FOURTH INTERNATIONAL MEDICAL CONGRESS

Scientific Achievements & Practical Experience in Cardiology, Oncology, Diabetes & Transplantations

11- 15 September 2013
Portoroz, Slovenia

Sofia, Bulgaria
2019

SOUTHEAST EUROPEAN MEDICAL FORUM

(SEEMF)

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Dear Colleagues,

I welcome you to the Fourth International Medical Congress, organized by the Southeast European Medical Forum, to be held in the period 11 - 15 September 2013 in Portoroz, Slovenia.

We are proud to announce that this year our Congress received very early European accreditation.

During the event we will have the chance to get acquainted with the scientific achievements and practical experience of outstanding specialists in important medical fields, such as Diabetes, Cardiology, Oncology, Transplantation, as well as to hold informal meetings and establish contacts. The Round Table on Health Funding and Role of Professional Associations will enable discussion on current healthcare issues.

The organizers will offer a large-scale event with presentations of over 50 eminent international speakers, which will guarantee the high scientific level of the Congress and its contribution to the development of the medical science and practice in this part of the world.

I believe that the Congress will address the priorities of the physicians, namely CME, ethics and topical health organization issues. It will contribute to authority of the profession and to the current and future status of the physicians and other health professionals.

Dr. Andrey Kehayov, MD, PhD
SEEMF President

Dear colleagues, dear friends,

It is my great pleasure to invite you to Portoroz, Slovenia to join us at the 4th International Medical Congress organised by Southeast European Medical Forum (SEEMF) in cooperation with the Slovenian Medical Association.

We are glad and proud that SEEMF successfully connects medical doctors, scientists and health professionals from east, south and central Europe countries. It represents the bridge between Eastern and Western Europe and enables the exchange of information and experience between countries. Further, one of the most important missions of SEEMF is an integral access. The congresses organised by our society are interdisciplinary, dealing with different topics from various braches of medicine providing presentations from prominent speakers who are superb in their fields.

I am convinced that the congress in Portoroz will continue the successful tradition of previous congresses to provide opportunity to represent new findings in different fields of medicine, to discuss controversies and to exchange experiences with the ultimate goal to reduce disease burden and find solutions for health problems. It will be the forum to listen and to learn but also to spread ideas between countries and different specialities.

The preliminary programme is very promising and I believe that it will be fully realised. We promise to do everything to fulfil your expectations.

Therefore, I would like to cordially invite you to attend this outstanding meeting, to come to Slovenia, to acquaint with our country in the heart of Europe. Slovenia inspires with its beauty and places of interest. There is so much to choose from, it is sometimes hard to decide where to go: from castles to nature parks, from museums to caves. You can have one eye on the sea, then look in the other direction and be surrounded by high mountains. This proximity of opposites and contrasts is a hallmark of our country. Everybody will find in Slovenia something interesting and exciting. The friendly, hospitable and attentive people will guarantee you a pleasant stay.

I do hope that you will come in great numbers to Slovenia, and I am sure that you will enjoy the science, the nature and Portoroz warm atmosphere.

Sincerely yours,

Prof. Dr. Pavel Poredos, M.D., Ph.D.
SEEMF Vice President

Dear colleagues,

Following the very successful Congresses held so far in Varna, Nesebar and Belgrade, the general conclusion has been that they were much more than just excellent professional events; SEEMF Congresses became also extraordinary cultural phenomena which showed that we have to take the every advantage to live and communicate in a world without political boundaries.

The SEEMF Board is making, as always, all efforts in a spirit of peace, friendship and collaboration continuously to strengthen the Forum and moreover to maintain it as reputable partner to other European and international associations.

Most of our countries had similar political systems, health care systems, pathology and underwent similar transitional processes. Therefore SEEMF Congresses besides acquainting with the best medical knowledge and practice, represent also an excellent opportunity to share our experience in the field of health financing, quality of care, patient safety, role of professional organizations, e.t.c.

Wise people build on their own experience, