with intravenous levothyroxine 200 mg/session three times a week (Table 1). Due to a change in our healthcare system, the patient could not receive intravenous treatment for about two months. The patient drank 450 micrograms of levothyroxine to overcome this problem by dissolving it in tap water. The patient's thyroid function tests, who came to the outpatient clinic in the first month of this treatment, were euthyroid. Euthyroidism was observed again in the patient who used the treatment he received for one more month (Table 2).

Table 1 Patient's history summary

Age (year), Gender	*60, Female*
Hypothyroidism etiology	*Medullary Thyroid Cancer*
Duration of hypothyroidism (year)	*7*
Levothyroxine dose	*600 mg/week/intravenous*
Pseudomalabsorption	*Negative*
Celiac panel	*Negative*
Helicobacter pylori antigen	*Negative*
LT4 + LT3	*No-response*
LT4 intake with vitamin C/sodas	*No-response*

Table 2 Oral levothyroxine only (450 mcg/day)

	1st month of treatment	2nd month of treatment
TSH (mU/l) (0,27-4,2)	**0,7**	**0,88**
Free T3(ng/dL) (0,93-1,7)	**0,8**	**1,0**
Free T4(pg/mL) (2,0-4,4)	**1,8**	**2,0**

Comment and new perspective:
The patient, who needed a total of 600 mg intravenous per week for seven years, switched to oral therapy because intravenous therapy could not be performed. Clinical response was obtained from the patient. In patients who do not respond to oral therapy in the first period, oral therapy can be tried later. This may indicate that intestinal levothyroxine absorption may increase after oral levothyroxine absorption is not taken for a while.
Keywords refractory hypothyroidism, switching, levothyroxine

DOI: 10.1530/endoabs.81.EP1154

EP1155

Refractory hypothyroidism and chronic gastritis

Mohamed Malad, Errahali Yassine, Malak Riznat & Guerboub Ahmed Anas
Mohamed V Military Training Hospital, Endocrinologie, Rabat, Morocco

Introduction
Refractory hypothyroidism is a fairly common situation in the practice of any endocrinologist, being defined by the persistence of hypothyroidism despite adequate doses of replacement therapy with Levothyroxine, generally supraphysiological. We report the case of refractory hypothyroidism under high doses of Levothyroxine.
Observation
she was a 54-year-old woman, diabetic Type2, followed for 06 years for papillary carcinoma of the thyroid gland, for which it was operated and irradiated, currently in clinical, biological and morphological remission. she was already under 325 µg/day of levothyroxine taken orally, or 4 µg/kg/day, for a target of TSH between 0.1 and 0.5, by the way as a TSH suppressant treatment. The patient recognizes having a regular pace of taking his medication without omission or errors related to the schedule of her medication. On examination, she shows symptoms of hypothyroidism, asthenia and pallor, with infiltration of the face and integuments. Biology revealed a TSH = 30 IU/ml, and FT4 at 0.58ng/dL (usual values between 0.7 and 1.5). An oral thyroid hormone absorption test was performed, at a dose of 1000 µg in a single dose on an empty stomach, under strict medical supervision. The FT4 assay was performed at times 0, 1h, 2h, 3h, and at 24h after intake. The results showed the absence of elevation of FT4, which is in favor of malabsorption. After elimination of the obvious causes, a malabsorption assessment was requested and returned without anomalies: the total cholesterol level at 1.8 g/l, ferretinemia at 77 mg/l, calcium phosphorus and vitamins B9 and B12 normal. A serology of celiac disease, anti-parietal antibodies, and digestive fibroscopy were requested. This finally led to the diagnosis of autoimmune gastritis, considered the cause of the malabsorption of levothyroxin. The patient was put under levothyroxine in the form of soft capsules and has marked a good evolution.
Conclusion
Our observation illustrates the interest of the thyroid hormone absorption test, a key examination to distinguish between true malabsorption and pseudo-malabsorption. This load test must lead to an etiological assessment in search of an organic cause for the malabsorption.

DOI: 10.1530/endoabs.81.EP1155

EP1156

Low testosterone: An unexpected journey

Jessica Lee[1], Edel Casey[1], Anna Hawkins[1], Antony Pittathankal[1, 2], Raj Tanday[1], Syed Imran[2], Gideon Mlawa[3] & Khash Nikookam[1,2]
[1]King George Hospital, United Kingdom; [2]Spire London East Hospital (Formerly Spire Roding Hospital), Ilford, United Kingdom; [3]Queen's Hospital, United Kingdom

A 68 year old gentleman referred to endocrinology clinic with a few years history of erectile dysfunction (ED), which manifested as reduced libido and partial erections. Investigations revealed primary hypogonadism with a low morning serum Testosterone of 4.8 (Ref: 7.9-31 nmol/l), raised FSH at 47 (Ref:1.5-12.4 iu/l) LH at 36.8 (Ref: 1.7-8.6iu/l) and normal thyroid function tests (TFTs). The patient declined testosterone replacement therapy following a discussion of pros and cons of the risk vs benefit. Clinical examination revealed a deep seated right thyroid lobe and also a possible right thyroid nodule. Ultrasound (US) thyroid showed a right U3 nodule of 6.3x4.1mm. Subsequent cytology following US guided Fine Needle Aspiration (FNA) of the right U3 nodule revealed Thy3f. According to the Royal College of Pathologists [1] Thy3f suggest follicular neoplasms whose characteristics are difficult to distinguish between benign or malignant nature. The Royal college of pathologists also states that the malignant potential of Thy3f nodules to be approximately 15-30% [1]. The options of surgery vs monitoring by means of US guided FNA of the thyroid nodule were discussed. Patient opted for the latter option, repeat Cytology showed Thy1 (non-diagnostic). In view of all of the above and the recommendation from the British Thyroid Association guidelines, patient elected for right hemithyroidectomy [2]. The histology revealed the presence of variable size thyroid follicles containing colloid material and no evidence of malignancy. Patient had an uneventful post-operative recovery, and subsequent examination showed a well healed post thyroidectomy scar.
Conclusion
While modern clinical practice tends to lean towards investigations and imaging to guide clinical management, a good history, thorough examination and patient engagement should always be at the cornerstone of every consultation. This in turn can lead to improved patient care and outcome.
References
1. The Royal College of Pathologists: Guidance on the reporting of thyroid cytology specimens. (2016). Accessed: February 02, 2022: https://www.rcpath.org/uploads/assets/7d693ce4-0091-4621-97f79e2a0d1034d6/g089_guidance_on_reporting_of_thyroid_cytology_specimens.pdf Perros, P. *et al* (2014) British Thyroid Association Guidelines for the Management of Thyroid Cancer. Clinical Endocrinology, 81 (Suppl. 1), 1-122

DOI: 10.1530/endoabs.81.EP1156

EP1157

From benign cytology to papillary thyroid carcinoma

Yasmin Nikookam[1], Bonnie Grant[1], Usman Shah[1], Gideon Mlawa[1], Anna Hawkins[1], Edel Casey[1], Antony Pittathankal[1, 2], Imran Syed[2] & Khash Nikookam[1,2]
[1]Barking, Havering and Redbridge University Hospitals NHS Trust, Greater London, United Kingdom; [2]Spire London East Hospital, Greater London, United Kingdom

Thyroid cancer is the most common endocrine malignancy with an increasing incidence globally predominantly due to the papillary thyroid carcinoma subtype. It is the 17th and 20th most common malignancy in females and males respectively. In 2018, Cancer Research UK reported 3865 new cases and 400 deaths. Mortality rates are predicted to continue to rise in the UK with an estimated rate of 1 per 100,000 deaths in 2035. We present a 42-year-old female

who presented with a 3-year history of lethargy, tiredness, poor concentration and hair loss. She had a history of iron deficiency anaemia previously requiring iron transfusions. On clinical examination and neck palpation rather tender and prominent thyroid isthmus noted. She was biochemically euthyroid with TSH 3.65 mU/l (range 0.27-4.2 mU/l), free T4 13.15 pmol/l (range 12-22 pmol/l) and free T3 4.7 pmol/l (range 3.1-6.8 pmol/l). Other blood tests showed vitamin D deficiency and an iron deficiency anaemia. Thyroid ultrasound (US) identified a large heterogenous exophytic left paracentral isthmus thyroid nodule measuring 2.1 x 1.1 cm with moderate vascularity within the nodule, classified as U3. Fine needle aspiration cytology (FNAC) described a colloid nodule (Thy2) with no malignant features seen. The management options were jointly discussed with the patient; do nothing, surveillance with repeat US and FNAC or referral for surgery. The patient opted for repeat US performed four months later which showed the nodule had slightly increased in size to 2.4 x 1 cm with significant heterogenicity within the solid and cystic components and moderate vascularity, classified again as a U3 nodule. Repeated FNAC was Thy2 with no malignant cells seen The options of doing nothing, repeated radiological surveillance or surgery were discussed further with the patient and she opted to undergo a left hemithyroidectomy. Histology revealed a 1.1mm focus of papillary thyroid carcinoma (pT1a) within the nodule. She recovered well post-operatively and thyroid function showed TSH 6.64 mU/l, FreeT4 11.2 pmol/l and Free T3 4.3 pmol/l for which she has been started on levothyroxine.

Conclusion

UK guidelines recommend an ultrasound (U) graded radiological examination in patients with thyroid nodules which then determines the patients who require fine needle aspiration cytology to aid diagnosis. This case highlights that thyroid nodule size, particularly if there has been an increase, may correlate with malignant potential. This has been emphasised in the American Thyroid Association management guidelines, but does not feature within UK guidelines.

DOI: 10.1530/endoabs.81.EP1157

EP1158

The combination of multi-nodular goiter and Thevenard's disease: about 3 familial cases

Ihssane Abidi, Kaoutar Rifai, Iraqi Hinde & Mohamed Elhassan Gharbi
University Mohammed 5 Rabat, Endocrinologie, Rabat, Morocco

Introduction

Thevenard's disease is a sensory neuropathy with a type of ulcerative-mutilating acropathy of progressive course. It has a hereditary character with autosomal dominant inheritance. It is a scarce disease, which usually affects feet but can also affect hands. It causes disorders of thermoalgesic sensitivity, leading to painless ulcerations at the pressure points and then bone deformities with osteoarticular destruction and 'cubic foot' appearance. Repeated superinfections, often with multi-resistant germs, are the cause of frequent amputations. Les surinfections à répétition, à des germes souvent multi-résistants, sont à l'origine des amputations fréquentes. We report the case of the three sisters who suffer from Thevenard's disease with multinodular goiter.

Cases

They are three sisters whose age varies between 30 and 40 years, they are under treatment for Thevenard's disease since the age of 18, with unilateral transtibial amputation in the three and deformities of the third phalanges of the hands in the youngest. They had multi-nodular goiter in euthyroidism (Tirades 2 and 3 nodules) revealed around the age of 30. The autoimmunity record was negative. They were operated on for signs of compression (dysphonia+). Anatom examination opathological was benign with signs of thyroiditis among the three sisters. The clinical and biological course was good under L-thyroxine. Note that there is no notion of goiter in their family or other predisposing factors.

Discussion

Thevenard's disease begins during adolescence or in adult age. Its diagnosis is made in practice, on bundles of clinical, electrophysiological and family arguments. Neuromuscular biopsy has only a differential diagnostic interest, discarding other polyneuropathies responsible for impaired thermoalgic sensitivity, such as diabetic, amyloid, para-amyloid and leprous neuropathies. The diagnosis of certainty requires the detection of a mutation in the SPTLC1 gene. Preventive treatment of skin lesions is the mainstay of the care of these patients because no curative treatment is available. Its association with multinodular goiter has not been reported in the literature. Moreover, this association among three sisters suggests a link between Thevenard's disease and nodular goiter which remains to be defined.

Conclusion

Goiter is most commonly caused by iodine deficiency, autoimmune or nodular diseases. Nevertheless, its appearance outside these circumstances and in association with serious diseases such as Thevenard's disease opens up a perspective for clinical and genetic research.

References

N.ghariani. Thevenard's disease: about a new observation, dermatology department, CHU Farhat Hached, Sousse, Tunisia, the journal of internal medicine, volume 40 supplement June 1, 2019, Pages A213-A214.

DOI: 10.1530/endoabs.81.EP1158

EP1159

Role of iratherapy in the treatment of Graves' disease in children: a case report

Kadiri Chaimae & Lachkar Hassan
Hôpital Cheikh Zayd, Endocrinology, Rabat, Morocco

Introduction

Graves' disease is a rare and severe disease in children with a marked female predominance. The diagnosis is made in front of a very suggestive clinical picture most often grouping together a goiter, an exophthalmos and a picture of thyrotoxicosis, confirmed biologically by the presence of hyperthyroidism with positive anti-TSH receptor antibodies and radiologically by diffuse, homogeneous, hypervascular goiter. There are three essential therapeutic weapons: synthetic antithyroid drugs, radioactive iodine or surgery. We report the observation of an adolescent girl in whom Graves' disease posed management difficulties.

Observation

We report the case of a 12-year-old patient, followed for Graves' disease for 4 years on 40 mg per day of carbimazole with poor adherence to therapy. She currently has a thyrotoxicosis syndrome made up of palpitations and thermophobia. Cervical examination revealed a diffuse and homogeneous goiter. Biological hyperthyroidism is confirmed by suppressed TSH. The thyroid scintigraphy showed hyperfixing goiter. The patient underwent iratherapy treatment at a dose of 20 mci with a good clinical course and obtaining biological hypothyroidism after 6 months. LT4 treatment was started.

Discussion and conclusion

Graves' disease is rare in children. It occurs in 0.02% of children. Its positive diagnosis is often easy, but its disease management remains a subject of controversy in pediatric endocrinology. Medical treatment with synthetic ant thyroid drugs is always attempted as a first-line treatment. Other treatment alternatives are surgery and iratherapy which allows rapid healing while avoiding complications from surgery.

DOI: 10.1530/endoabs.81.EP1159

EP1160

Surgical treatment of Graves' disease

Mohamed Masmoudi, Marwa Regaeig, Wadii Thabet, Azer Chebil, Mehdi Hasnaoui & Khalifa Mighri
Tahar Sfar Hospital, Mahdia, Otorhinolaryngology, Tunisia

Introduction

Graves' disease is an autoimmune disease of the thyroid gland, which represents the most common cause of hyperthyroidism, accounting for 50 - 80% of all cases. Three treatment options are available for Graves' disease: anti-thyroid drugs, radioactive iodine and thyroidectomy. But therapeutic management is still controversial. The aim of our study is to discuss, after a review of the literature, the role of surgery in the treatment of Graves' disease.

Patients and methods

We conducted a retrospective study of medical records of 40 patients who underwent surgery for Graves' disease in our department between 1996 and 2019.

Results

Our series included 30 women and 10 men, aged between 11 years and 63 years. All our patients had hyperthyroidism. Thirty-eight patients had a diffuse goiter whereas the gland was not palpable in 2 patients. A vascular thrill was perceived in 4 patients. Twelve patients had Graves' orbitopathy. All our patients were treated with anti-thyroid drugs and β blockers. The average duration of medical treatment was 18 months. No patient in our series was treated with radioactive iodine. Indications for surgery were: failed medical therapy after 2 years of treatment (29 cases), a compressive goiter (4 cases), concomitant suspicious thyroid nodules (4 cases), second effect of antithyroid drugs (2 cases) and pregnancy (1 case). All our patients had a total thyroidectomy. Seven patients

developed post operative complications: transient hypocalcemia in six cases and recurrent laryngeal nerve palsy in one case. No case of recurrent disease was noted.
Conclusion
Total thyroidectomy is the more efficient radical method for treating patients with Graves' disease. It offers rapid and durable control of hyperthyroidism.

DOI: 10.1530/endoabs.81.EP1160

EP1161

Case report: Amiodarone-induced thyroid dysfunction

Faten Haj Kacem Akid, Oumeyma Trimeche, AbdelMouhaymen Missaoui, Dhoha Ben Salah, Mnif Fatma, Nadia Charfi, Mouna Mnif, NABILA REKIK MAJDOUB, Mouna Elleuch & Mohamed Abid
Hedi Chaker Hospital, Endocrinology, Sfax, Tunisia

Amiodarone is considered by many the most potent antiarrhythmic drug. The other side of the coin is that it's associated with many side effects including disturbances in the thyroid function, which can be seen in 14 to 18 % of the cases (1). This case is about a 56-year-old male patient with a history of mitral valve disease who was on Amiodarone for 3 years. His personal history was notable with Epilepsy of unknow etiology for which he was on sodium valproate. During follow-up, the thyroid function was assessed twice at a 1-month interval and results were consisting with a patent hyperthyroidism. One month later, the patient was referred for our endocrine department and lab work revealed this time hypothyroidism. Thus, the patient was treated with levothyroxine. This case highlights the effects of Amiodarone on the thyroid gland and demonstrate the possible spontaneous evolution of amiodarone induced thyrotoxicosis into hypothyroidism.
References
1. Martino E, Bartalena L, Bogazzi F, Braverman LE. The Effects of Amiodarone on the Thyroid*. Endocr Rev. 1 avr 2001;22(2):240–54.

DOI: 10.1530/endoabs.81.EP1161

EP1162

Hypothyroidism : the interest of thyroid hormone test

Yasmine Mouelhi, Nadia Khessairi, Ameni Terzi, Wafa Grira, Meriem Yazidi & Melika Chihaoui
Rabta Hospital, Endocrinology, Tunis, Tunisia

Introduction
Hypothyroidism is a common endocrine disease with reduced systemic metabolism and its treatment consists on hormonal supplementation. However, despite concurrent replacement therapy with high doses of L-thyroxin, some patients might be seen with clinical and biochemical evidence of hypothyroidism. We report a case of persistent hypothyroidism on high dose of levothyroxin.
Case presentation
It was a 41-year-old female, with a history of recurrent chronic Helicobacter pylori gastritis and total thyroidectomy for a multinodular goitre in 2017, treated with 900 µg per day of L-thyroxin with good compliance and regular intake. She was admitted in our department in December 2021 for exploration. Clinically, she had signs of hypothyroidism: asthenia, puffy face, pudgy fingers and macroglossia. Biology revealed a TSH= 55.32 µUI/ml and a FT4 < 0.42 ng/dl. A levothyroxin absorption test under medical supervision was performed with 600µg of L-thyroxin. TSH and FT4 were measured before the test and at 2h, 4h, 6h and 24h after the test. The FT4 remained low with a peak at 0.48 ng/dl (2h after the start of the test). The test concluded that there was malabsorption of thyroid hormones. Serological markers for celiac disease and a new digestive fibroscopy were requested.
Conclusion
This case illustrates the interest of the thyroid hormone test which allows to distinguish between malabsorption and pseudomalabsorption, non compliance to the treatment. If the diagnosis of malabsorption is retained, further investigations for etiological purposes should be carried out.

DOI: 10.1530/endoabs.81.EP1162

Late Breaking

EP1163

Sex difference in the association of cortisol excess severity with osteoporosis and osteopenia prevalence in cortisol-producing adrenal adenoma

Shoichiro Izawa[1], Kazuhisa Matsumoto[1], Kazuhiko Matsuzawa[1], Takuyuki Katabami[2], Takanobu Yoshimoto[3], Michio Otsuki[4], Masakatsu Sone[5], Yoshiyu Takeda[6], Shintaro Okamura[7], Takamasa Ichijo[8], Mika Tsuiki[9], Tomoko Suzuki[10], Mitsuhide Naruse[11] & Akiyo Tanabe[12]
[1]Tottori University Faculty of Medicine, Division of Endocrinology and Metabolism, Yonago, Japan; [2]St. Marianna University School of Medicine Yokohama City Seibu Hospital, Division of Metabolism and Endocrinology, Department of Internal Medicine, Yokohama, Japan; [3]Tokyo Medical and Dental University, Department of Molecular Endocrinology and Metabolism, Tokyo, Japan; [4]Tokyo Women's Medical University, Department of Endocrinology, Tokyo, Japan; [5]St. Marianna University School of Medicine, Division of Metabolism and Endocrinology, Department of Internal Medicine, Kawasaki, Japan; [6]Graduate School of Medical Science, Kanazawa University, Department of Internal Medicine, Kanazawa, Japan; [7]Tenri Hospital, Department of Endocrinology, Tenri, Japan; [8]Saiseikai Yokohama-shi Tobu Hospital, Department of Diabetes and Endocrinology, Yokohama, Japan; [9]National Hospital Organization Kyoto Medical Center, Department of Endocrinology and Metabolism, Kyoto, Japan; [10]International University of Health and Welfare School of Medicine, Department of Public Health, Narita, Japan; [11]Ijinkai Takeda General Hospital, Endocrine Center; [12]National Center for Global Health and Medicine, Division of Endocrinology, Tokyo, Japan

Objective
Osteoporosis and osteopenia (OS/OP) are frequent in patients with cortisol-producing adrenal adenomas (CPA) associated with severity of cortisol excess (CE). However, the relationship between OS/OP and CE severity considering sex differences is unknown.
Patients and Methods
This was a retrospective cross-sectional observational study conducted as a part of the Advancing Care and Pathogenesis of Intractable Adrenal Disease in Japan (ACPA-J) study, which was based on a registration system for a cohort of patients with adrenal tumors. A total of 237 patients aged 20 to 90 who were diagnosed with mild autonomous cortisol secretion (MACS) and overt Cushing's sindrome (CS) originated from CPA between January 2006 to December 2015 in 10 referral centerswere included in the study. MACS was defined by 1-mg overnight dexamethasone suppression test (DST) cortisol level >1.8 µg/dL (50 nmol/l). OS was defined by less than -2.5 SD of the bone miniral density (BMD) T-score obtained from the lumbar spine or femoral neck, fragility fractures, and medication for osteoporosis. OP was defined as a value of -2.5 SD $<$ BMD T-score <-1.7 SD, without a history of fragility fracture and medication for osteoporosis.
Results
In total,112 of 237 patients, who were predominantly female ($P<0.001$) and had lower BMI ($P=0.013$), had OS/OP. Patients with OS/OP was significantly affected by CE ($P<0.01$) than those without. The adjusted odds ratio (OR) for predicting OS/OP was obtained in multivariate logistic regression analysis. Clinical measures of CE, 1-mg DST cortisol levels, were positively associated with OS/OP in total cases (OR 1.124, 95% CI: 1.070–1.181, $P<0.001$) and the cases with MACS (OR 1.156, 95%CI: 1.046–1.278, $P=0.005$). A cutoff value of 1-mg DST cortisol level >5.0 µg/dL was associated with OS/OP differently between men and women. OS/OP risk in men with MACS was significantly affected only by 1-mg DST cortisol levels (OR 1.221, 95%CI: 1.027–1.452, $P=0.024$). However, multivariate logistic regression analysis suggested that OS/OP risk in women with MACS was significantly affected by 1-mg DST cortisol levels (OR 1.129, 95% CI: 1.005–1.267, $P=0.041$) and age (OR 1.047, 95% CI: 1.006–1.090, $P=0.024$).
Conclusions
CE severity in CPA is positively associated with OS/OP. However, the associated factors of OS/OP in the patients with MACS are different between men and women.
Funding Statement
This study was supported by AMED, Japan (Grant Number JP17ek0109122 and JP20ek0109352) and National Center for Global Health and Medicine, Japan (27-1402, 30-1008 and 21A1015).

DOI: 10.1530/endoabs.81.EP1163

EP1164

Fresh pair of eyes for peri-menopausal lady

Yin Yin & Christopher McGettigan
QEQM Hospital, East Kent University Hospital NHS Foundation Trust, Endocrine and DM, Margate, Kent, United Kingdom

A 50-year-old peri-menopausal lady has had a background history of hypertension on single-agent antihypertensive medication (ACEI), chronic headache, recurrent collapses, and panic attacks for the past 14 years. She has been visited by her GP frequently and performed countless blood tests including FSH, LH, and TSH which confirmed that her symptoms were neither related to menopause nor hyperthyroidism. She also presented to the Emergency Department a dozen times and called paramedics 8 times for similar symptoms. She was diagnosed with panic attacks or investigated for meningitis. Her symptoms have never been resolved or getting better after discharge from the hospital. Unfortunately, her chronic catecholamines symptoms were controlled with anti-depressants and analgesics. Subsequently, she was relocated to a new place in 2014 and registered with a new GP for symptom relief medications. The GP reviewed her before issuing a repeat prescription and re-investigated the unresolved symptoms. 24-hour urine catecholamines were markedly elevated which were evident by urine volume of 3.7l, Noradrenaline 54327 nmol/24 h (0-570 nmol/l), Adrenaline 78nmol/24 h (0-100 nmol/l), urine dopamine 1468 nmol/24 h (0-2500 nmol) respectively. Finally, she was referred to the endocrine clinic for further evaluation and management. She was a slim and well-presented lady with a slightly anxious disposition. Her BP was 150/90 with a pulse rate of 100 beats/min. Hypertensive retinopathy grade 1 was detected in fundoscopy. There was no postural drop and no thyroid nodules. MRI adrenals showed 39 mm high intensity right adrenal lesion. Alpha blockade with Phenoxybenzamine was used before surgery. She underwent laparoscopic right adrenalectomy in January 2015 and the histology reported encapsulated tumour without lymphovascular invasion and low risk for malignancy. The adrenergic symptoms were entirely resolved postoperatively. She became normotensive and Urinary catecholamines were dramatically normalized although she required hydrocortisone replacement for a few months due to the suboptimal short synacthen test. It was stopped subsequently as her adrenal response has recovered fully thereafter. She has been followed up in endocrine outpatient clinic from 2015 to 2020 with 6-monthly urinary catecholamine but there is no biochemical as well as clinical features of pheochromocytoma relapse.

Discussion

The diagnosis of a very rare and potentially life-threatening endocrine tumour was made by a General Practitioner instead of an endocrinologist. This case also highlighted that the definitive treatment is not only curative and reducing cardiovascular risks, but also improving her quality of life.

DOI: 10.1530/endoabs.81.EP1164

EP1165

Prevalence of endocrine autoimmune pathology in adult patients with vitiligo

Nurana Nuralieva[1], Marina Yukina[1], Ekaterina Troshina[1], Vitaliy Petrov[2] & Vladimir Volnukhin[2]
[1]Endocrinology Research Centre, Moscow, Russian Federation; [2]Moscow Scientific and Practical Center of Dermatovenereology and Cosmetology, Moscow, Russian Federation

Introduction

In Russia, full-scale studies aimed at assessing the incidence of endocrine autoimmune diseases (eAID) in adult patients with vitiligo have not been conducted.

Objectives

analysis of occurrence of eAID in patients with vitiligo.

Methods

1) The first part of the study included 39 patients aged 19-73 years with endocrine pathology and vitiligo, who were initially examined in Endocrinology Research Centre. 2)The second part of the study included 26 patients aged 19-71 years with vitiligo who were initially examined in Moscow Scientific and Practical Center of Dermatovenereology and Cosmetology.

Results

1) eAID were diagnosed in 85% of cases ($n=$ 33): 38,5% of patients ($n=$ 15) had one eAID, 46,1% of patients ($n=$ 18) had multiple eAID, other participants ($n=$ 6, 15,4%) had antibodies to thyroid or insular apparatus of pancreas without disruption of their functions. Autoimmune leison of thyroid (ALT) was diagnosed in 69% of cases ($n=$ 27, of these n=19 (70%) – primary hypothyroidism and n=8 (30%) – Graves' disease (GD)), Addison's disease was diagnosed in 28% of cases ($n=$ 11), type 1 diabetes mellitus was diagnosed in 21% of cases ($n=$ 8), hypoparathyroidism was diagnosed in 13% of cases ($n=$ 5), hypergonadotropic hypogonadism was diagnosed in 10% of cases ($n=$ 4), endocrine ophthalmopathy was diagnosed in 10% of cases ($n=$ 4). Multiple eAID were presented by autoimmune polyglandular syndrome (APS)-2 in 61% of cases ($n=$ 11) and APS-1 in 22% of cases ($n=$ 4), 3 patients (17%) had GD in combination with endocrine ophthalmopathy. Vitiligo preceded the manifestation of eAID in 30% of cases ($n=$ 10) and developed simultaneously with eAID in 12% of cases ($n=$ 4). 97% of patients ($n=$ 38) had the non-segmental vitiligo. One patient (3%) with APS-2 (Addison's disease, primary hypothyroidism, autoimmune gastritis) had universal vitiligo. 2) ALT was found in 15% of patients ($n=$ 4, of these n=3 (75%) – primary hypothyroidism and n=1 (25%) – GD), other eAID were not detected. Carriage of antibodies to thyroid or insular apparatus of pancreas without disruption of their functions was detected in 19% of patients ($n=$ 5). Vitiligo preceded the manifestation of eAID in 50% of cases ($n=$ 2) and developed simultaneously with eAID in 25% of cases ($n=$ 1). 96% of patients ($n=$ 25) had the non-segmental vitiligo. One patient (4%) without manifest eAID and antibodies carriage had segmental vitiligo.

Conclusion

The non-segmental vitiligo is most often associated with the development of eAID, especially ALT. The development of vitiligo precedes the manifestation of eAID in 30-50% of cases, which necessitates a regular screening examination of these patients.

DOI: 10.1530/endoabs.81.EP1165

EP1166

Does Autonomic cortisol secretion really affect metabolic parameters? preliminary results

Seda Karslı[1], Seda Turgut[1], Didem Acarer Bugün[1], Naim Pamuk[1], Hamide Piskinpasa[1], İlkay Çakir[1], Meral Mert[1] & Sema Ciftci[1]
[1]University of Health Science Bakırköy Dr. Sadi Konuk Training and Research Hospital, Endocrinology and Metabolism, İstanbul, Turkey

Aim

Autonomic cortisol secretion (ACS) is a clinical picture without overt signs of Cushing's Syndrome despite adrenal adenoma and ACTH-independent cortisol secretion. These patients, who currently do not have a standard treatment, are followed up, especially for known comorbidities of hypercortisolemia such as obesity, diabetes mellitus (DM), hypertension, osteoporosis, and hyperlipidemia. However, it remains unclear how long the patients will be followed and when the treatment should be begun. This study aimed to evaluate the parameters to be examined in the clinical follow-up by comparing the metabolic and hormonal parameters of ACS patients with the control group with non-functional adenoma (NFA).

Material and methods

Our study included 54 female patients diagnosed with ACS ($n=$ 30) and age-matched NFA ($n=$ 24) as the control group. 1 mg overnight dexamethasone suppression test cut-off point was accepted as $\geq$1.8 mg/dL in ACS diagnosis. Age, body mass index, waist circumference, fasting blood glucose, HbA1c, AST, ALT, lipid profile, thyroid function tests, basal cortisol, ACTH, DHEAS, maximum mass size of adrenal adenoma, 25-hydroxyvitamin D, HOMA-IR measured, and visceral adiposity index (VAI) were calculated for both groups.

Results

The mean age of ACS was 52.13 $\pm$8.8 years, while the mean age of NFA was 49.04 $\pm$6.8 years ($P>0.05$). The prevalence of hypertension and DM was similar ($P>0.05$). There were significant differences between the two groups in terms of maximum adenoma size ($P=0.007$), DHEAS levels ($P=0.013$), and TSH levels ($P=0.01$). No significant difference was found in other comparisons ($P>0.05$). Maximum adenoma size showed a significant positive correlation with waist circumference ($r=$ 0.331, $P=0.018$), and significant negative correlations with DHEAS and ACTH ($r=$ -0.519, $P<0.001$, $r=$-0.289, $P=0.049$, respectively). There was no significant difference in VAI scores between the two groups ($P>0.05$).

Conclusion

In our study, no significant difference was found between ACS and NFA patients in terms of metabolic disease frequency. While the maximum adenoma size was found to be significantly higher in ACS patients than in NFA patients, DHEAS and TSH levels were shown to be lower in those patients. These results were consistent with the possible effects of mild hypercortisolemia. Our study showed that DHEAS and TSH levels might play a role in patient follow-up, and it was emphasized that the diagnosis of ACS should be considered, especially in patients with larger adenoma sizes. Further studies are needed to eliminate the uncertainties in the diagnosis and follow-up of ACS.

DOI: 10.1530/endoabs.81.EP1166

EP1167

Silent giant pheochromocytoma : about a rare entity

Chtioui Sara, Ahmed Boukhalfa, Rafi Sanaa, El Mghari Ghizlane & El Ansari Nawal
Mohamed VI Hospital University, Endocrinology Department, Marrakesh, Morocco

Introduction
Pheochromocytomas are catecholamine producing tumors which arise from chromaffin cells within the adrenal medulla. Silent pheochromocytomas are rare entities that do not present with the classical symptoms commonly seen in catecholamine-secreting tumors.
Case report
We report a case of 70-year-old-woman patient who presented with left sided abdominal pain and discomfort for 6 months. A preoperative Computed tomography (CT) scan showed a huge left suprarenal tumor 09×112×153mm in size. The right adrenal gland was normal and there were no finding of distant metastatic. The urinary catecholamines were very elevated. The patient underwent a laparoscopic surgical resection without untoward intraoperative and postoperative events. In the pathological evaluation, the mass weighed 1137 g and showed a pheochromocytoma with a PASS score of 8. The patient is on long term follow up. She was well and completely asymptomatic at last review six months after surgery.
Conclusion
This case brings to the attention of clinicians the need to have a high index of suspicion of a giant pheochromocytoma in a patient presenting with vague abdominal symptoms whose CT scan shows a large retroperitoneal tumor, even in the absence of clinical symptoms. Key-words : Pheochromocytoma-silent-giant tumor-surgery

DOI: 10.1530/endoabs.81.EP1167

EP1168

A rare case of hypocortisolism in hypercoagulable state

Htet Htet Aung[1], Amna Zeeshan[1], Dmitriy Chernov[1], Nizar Damani[2], Rahat Tauni[1] & Melina Kostoula[1]
[1]West Hertfordshire NHS Trust, Diabetes and Endocrinology, Watford, United Kingdom; [2]West Hertfordshire NHS Trust, Radiology Department, Watford, United Kingdom

We report a case of 39-year-old woman presenting with sudden severe abdominal pain and vomiting. She had a past medical history of anti-phospholipid antibody syndrome (APLS) diagnosed in the United States (US) 20 years ago. She had multiple episodes of vomiting over the last 10 years and was diagnosed with cyclical vomiting as investigations including CT abdomen and endoscopy did not reveal a structural cause. She was taking warfarin for APLS. She was haemodynamically stable and clinical examination was unremarkable. Investigations showed normal electrolytes, subtherapeutic international normalised ratio (INR), raised cardiolipin antibody and raised activated partial thromboplastin time (APTT). CT abdomen showed enlarged bilateral adrenal glands with heterogenous parenchyma suggestive of adrenal haemorrhage and warfarin was stopped. A morning cortisol level was 171 nmol/l and short synacthen test showed inadequate cortisol response rising from 166 mmol/l only to 179 nmol/l at 30 minutes confirming the diagnosis of primary adrenal insufficiency. She was commenced on oral hydrocortisone. Subsequent MRI adrenals confirmed stable bilateral adrenal haemorrhage with cystic area of peripheral methaemoglobin and central haemosiderin. As the adrenal haemorrhage was non-progressive, anticoagulation was restarted due to high risk of thrombosis in the future. She is being followed up in the endocrine clinic with full adrenal work up including renin and aldosterone awaited. Adrenal infarction or haemorrhage is a rare complication of APLS, and hypercoagulable state may lead to adrenal vein thrombosis with haemorrhagic transformation of adrenal glands. The presenting features of adrenal thrombosis and haemorrhage include localised pain and/or adrenal insufficiency but often such patients do not have any symptoms. Patients with APLS and adrenal insufficiency may not present with hypotension as patients with APLS are commonly hypertensive, therefore masking hypotension. Unless promptly treated with intravenous glucocorticoids, complete adrenal insufficiency associated with vascular phenomenon of APLS can potentially be fatal. Therefore, physicians should have a high index of suspicion in such cases. Decision about anticoagulation should be individualised but most patients need anticoagulation as they remain at high risk of thrombotic phenomenon elsewhere.

DOI: 10.1530/endoabs.81.EP1168

EP1169

Silent primary adrenal insufficiency: a case of treatment-resistent hyponatremia

Deniz Cengiz
Ankara Ataturk Sanatoryum Training and Research Hospital, Internal Medicine, Ankara, Turkey

64 year old male with known hypertension presented with fatigue and mild vertigo to the emergency department. Blood pressure was 110/65 mmHg. Physical examination revealed bilateral inspratory crackles with bilateral pedal oedema. There was not any skin discolourisation or bruises. Patient history indicated a suspected lung malignancy but pathological diagnosis was yet to be concluded. Laboratury test showed that sodium level was 117 mEq/l, potassium level was 5.2 mEq/l, venouse blood gas ph was 7.37, HCO_3 level was 22 mmol/l, $PaCO_2$ was 44 mmHg. Spot urine sodium8 mEq/l, serum osmolarity was 271 mOsm, urine osmolarity was 425 mOsm/l. Other renal, liver, thyroid function tests and lipid levels were within normal laboratory values. He had no obvious hyponatremia sypmtoms other than fatigue and mild nausea without vomitting. Previous medical center initiated hypertonic saline for two days, yet sodium level did not improve. He was transferred with the suspicioun of inappropriate ADH syndrome. Lung imaging showed a right mid-zone opacity with bilateral basal pleural effusion. Further investigations revaled no head injury or cranial pathology, morning serum cortisol level was 26 µd/dl. Patient admitted and started on furosemid and water restriction to 1.5 L for hypervolemia. Due to two days without improvement, PET-CT imaging was requested for evaluation. A 85x60 mm heterogeneous, hypodens mass at left adrenal gland with metabolic activity (suv maks 6.93) was reported. Despite patient's lack of metabolic acidosis, hypotension or confusion, it is suspected to be adrenal function disorder and insufficiency. Serum ACTH, cortisol, renin, aldosterone levels were sent and short synachten test was performed before corticosteroid treatment with 100 mg hydrocortizon four times daily started. Second cortisol level was 11 µd/dL and latter Synachten test was consisted with primary adrenal insufficiency. Patients' sodium level was improved after two days of steroid treatment and increased to 128 mEq/l. Later on, patient was diagnosed with squamous cell lung cancer with adrenal and lymph node metastasis. This case was complicated with mild nonspesific symptoms with initial high basal cortisol levels and absence of hyperpigmentation. It is suggested that patients with low plasma sodium should be carefully evaluated for laboratory errors, differantial diagnosis; and adrenal functions should not be overlooked.

DOI: 10.1530/endoabs.81.EP1169

EP1170

Post-thyroidectomy hypocalcemia: a single-center retrospective study

Paloma Iglesias[1], Ana Laura Salguero[1], Jose Antonio Rosado[1], Maria Merino[2], Guadalupe Guijarro[1], Cristina Navea[1] & Isabel Pavon[1]
[1]Hospital Universitario de Getafe, Endocrinology, Madrid, Spain; [2]Hospital Universitario de Getafe, Endocrinology, Spain

Background
Post surgery hypocalcemia is the most common sequel of thyroidectomy. An accurate prediction of hypocalcemia in the immediate postoperative period would enable the selection of patients for appropriate treatment and facilitate early discharge.
Objective
This study aims to investigate the prevalence of hypocalcemia after thyroidectomy and to identify potential risk factors.
Methods
This is a retrospective cohort study of 91 patients who underwent total thyroidectomy in a tertiary center between 2017 and 2019. Data were extracted from patient medical records. Hypocalcemia was evaluated in relation to risk factors (age, sex, body mass index and type of thyroid disease). Serum parathyroid hormone (iPTH) was measured 24 h (h) after surgery. Serum ionized calcium ($Ca2+$) was analyzed 8h, 24h and 48h post-surgery.
Results
Hypocalcemia was noted in 28 (30%) of 91 patients who underwent thyroidectomy. There was no significant relationship between the occurrence of hypocalcemia and age, sex, body mass index and type of thyroid disease. The best cut-off values of serum iPTH to predict hypocalcemia was found to be 19 pg/ml at 24h post total thyroidectomy with a sensitivity and specificity of 92.45% and 100%, respectively.
Conclusion
Clinical factors are not reliable predictive markers of immediate post-thyroidectomy hypocalcemia. Prediction of hypocalcemia using serum iPTH

seems to be a promising approach. In our cohort, a cut-off value of 19 pg/ml at 24h after surgery showed a good sensitivity and specificity. Serum vitamin D levels were not performed preoperatively. This can be considered a limitation of our study.

DOI: 10.1530/endoabs.81.EP1170

EP1171

A case of postgravid osteoporosis

Nodira Alikhanova, Lola Abboskhujaeva, Feruza Takhirova, Gulzoda Akramova & Munavvara Shokirova
Republican Specialized Scientific and Practical Medical Center of Endocrinology named after academician Yo.Kh.Turakulov, Tashkent, Uzbekistan, Diabetology, Osteoporosis and Metabolism

Introduction
Of interest are cases of osteoporosis of unknown etiology after a recent delivery.
Matherials and methods
A 33-year-old woman complained of frequent fractures of the bones of both feet (four times in the last year) after the birth of her third child. For the woman, this was the fourth pregnancy, according to her, after the birth of her second child, she had pain in the lower back, which aggravated with physical exertion (at 24 years old).
Results
The patient's calcium level was 2.37 mmol/l, phosphorus 1.25 mmol/l, vitamin D - 20.07 ng/ml, parathyroid hormone - 50.04 pg/ml, NTx - 79.74 nM BCE (normal 17- 94 nM BCE), osteocalcin - 5.28 ng/ml (normal 6-43 ng/ml), alkaline phosphatase - 60.0 U/l. Dual-energy x-ray absorptiometry (DEXA) showed that the Z-score of 1-4 lumbar vertebrae was -3.3, the left hip was -2.2, the neck of the left femur -2.3, the right hip -2.8, the neck right thigh -2.0. The analysis of the obtained results showed that the resorption markers were within the normal range, and the formation markers were below the norm, therefore it was advisable to prescribe teriparatide, but due to the lack of access to teriparatide in our country, we prescribed the patient a calcium preparation 1000 mg per day, osteogenon 6 tablets per day, alendronic acid 70 mg per week and vitamin D at a dose of 300,000 IU. Repeatedly after 2.5 months, all parameters remained unchanged, except for vitamin D (20.07 → 34.89) and NTx (79.74 → 75.60), osteocalcin (5.28 → 2.93), alkaline phosphatase also decreased (60 → 54). The patient was then switched to teriparatide 20 mg subcutaneously once daily. After 6 months, during therapy with teripartide, osteocalcin increased from 2.93 to 13.82, the same situation was observed in relation to alkaline phosphatase (54 → 185). X-ray densitometry parameters also had positive shifts: Z-score of 1-4 lumbar vertebrae increased from -3.3 to -2.6, Z-score of the left hip -3.2 → 2.9, right hip -2.8 → 2, 6. Based on the positive changes in the results of laboratory and functional studies, it was recommended to continue therapy with teriparatide. The patient is being monitored.
Conclusion
Pregnancy and the lactation period are physiological for a woman's body, the development of osteoporosis during pregnancy and lactation, not due to other reasons, requires further research.

DOI: 10.1530/endoabs.81.EP1171

EP1172

Osteoporosis after menopause: interaction between genes related to iron metabolism and estradiol

Laura Aguiar[1,2,3], Joana Ferreira[1,2,3], Raquel Binda Pereira[2], Ana Paula Barbosa[3, 4], Mário Rui Mascarenhas[3,4], Paula Faustino[3, 5], Ângela Inácio[1,2,3] & Manuel Bicho[1,2,3]
[1]Instituto de Investigação Científica Bento da Rocha Cabral, Lisbon, Portugal; [2]Laboratório de Genética, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal; [3]Instituto de Saúde Ambiental, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal; [4]Clínica de Endocrinologia, Diabetes e Metabolismo de Lisboa, Lisbon, Portugal; [5]Departamento de Genética Humana, Instituto Nacional de Saúde Doutor Ricardo Jorge, Lisbon, Portugal

Introduction
Osteoporosis is a common metabolic bone disease characterized by reduced bone mass and increased risk of fragility fractures. The pathogenesis of this disease is complex and influenced by multiple risk factors, where genetic factors play an important role. Menopause predisposes women to osteoporosis due to declining estrogen levels. Osteoporosis and iron metabolism have an important relationship. Iron overload suppresses osteoblast formation and stimulate osteoclast resorption of bone, suggesting that polymorphisms in genes affecting iron homeostasis can increase the susceptibility for the development of osteoporosis.
Objectives
This study aimed to investigate the potential implication of genetic polymorphisms in genes related to iron metabolism and their interaction with estradiol in the development of osteoporosis in a sample of postmenopausal women.
Material and methods
A case-control study was carried out for a sample of 169 Portuguese postmenopausal women, of which 78 had osteoporosis and 91 had normal bone mass. Polymorphic analyzes on the *HFE* gene (H63D and C282Y) were performed by PCR-RFLP. The haptoglobin (*Hp*) phenotype was determined by polyacrylamide gel electrophoresis. Plasma 17β-estradiol concentration was determined by ELISA. All statistical analyzes were performed using SPSS software, version 24.0.
Results
An association was found between lower levels of 17β-estradiol and osteoporosis [OR (95% CI) = 5,946 (2,199-16,079); $P<0.001$]. When the genes were analyzed separately, no significant differences were found between the two populations in relation to the polymorphisms under study. However, women with the presence of the H allele of the H63D polymorphism of the *HFE* gene and lower levels of estradiol had an increased risk of developing osteoporosis [OR (95% CI) = 22,750 (2,492-207,731); $P=0.001$], as well as the presence of the CC genotype of the C282Y polymorphism of the *HFE* gene and lower levels of estradiol [OR (95% CI) = 11,667 (2,139-63,638); $P=0.002$]. Also women who had the *Hp* 2 allele and lower levels of estradiol had an increased risk of developing osteoporosis [OR (95% CI) = 7,023 (1,813-27,200); $P=0.005$].
Conclusion
Since these genes are related to iron metabolism, the results of this study suggest an action of this metabolism in interaction with estradiol levels in the development of osteoporosis in postmenopausal women.

DOI: 10.1530/endoabs.81.EP1172

EP1173

Primary hyperparathyroidism-induced osteoporosis: lessons from the DENOCINA trial

Valentim Lopes & Adriana Lages
Braga Public Hospital, Braga, Portugal

An 89 years old caucasian female patient with antecedents of hemithyroidectomy in 2016 due to benign nodular disease, and actually suplemented with 0.1 mg/day of levothyroxine, was referred to the Endocrinology consultation because of a primary hyperparathyroidism diagnosed in the sequence of the study of an episode of nephrolitiasis that happened in 2012 and a diagnosis of osteoporosis that was established in 2017. A 99mTc-Sestamibi revealed an augmented right inferior parathyroid gland. Although the patient had surgical indication for paratiroidectomy (symptomatic hyperparathyroidism), it was decided to treat the patient medically, because of her age and functional dependence, with the agreement of the patient and her family. She was initially treated with alendronic acid 70 mg once week during 5 years, but without significant response in terms of bone mineral density, hypercalcemia and osseous pain. The treatment was then switched to denosumab 60 mg twice year in 2020, and, in 2021, because the hypercalcemia didn't ameliorate, inspired by the results of the DENOCINA trial, we decided to introduce, in add-on, cinacalcet, initially in the dose of 30 mg/day. The calcium was 11.5 mg/dL and the PTH was 147 pg/mL (with adequate levels of vitamin D) before the initiation of cinalcalcet. Actually, 4 months after the initiation of cinacalcet, with a dose that was titrated to 60 mg/day, the calcium is in the upper limit of the normality (10.5 mg/dL) and the PTH has fallen to 85 pg/ml. But most important, the patient tolerated well both drugs, did experience an improvement in the osseous pain and gained more autonomy in the accomplishment of her daily activities.

DOI: 10.1530/endoabs.81.EP1173

EP1174

miR-15b mediates the obesity-induced adipocyte insulin resistance by targeting insulin receptor

Xingjing Liu

Zhongda Hospital, Institute of Diabetes, Medical School, Southeast University, Department of Endocrinology, Nanjing, China

Background
In recent years, the morbidity of obesity has been increasing rapidly worldwide, which is a major risk factor for type 2 diabetes mellitus (T2DM). Obesity, mainly characterized by abnormal and excessive white adipose tissue accumulation, is the most common cause of insulin resistance (IR), where the insulin target tissues fail to respond normally to circulating insulin. However, the precise mechanism by which obesity affects insulin resistance in the major insulin sensitive tissues remains unclear. Adipose glucose uptake plays a significant role in systemic insulin sensitivity, therefore clarifying the regulatory factors of adipose insulin sensitivity is of great significance to find effective therapeutic targets of obesity. Obesity causes the increase of hepatic miR-15b, which provokes hepatocyte insulin resistance, but has no effect in skeletal muscle. The upregulation of miR-15b induced by obesity causally resulted in an impairment of hepatocyte insulin signaling and the decrease of the insulin receptor (INSR) expression. However, no studies have explored whether miR-15b is involved in adipose tissue insulin resistance induced by obesity so far.
Aim
To study the role of miR-15b in the adipose tissue of DIO mice and IR 3T3-L1 adipocytes
Method
We fed mice with high-fat diet (HFD) for 10 weeks to construct obese and insulin-resistant (IR) mice models, and treated3T3-L1 adipocytes with chronic hyperinsulinemia to establish IR adipocyte models. Cell transfection was performed using riboFECTTMCP or Lipofectamine2000. Insulin stimulated fluorescence labeled 2-NBDG uptake assay was used to detect the capacity of glucose uptake in adipocytes. The expression levels of miR-15b, the insulin receptor (INSR) and its downstream insulin signaling molecules were detected by real-time PCR and Western blot respectively.
Resluts
We found that expression of miR-15b was increased, while INSR expression was downregulated in adipose tissue of diet-induced-obese (DIO) mice. In IR 3T3-L1 adipocytes, the expression of miR-15b also ascended, accompanied by the decrease of INSR expression. Bioinformatics analysis and luciferase reporter analysis suggested that INSR was a potential target of miR-15b. Overexpression of miR-15b led to decreased INSR expression and impaired insulin signal transduction in adipocytes, and inhibition of endogenous miR-15b can reverse the downregulation of INSR and insulin resistance induced by high insulin. In addition, when miR-15b was overexpressed, the simultaneous overexpression of INSR partially alleviated the insulin resistance in adipocytes.
Conclusion
These results suggested that the impaired insulin signaling in adipocytes caused by obesity was at least partially mediated by the downregulation of INSR induced by elevated miR-15b.

DOI: 10.1530/endoabs.81.EP1174

EP1175

Greece: Study of people's mobility in parks vis-à-vis internet searches for diet or obesity in the Covid-19 era

Ioannis Ilias[1], Charalampos Milionis[1], Athanasios Tselebis[2] & Eftychia Koukkou[1]
[1]Elena Venizelou Hospital, Department of Endocrinology, Diabetes & Metabolism, Athens, Greece; [2]Sotiria Hospital, Department of Psychiatry, Athens, Greece

Introduction
In the Covid-19 era mass media present people worldwide, including in Greece, to transiently flock to green spaces and parks. A study from the Western United States in 2020, indicated that indeed, park visitation may have increased by 20% compared to baseline (the immediate pre-Covid-19 period). The Google mobility index (GMI) is based on location data/visits - from smartphone users - to various areas; among areas of mobility the GMI can focus specifically on visits to parks. Studies have shown that internet searches honed on diets may have fluctuated during the Covid-19 era, while obesity may have increased.
Aim
To assess whether the GMI for parks, as a surrogate of physical activity, is related to Google Trends (GT) searches for diet and obesity.
Methods
We extracted the GMI data for Greece, regarding people's mobility in parks, from March 2020 to February 2022; the data were analyzed by two-way analysis of variance (ANOVA) vis-à-vis season and non-lockdown (NLD)/lockdown (LD) time. For the same time period we also extracted the GT data for internet searches in Greece regarding 'diet' and 'obesity' (in English and Greek). We assessed the autocorrelation of the parameters, to search for periodicity/seasonality, and we performed cross-correlation analysis of the GMI vis-à-vis GT searches. Separate cross-correlation analyses were done for NLD and LD time periods also.
Results
Park visitations' GMI vs baseline had a markedly dimorphic aspect during NLD/lD time periods; in winter, NLD: +16%, LD: -11%, in spring, NLD: +38%, LD: +9%, in summer, NLD only: +150%, in autumn, NLD: +76%, LD: -5% (p were 0.067 for comparisons by season and <0.001 for comparisons by NLD/lD status). The autocorrelations for periodicity/seasonality of the parameters did not reach statistical significance. Mostly negative cross-correlation coefficients for GMI against GT, lagging mainly from to +2 to +11 weeks (with GT trailing GMI) were noted, ranging from - 0.22 to - 0.56 ($P<0.05$). Analyses done separately for NLD and LD periods yielded analogous results.
Discussion
Surprisingly, during LD periods, when stay-at-home mandates were in effect, whereas walking in parks was allowed for exercise, park visitations mostly declined. Moreover, periods of increased mobility in parks during the Covid-19 era were coupled, with a time delay, to a drop in internet searches for 'diet' and 'obesity'. Whether this represents a counterintuitive perception in the community, in Greece, that physical activity in parks renders dieting superfluous remains to be evaluated.

DOI: 10.1530/endoabs.81.EP1175

EP1176

The level of biomarkers of early kidney damage in patients with prediabetes

Dilara Isakova[1], Ivan Petrov[2], Irina Troshina[1] & Tatyana Vasilkova[1]
[1]Tyumen State Medical University, Department of Hospital Therapy with courses in Endocrinology and Clinical Pharmacology, Tyumen, Russian Federation; [2]Tyumen State Medical University, Department of Research and Innovation, Tyumen, Russian Federation

Purpose
To assess the level of biomarkers of early kidney damage (urinary and plasma cystatin C) in patients with prediabetes and to characterize their association with risk factors for the development of nephropathy.
Materials and methods
The object of the study were 60 patients (32% men, 68% women) with early disorders of carbohydrate metabolism (impaired fasting glycemia (IFG) and impaired carbohydrate tolerance (IGT), WHO criteria, 2009). The mean age in the group was 44.3 ± 7.8 years. The average level of fasting glycemia diagnosis was 5.7±0.42 mmol/l, the average level of glycated hemoglobin was 5.96±0.36%. The mean BMI was 31.6±5.4 kg/m^2. All participants underwent a morning urine test for microalbuminuria (MAU), assessment of creatinine levels, followed by calculation of GFR (MDRD). Urinary and plasma levels of cystatin C were analyzed by enzyme immunoassay using the Cystatin C-ELISA-Best test system. Statistical processing of the results was carried out using the program Statistica 7.0. using: $\chi 2$ test, Mann-Whitney U-test for two independent samples, Spearman test. Differences were considered significant at $P<0.05$.
Results
The mean urinary cystatin C was 10.3±1.2 mg/l. An elevated urinary level of cystatin C was observed in 54.6% of the subjects. There were significant differences in the level of the analyzed urinary marker in the group of patients with MAU ($P<0.001$). A direct correlation was also established between the concentration of cystatin C in urine with BMI ($r=0.42$, $P<0.01$), SBP ($r=0.59$, $P<0.05$), DBP ($r=0.34$, $P<0.05$), creatinine level ($r=0.68$, $P<0.001$), glycemia during oral glucose tolerance test 2 h after exercise ($r=0.51$, $P<0.01$) and negative correlation relationship with GFR level ($r=0.59$, $P<0.01$). The mean plasma level of cystatin C was 1.02 mg/l. There were significant differences in the level of the analyzed plasma marker in the group of patients with MAU ($P<0.01$). Direct relationship was established between the concentration of cystatin C and blood creatinine ($r=0.61$, $P<0.001$), the severity of MAU ($r=0.61$, $P<0.001$), the age of patients ($r=0.42$, $P<0.05$) and an inverse relationship with the level of GFR ($r=-0.65$, $P<0.01$).
Conclusions
An increase in the level of analyzed markers in patients with prediabetes demonstrates kidney damage at the stage of early carbohydrate metabolism disorders. The revealed changes in the levels of urinary and plasma cystatin C, compared with traditional nephrological markers (MAU, GFR), indicate a higher

diagnostic significance in the light of early detection and enable preventive intervention in terms of prevention.

DOI: 10.1530/endoabs.81.EP1176

EP1177

Prolonged oral glucose tolerance test in the diagnosis of postprandial non-diabetic hypoglycemia

Marina Yukina, Nurana Nuralieva & Ekaterina Troshina
Endocrinology Research Centre, Moscow, Russian Federation

Introduction
tests alternative to the fasting test are necessary for the diagnosis of numerous causes of non-diabetic hypoglycaemia (NDH), that not provoked by starvation (postprandial hypoglycemia), such as insulin autoimmune syndrome (IAS) and noninsulinoma pancreatogenous hypoglycemia syndrome (NIPHS). However, there is no consensus on the most optimal test (prolonged oral glucose tolerance test (pOGTT) or mixed meal test (MMT)) in this cohort of patients.
Objectives
1)To determine the accuracy of pOGTT and MMT in the diagnosis of postprandial NDH. 2)To compare the glycemic curves during pOGTT in patients with IAS and NIPHS.
Methods
We included152 patients aged 18-74 years: with IAS ($n=$ 14), NIPHS ($n=$ 9), fasting NDH ($n=$ 108) and without NDH ($n=$ 21). All patients underwent pOGTT and MMT. During pOGTT the analysis of venous blood for glucose was performed at baseline, 120 minutes after a 75 g oral dextrose load, and then every 30 minutes until reaching 6 h, if hypoglycemia in venous blood has not been previously recorded. During the MMT the analysis of venous blood for glucose was performed at baseline, and then every 30 minutes after a mixed meal (containing 36.8 g of carbohydrates, 12 g of proteins, 11.6 g of fats (calorie content - 300 kcal)) oral load until reaching 5 h, if hypoglycemia in venous blood has not been previously recorded. During both pOGTT and MMT, analysis of insulin and C-peptide levels was performed once in a blood sample with diagnosed hypoglycemia.
Results
1)Sensitivity, specificity, AUC of the pOGTT were: 100,0% [82,7%; 100,0%]; 61,1% [44,8%; 75,2%]; 80,6% [72,5%; 88,6%], respectively. Sensitivity, specificity, AUC of the MMT were: 22,2% [5,7%; 55,9%]; 77,4% [67,2%; 85,0%]; 49,8% [34,7%; 64,9%], respectively. When comparing the AUCs of pOGTT and MMT the significant difference was found, $P<0.001$. 2)The minimal level of glycemia in patients with IAS and true positive result of pOGTT (2,84 [2,60; 2,93] mmol/l) and in patients with NIPHS and true positive result of pOGTT (2,52 [2,15; 2,63] mmol/l) didn't differ significantly, p=0,130. Patients with IAS developed hypoglycemia at the 180-300 minutes after beginning of the pOGTT, and patients with the NIPHS developed hypoglycemia at the 120-180 minutes after beginning of the pOGTT.
Conclusion
1)Patients with suspected NDH should undergo 5-hour pOGTT for the purpose of postprandial hypoglycemia excluding. 2)Patients with NIPHS develop postprandial hypoglycemia earlier, than patients with IAS.

DOI: 10.1530/endoabs.81.EP1177

EP1178

Dietary education for patients with type 2 diabetes : state of art

Mehrez Achwak, Wafa Alaya, Selma Mohsen, Najoua Lassoued, Fedia Boubaker, Baha Zantour & Mohamed Habib Sfar
Taher Sfar University Hospital, Tunisia

Introduction
Dietary practices are essential in diabetes control and acquiring HbA1c target. The aim of our work is to evaluate the prevalence of dietary education practice in a type 2 diabetes population and its associated factors.
Methods
Cross-sectional study enrolling 84 type 2 diabetes patients followed up in the outpatient endocrinology department. The data was collected through a questionnaire in face-to-face interviews with patients. Age, body mass index (BMI), diabetes duration, glycosylated hemoglobin (HbA1c) and serum lipid profile were assessed.
Results
The mean age was 59 $\pm$ 12 years. Of the study population, 42 % were females. The mean diabetes duration was 9.4 $\pm$ 6.4 years. The mean HbA1c was 9.9% $\pm$ 2.4. The mean BMI was 27.7 $\pm$4.7 kg/m^2. More than two-third (71%) of the patients were overweight/obese. Less than the the half of the participants (45%) were measuring their blood glucose level at their home. Only 33% got nutrition education on diabetes diet from a health professional. The rest of respondents reported getting dietary information from media in 30% and from friends and family in 37%. Recieving nutrition education from a health care professional was associated with following dietary recommendations ($P=10^{-3}$), self monitoring of blood glucose ($P=0.04$) and a better glycemic control ($P<10^{-3}$). Patients who got a dietary education had lower BMI (26.6 $\pm$ 3.1 kg/m^2 vs 28.3 $\pm$ 5.2 kg/m^2 $P=0.06$) and better serum lipid profile including a lower triglycerides levels (1.09 $\pm$0.36 mmol/l vs 1.52$\pm$ 1.1 mmol/l; $P=0.009$). Getting nutrition education was significantly associated with good dietary practices including : getting meals meals based on a diet plan ($P<10^{-3}$), knowing diffrent food groups ($P=0.003$) and reducing sweets and sugary consumption ($P<10^{-3}$). Patients who recieved a nutrition education insisted more on the importance of having a physician nutrition specialist ($P=0.002$)
Conclusion
Among the patients, diabetic dietary awareness and management are still a major challenges faced by healthcare professionals. This study highlights the importance of reinforcement of an active dietary education through health-care providers (physician nutrition specialist, dietitician…) to encourage patient to make changes in their nutritional habits and improve their dietary knowledge and practices.

DOI: 10.1530/endoabs.81.EP1178

EP1179

Differential effect of vitamin D therapy on insulin resistance in vitamin D deficient women

Stavroula Psachna, Evangelia Vogiatzi, Christina Kogia, Dimitrios Ioannidis, Dimitrios Lilis, Maria Drakou, Antonis Polymeris & Peter Papapetrou
Sismanoglio- Amalia Fleming - General Hospital, Department of Endocrinology, Metabolism and Diabetes Mellitus, Greece, Melissia, Greece

Forty-one vitamin D deficient women (aged 26-75 years, mean 56.2, median 57) were treated with Vitamin D3 (50000 IU/week for 1.5 month and 25000 IU/week for another 1.5 month). Before treatment their serum 25(OH)D was 17.3$\pm$6.1 ng/ml (mean$\pm$SD) and after treatment 37.0$\pm$7.5 ($P<0.0001$). Their HOMA-IR was 2.2$\pm$1.1 before and 2.3$\pm$1.1 after ($P=$NS), serum insulin 9.0$\pm$4.2 mIU/l before and 9.6$\pm$4.5 after (NS), glucose 96.2$\pm$8.2 mg/dl before and 97.0$\pm$10.0 after (NS), calcium 9.4$\pm$0.4 mg/dl before and 9.2$\pm$0.5 after (NS), parathyroid hormone (PTH) 82.5$\pm$34.2 pg/ml before and 61.4$\pm$29.4 after ($P<0.0001$), and BMI 26.2$\pm$3.8 before and 26.3$\pm$3.8 (NS) after treatment. The change in HOMA-IR and Insulin after therapy was not uniform in all the women. In 24 women (group I) HOMA-IR increased significantly: from 1.7$\pm$0.7 before to 2.4$\pm$1.2 after treatment ($P<0.0001$), and Insulin from 7.2$\pm$2.7 to 9.9$\pm$5.0 ($P=0.0003$). In 17 women (group D) HOMA-IR decreased significantly: from 2.9$\pm$1.2 to 2.2$\pm$1.0 ($P<0.0001$), and Insulin from 11.7$\pm$4.5 to 9.2$\pm$3.9 ($P<0.0001$). HOMA-IR and Insulin were significantly different before treatment ($P=0.0002$ and $P=0.0003$) between the two groups I and D, but they were not significantly different after treatment. PTH was not significantly different between the two groups either before or after treatment. The values of some parameters before and after treatment were combined and thus for group I the number of cases became n=48 and for group D n=34. There was a negative significant correlation between the combined values of PTH and 25(OH)D in group D but not in group I. The values of 25(OH)D were not significantly correlated with those of HOMA-IR in both groups. However, there was a significant negative correlation between HOMA-IR and PTH in group I ($P=0.04$), but a significant positive correlation between HOMA-HR and PTH in group D ($P=0.04$). Similar were the correlations between 25(OH)D or PTH with Insulin in both groups. Our conclusion is that during vitamin D therapy of vitamin D deficient women there is no direct effect of the serum 25(OH)D level on HOMA-IR or Insulin. The effect of the treatment is mediated by the level of PTH which is significantly correlated with HOMA-IR or Insulin. This conclusion is in keeping with the known from the literature direct effect of PTH on the beta cells of pancreatic islets affecting the secretion of insulin. It seems that the treatment increases the HOMA-IR in women with relatively low baseline values, but it decreases it in those with relatively high baseline HOMA-IR values.

DOI: 10.1530/endoabs.81.EP1179

EP1180

The Global Threat of non-communicable Diseases

Sophie Kiefer[1], Anna Scherdjow[1], Jonas Lüske[2] & Annina Althaus[3]
[1]FOM University of Applied Sciences | Elsenheimerstraße, München, Germany; [2]Charité – Universitätsmedizin Berlin, Berlin, Germany; [3]Berlin International University of Applied Sciences, Berlin, Germany

Background
Since the last decade, the disease pattern has significantly changed around the world. Non-communicable diseases, most commonly diabetes mellitus, have become the main threat to global health. The incidence of diabetes mellitus type 2 (DM2) is rising steadily, accounting for about two-thirds of deaths in Germany. Based on a prevalence of 9 million diabetic patients per year, DM2 constitutes a considerable medical and economic burden in Germany. However, the healthcare spending and its cost drivers are not yet sufficiently known.
Aims of the study
The primary objective of this study was to describe healthcare resource use and cost development of DM2 treatment in Germany, focusing on the most significant cost drivers and opportunities for cost-savings. The secondary objective was to analyse the impact of technical progress on diabetes care.
Methods
A systematic literature search was conducted in PubMed and Embase. Additionally, publications of the national health authorities (Robert Koch Institute RKI), Federal Joint Committee (Gemeinsamer Bundesausschuss G-BA) and the German Diabetes Society (Deutsche Diabetes Gesellschaft DDG) were included. Following the PRISMA guidance, the review identified the study design, epidemiological approach, analytical perspective, and data collection approach in each of the included studies.
Results
From 1.965 records, the final sample was composed of 41 articles. Most of the studies addressed direct costs and were based on calculations by extrapolations. The annual diabetes-specific direct costs of DM2 were between 542 and 6.323 € per patient. The most used method is the incremental or excess cost approach (1.8-fold higher costs compared to individuals without DM2). Confirmed risk factors included physical inactivity, obesity, genetic predispositions, and tobacco use. People with low social and income status had a significantly increased risk of developing DM2. The major cost drivers are demographic change with aging, exponentially increasing obesity, the availability of medications and therapies and the increased use of medical services by patients due to available treatment options of diabetic complications. Increasing prevalence, especially in childhood, is a major cost driver on its own. The preventive measures taken so far have not yet paid off. The potential financial savings from medical-technological progress are eroded by increasing age and use of medical services.
Conclusion
DM2, based on the results of this study, constitutes a considerable medical and economic burden in Germany and has a serious impact on the government health expenditures. To successfully combat diabetes and reduce health care expenditures, preventive efforts must be intensified.

DOI: 10.1530/endoabs.81.EP1180

EP1181

Knockdown of CASK in Pancreatic β Cells Affects Adipocyte Insulin Sensitivity by Reducing Exosome Release

Ting Xiao & Yao Wang
Southeast University, Department Of Clinical Medicine, Nanjing, China

Objective
Previously, we identified that knockdown of calcium/calmodulin-dependent serine protein kinase (*Cask*) in β cells *in vitro* resulted in decreased insulin secretion. We then used the Cre-loxP system to specifically delete the *Cask* gene in β cells of mice, and the mice exhibited impaired glucose tolerance and glucose-stimulated insulin secretion under a normal chow diet. However, under a high-fat diet (HFD), the insulin sensitivity and glucose tolerance of KO mice were significantly improved than wild-type. The insulin-stimulated phosphorylation levels of IRS1 and AKT in adipose tissue of HFD-KO mice increased significantly, but there were no significant changes in insulin sensitivity in liver and skeletal muscle. Study shows that β cells can regulate the function of target organs by secreting miRNAs via exosomes. Therefore, this study mainly discussed whether knockdown of *Cask* in β cells specifically affected the insulin sensitivity of adipocytes by regulating the release of exosomes and their contents.
Methods
Cask-siRNA was used to knockdown the *Cask* gene in MIN6 cells. The secretion of exosomes was detected by NTA and WB. Fluorescent labeling exosomes released by β cells were co-incubated with mature 3T3-L1 adipocytes for observing the uptake of exosomes. Adipocytes were treated with exosomes from the supernatant of MIN6 cells, and the expression of insulin signaling pathway related proteins was detected. The exosomes were sequenced, and differentially expressed miRNAs were screened and analyzed. 3T3-L1 adipocytes were transfected with miR-15b minics/inhibitors to detect the expression of its target gene INSR and the downstream proteins.
Results
We found that knockdown of *Cask* in β cells reduced the secretion of exosomes, and adipocytes could absorb exosomes derived from β cells. The number of exosomes absorbed by adipocytes also decreased after *Cask* deletion. The insulin sensitivity of adipocytes treated with exosomes from *Cask*-knockdown MIN6 cells was significantly higher than control. In addition, it was found that the content of miR-15b in the exosomes of MIN6 cells decreased after knockdown of *Cask*, and miR-15b can inhibit the insulin signaling pathway. Overexpression of miR-15b in 3T3-L1 adipocytes reduced the expression of INSR and the insulin signaling pathway was blocked. While inhibiting miR-15b in insulin-resistant adipocytes rescued the damaged insulin signaling.
Conclusion
Cask participates in the release of exosomes in β cells. Knockdown of *Cask* reduces the release of exosomes, thus reducing the content of miR-15b in them. Adipocytes can absorb the exosomes from β cells, which causes the changes of insulin sensitivity through miR-15b.

DOI: 10.1530/endoabs.81.EP1181

EP1182

Association between lipid profile and diabetic nephropathy in type 1 diabetes mellitus

Patricija Poskaite[1,2], Lina Radzeviciene[2] & Rasa Verkauskiene[2]
[1]Lithuanian University of Health Sciences (LUHS), Department of Endocrinology, Kaunas, Lithuania; [2]Lithuanian University of Health Sciences, Kaunas, Lithuania

Introduction
Diabetic nephropathy (DN) is a severe complication of type 1 diabetes mellitus (T1DM) and has become common primary disease leading to end-stage renal disease worldwide. Abnormalities in lipid metabolism is very important in the progression of renal damage in patients with T1DM.
Aim
to assess the relationship between lipid abnormalities and diabetic nephropathy in type 1 diabetes mellitus patients.
Methods
we performed a retrospective analysis of clinical data from Litdiane database from 2013 to 2016. 18-67-year-old 100 patients with type 1 diabetes were enrolled in the study. Participants filled questionnaires about T1DM, disease duration, complications and treatment. Anthropometric parameters height and weight were measured. Laboratory tests including total cholesterol, triglycerides, low-density lipoprotein (LDL) and high-density lipoprotein (HDL) cholesterol, glycated hemoglobin (HbA_{1c}), creatinine, albumin in 24h urine sample were performed. Study included group 1 of 50 T1DM patients with DN and group 2 of 50 T1DM patients without DN. Patients taking statins and patients with eGFR $<$ 30 ml/min were excluded from the trial.
Results
62 females and 38 males participated in the study. Mean age in DN group was 38.4 ± 11.2 years and in group without DN 30.4 ± 10.3 years. Mean duration of diabetes was 17.7 ± 11.1 years, average body mass index (BMI) was 24.2 ± 3.9 kg/m^2, HbA1c 9 $\pm$ 2.2 %, eGFR 92 ± 30.9 ml/min/1.73m^2. Patients with macroalbuminuria (26%) and microalbuminuria (40%) had significantly increased serum cholesterol ($P < 0.05$). LDL cholesterol was significantly higher (3.3 ± 0.9) in DN group ($P = 0.005$). Cases of hypertriglyceridemia were significantly more frequent between males than females (39.5% vs 9.7% $P < 0.001$). Statistically significant relationship was verified between higher serum cholesterol (5.8 ± 1.5) and DN group ($P = 0.001$).
Conclusion
lipid metabolism is significantly impaired among patients with diabetic nephropathy. Early monitoring, regular screening and appropriate lipid-lowering drug therapy may delay further renal complications in type 1 diabetes mellitus patients.

DOI: 10.1530/endoabs.81.EP1182

EP1183

Weight loss induced by bariatric surgery may improve systemic inflammation: Preliminary results

Naim Pamuk[1], Seda Turgut[1], Hakan Seyit[2], Didem Acarer Bugün[1], Hamide Pişkinpaşa[1], Evin Bozkur[1], Mehmet Karabulut[2] & İlkay Çakır[1]
[1]University of Health Science Bakırköy Dr. Sadi Konuk Training and Research Hospital, Endocrinology and Metabolism, Istanbul, Turkey; [2]University of Health Science Bakırköy Dr. Sadi Konuk Training and Research Hospital, General Surgery, Istanbul, Turkey

Background
Obesity is a widespread disease that causes chronic low-grade inflammation and related chronic diseases such as steatohepatitis, metabolic syndrome, diabetes mellitus (DM), and cancer. It is known that weight loss positively affects life expectancy by reducing obesity-related complications. Therefore, effective management of particularly morbidly obese patients is getting prominent in clinical practice. Bariatric surgery (BS) is the main effective treatment option and weight loss method for morbid obesity. This study aimed to investigate the impact of bariatric surgery on systemic inflammation and metabolic parameters.
Methods
Morbid obesity patients who underwent BS between December 2014 and June 2020 were screened retrospectively. Patients with inadequate data or diagnosed acute or chronic inflammatory disease were excluded. A total of 693 patients between 18 and 65 years were included in the study. The preoperative and postoperative 12th-month data were analyzed. A novel hematologic and immune biomarker systemic inflammation response index (SIRI) was calculated to evaluate inflammation. ΔSIRI computed as the preoperative SIRI (SIRI1) minus the postoperative 12th-month SIRI (SIRI2). The percent of total weight loss (%TWL) was also calculated to classify participants. The patients with %TWL < %40 were defined as Group 1, and patients with %TWL ≥ %40 were defined as Group 2. All parameters were compared between the groups.
Results
The mean age of 693 patients (152 female/541 male) was 39.9 ± 10.3 years. The mean body mass index was 47.7 ± 6 preoperatively and 30.2 ± 5.4 postoperatively at the 12th month. The mean SIRI1 (1.14 ± 0.54) was significantly higher than the mean SIRI2 (0.77 ± 0.45) for all patients ($P < 0.001$). Group 2 had significantly higher ΔSIRI and lower age than Group 1 ($P = 0.001$, $P < 0.001$, respectively). In addition, the frequency of both diabetes and hypertension increased in group 1 ($P < 0.001$ for both). After controlling for age, gender, hypertension, and DM covariates, only ΔSIRI levels sustained the significant difference status ($P = 0.007$). All metabolic parameters significantly improved after bariatric surgery ($P < 0.05$).
Conclusion
The present study showed that regardless of age, DM, and hypertension, increased inflammation recovery is significantly associated with effective weight loss. In the light of this finding, we suggest BS may give an independent contribution to the improvement of chronic inflammation induced by obesity. Further prospective studies in larger populations may improve the management of morbidly obese patients by clarifying the inflammation mechanism and process.

DOI: 10.1530/endoabs.81.EP1183

EP1184

The relevance of managing ketoacidosis in otologic mucomycosis

Meherzi Abir, Safa Jemli, El Omri Malika, Marwa Ben Njima, Habiba Ben Shgaeir, Mouna Bellakhdher, Jihene Houass, Kermani Wassim & Abdelkefi Mohamed
ENT Department Farhat Hached Hospital Sousse, Sousse, Tunisia

Background
Uncontrolled diabetes mellitus in ketoacidosis, as well as other kinds of metabolic acidosis, are major risk factors for mucormycosis. As the frequency of diabetes mellitus increase, so does the number of individuals at risk for this lethal infection. However, a lack of symptoms could lead to a delay in diagnosis. The aim of this paper is to study the clical features of otologic mucomycosis and to analysis the impact ketoacidosis the disease's course.
Materials and methods
The zygomycete infection was confirmed by either or both histologically and mycological examination of specimens.
Result
Auricular mucormycosis was diagnosed in 4 patients. Patient ages ranged from 3 to 78 years, with a median age of 58.75 years. There were 3 (75 %) male subjects. The underlying diseases were kidney failure in one patient, cell-mediated immunity defect in another one and diabetes mellitus was noted in one case. No underlying condition was registred in one case. Auricular mucormycosis involved otocerebral (2 patients), chronic otitis media (1 patient) and malignant otitis externa (1 patient). Diagnosis was obtained by positive histology, positive direct microscopy and fungal culture in all patients. The species identified were Lichtemia corymbifere in two cases, Rhizopus arrhizus in one case, and Rhizopodiformis in the latter case. The quasi majority of antifungal-treated patients (3/4cases) received an amphotericin B formulation (amphotericin B deoxycholate in two cases and liposomal amphotericin B (L-AmB) in one case). Two (2/3) of these patients received amphotericin B in combination with other antifungals (fluconazole in one case and itraconazole in the other case). Mucormycosis was considered responsible for death in one patient.
Conclusion
Ketoacidosis is a significant factor in the development and in the control of this lethal infection. thereby it is important to optimalize information for clinicians in charge of diabetic patients.

DOI: 10.1530/endoabs.81.EP1184

EP1185

The role of preoperative thyroid function tests in weight loss after bariatric surgery in morbidly obese patients

Didem Acarer Bugün[1], Seda Turgut[1], Hakan Seyit[2], Naim Pamuk[1], Hamide Pişkinpaşa[1], Evin Bozkur[1], Mehmet Karabulut[2] & Meral Mert[1]
[1]University of Health Science Bakırköy Dr. Sadi Konuk Training and Research Hospital, Endocrinology and Metabolism, Istanbul, Turkey; [2]University of Health Science Bakırköy Dr. Sadi Konuk Training and Research Hospital, General Surgery, Istanbul, Turkey

Background
Obesity is one of the most critical problems nowadays, its frequency and consequences. Since the risk of morbidity and mortality increases in obese individuals, lifestyle changes, pharmacotherapy, and bariatric surgery (BS) methods are used for treatment. BS is generally considered the most effective method to treat morbid obesity. However, it is known that thyroid function has a role in weight regulation, the effect of preoperative thyroid function on weight loss after BS is not fully understood. Therefore, we aim to evaluate the impact of thyroid function tests and metabolic variables on weight loss after BS.
Methods
The patients who underwent bariatric surgery between 01.12.2014 and 01.06.2020 in our hospital were retrospectively screened. Patients with a history of thyroid disease treated with thyroid hormone or antithyroid drugs were excluded from the study. A total of 635 patients between 18 and 65 years were included, preoperative and postop 1st-year data were recorded, and the percent of total weight loss (%TWL) was calculated, in our study. Patients were divided into two groups in terms of %TWL. Those with %TWL < 35 were defined as Group 1, and those with %TWL < 35 were defined as Group 2. All parameters were compared between the groups. Regression analysis was applied to evaluate which factors affected postoperative weight loss contributed more to the outcome.
Results
The mean age of 635 patients (154 male/481 female) was 39.3 ± 10.6 years. Age, pre-and postop fasting plasma glucose (FPG), postop ALT levels were significantly higher in Group 1 than Group 2 ($P < 0.001$, $P = 0.011$, $P < 0.001$, $P = 0.009$, respectively). FT3 level was significantly higher in Group 2 than Group 1 ($P = 0.005$). While there was no significant difference between the two groups regarding gender, DM and HT patients were significantly more frequent in Group 1 ($P = 0.003$, $P = 0.005$, respectively). The regression analysis determined that increasing fT3 levels raised the probability of being in %TWL ≥ 35 group by 1.6-fold (OR = 1.577, $P = 0.027$).
Conclusion
Weight loss after BS varies according to individuals. Therefore, predicting patients who will respond better to surgery is essential for the clinical management and follow-up of patients with obesity. In this regard, the present study showed that increasing fT3 levels, even if in the normal range, raised the probability of losing weight adequately.

DOI: 10.1530/endoabs.81.EP1185

EP1186

Hypobetalipoproteinemia: case report and literature review

Matheus Kowal Rosales[1], Laura Vilas Boas[2], Thielsen Cardoso da Silva[2], Jéssica Maria Telles[1], Gabrielle Andrusko dos Santos[1], Marcela Malinoski Munoz[3] & Mirnaluci Paulino Ribeiro Gama[1]
[1]Hospital Universitário Evangélico Mackenzie, Brazil; [2]Evangelical Mackenzie Faculty of Parana, Brazil; [3]Federal University of Paraná - UFPR, Brazil

Introduction
Primary hypobetalipoproteinemia corresponds to a series of congenital disorders that have a variable incidence from 3.2% to less than 1 in 1 million, depending on the type of genetic mutation. The diseases that comprise it occur due to different types of mutations in genes that will encode important proteins at different stages of lipid metabolism. Individuals with determinant mutations of severe phenotypes, such as Bassen-Kornzweig syndrome, as known as Abetalipoproteinemia (ABL), chylomicron retention disease (CRMD), homozygous familial hypobetalipoproteinemia (FHBL), may present manifestations even during childhood with a picture of malabsorption of fats with vomiting, steatorrhea and weight-height deficit, and later on, they progress with progressive affections resulting from deficiency of fat-soluble vitamins, such as retinal degenerations and neuropathies. Heterozygous individuals are often asymptomatic although they may develop fatty liver disease and eventually some vitamin deficiencies.
Case report
A 20-years-old male patient was referred to endocrinology service due to a lipogram alteration. Asymptomatic, reported having a balanced diet, without being submitted to any type of diet. Maintained a preserved intestinal habit, with no significant history of diarrheal conditions. Laboratory tests showed total cholesterol 61 mg/dl, HDL 30.4 mg/dl, LDL 17.4 mg/dl. VLDL 10.6 mg/dl and triglycerides 53 mg/dl are associated with a deficiency of fat-soluble vitamins (vitamin D, E, and K). Apolipoprotein B dosage was 24 mg/dl (RV: 55 to 155 mg/dl) and also had an abdominal ultrasound with evidence of mild hepatic steatosis.
Conclusion
Hypobetaliproteinemia corresponds to a heterogeneous group of diseases. Most of them do not cause serious manifestations and go unnoticed. However, even these can lead to late repercussions such as liver disease and hypovitaminosis. Therefore, it is important to be attentive to patients with low levels of LDL and total cholesterol, avoiding dismissing these findings as "benign" changes. Despite this, it must be recognized that, possibly, these patients have some cardiovascular protection due to low LDL titers. The severe forms, despite being very rare, lead to evident clinical manifestations in the first years of life, showing the importance of lipids for humans.

DOI: 10.1530/endoabs.81.EP1186

EP1187

Endocrinological and inflammatory markers in individuals with spinal cord injury: A systematic review and meta-analysis

Gabriela Böhl[1], Peter Francis Raguindin[1,2,3], Ezra Valido[1, 4], Alessandro Bertolo[1, 5], Oche Adam Itodo[1,2,3], Beatrice Minder[6], Patricia Lampart[7], Anke Scheel-Sailer[7], Alexander Leichtle[8], Marija Glisic[1, 2] & Jivko Stoyanov[1,2]
[1]Schweizer Paraplegiker-Forschung, SCI Population Biobanking and Translational Medicine Group, Nottwil, Switzerland; [2]University of Bern, Institute of Social and Preventive Medicine, Bern, Switzerland; [3]University of Bern, Graduate School for Health Sciences, Bern, Switzerland; [4]University of Lucerne, Department of Health Sciences and Medicine, Luzern, Switzerland; [5]Inselspital, Department of Orthopedic Surgery, Bern, Switzerland; [6]University of Bern, Public Health & Primary Care Library, Bern, Switzerland; [7]Schweizer Paraplegiker-Zentrum, Nottwil, Switzerland; [8]Inselspital, University Institute of Clinical Chemistry, Bern, Switzerland

Background
Spinal cord injury (SCI) can lead to dramatic physiological changes which can be a factor in developing secondary health conditions and might be reflected in biomarker changes in this elevated risk group. We focused specifically on the endocrine and inflammation profile differences between SCI and able-bodied individuals (ABI).
Objectives
To determine the differences in inflammatory and endocrine markers profiles between individuals with SCI and ABI.
Methods
We systematically searched 4 electronic databases for relevant studies. Data was extracted and assessed by two independent reviewers. Weighted mean difference between SCI and ABI was calculated using random-effects models. Heterogeneity was computed using I^2 statistic and chi-squared test. Study quality was evaluated through the Newcastle-Ottawa Scale.
Results
The search strategy yielded a total of 2,603 records after duplicates were removed. Titles and abstracts of records were screened, from which 256 articles were selected for full-text assessment. Sixty-two studies were included in the meta-analysis. Most of the studies were conducted only among male SCI individuals (68%), had a sample size of or fewer than 100 participants (74%), and were conducted in North America (40%). The mean age of the study population ranged from 16 to 64 years and the mean injury duration ranged from <1 to 29 years, with the majority of studies containing both individuals with tetraplegia and paraplegia (77%). One-third of the studies (31%) included individuals with complete injury, while 40% of the studies had both complete and incomplete injury. Most of the studies were classified as being of moderate quality (71%). SCI individuals had higher levels of pro-inflammatory C-reactive protein and IL-6 than ABI. Creatinine and Vitamin D levels were lower in SCI than ABI. Total testosterone levels and IGF-1 were also found to be lower, while cortisol and leptin levels were higher in SCI when compared to ABI. However, no significant differences were found regarding glucose and insulin. Accordingly, meta-regression, subgroup analysis, and leave-one-out analysis, were performed, however they were able to only partially explain the high levels of heterogeneity.
Conclusion
Individuals with SCI show higher levels of inflammatory markers and present significant endocrinological changes when compared to ABI. Moreover, higher incidence of obesity, diabetes, osteoporosis and hypogonadism in SCI individuals, together with decreased creatinine levels reflect some of the readily measurable aspects of the phenotype changes in the SCI group. These findings need to be considered in anticipating related medical complications and personalizing SCI medical care.

DOI: 10.1530/endoabs.81.EP1187

EP1188

The relationship between free thyroid hormones and diabetic retinopathy in euthyroid patients with type 2 diabetes mellitus

Leyla Akdoğan[1], Şefika Burç ak Polat[1], Nagihan Uğurlu[2], Ahmet Dirikoç[1], Didem Özdemir[1], Oya Topaloğlu[1], Reyhan Ersoy[1] & Bekir Çakır[1]
[1]Ankara Yildirim Beyazit University Faculty of Medicine, Ankara Bilkent City Hospital, Department of Endocrinology and Metabolism, Ankara, Turkey; [2]Ankara Yildirim Beyazit University Faculty of Medicine, Ankara Bilkent City Hospital, Department of Ophtalmology, Ankara, Turkey

Introduction
The prevalence of diabetes mellitus (DM) continues to increase worldwide. Diabetic retinopathy (DRP) is one of the most common complications of Type 2 DM. Recently, the effect of thyroid hormones on diabetic microvascular complications has gained much attention. This relationship is explained by the important effects of thyroid hormones on endothelial function. There are studies investigating the relationship between TSH and diabetic nephropathy and DRP. There are very few studies evaluating free thyroid hormone levels. In this study, it was aimed to investigate the relationship between free thyroid hormone levels and DRP in euthyroid patients with type 2 DM.
Method
In this study, the biochemical records of patients with Type 2 DM who had euthyroid status and evaluated for retinopathy, applied to the endocrinology and ophtalmology clinics of our hospital between January 2018 and August 2018. Demographic data of the patients and characteristics that may be associated with diabetic retinopathy were evaluated. Whether the patients had DRP and, if any, retinopathy levels were recorded. It was evaluated whether there was a difference in free thyroid hormone levels between the groups with and without DRP.
Results
A total of 171 patients, 106 men and 65 women, were included in the study. Mean age was 57.19 $\pm$10.81 years. DRP was not present in 127 patients (74.2%), nevertheless 36 patients (21%) had nonproliferative DRP and 8 patients (4.6%) had proliferative DRP. There was no difference between the groups in terms of age, gender, hypertension, cardiovascular disease, fasting plasma glucose, serum creatinine, lipid levels and microalbuminuria. The duration of diabetes was longer in the nonproliferative DRP group ($P=0.026$). HbA1c levels were higher in the proliferative DRP group ($P=0.05$). No significant difference was found in terms of TSH levels and free thyroid hormone levels in all three groups.
Conclusion
In our study, the relationship between free thyroid hormone levels and DRP in euthyroid type 2 DM patients was investigated. Diabetes duration and Hba1c levels were found to be risk factors in DRP similar to the literature. When the

groups with and without DRP were compared, no difference was found in TSH and free T4 and free T3 levels.

DOI: 10.1530/endoabs.81.EP1188

EP1189

Diabetes mellitus in the Tashkent region of Uzbekistan

Feruza Takhirova & Nodira Alikhanova
Republican Specialized Scientific And Practical Medical Center Of Endocrinology named after academician Yo.Kh.Turakulov, Diabetology, Tashkent, Uzbekistan

Objective
Studying the prevalence of diabetes mellitus is necessary to assess the epidemiological situation in the region
Aim
To study the prevalence of diabetes mellitus in the Tashkent region.
Methods
The source of information was the data of the statistics office of the endocrine dispensary of the Tashkent region for the period 2018-2020. For the statistical processing of the data, the Microsoft Excel 2010 program was used.
Results
The largest number of patients is observed in Zangiata district of Tashkent region, which is 2.29% of the adult population of the district, the lowest prevalence of diabetes is observed in Bekabad and Bustanlik districts (1.11%); the number of diagnosed patients with diabetes in 2020 in the Tashkent region was 3416 people (0.17%); the highest percentage of type 1 diabetes mellitus type 2 diabetes is observed in the Angren region 26.3% to 73.7%.
Conclusion
Analysis of the situation with diabetes mellitus in the Tashkent region showed that, like throughout the Republic of Uzbekistan, there is late diagnosis of type 2 diabetes mellitus, and not all patients are registered.

DOI: 10.1530/endoabs.81.EP1189

EP1190

NanoLuc® Binary Technology to explore the mechanism of action of a Magmas inhibitor

Patricia Borges de Souza, Irene Gagliardi, Maria Rosaria Ambrosio, Marta Bondanelli & Maria Chiara Zatelli
Unifersity of Ferrara, Department of Medical Sciences Section of Endocrinology, Ferrara, Italy

Introduction
Magmas encodes for an integral constituent of the TIM23 translocase complex located in the mitochondrial inner membrane that drives proteins from the intermembrane space into the mitochondrial matrix by functionally interacting with Tim14. We previously demonstrated that Magmas silencing is able to sensitize ACTH-secreting mouse pituitary adenoma cells to pro-apoptotic stimuli, reduce DNA synthesis, accumulate cells in G0/G1 phase with concomitant decrease in S phase, supporting the hypothesis that Magmas may play a role in tumor development by protecting neoplastic cells from apoptosis and by promoting cell proliferation. We then synthesized a protein Magmas inhibitor, reported herein as "Compound 5", which does not affect viability of cancer cells, but sensitizes them to the pro-apoptotic effects of chemotherapeutic agents such as Staurosporine, Doxorubicin and Cisplatin. These studies provide evidence for a role of Magmas in chemoresistance and indicate that Compound 5 may be useful to restore sensitivity of chemoresistant cancers cells, possibly allowing for a reduction in chemotherapeutic agent effective dose, with consequent decrease in side effects.
Aim
The purpose of this research is to understand whether the mechanism of action of Compound 5 is to disrupt Tim16-Tim14 interaction. This issue is important to explore the key features of Magmas inhibitors, providing information as to the better chemical structure of these compounds which might increase their chemosensitizing effects.
Methods
Tim16 and Tim14 were amplified from pCMV6-Entry vectors and cloned into NanoBiT® Expression Constructs using unique restriction enzyme sites present in the MCS of each vector. The resulting vectors containing Tim16 or Tim14 genes were transformed into One Shot® TOP10 Chemically Competent *E. coli* and the resulting ligation DNA was miniprepped. For each gene of interest, 4 possible ligation combinations may exist considering both -C and -N terminal tags. These constructs were transfected into chemoresistant cells 2 by 2 (Tim16:Tim14). After 48 h Compound 5 was added at a final concentration of 5uM and after 3 h luminescence from living cells was detected by use of furimazine for up to 2 h.
Results
Tim16 and Tim14 interaction was confirmed by measuring luminescence, developing when Tim16 and Tim14 were -C terminal tagged. The addition of Compound 5, on the other hand, decreased by $>65\%$ luciferase emission ($P<0{,}0001$).
Discussion
Compound 5 could be further developed to aid the treatment of chemoresistant cancer. Not only it is devoid of toxic activity, but enhances the pro-apoptotic stimuli of chemotherapy, by specifically targeting Tim16-Tim14 interaction.

DOI: 10.1530/endoabs.81.EP1190

EP1191

Hypoglycemia due to non islet cell tumor in a non-diabetic patient- a case report

Hanaan Ashraf[1] & Idrees Mubarik[2]
[1]Aster DM Healthcare, Internal Medicine, Dubai, United Arab Emirates; [2]Aster DM Healthcare, Endocrinology, Dubai, United Arab Emirates

Background
Non-islet-cell tumor hypoglycemia (NICTH) is a rare but severe complication of malignancy. NICTH has been related to the production of IGF II by tumours of mesenchymal or epithelial origin. It gives rise to frequent episodes of severe hypoglycemia and can have negative impact on quality of life. This case report describes a case of Non Islet cell tumor hypoglycemia due to hepatocellular carcinoma with hypoglycemia as the first presentation.
Clinical presentation
34 years old male patient brought to the ER by ambulance as patient was found unresponsive with blood sugars of 30 mg/dl. Patient was started on dextrose infusion and regained consciousness. On history patient has been having episodes of headache and increased hunger and abdominal discomfort for the past 1 month duration. These episodes occurred thrice a week. He had noticed increase in size of abdomen, fullness and loss of appetite. Patient denied history of Alcohol or Drug use. He had no positive past medical/surgical/family history. On examination patient was cachexic, Abdomen non tender hepatomegaly and ascites. Cardiovascular and Respiratory system examinations were normal. Laboratory investigation of the patient revealed Hb 10.9 mg/dl, WBC-5.8(n- 67.6, l-19.7), PLT-363, LFT: AST-83, ALT-39, GGT-399, Alk phosphatase 278, Insulin-0.20 mIU/ml, C-peptide 0.68 ng/ml, creatinine 0.78, Hba1c-4.5, Insulin antibodies negative, Hepatitis B + ve. USG Abdomen revealed large heterogenous predominantly hyperechoic lesion of right lobe of liver with the possible thrombotic occlusion of right portal vein seen likely suggestive of neoplastic aetiology, ascites present. CT abdomen and pelvis reported hepatomegaly and large mass lesion involving right lobe of liver measuring 18.2 x 14.4 x 13.5 cm in size. The mass had invaded portal vein confluence and right branch of portal vein. Patient was subsequently evaluated for AFP-181500 IU/ml, IGF-1-36.74 ng/ml, CEA-0.50 ng/ml. The diagnosis of Hepatocellular carcinoma was made, Multidisciplinary team was formed, patient was treated for hypoglycemia with dextrose infusion and prednisolone 60 mg/day, planned for PET scan to check for metastasis, debulking/palliative care for relief from hypoglycemia.
Conclusion
NICTH is a rare condition and its incidence is unknown. It is more likely to develop in those with large tumor burden. The diagnosis can be confirmed by a combination of suppressed serum insulin levels and suppressed C peptide and growth hormone concentrations in the setting of hypoglycemia, along with elevated IGF-II levels. Initial treatment aims at maintaining euglycemia, managed with parenteral dextrose infusion. Identification of NICTH and complete tumor resection represents ideal management.

DOI: 10.1530/endoabs.81.EP1191

EP1192

Insulin autoimmune syndrome (hirata's disease) -a case report

Hanaan Ashraf[1] & Idrees Mubarik[2]
[1]Aster DM Healthcare, Internal Medicine, Dubai, United Arab Emirates; [2]Aster DM Healthcare, Endocrinology, Dubai, United Arab Emirates

Background
Insulin autoimmune syndrome (IAS) or Hirata disease, is a rare cause of hyperinsulinemic hypoglycemia characterized by autoantibodies to endogenous insulin in individuals without previous exposure to exogenous insulin. IAS has been described as a form of type VII hypersensitivity, characterized by the presence of autoantibodies against a circulating antigen. The cornerstone of the IAS is the appearance of circulating insulin autoantibodies (IAA), which have a pathogenic role in the development of the syndrome. Occasionally It develops when a triggering factor that is a medication or a viral infection acts on an underlying predisposing genetic background. Here, we report a case of Insulin Autoimmune Syndrome.
Clinical presentation
43 years old Asian woman presenting to the ER with diaphoresis and tremors for the past 10 days duration. She had 3-4 episodes/day and were triggered by fasting and exercise. Her blood glucose when checked was noted to be 45 mg/dl. Patient was administered dextrose infusion and evaluated for hypogylcemia. She is non diabetic, no other comorbidities and was not on any medications. General physical examination revealed an obese, alert and healthy female. Her blood pressure 130/82 mmHg and pulse rate was 84/min. She was admitted for 72 hour fast test, patient was kept NPO and closely monioted for symptomatic hypoglycemia. Patient developed diaphoresis and tremors, blood glucose of 50 mg/dl, Samples for insulin, C- peptide, Pro Insulin, serum Beta hydroxy butyrate, and urine ketones were collected, fast terminated and patient was given oral carbohydrates and her condition improved confirming presence of Whipples triad. Her laboratory investigations revealed renal function, liver function tests, thyroid profile and hemogram to be normal. Her 8 am cortisol 12, Hba1c:5.5, Insulin $>$ 1000.0 mIU/ml, Pro insulin 69.70 pmol/l ($<$11), Beta butyric acid $<$60 umol/l.C-peptide 6.29 ng/ml (0.78-5.19), Insulin antibody $>$100 U/ml ($>$10 positive). Usg Abdomen was normal. Contrast enhanced CT abdomen was performed to look for pancreatic pathology and was normal. Diagnosis of Insulin autoimmune syndrome is made. She was adviced frequent small meals and also treated with steroids for a week. On follow up she had resolution of her symtpoms.
Conclusion
The diagnosis of IAS is challenging and should be considered in any patient undergoing evaluation for hypoglycemia. Discrepancies between an unusually high insulin concentration and slightly raised proinsulin and C-peptide levels, with a concurrent insulin to C-peptide molar ratio of $>$ 1, are suggestive of IAS.

DOI: 10.1530/endoabs.81.EP1192

EP1193

Higher blood lead level with menopause and weight recycling in korean women

Kyu Rae Lee
Gachon University Of Medicine And Science, Family Medicine, Incheon, Rep. of South Korea

Background
Previous studies show that lead levels are closely related with obesity, and severe weight reduction in obese women increases skeletal bone mobilization and blood lead levels especially postmenopausal women. However, it is under the curtain if blood lead level is associated with menopause, weight recycling in women until now.
Methods
We assessed weight, height, waist circumferences and obtained past medical histories, blood lead levels as well as socio-demographic, cardio-metabolic variables of 1043 women participated KNHANES (Korea National Health Analysis Nutrition Examination Survey) in 2018. All participants were recategorized into four groups [premenopausal weight loss (-1), premenopausal weight stable (0), postmenopausal weight stable (1), postmenopausal weight gain (2)]. ANCOVA tests were performed using by SPSS for window (Ver. 18, Il, USA) and probabilities less than 0.05 was significant at both sided.
Results
Higher blood lead levels showed significantly associated with higher cardio-metabolic risk variables (hypertension, hyperglycosemia, hypertriglyceridemia, and low HDL cholesterolemia), more obese in postmenopausal weight recycling gain group. ($P<0.01$)
Discussion and Conclusion
Further controlled clinical trial would be considered in the future. We concluded that higher blood lead levels were associated with postmenopausal Korean women with weight recycling.
Keyword: blood lead level, obesity, menopause, weight recycling, women

DOI: 10.1530/endoabs.81.EP1193

EP1194

Acromegaly presenting with type 2 diabetes: a case report

Yilmaz Cankurtaran[1] & Zehra Yagmur Sahin Alak[2]
[1]Aydın, Bozdoğan Rasim Menteşe State Hospital, Internal Medicine Department, Aydın, Turkey; [2]Bursa, Health Sciences University, Bursa Yuksek Ihtisas Research and Training Hospital, Endocrinology and Metabolism, Bursa, Turkey

Introduction
Alterations in glucose homeostasis and diabetes mellitus (DM) are the most common metabolic comorbidities in acromegaly. DM has been reported in 16–56% of patients with acromegaly. It is estimated that 20% of patients with acromegaly have developed DM before the formal diagnosis of acromegaly. We report a case of a patient with acromegaly secondary to a pituitary macroadenoma who presented with diabetes.
Case report
A 47- year-old female patient was admitted to our internal medicine clinic for control and assessment of diabetes before tooth extraction due to dental caries. She had suffered from type 2 diabetes for ten years. She had been unable to control the blood glucose level adequately, 1- year history of amenorrhea, generalized fatigue and weight loss for the last one year. She had been on oral antidiabetic therapy (metformin, dapagliflozin, gliclazide, and sitagliptin) for one year with bad glucose values. On examination, her vital signs were within normal. Physical examination revealed acromegalic coarsened facial features but she had no clear-cut cushingoid features and acral enlargement. Anthropometry and laboratory tests were as follows: Height, 150 cm; body weight 55 kg; body mass index (BMI), 24.44 kg/m^2 basal and postprandial glycemia 202, and 280 mg/dL respectively, A1c level of 11.8%. Investigations revealed high IGF-1 levels of 735 mg/l (101–267 mg/l) and growth hormone nadir (1 hour after a 75-g oral glucose load) was 30 ng/mL ($<$1 ng/mL). Complete pituitary hormonal profile revealed prolactin 28.29 ng/mL (4–25 ng/mL), thyroid-stimulating hormone 1.02 uIU/mL (0.35–4.94 uIU/mL), FT3 2.81 pg/mL (2.3–4.2 pg/mL), FT4 1.25 ng/dL (0.89–1.76 ng/dL), follicle-stimulating hormone 57.78 mIU/mL (3.35-21.63 mIU/mL), luteinizing hormone 15.94 mIU/mL (2.39-6.6 mIU/mL), adrenocorticotropic hormone 26.7 pg/mL (7.2-63.3 pg/mL) and cortisol 22.71 mg/dl (5.27-22.45 mg/dl). Magnetic resonance imaging of the sella demonstrated a 17x14 mm pituitary adenoma. The patient was diagnosed with acromegaly, and acromegaly-associated exacerbation of diabetes mellitus. Trans-sphenoidal resection was performed and histopathologic and immunohistochemical findings indicated GH and PRL -producing pituitary adenoma.
Discussion
Acromegaly is often develop insidiously and diagnosis may be delayed as a consequence. The present report outlines a case of missed diagnosis of acromegaly associated with severe hyperglycemia. Clinical suspicion of acromegaly is generally difficult during anamnesis of patients with DM, particularly in the absence of disease-related symptomatology. When treating patients diagnosed with diabetes, secondary causes should not be neglected.

DOI: 10.1530/endoabs.81.EP1194

EP1195

What predictive factors influencing stature gain during the first year GH therapy?

Wahiba Abdellaoui[1], Tahri Abir[1], Nada El Yamani[1], Siham Rouf[1, 2] & Hanane Latrech[1,2]
[1]Mohammed VI University Hospital, Medical School, Mohammed the First University, Department of Endocrinology-Diabetology-Nutrition, Morocco; [2]Laboratory of Epidemiology, Clinical Research and Public Health, Faculty of Medicine and Pharmacy of Oujda, Mohammed the First University, Morocco

Introduction
Growth Hormone deficiency (GHD) is a rare etiology of short stature. The lack of early diagnosis and adequate treatment have adverse consequences, especially the small final height with the resulting psychological impact. The aim of this study is to identify some of the predictive factors influencing stature gain during the first year of GH therapy.
Matherials and methods
This is a retrospective and analytical study regarding 36 children with GHD, collected in the endocrinology department of Mohammed VI Hospital. The data were collected and processed using SPSS software V21.
Results
The prevalence of patients with GHD is 16.36% among 220 cases with short stature requiring exploration. The mean chronological age (CA) at the start of

treatment was 11,6 years. Mean height Z-score at time of diagnosis was −4,3 SD. The delay of bone age (BA) over the chronological age was of 4,2 years on average. The mean therapeutic dose was 0.025 to 0.035 mg/kg/day. The average stature gain at the end of the first year of GH treatment was 10,5 cm. Correlation analysis showed that a change in height gain in the first year had a significant correlation with the age at the start of treatment ($P<0.001$), the severity of growth hormone deficiency ($P=0,047$) and the presence of multiple pituitary hormone deficiencies ($P=0.18$). No correlation was found between height gain and sex gender, body mass index, and abnormalities on pituitary magnetic resonance imaging.
Conclusion
Despite a very evocative clinical features, the diagnosis of GHD remains difficult and relatively late in some patients. The height gain is more important during the first year of GH therapy. The earlier the treatment is administrated, the better the results will be in case of a severe deficiency.

DOI: 10.1530/endoabs.81.EP1195

EP1196

Permanent central diabetes insipidus after traumatic brain injury

Ludmila Astafyeva[1], Yuliya Sidneva[1], Inna Badmaeva[1], Pavel Kalinin[1], Svetlana Valiullina[2] & Andrey Marshintsev[2]
[1]Burdenko Neurosurgery Center, Moscow, Russian Federation; [2]Clinical and Research Institute of Emergency Pediatric Surgery and Trauma (CRIEPST), Moscow, Russian Federation

The article presents a case of permanent central diabetes insipidus (CDI) in a patient after severe traumatic brain injury (TBI) in traffic accident. A 16-year-old boy entered to a medical facility in the coma (6 points of Glasgow Coma scale (GCS)). Diagnosis: acute TBI; severe cerebral contusion; subarachnoid hemorrhage; depressed comminuted cranial vault fracture; basilar skull fracture; visceral contusion. CDI diagnosed three days after injury when polyuria and hypernatremia (155 mmol/l) developed. Desmopressin therapy started through a feeding tube. Thirst was appeared when patient out of coma on day 21 while desmopressin therapy was continuing. Because of persistent thirst and polyuria desmopressin therapy continued in the spray form. Against this backdrop polyuria reduced to 3-3.5 liters per day while nasal desmopressin therapy was continuing. The symptoms of CDI persisted in the long-term period two years after TBI while the intact adenohypophysis function. This case demonstrates a rare development of permanent diabetes insipidus in a boy after TBI. CDI manifested only as polyuria and hypernatremia in a coma. Thirst joined at rising levels of consciousness. The probable causes of CDI were neurohypophysis and his tract injury as a result of extended basilar skull fracture and/or irreversible secondary hypothalamus injury because of brain diffuse axonal damage after head trauma.

DOI: 10.1530/endoabs.81.EP1196

EP1197

Pilomyxoid astrocytoma revealed by a failure to thrive: An uncommon case report

Salma Ben Yakhlef, Achwak ALLA, Wahiba ABDELLAOUI, Siham ROUF & Hanane Latrech
Mohammed VI University Hospital, Mohammed I University, Oujda, Morocco, Department of Endocrinology- Diabetology, Oujda, Morocco

Introduction
Pilomyxoid astrocytoma (PMA) is a rare entity usually described in the hypothalamic-chiasmatic area. It generally concerns infants and very young children. Clinical presentation is not well-defined. But, the therapists should be aware of diencephalic syndrome as an unconventional cause of failure to thrive during early childhood. We report a case of PMA exhibited by failure to thrive;which is a rare outlined association in the litterature.
Case report
An 11-month-old boy was admitted to our university hospital for further exploration of poor weight gain (<3rd percentile). The physical examination revealed pallid and dry skin besides lack of subcutaneous fat. He had a sunken anterior fontanel, muscle atrophy and left eye's nystagmus. Brain magnetic resonance imaging (MRI) exhibited a suprasellar mass measuring 59*41*40 mm, isointense on T1-weighted MRI and hyperintense on T2-weighted MRI and homogeneously enhanced upon contrast administration. The lesion extended into retro-sellar region, optic chiasm and right hypothalamus. The lesion compressed mainly temporal lobes, cerebral pedicles and the anterior surface of the pons. The patient underwent a right pterional craniotomy besides a subtotal tumor resection (95%). After the surgery, the child's clinical course declin ed with blindness of the left eye and left-sided mild hemiparesis besides focal seizures prevented by Levetiracetam twice a day. Hormonal assessment in post op period showed a panhypopituitarism. Therefore, hormonal replacement medications have been immediately introduced. Histological examination revealed monomorphous bipolar cells with a generous myxoid matrix and an angiocentric disposition of the tumor cells. Immunochemistry showed oligo-dendrocyte lineage transcription factor 2(oligo-2)and S-100 positively stained cells while they seemed negative for IDH1 and P53. The proliferation index of Ki 67 was about 8%. During a 6-month follow-up, MRI showed a residual supra-sellar mass with a sellar component compressing optic chiasm, cerebral pedicles, and pons anterior surface, with cystic component extending to third and lateral ventricles.A chemotherapy was suggested instead of surgical reintervention and the patient died after 2 sessions due to medullary anaplasia.
Conclusion
The non specific clinical aspects of diencephalic syndrome and its fluctuating presentation deeply reflects the lack of understanding of its pathogenesis and should keep in mind the necessity of brain MRI within etiological investigations to make diagnosis as early as possible and plan an adequate therapy.

DOI: 10.1530/endoabs.81.EP1197

EP1198

Spectrum of radiological abnormalities of children with growth hormone deficiency at the endocrinology-diabetology-nutrition department of oujda's university hospital

Wahiba Abdellaoui[1], Nada El Yamani[1], Tahri Abir[1], Siham Rouf[1, 2] & Hanane Latrech[1]
[1]Mohammed VI University Hospital, Medical School, Mohammed the First University, Department of Endocrinology-Diabetology-Nutrition, Morocco; [2]Laboratory of Epidemiology, Clinical Research and Public Health, Faculty of Medicine and Pharmacy of Oujda, Mohammed the First University, Morocco

Introduction
Growth hormone deficiency (GHD) is a non-exceptional cause of short stature. Hormonal evaluation and hypothalamic-pituitary MRI are essential to establish the etiological diagnostic. The objective of our study is to assess the different pituitary lesions found in a group of children with GHD.
Patients and methods
This is a retrospective longitudinal study of 36 cases of GHD who underwent pituitary MRI examination collected in the Endocrinology-Diabetology Department of Mohammed VI University Hospital.
Results
The mean age at diagnosis was 11.6 years with a sex ratio (M/F) of 1.57. Mean height Z-score at time of diagnosis was −4.3 SD. The mean bone age (BA) at the time of diagnosis was 7.6 years. The delay of BA over the chronological age was of 4.2 years on average. The diagnosis of total GHD was found in 66.7% of patients and partial GHD in 33.3% of patients. The isolated deficiency was noted in 52.8 % of cases and multiple deficiencies in 47.7% of cases. Magnetic resonance imaging of the hypothalamic-pituitary region was normal in 33.3% of cases. Pituitary stalk interruption was observed in 41.7% of patients, pituitary hypoplasia was observed in 11.1% of patients, an empty sella was observed in 8.3% of patients, and agenesis of anterior pituitary in 5.6% of patients.
Conclusion
The multiplanar capability of MR imaging plays an important role in the assessment of the hypothalamic-pituitary area and in determining the underlying cause of various pituitary diseases in GHD.

DOI: 10.1530/endoabs.81.EP1198

EP1199

Aggressive corticotropic pituitary adenoma: when to think about? about a clinical case

Aicha Ahmed[1], Cheibetta Zekeria[1], Mohamed Ali Boutheina[1], Rifai Kaoutar[2], Iraqi Hind[2] & Gharbi Mohamed Hassan[2]
[1]Ibn Sina, Endocrinology, Rabat, Morocco; [2]Chu Ibn Sina, Endocrinology, Rabat, Morocco

Introduction
Most pituitary adenomas are benign. However, there are invasive forms with rapid growth rate and particular histological signs (atypical adenomas), making them considered pituitary carcinomas without metastases.
Observation
A 63-year-old patient was followed for 10 years for Cushing's disease in the pituitary macrodenoma. Clinical evaluation found Cushing syndrome, pituitary tumor syndrome associated with diplopia, and trigeminal neuralgia. At the endocrine level, it presents substituted thyrotropic and gonadotropic insufficiency. Metabolically, severe osteoporosis complicated by vertebral fracture. He was operated on by the transphenoidal route and irradiated three times by gamma-knife radiosurgery without clear remission. Immunohistochemistry expressed only ACTH. Currently, the patient has persistent Cushing's disease with eight times normal urinary free cortisol (UFC). MRI showing an invasive pituitary macrodenoma with extension to the cavernous sinus. Anticortisolic treatment (ketoconazole) was started with an improvement in CLU to 3 times normal. For the treatment of macroadenoma, surgical treatment has been discussed but rejected by surgeons. So, we indicated a somatostatin analogue 'pasireotide', but it is not available in Morocco.
Discussion
Aggressive pituitary adenomas (AHA) are said to be atypical and have suprasellar and parasellar extension with invasion of the cranial nerves, cavernous sinus. Usually, they are resistant to conventional treatments (surgery and radiation therapy). It is important to differentiate them from pituitary carcinomas according to histological criteria. Treatment of these forms of aggressive adenoma consists of a combination of several surgical, pharmacological, and radiotherapy therapies. Pasireotide, which is an analogue of somatostatin, has particularly demonstrated efficacy in corticotropic pituitary adenomas. New therapeutic prospects based on chemotherapy using temozolomide have also been shown to be effective. These pituitary tumors must be recognized and aggressively treated to prevent complications.
References
1) Steven W. J. Lamberts Æ Leo J. Hofland. Future treatment strategies of aggressive pituitary tumors Pituitary (2009) 12 :261–264. 2) McCormack A, Wass A. and Grossman A. Aggressive pituitary tumours: the role of temozolomide and the assessment of MGMT status. Eur J Clin Invest 2011; 41 (10): 1133–114. 3) Annamaria Colao, Stephen. Petersenn and al. A 12-month phase 3 study of pasireotide in cushing's disease. N Engl J Med 2012;366:914-24.

DOI: 10.1530/endoabs.81.EP1199

EP1200

Change in the size of somatotropin after radiation therapy depending on age

Zamira Khalimova[1], Saodat Issaeva[1] & Mukhlisa Khokimboeva[2]
[1]Republican Center of Endocrinology, Neuroendocrinology, Tashkent, Uzbekistan; [2]General Secondary School, Tashkent, Uzbekistan

Aim
To study the relationship between the age of patients and the dynamics of the size of somatotropinomas after radiation therapy (RT).
Materials and methods
The object of the study is 94 patients with acromegaly who received RT. The average age was 43.8 ± 10.4 years. The patients were divided by age into the following groups: Group I 16-29 years old (9 patients); II group 30-44 years old (44 patients); III group 45-59 years old (34 patients); IV group 60-74 years old (7 patients).
Results
The analysis shows that before RT in group I, macroadenomas were observed in 84.9% of cases, microadenomas in 3.8% and giant adenomas in 11.3% of cases. In group II, microadenomas accounted for 3%, macroadenomas - 82.4%, giant adenomas - 14.7%. In group III, macroadenomas were 85.7%, giant adenomas - 16%. Moreover, giant adenomas tended to increase in parallel with increasing age also if in patients of group I they accounted for 11.3% of cases, increased to 14.7% and 16.3% in groups I and III, respectively. Assessment of the dynamics of the size of education in different age groups against the background of RT also revealed interesting results. After RT in group I, cases of microadenomas increased to 30.2%, macroadenomas decreased 1.3 times and amounted to 67.9%, and giant adenomas 1.89%. In group II, up to the stage of microadenomas decreased in 38.2% of patients (due to a decrease in cases of macroadenomas and giant adenomas), cases of macroadenomas decreased almost 1.5 times, and one patient experienced a recurrence of pituitary adenoma. So, in the long-term periods of post-radiation therapy, a significant decrease in the size of somatotropinoma was observed ($P<0.01$). In group III of patients, 43% of patients had microadenomas, the frequency of macroadenomas decreased by 1.5 times - in 57% of patients, no giant adenomas were detected.
Conclusion
The use of RT leads to a significant decrease in the size of the growth hormone in all age periods. In the age period from 30 to 59 years, a significant improvement in the results was observed in the long term after RT.

DOI: 10.1530/endoabs.81.EP1200

EP1201

Impact of COVID-19 outbreak on acromegaly patients management

Elisa Filippi, Silvia Camerini, Marica Spinello, Roberto Vettor, Pietro Maffei & Francesca Dassie
UOC Clinica Medica 3, DIMED, Padova, Italy

Introduction
Acromegaly is a chronic disease that requires continuous follow-up and examinations over time. During the COVID-19 pandemic outbreak many endocrinological scientific societies recommend to reduce pituitary patient access to hospital facilities to decrease risk of infection.
Aim
The aim of our study is to evaluate the impact of restrictions on outpatient access in the clinical management of the patient with acromegaly during COVID19 pandemic outbreak.
Methods
We enrolled 41 patients with acromegaly, who had at least one clinical evaluation during the year 2018 (period before COVID-19) and a re-evaluation in the COVID19 period between 2020-2021. We collected the following data: anthropometric measures, disease activity status, ACROQoL score, comorbidities, previous treatments, ongoing medical treatments, pituitary adenoma characteristics, Sign and Symptoms Score (SSS), SAGIT® and ACRODAT®.
Results
The 41 patients (24 females and 17 males) had a mean age of 53.27 ± 11.43 years at 2018 evaluation, among these patients 6 were infected with SARS-COV-2 during the considered period. In the entire cohort of patients analysed, there was a significant reduction in IGF-1 values (2018 vs 2021: IGF-1 256.61 ± 165.60 mg/l vs 201.44 ± 87.44 mg/l, $P = 0.004$) with a significant increase in patients who had IGF-1 ULN values <1.2 in 2021 (2018 vs 2021 54% vs 76%, $P=0.004$). GH values decreased over time but not significantly (2018 vs 2021: 6.43 ± 23.51 vs 1.37 ± 1.12 mg/l, $P=$NS), while SSS showed a worsening of referred acromegaly related symptoms at the second evaluation (2018 vs 2021: 1.987 ± 0.70 vs 2.32 ± 0.61, $P=0.001$). There was also a trend towards reduced disease activity at ACRODAT assessment (2018 vs 2021: 61.63% ± 38.30 vs 49.29 ± 33.63, $P=0.047$; red 46.34 vs 24.39 yellow 24.39 vs 34.15 green 39.27 vs 41.46, $P=$NS) which was not confirmed by SAGIT (2018 vs 2021: 6.78 ± 3.67 vs 7.08 ± 2.55, $P=$NS). The ACROQoL and the percentage of cardiovascular, osteo-skeletal, respiratory and cancer comorbidities of the patients remain stable over time. These findings were also confirmed in the cohort of patients undergoing medical treatment (excluding patients in remission, first disease diagnosis and immediate post-surgical period).
Conclusions
COVID-19 pandemic status and its consequent limitations do not seem to have affected outpatient access and achievement of good disease control within the analysed sample. Pandemic seems to not affect quality of life even if reported symptoms have worsened.

DOI: 10.1530/endoabs.81.EP1201

EP1202

Mycophenolate mofetil as a treatment for infundibulo-neurohypohysitis related to Gougerot-Sjögren's syndrome revealed by postpartum diabetes insipidus: A case report

Rachid Smaili[1], Ikram Raaidi[1], El Bachiri Soumaya[1], Lahbib Hafsa[2] & Myriem Bourkia[1]
[1]University Hospital of Tangier, Morocco, Internal Medicine and Clinical Immunology, TANGER, Morocco; [2]University Hospital of Tangier, Endocrinology Department, TANGER, Morocco

Infundibulo-neurohypophysitis is an inflammation of the pituitary stalk and posterior gland. It is an autoimmune disease characterized by lymphocytic infiltration of the pituitary gland. It occurs mainly at the end of pregnancy or in the postpartum period, and is related to autoimmune diseases, including autoimmune thyroiditis. But it is rarely related to Gougerot-Sjogren syndrome, which is an autoimmune connective tissue disease with lymphocytic infiltration of the exocrine glands. We report unusual case of a 25-year-old woman with a history of atopic dermatitis who presented in the early postpartum period with central diabetes insipidus and visual hallucination, dry eyes and mouth. Investigation showed a typically imaging of an infundibulo-neurohypophysitis in the pituitary MRI, associated with a primary Gougerot-Sjogren's syndrome confirmed at the salivary gland biopsy. Patient was treated with mycophenolate mofetil at 1 gramme by day, and desmopressin replacement therapy with a good clinical and radiological improvement at one year of follow-up.

Key words: Infundibulo neurohypophysitis- gougerot sjogren's syndrome – postpartum period - mycophenolate mofetil.

DOI: 10.1530/endoabs.81.EP1202

EP1203

Profil of vitamin D in children with growth hormone deficiency at the Endocrinology-Diabetology-Nutrition Department of Oujda's University Hospital

Wahiba Abdellaoui[1], Nada El Yamani[1], Salma Ben Yakhlef[1], Siham Rouf[1,2] & Hanane Latrech[1,2]
[1]Mohammed VI University Hospital, Medical School, Mohammed the First University, Department of Endocrinology-Diabetology-Nutrition, Morocco; [2]Laboratory of epidemiology, Clinical Research and Public Health, Faculty of Medicine and Pharmacy of Oujda, Mohammed the First University, Morocco

Introduction
Hypovitaminosis D is prevalent in children with growth hormone deficiency. Infants and young children are special risk groups of vitamin D deficiency due to their rapid growth with high nutritional requirements. The lack of early diagnosis and adequate treatment have adverse outcomes. It impairs particularly bone maturation and increases metabolic risk. The purpose of our study is to assess the vitamin D status of children followed up for GHD in the Endocrinology-Diabetology and Nutrition department of Mohamed VI University Hospital Center.
Matherials and methods
This is a retrospective and analytical study regarding 36 children with GHD who underwent a vitamin D dosing, collected in the endocrinology department of Mohammed VI Hospital. The data were collected and processed using SPSS software V21.
Results
The mean age at diagnosis was 11.6 years with a sex ratio (M/F) of 1.57. The average standard deviation score was 4.3 SD for height and 2.9 SD for weight. The median difference in bone age from chronological age was 4.2 years. The insulin growth factor 1 (IGF1) was low related to pubertal stage in 77,8 % of patients. Bone X-rays were performed in all patients and did not reveal any abnormalities. The diagnosis of total GHD was assessed in 66.7% of patients and partial GHD in 33.3% of the cases. The mean vitamin D value was around 22,3 ng/ml, and ranged between 10–30 ng/ml in 66.7 % of the patients. It was less than 10 ng/ml in 11.1%, and greater than 30 ng/ml in 22.2% of the cases. Patients with total GH deficiency had a significantly lower vitamin D levels ($P=0.036$). The reminder of phosphocalcic laboratory tests was normal in all patients.
Conclusion
Vitamin D deficiency increases metabolic risk and skeletal consequences of growth hormone and IGF1 deficiency. The strong link between vitamin D and IGF1 levels requires vitamin D replacement therapy in order to improve their height growth velocities. The results of our study highlighted the value of vitamin D dosing in children with GHD, in order to detect any deficiency which may affect the growth of children with GHD.

DOI: 10.1530/endoabs.81.EP1203

EP1204

Role and expression of miRNAs (miRNA 548e_5p, miRNA 873_5p, miRNA 378b) in fetal development and incidence of Preeclampsia in pregnancy

Ramesh Bangaraiahgari[1], Rajesh Bangaraiahgari[2], Bhargav Panchangam[3], Udaya Kumar U[4], Vinaya V[5] & Banala Rajkiran[6]
[1]Arundathi Institute of Medical Sciences, Department of Biochemistry, Telangana, India; [2]Arundathi Institute of Medical Sciences, Department of Anatomy, Telangana, India; [3]Endocrine Hospitals, Vijayawada, India; [4]Arundathi Institute of Medical Sciences, Department of Pediatrics, Telangana, India; [5]Apollo Institute of Medical Sciences and Research, Telangana, India; [6]Sunshine Hospital, Telangana, India

Background
Preeclampsia (PE) continues tochallenge both the clinicians and researchers worldwide, as the existing knowledge on its etiopathology does not come up with an efficient and foolproof treatment regime due its progressive nature and uncertain diagnosis and prognosis. In this context, miRNAs represent a potential therapeutic target and a diagnostic tool.
Objectives
Circulating microRNAs present in maternal blood play an important role in the etiopathology of PE. The aim of this study is create the panel of miRNAs and quantify their real time expression in peripheral blood of PE patients (from early-onset PE (EOPE) ($<$ 34 weeks), and late- onset PE (LOPE) ($\geq$34 weeks)) and compare with thecontrols.
Study design
Using real time polymerase chain reaction (RT-PCR) method, we quantify the miRNA's expression (miRNA 548e_5p, miRNA 873_5p, miRNA 378b) in EOPE ($n=$ 50) and LOPE ($n=$ 50) and compare with the controls ($n=$ 50), through this we will find out their association with PE and its onset.
Outcome measures
Expression of the target miRNA in EOPE and LOPE patient samples will be compared to the controls and quantification will help in studying the specific miRNA and role in fetal growth or elevation of blood pressure, etc. Once, the panel of targeted miRNA is preparedand quantified it will help in diagnosis and therapeutics.
Results
Basesd on the rt-pcr analysis the expression of mi-RNA (miRNA 548e_5p, miRNA 873_5p) was significant in EOPE & LOPE where as micro RNA 378b expression was higher in controls samples. miRNA 548e_5p plays to role role down regulate ZEB gene which is involved in epithelial to mesenchymal transition. miRNA 873_5p plays to role down regulate JMJD _8 gene. Jumonji C domain _containing protein which is involved in endothelial differentiation. Micro RNA 378b was found in controls, and not in PE. It down regulates the expression of TGFbeta3.
Conclusion
The expression of miRNA 548e_5p, miRNA 873_5p is only found in patients with PE, Where as miRNA 378b is found only in controls.

DOI: 10.1530/endoabs.81.EP1204

EP1205

Psychological stress levels in men with infertility

Gesthimani Mintziori, Stavroula Veneti, Athanasios Mousiolis & Dimitrios Goulis
Aristotle University of Thessaloniki Medical School, Unit of Reproductive Endocrinology, First Department of Obstetrics and Gynecology, Thessaloniki, Greece

Aim
Infertility, defined as the non-achievement of pregnancy by a couple after 12 months of free sexual intercourse, affects 4 - 17% of couples worlwide. In 20% of cases, the cause is found exclusively or mainly in the man. The purpose of this study is to evaluate infertility as a risk factor for increased psychological stress.

Material and Methods
A case – control study was conducted in which the levels of psychological stress of men with infertility and fertile healthy men were assessed. The primary research question was whether male infertility was associated with increased psychological stress. The Greek editions, validated for the Greek population of the Perceived Stress Scale -14 (PSS-14) and Spielberger State-Trait Anxiety Inventory (STAI) questionnaires were used to assess the latter.
Results
The study involved 91 men: 47 infertile men with mean ($\pm$ SD) age 37.5 $\pm$ 0.9 years and mean body mass index (BMI) 24.4 $\pm$ 1.1 kg/m^2 and 44 fertile with mean age 37.9 $\pm$ 0.7 years and BMI 24.1 $\pm$ 1.2 kg/m^2. No differences in stress scales were observed between infertile patients and fertile men (STAI 45.9 $\pm$ 0.4 vs. 44.86 $\pm$ 0.493, $P=$ 0.105 and PSS-14 29.66 $\pm$ 0.75 vs. 28.89 $\pm$ 0, 5, $P=$ 0.436 in infertile and fertile men, respectively).
Conclusion
There was no statistically significant difference in psychological stress levels between infertile and fertile men, although levels were relatively high in both groups. One possible cause is the SARS-CoV-2 pandemic, which by affecting lifestyle can lead to high levels of stress and mitigation of any differences between the groups.

DOI: 10.1530/endoabs.81.EP1205

EP1206

The impact of gh treatment in turner syndrome

Anamaria Hrisca[1], Teodora Dumitru[2], Diana Andrei[2], Alexandru Florescu[1, 2], Letitia Leustean[1, 2], Cristina Rusu[4, 5], Cristina Preda[1, 2] & Maria Christina Ungureanu[1, 2]
[1]University of Medicine and Pharmacy 'Grigore T. Popa', Endocrinology, Iasi, Romania; [2]'St. Spiridon' Clinical and Emergency Hospital, Endocrinology, Iasi, Romania; [4]University of Medicine and Pharmacy 'Grigore T. Popa', Clinical Genetics, Iasi, Romania; [5]'St Mary' Emergency Children Hospital, Clinical Genetics, Iasi, Romania

Introduction
The treatment with growth hormone (GH) plays an essential role in the Turner syndrome (TS) management. This study evaluated its efficacy in improving adult height (AH) and metabolic parameters.
Material and methods
We retrospectively analysed auxological, biochemical, genetic and pharmacological parameters of 56 girls with confirmed TS. They were categorised according to their karyotype as X monosomy (62%), isochromosome (17%), X mosaicism (11%) and ring X chromosome (10%). They were aged 10.85 $\pm$4.008 years at the initiation of the treatment, and the average GH treatment duration was 4.36 $\pm$ 2.82 years with a dose of 0.035-0.05 mg/kg/day.
Results
The GH treatment significantly increased height between the first and the last visit (123.36 $\pm$ 17.78 cm vs 150.45 $\pm$ 7.37 cm). There was a significant correlation between the initial age and the final height. IGF1 serum level was low in 15 patients before treatment and raised to normal values during treatment. Nine patients were overweight and the BMI did not significantly change during treatment. The total cholesterol and triglycerides decreased after the initiation of the treatment (from 173.87 $\pm$ 27.59 mg/dl to 155.69 $\pm$ 31.06 mg/dl and 79.25 $\pm$ 44.07 to 75.6 $\pm$ 34.61). Fasting plasma glucose raised from 87.53 $\pm$ 10.57 to 93.85 $\pm$ 9.35 mg/dl, with only a few isolated cases of hyperglycemia (6 patients). There was no significant change in terms of hepatic enzymes during treatment. Vitamin D deficiency was identified in 17 patients (16.13 $\pm$ 4.3 ng/ml). Eleven girls (19.6%) presented autoimmune thyroiditis, ten girls - cardiac anomalies, 2 - renal malformation and 4 - celiac disease. The treatment had no negative impact on cardiac function.
Conclusion
Our study strengthens the literature findings that GH treatment at an early age effectively improves the final height. GH therapy has additional positive effects on serum lipids, without adverse effects on carbohydrate metabolism, hepatic function or cardiac modifications, confirming treatment safety in TS girls.

DOI: 10.1530/endoabs.81.EP1206

EP1207

Ultrasound EU-TIRADS classification of thyroid nodules and its correlation with fine-needle aspiration results : Experience of the endocrinology, diabetology and nutrition department of the Mohammed VI University Hospital of Oujda

Achwak Alla[1], Salma Ben Yakhlef[1], Siham ROUF[2] & Hanane Latrech[2]
[1]Chu Mohammed VI Oujda, Endocrinology Diabetology and Nutrition Department, Oujda, Morocco; [2]Chu Mohammed VI Oujda, Endocrinology Diabetology and Nutrition Department, Laboratory of Epidemiology, Clinical Research and Public Health, Faculty of Medicine and Pharmacy, Mohamed I University, Oujda, Morocco, Oujda, Morocco

Introduction
Nodular thyroid pathology is very frequent. Its exploration requires a clinico-biological evaluation, a cervical ultrasound to look for the ultrasound criteria of malignancy allowing to classify the thyroid nodules according to the EU-TIRADS classification in order to orientate the diagnosis and to indicate the Fine needle aspiration, to finally allow a targeted management. The aim of our study is to investigate the correlation between the EU-TIRADS classification and the Fine-Needle aspiration outcomes.
Materials and Methods
This is a retrospective study including 85 patients with thyroid nodules. Conducted at the Endocrinology, Diabetology and Nutrition Department of the Mohammed VI University Hospital Center of Oujda in MOROCCO.
Results
The average age of our patients was 45 $\pm$ 14.1 years with a female predominance of 88%. According to the EU-TIRADS 2017 classification, we noted 2.2% of cases classified as EU-TIRADS2, 35.2% of cases classified as EU-TIRADS3, 49.5% of cases classified as EU-TIRADS 4, and 14.1% of cases classified as EU-TIRADS5. Fine-needle aspiration was performed in 86.9% of cases, 13% of cases came back malignant. The calculated risk of malignancy for each score is 0% for EUTIRADS 2, 9% for EUTIRADS 3, 12% for EUTIRADS 4, 60% for EUTIRADS 5. The EU-TIRADS and Bethesda 2017 correlation had a statistically significant relationship ($P=$ 0.004).
Discussion and Conclusion
The EU-TIRADS system has been prospectively validated and its diagnostic value was confirmed by Yoon *et al* (1) in a study of 4696 nodules. Compared with other risk stratification systems, the main objective of EU-TIRADS is to provide easy indications to detect thyroid carcinomas with high sensitivity while maintaining high negative predictive value. This, in turn, should reduce unnecessary cytopunctures. In 2017, Russ *et al* (2) found a correlation between the EU-TIRADS score and the risk of malignancy for each score, and concluded that the risk of malignancy increased with increasing EU-TIRADS score.
1. Yoon JH, Han K, Kim EK, Moon HJ, Kwak JY. Diagnosis and management of small thyroid nodules: A comparative study with six guidelines for thyroid nodules. Radiology. 2017;283(2):560–9.
2. Russ G, Bonnema SJ, Erdogan MF, Durante C, Ngu R, Leenhardt L. European Thyroid Association Guidelines for Ultrasound Malignancy Risk Stratification of Thyroid Nodules in Adults: The EU-TIRADS. Eur Thyroid J. 2017;6(5):225–37.

DOI: 10.1530/endoabs.81.EP1207

EP1208

Biological profile of patients with Graves' disease after treatment with iodine 131: experience of the nuclear medicine department of Tlemcen hospital

Khelil Nour El Houda[1], Meghelli Sidi Mohammed[2], Benmansour Fatéma Zohra[3] & Bouhadjer Nassima[3]
[1]Faculty of Medicine (Tlemcen), Department of Endocrinology - Tlemcen Hospital, TLEMCEN, Algeria; [2]Faculty of Medicine (Tlemcen), Department of Nuclear Medicine - Tlemcen Hospital, TLEMCEN, Algeria; [3]Faculty of Medicine (Tlemcen), TLEMCEN, Algeria

Hyperthyroidism is a clinical situation characterized by an excess of thyroid hormones in the circulation, the most common etiology of which is Graves' disease. Its treatment is based on ATS, iodine 131 and surgery. The iratherapy, object of our study, is a treatment of current practice. It is a simple and radical treatment whose goal is to switch to euthyroidism or hypothyroidism. In case of failure or recurrence, a 2nd or even a 3rd cure is prescribed. We conducted a retrospective, descriptive study with the aim of clarifying the future of patients followed in the nuclear medicine department of the CHU Tlemcen after metabolic radiotherapy with iodine 131 for Graves' disease. Out of 101 patients, 3 groups were identified: the first with 87 patients having received a single course of iodine 131, the average activity administered is 9.89 mCi, the success rate at 18 months

is 75%. The second group with 13 patients who received 2 courses of iodine 131 whose mean activity administered in the first course was 10.01 mCi, after failure and persistence of hyperthyroidism they received a second course whose mean activity administered is of 10.11 mCi, the success rate at 18 months this time is 77.7%. Finally, a third group consists of a single patient who received 3 courses of iodine 131 with a cumulative activity of 35.08 mCi. The latter found himself in hypothyroidism after the 3rd treatment. Radiation therapy has its place as a therapeutic alternative for Graves' disease after failure or intolerance to medical treatment

DOI: 10.1530/endoabs.81.EP1208

EP1209

Differentiated thyroid cancer staging after total thyroidectomy and their respective ablative radioiodine doses

Camila Mannes[1], Laura Vilas Boas[1], Luiz Martins Collaço[1,2], Carmen Australia Paredes Marcondes Ribas[1,2], Osvaldo Malafaia[1, 2], Gleyne Biagini[1, 2] & Giuliana Biagini[3]
[1]Evangelical Mackenzie Faculty of Parana, Brazil; [2]Hospital Universitário Evangélico Mackenzie, Brazil; [3]Carlos Chagas Institute, Fiocruz, Brazil

Differentiated Thyroid Cancer (DTC) is the most common malignant tumor in endocrinology, being the papillary subtype frequently found. The DTC is usually indolent and with a more favorable clinical prognosis of survival in 10 years, which has been diagnosed more frequently after the development and dissemination of complementary detection methods, according to the world literature. However, access to imaging exams with increasing resolving power makes a large number of low-risk patients suffer unnecessary and aggressive treatment. To overcome this new reality, the current guidelines, such as ATA 2015, have changed the way that this disease is treated and classified, in order to prevent the low-risk patients to be overtreated. The objective of this paper was toidentify if the current treatment guidelines for DTC have impacted the decision to use less iodine therapy after thyroidectomy. We performed a retrospective cross-sectional, quantitative, observational analysis of patients diagnosed with DTC, submitted to thyroidectomy with their respective treatment histories and clinical and laboratory follow-up data. In the sample of 201 patients, of the 54 staged as intermediate risk by ATA 2009, 16 (30%) were stratified to low risk by ATA 2015. A percentage of 26,5%($n=$ 18) of microcarcinomas were diagnosed since 2015, being significantly larger ($n=$ 17 (12,8%) than those treated before the new classification (p-value = 0,019). However, patients who maintained the low-risk classification had a mean ablative dose of 61,92 mCi, while the 16 patients who were reclassified from intermediate to low risk in 2015, has a mean dose of 97,5 mCi. In conclusion, the DTC is being treated in smaller tumors but continues to be treated with high doses of radioiodine associated with total thyroidectomy, when they could have been submitted to cheaper surgery or even active surveillance. Thus, despite a significant change in estranging due to updates in the latest guideline, in medical practice there I still a wide variation in the management of low-risk DTC.

DOI: 10.1530/endoabs.81.EP1209

EP1210

Correlation of ultrasound predictors of malignancy and risk of thyroid cancer in patients with thyroid nodules - about 85 cases -

Achwak Alla[1], Nada Derkaoui[1], Siham ROUF[2] & Hanane Latrech[2]
[1]Chu Mohammed VI Oujda, Endocrinology Diabetology And Nutrition Department, Oujda, Morocco; [2]Chu Mohammed VI Oujda, Endocrinology Diabetology And Nutrition Department, Laboratory of Epidemiology, Clinical Research and Public Health, Faculty of Medicine and Pharmacy, Mohamed I University, Oujda, Morocco

Introduction
Thyroid pathology, particularly nodular, is very frequent. It is in most cases benign, thyroid cancer remains rare (5% of nodules). Thyroid ultrasound is the reference examination and should be performed in all patients with known or suspected thyroid nodules. It will allow the detection, diagnosis, search for signs of malignancy and monitoring of these nodules. The aim of our study is to investigate the correlation between the ultrasound signs of malignancy and the risk of thyroid cancer.

Materials and methods
This is a retrospective study including 85 patients with thyroid nodules. Conducted at the Endocrinology, Diabetology and Nutrition Department of the Mohammed VI University Hospital Center of Oujda in the East of MOROCCO.
Results
The average age of our patients was 45 $\pm$ 14.1 years with a female predominance of 88%. The location of thyroid nodules was variable with no statistically significant relationship with the risk of malignancy ($P=0.348$). The mean size of benign nodules was 35.1 mm, whereas malignant nodules had a mean size of 31.8 mm ($P=0.580$). The nodules were taller than wide in 8.7% of cases with a statistically significant relationship with the risk of malignancy ($P=$ 0.004). We did not find a significant relationship between hypoechoic or isoechoic nodules and malignancy ($P=0.168$). On the other hand, irregularity of the contours was noted in 12% of the cases and had a statistically significant relationship in predicting cancer ($P=0.015$). We had the same finding for microcalcifications ($P=0.017$) and central vascularization ($P=0.021$). We noted 2.2% of cases classified as EU-TIRADS2, 35.2% of cases classified as EU-TIRADS3, 49.5% of cases classified as EU-TIRADS 4 and 14.1% of cases classified as EU-TIRADS5. Fine-needle aspiration was performed in 86.9% of cases, 13% of cases came back malignant. The EU-TIRADS and Bethesda 2017 correlation had a statistically significant relationship ($P=$ 0.004).
Discussion and conclusion
Our results were consistent with the literature, allowing us to conclude that a good diagnostic approach using ultrasound by an experienced clinician, followed by fine-needle aspiration, when indicated, facilitates the therapeutic management of these thyroid nodules, promoting high quality care while minimizing cost and unnecessary surgeries.

DOI: 10.1530/endoabs.81.EP1210

EP1211

Study of Correlation between Serum Osteoprotegerin, TNF-alfa and Biomarkers of Bone Metabolism in Patients with treatment naive Graves' Disease. - A cross sectional study

Kishore Behera[1], Suchanda Sahu[2], Kanhaiyalal Agarwal[3], Girish Kumar Parida[3], Uttam Kumar Soren[1] & Anand Srinivasan[4]
[1]All India Institute of Medical Sciences, Endocrinology & Metabolism, Bhubaneswar, India; [2]All India Institute of Medical Sciences, Biochemistry, Bhubaneswar, India; [3]All India Institute of Medical Sciences, Bhubaneswar, Nuclear Medicine, Bhubaneswar, India; [4]All India Institute of Medical Sciences, Bhubaneswar, Pharmacology, India

Objectives
Primary - Study of Correlation between Serum Osteoprotegerin, and Biomarkers of Bone Metabolism in Patients with treatment-naive Graves' Disease (GD). Secondary- Serum level of Osteoprotegerin, TNF alfa and Biomarkers of Bone Metabolism in Patients 3 months after treatment of GD with methimazole (MMI).
Material and Methods
A total of thirty-five treatment-naive newly diagnosed GD were recruited for the study, most of them were female. All patients were started with MMI for the treatment and various blood parameters were measured at baseline and after 3months of treatment.
Measurements
Serum calcium, phosphorus, and bone-specific alkaline phosphatase (B-ALP), OPG (osteoprotegerin), TNF-alpha and urine deoxypyridinoline (Udpd) along with serum-free T3 and T4, TSH and TR-ab were analysed at baseline and three months after MMI treatment. All the patients were euthyroid at 3months of MMI treatment.
Results
Mean Serum OPG (0.94 ± 1.39 v $0.63\pm.27$ng/ml; $P=0.262$)level at base line and after treatment with MMI did not show any significant change. Mean TSH level (0.207 0.59 vs 1.00 1.95, $P=0.025$) was significanly low at base line than after treatment;FT4 (5.9 ± 5.22 v 1.77 ± 1.89 ng/dl;$P<0.001$), FT3 (12.19 ± 6.91 v 4.99 ± 3.55pg/ml;$P<0.001$), and TNG -alfa values decreased significanly after treatment, however PTH (58.09 ± 28.75 v 75.57 ± 41.50;$P<0.026$) increased significantly after treatment. There is no correlation of OPG with thyroid hormone profile, TSH, thyroid receptor antibody (TR-ab) and bone metabolic parameters such as serum calcium, phosphorus, and bone-specific alkaline phosphatase (B-ALP), TNF-alpha and urine deoxypyridinoline (Udpd) in our study. Mean TNF-alfa decreased significantly (393.43 ± 270.473 v 139.34 ± 101.264pg/ml; $P=0.001$)level after treatment with MMI. TNF-alfa was positively correlated with TR-ab ($r=$ 0.374; $P=0.027$)and B-ALP ($r=$ 0.388;p0.021).
Discussion
The bone turnover marker in GD seems to be mediated other than OPG. We observed increased circulating TNF-alfa in GD with a significant decrease after

treatment. TNF-alfa could be a marker of GD activity as evidenced by a close positive correlation with TR-ab a sensitive marker of GD autoimmunity. TNF-alfa could be the factor associated with the bone turnover marker in GD despite the euthyroid state.

DOI: 10.1530/endoabs.81.EP1211

EP1212

Post COVID 19 subacute thyroiditis -de Quervain

Merita Emini[1], Izet Sadiku[2] & Mimoza Ramadani Piraj[1]
[1]Pristina, Clinic of Endocrinology, University Clinical Center of Kosovo, Pristina, Kosovo; [2]Pristina, Clinic of Infection Diseases, University Clinical Center of Kosovo, Pristina, Kosovo

Introduction
COVID-19 in Kosovo was introduced in March 2020 as a global pandemic started in Wuhan, China in December 2019. The link between COVID-19 and diabetes was seen in the first cases but was if this disease is interfering in other endocrine glands was still unclear. In May 2020 we found the first case of subacute thyroid immediately after COVID-19 which case trigger us for further observation of its spread.
Aim
To investigate the clinical forms and laboratory follow-up of cases with subacute thyroiditis in COVID-19.
Material and methods
In this presentation we report for 7 patients with subacute thyroid de Quervain and positive serology for COVID-19 with demographic, biochemical, clinical and imaging data.
Results
From 7 patients (6 female and 1 male), biochemical data showed increases in C-reactive protein (in some of them triple digits), increased erythrocyte sedimentation rate, increased free fractions of triiodothyronine and thyroxine hormones such as inhibition of thyrotropin, serological tests (IgM and IgG) were positive for infection with COVID-19. All cases presented with neck pain followed with headache in some of them, fatigue and marked laziness as well as fever. Typical changes of subacute thyroiditis have been identified on ultrasound (Fig.1) and scintigraphy (Fig.2). The ways in which they were get infection with COVID 19 differed diametrically. Almost all have been treated with corticosteroids with complete improvement of inflammatory parameters and normalization of thyroid hormones.
Conclusion
The presentation of such cases helps physicians of different profiles to identify complications of COVID-19 and especially such rare cases of subacute thyroiditis which may be underestimated during clinical practice. Keywords: subacute thyroiditis, COVID-19, Kosovo

DOI: 10.1530/endoabs.81.EP1212

EP1213

Refractory graves' disease dramatically responded to adjunctive colestyramine, case report and literature review.

Mohammad Bilal Jajah, Heng Chun Wong & Jayamalee Jayaweera
West Suffolk Hospital, Bury St Edmunds, United Kingdom

Background
Graves' Disease usually responds well to medical treatment with thionamides. However, in some cases, it fails to respond to this treatment, even at maximum doses. A few reported cases have shown that colestyramine helps to restore normal thyroid function when added to the ongoing anti-thyroidal medications in refractory thyrotoxicosis. We reported a case of relapsing refractory Graves' disease, in which colestyramine has helped to restore normal thyroid function tests and allowed for subsequent total thyroidectomy.
Case Presentation
A 21-year-old female presented with relapsing Graves' Disease after 5 years of remission. She was planned for surgery and started on carbimazole in order to restore a euthyroid state before the procedure. This was not achieved despite carbimazole doses being increased to 60 mg over a period of 8 weeks. Colestyramine, 4 mg four times a day, was added as an adjunct, which normalized her thyroid function after 2 weeks of treatment. The patient underwent successful total thyroidectomy subsequently.
Discussion
Bile acid sequestrants (e.g. colestyramine) have been found to reduce thyroid hormone levels in thyrotoxic patients by interfering with enterohepatic circulation and recycling of thyroid hormone. Cholestyramine, given in a dose of 4 g four times daily with thionamides, lowers serum T4 and T3 concentrations more rapidly than thionamides alone and may be useful adjunctive therapy in selected patients who require rapid amelioration of hyperthyroid symptoms. A few case reports have noted that colestyramine, when added to antithyroid drugs in patients with refractory thyrotoxicosis, has successfully achieved a euthyroid state within a few weeks of treatment. This case further supports the growing body of evidence that in medically refractory thyrotoxicosis, colestyramine could be used as an adjunct in reducing thyroid hormone levels to acceptable ranges for surgery to be done. Further studies including randomized control trials could be done to examine the effects of colestyramine in this group of patients.
Conclusion
Colestyramine could be an effective additional treatment in refractory thyrotoxicosis when maximum doses of thionamides fail to restore normal thyroid function.

DOI: 10.1530/endoabs.81.EP1213

EP1214

EBV-associated lymphoepithelioma like carcinoma of thyroid : a case report

Talbi Dounia, Lamia Echchad, Kaoutar Rifai, Hinde Iraqui & Mohamed El Hassan Gharbi
Chu Ibn Sina, Endocrinology, Rabat, Morocco

Introduction
Epstein-Barr virus (EBV) is a well-known human tumor virus with a very high prevalence in the population, this virus is associated with epithelial and lymphoid malignancies, including lymphoepithelioma carcinoma of thyroid. This subtype of thyroid carcinoma is characterized by histologic features similar to those of undifferentiated carcinoma of the thyroid.
Case Report
A 17-year-old male patient, his medical and family histories were non-specific. the physical examination found a large cervical swelling painful on palpation. The neck ultrasonography was performed revealed a left thyroid nodule of 46*26mm classified Tirads5 accompanied by three enlarged neck lymph nodes in the left level II and level III regions. Thyroid functional tests, calcitonin, and thyroid antibodies were within normal limits. A total thyroidectomy was scheduled for the patient ans bilateral neck lymph node dissection. The histologic slides of the thyroid tumor revealed EBV-associated lymphoepithelioma thyroid carcinoma with gonglion metastases. he subsequently benefited from chemotherapy and radiotherapy. and was put on Levothyroxine suppression therapy.
Discussion
EBV has been revealed to be associated with the development of many cancers, such as gastric cancer, nasopharyngeal carcinoma, and Hodgkin's lymphoma. However, the relationship between thyroid tumorigeneses and EBV has not been fully elucidated with conflicting results. The preliminary investigation of EBV in thyroid lymphoma was inspired by EBV persistently infecting B lymphocytes, it can also infect T lymphocytes, myocytes, and epithelial cells, Once EBV infects a host cell, it starts to induce a lytic or latent infection with diverse genes expressed. These genes collaborate to induce tumorigenesis by causing systematic inflammation, suppressing the antitumoral immune system, and preventing anoikis The Chronic inflammation induced by EBV infection may play a significant role in the progression of lymphoepithelioma carcinoma of thyroid.
Conclusion
Lymphoepithelioma-like carcinoma is a rare entity among thyroid tumors, We reported a patient with an EBV-associated thyroid carcinoma. However, whether these rare thyroid malignancies are related to EBV infection requires further investigation.
Reference
1. Shimakage M, Kawahara K, Sasagawa T, Inoue H, Yutsudo M, Yoshida A, Yanoma S. Expression of Epstein-Barr virus in thyroid carcinoma correlates with tumor progression. *Hum Pathol.* 2003;**34**(11):1170–1177.

DOI: 10.1530/endoabs.81.EP1214

EP1215

Aggressive thyroid tumor with difficult histological diagnosis

Malika El Omri[1], Mouna Khalifa[1], Abir Meherzi[1], Safa Jemli[1], Jihen Hwas[1], Moni Ghammem[2], Mouna Bellakhdher[1], Wassim Kermani[1] & Mohamed Abdelkefi[1]
[1]Farhat Hached Hospital, ENT, Sousse, Tunisia; [2]Farhat Hached Hospital, Sousse, Tunisia

Introduction
Oncocytic tumors of the thyroid include adenomas and carcinomas. The distinction between malignancy and benignity represents a major difficulty on the histological level. From this aspect arise constraints in the attitude therapy to adopt.
Material and methods
we present one rare case of an oncocytic carcinoma of the thyroid with laryngotracheal invasion in a 54 male patient operated in ENT department of Farhat Hached hospital of Sousse.
Observation
This is the case of a 54 years old patient who presented with a left basicervical mass evolving for 6 months without other associated signs such as local compression signs or clinical dysthyroidism. There was no history of pain, fever, dysphagia or resiratory difficulties. On examination, there was a large swelling occupying the anterior basicervical region; of 3 centemeters in the right side an of 6 centemeters in the left side; with ferm, nontender, and nonpulsatile consistency. The examination did not find any cervical lymph nodes and nasofibroscopy showed normal vocal cords in aspect and in mobility. Free thyroxine (fT4) and thyroid stimulating hormone (TSH) levels were normal. Thyroid ultrasound confirmed the thyroid origin of the mass and showed no signs of malignancy. A total thyroidectomy was performed. Extemporaneous and definitive histological examination concluded to an oncocytic adenoma. Five years later, the patient came back with an anterior basicervical mass of 5 centemeters, associated with moderate dyspnea. CT scan concluded to thyroid mass of 4 centemeters with a subglottic tissue process with necrotic center of 3 centimeters. Also, pulmonary metastasis was noted. He had a direct laryncoscopy with tracheoscopy showing an infiltration of tracheal wall 2 centimeters from the glottic plane. Histological exaination of the biopsy concluded to an infiltration of the tracheal wall by an oncocytic tumor. We concluded to a recurrence of a misdiagnosed oncocytis thyroid carcinoma as an oncocytic adenoma. The patient had a tumorectomy associated to a sub-isthmic tracheotomy followed by 3 courses of radioactive iodine treatment. The patient was forseen for target therapy but wasunfortunatelylost to follow.
Conclusion
Oncocytic cell carcinoma is commonly retained as an aggressive tumor with low survival rate. Surgery is the mainstay of treatment for carcinoma and planning its appropriate initial surgical management is especially important as curative procedure.

DOI: 10.1530/endoabs.81.EP1215

EP1216

T4 + T3 combination therapy of refractory hypothyroidism to levothyroxine treatment, in a subject after ablative radioactive iodine treatment for differentiated thyroid cancer. A case report and review of literature.

Marjeta Kermaj[1], Irsa Zaimi[2], Klotilda Resuli[3], Mariola Kapia[4] & Agron Ylli[1]
[1]UHC 'Mother Tereza', Endocrinology, Tirana, Albania; [2]Fier Regional Hospital, Endocrinology, Fier, Albania; [3]Vlora Regional Hospital, Endocrinology, Vlora, Albania; [4]Health Center 6, Endocrinology, Tirana, Albania

Introduction
Hypothyroidism is considered refractory to oral levothyroxine substitution, when there is biochemical (serum level of TSH (thyroid stimulating hormone) above the upper target level) or clinical evidence of hypothyroidism, despite increasing dosages of oral levothyroxine beyond 2.5 μg/kg daily. In these circumstances, further increments in the dosage of levothyroxine may not always be the most appropriate intervention. In such a situation, physicians need to search for causes of decreased absorption of levothyroxine or increased demand for thyroxin and the solution.
Case report
We present the case of a 55-year-old woman who underwent total thyroidectomy for multinodular goiter, then ablative treatment with 30 mci of radioactive iodine 131, after postoperative biopsy resulted in papillary thyroid cancer. She then started treatment with the levothyroxine replacement dose. In control after 6 weeks of treatment with levothyroxine, TSH level was high and her complaints related to hypothyroidism. We gradually increased the dose of levothyroxine after each periodic TSH test, reaching more than 300 mg of levothyroxine/day, but the TSH level remained high. We searched for the cause of refractory hypothyroidism, but found neither poor compliance nor malabsorption. In our case where it was necessary and urgent to inhibit TSH, following the protocol of differentiated thyroid cancer to control the progression of papillary thyroid cancer, we tried combination therapy with T4 (Thyroxin) and T3(triiodothyronine), and in the next control TSH decreased. We adjusted the T4/T3 doses gradually and after a few checks, the desired TSH levels were reached and the patient felt clinically well.
Conclusion
Whilst current guidelines do not suggest routine use of combination T4/T3 therapy, they do acknowledge a trial in patients with refractory hypothyroidism to levothyroxine treatment, may be appropriate. Our case confirms that.

DOI: 10.1530/endoabs.81.EP1216

EP1217

Mantle cell lymphoma in the thyroid gland : clinical features and management case report

Meherzi Abir, Safa Jemli, El Omri Malika, Marwa BEN NJIMA, Mouna Bellakhdher, Jihene Houass, Kermani Wassim & Abdelkefi Mohamed
ENT Department Farhat Hached Hospital Sousse, Sousse, Tunisia

Background
Primary thyroid non Hodgkin's lymphoma (PT-NHL), which defined as a lymphoma occurring in the thyroid gland with or without the involvement of regional lymph nodes, is a quite rare pathologic entity, accounting for 1,3-1,5 % of thyroid neoplasm, and 0,5% of lymphoma. there exists insufficient data to describe the incidence of mantle cell lymphoma in the thyroid gland. Due to this rarity and non specific clinical presentation, it seems essentiel to better understand the disease course. Thus we report this case in order tu study its clinical features and discuss management particularities.
Case presentation
A 58-year-old man, without pathological history, complaining from acute progressive dyspnea and dysphagia, associated with an enlarging anterior neck mass that increased rapidly through the last few weeks. On the clinical examination, we found a painless, hard huge goiter which depends mainly on the left lobe, fixed to the musculature, associated with bilateral lymph nodes. The laryngeal fibroscopy showed severe edema of the larynx, without modification of cordal mobility showed diffuse swelling of the thyroid compressing the airway tract. We proceed for diagnosing by a biopsy guided by the ultrasound imaging which confirms the mantle lymphoma of the thyroid; we complete the general evaluation by realizing a full body computed tomography in which we note the absence of other lymph node and a gastroscopy that eliminated the stomach localization. The disease was staging according to the classification proposed by Ann Arbor and modified by Myssof: stage IV. After 5 courses of chemotherapy R-CHOP, A complete remission was achieved. After a follow-up of 3 years, no relapse has occurred.
Conclusion
MCLs are usually diagnosed at an advanced stage, with mostly extranodal involvement, MCLs are classified as an aggressive lymphoma, with median survival of 3–5 years. Treatment options for MCL have been evolving. Chemotherapy and CHOP regimens have usually been used (cyclophosphamide, vincristine, doxorubicin, and prednisone). Immunotherapy (rituximab) and autologous stem cell transplantation have recently been used to treat patients.

DOI: 10.1530/endoabs.81.EP1217

EP1218

Oncocytic carcinoma of the thyroid: Therapeutic and diagnostic challenge

Meherzi Abir, Marwa Ben Njima, Safa Jemli, Habiba Ben Sghaier, Mouna Bellakhdher, Jihene Houass, Kermani Wassim & Abdelkefi Mohamed
ENT Department Farhat Hached Hospital Sousse, Sousse, Tunisia

Background
To study the diagnostic difficulties, the clinical characteristics, as well as the therapeutic modalities of this entity.
Material and method
Report a case of oncocytic carcinoma of the thyroid of aggressive evolution collected in the ENT department and CCF Farhat Hached in Sousse.
Result
This is a 54-year-old patient, with no notable history, who was operated on in 2012 for a large goiter evolving for 3 years previously, having had a total thyroidectomy, with an anatomopathological examination objectifying an oncocytic adenoma on a goiter multi nodular. The patient was lost to follow-up, then reconsulted 5 years later, for the reappearance of a voluminous right anterior cervical swelling and cervical polyadenopathy, associated with dyspnea and hemoptysis. A cervico-thoracic CT showed a tumoral process above and below the glottic laryngeal with signs of locoregional extension, a tumoral process of the thyroid compartment and pulmonary lesions of secondary appearance. A histological re-reading was requested, correcting the diagnosis towards an oncocyte-type vesicular carcinoma. The patient had a lumpectomy with an anapath result confirming tumor recurrence. Additional radiation therapy was performed and the patient was put on L-thyroxine at a restraining dose. He was again lost sight.
Conclusion
Oncocytic carcinoma of the thyroid is a rare, aggressive tumor with metastatic potential posing an anatomopathologic diagnostic and therapeutic problem, requiring careful histological verification and adequate surgical management.

DOI: 10.1530/endoabs.81.EP1218

EP1219

Thyrotoxicosis after the cessation of amiodarone treatment
Ivana Bozic-Antic[1,2]
[1]Euromedic Healthcare System, Belgrade, Serbia; [2]Faculty of Dentistry Pancevo, University Business Academy in Novi Sad, Serbia

Introduction
Amiodarone is an effective drug for treating heart arrhythmias. High iodine content and specific metabolism of this drug, in 15-20% of patients lead to thyroid function disorder. Amiodarone induced thyrotoxicosis (AIT type 1 or type 2) usually occurs during the use of the drug, while it is rare after the drug cessation.
The aim
A case report of a patient with type 2 AIT that manifested after the cessation of short-term amiodarone treatment.
Case presentation
A 73-year-old patient was treated for atrial fibrillation with amiodarone for six months. Two months after the drug cessation, clinical manifestations of thyrotoxicosis (weight loss, sweating, tachycardia) occured. Laboratory tests showed overt thyrotoxicosis with normal antithyroid antibodies and high thyroglobuline (TSH 0.01 uIU/ml, fT4 45.4 pmol/l, fT3 10.8 pmol/l, antiTPO 6 IU/ml, antiTg 11 IU/ml, TSH-receptor antibodies 0.9 IU/l, thyroglobuline 232 ng/ml). Blood cell count and sedimentation rate were normal. The thyroid gland was painless, normal size, normoechogenic, with normal vascularisation and without nodal lesions. The patient was succesuflly treated with corticosteroids (at the beginning 60 mg/day with gradual drug suspension). After 10 weeks patient was euthyroid. One month later hypothyreosis occured, and levotyroxine substitution was started.
Conslusion
This case report showes a patient with type 2 AIT which occured two months after the cessation of short-term treatment with amiodarone. The elimination of amiodarone from the body is variable and iodine depot in the body can remain increased for up to 9 months after the drug is stopped. For this reason, it is necessary to monitor patients not only during amiodarone treatment, but also months after the suspension of the therapy.

DOI: 10.1530/endoabs.81.EP1219

EP1220

Iatrogenic agranulocytosis in a woman with hyperthyroidism
Mubina Hodžić[1], Alma Badnjevic-Cengic[2] & Amila Cerim-Aldobasic[2]
[1]Cantonal Hospital, Internal Diseases, Endocrinology Unit, Zenica, Bosnia and Herzegovina; [2]Cantonal Hospital, Zenica, Bosnia and Herzegovina

Hyperthyroidism is a condition with the overproduction of thyroid gland's hormones. One of the treatment option is methimazole, blocking the synthesis named hormones, usually before thyroid surgery or radioactive iodine therapy. I report a 68-year old woman who admitted to hospital in November 2021. after a hematological examination due to leucopoenia and agranulocytosis. She is been treating the hyperthyroidism last 12 years with methimazole. In the beginning she was taking twice daily 10 mg, and later once daily 10 mg of methimazole. Blood counts were normal before as she recalls. She also was treating depression syndrome from the beginning as a hyperthyroidism. Since last year she is been having tonsil problems, difficult swallowing. Last ten days before admitted she had a throat pain, ear pain, no fever and chills. No losing weight. In laboratory findings there were leucopoenia with agranulocytosis leucocyte 1.15/neutrophils 0.33(Absolute number). Her hormones of gland thyroid were in hyperthyroidism range (TSH 0.001 referral range (0.34-5.5), fT3 5.84 ref.r.(2.5-4.5), fT4 2.39 ref.r.(0.58-1.64)). She received a granulocyte grow factor in hematology admission. She had frequent controls of blood count till the leucocyte raised over 1x 10*9 per liter. Her immunology test were negative, other non specific laboratory, ultrasound, radiological chest results. PCR SARS CoV-2 was negative. Palpatory the thyroid gland was large. In ultrasound the lobes were largly, hypoechoic and non homogeneous, roughly echo picture, with several hypoechoic nodule. We consulted the nuclear specialist. The therapy was propylthiouracil 50 mg 1tablet daily with Lugol solution 3 times a day per 2 drops. The control hormones of gland thyroid were: TSH was suppressed, fT3 and fT4 were in referral range. The scintigraphy of thyroid gland was perform with Technetium -99m, where radiopharmaceutical was very weak binding diffuse with some intense binding in one of the nodule in right lobe, and several small ones in left lobes. The therapy option was total thyroidectomy. Her blood count was normal (total recieved 2 ampules of Leucocyte growth factor). She was discharged from hospital. In Decembar she came to check up. No symptoms on her side, blood count with differential blood count were normal. Her TSH was still suppressed, and other hormones of gland thyroid were in referral range. Therapy was the same with recommendations to surgery option
Key words:hyperthyreoidism, methimazole, agranulocytosis, granuloyte growth factor

DOI: 10.1530/endoabs.81.EP1220

EP1221

Case report: Toxic multinodular goiter in pregnant women
Sanaa Bammou, Sana Rafi, Ghizlane EL Mghari & Nawal EL Ansari
Mohamed VI University Hospital Center, Department of Endocrinology, Diabetology, Metabolic Diseases Nutrition, Marrakech, Morocco

Introduction
-Thyroid disorders can predate or develop during pregnancy.
-The effects on the fetus vary depending on the disease and the drugs used for treatment. But usually, untreated or undertreated hyperthyroidism can lead to harmful complications.
Case report
It's a 26-year-old patient with a history of goiter since childhood, history of goiter in the mother; grandmother and maternal aunt. the patient is 18 weeks pregnant, the pregnancy is unplanned. Anamnesis:the notion of weight loss; palpitation and dyspnea The clinical examination revealed a: goiter Grade 3 with turgidity in the jugular veins. Investigations showed: white blood cell 11440/mm3 Neutrophil : 6115/mm3 Hemoglobin:12.7 g/100ml blood platelets :19400/mm3 ALAT :10 UI/I ASAT:19 UI/I TSH:0.005uUI/ml T4:16;6 pmol/l T3:7,2 pmol/l On cervical ultrasound: nodular goiter classified EU TIRADs 3; the largest measuring on the right 42*32 mm and on the left 23*21mm Patient was started synthetic antithyroid drug and she was sent to surgery after euthyroidism.
Discussion
The association of thyroid disease and pregnancy is relatively common [1-4]. The increase in thyroid volume during pregnancy has been known since antiquity. In fact, pregnancy is favored by the increase in the need for thyroid hormones, and the hormonal variations that accompany it, an increase in the functional activity of the thyroid gland, and the nodular remodeling of goiters, and potentially the growth of possible nodules. cancer [2,3]. Thyroid surgery, in the event of pregnancy, is indicated in cases involving the vital prognosis of the mother and/or fetus (bulky goiters compressing the esophagus or the trachea, a state of hyperthyroidism difficult to balance such as the case of of Basedow) at any time, preferably during the second trimester to avoid first-trimester abortion and third-trimester preterm delivery [1,4]. It is also indicated during pregnancy for medullary carcinoma [4].
Conclusion
Pregnancy is a test for the thyroid gland. The latter has significant adaptive capacities which allow it on the whole to cope with the increase in hormonal needs, the depletion of the iodine load. But imbalances are possible, which is not without consequence on the maternal and fetal situation. All the interest of the preconception and prenatal consultation and its role in detecting pathologies early and treating them in time and by the optimal means.

DOI: 10.1530/endoabs.81.EP1221

Author Index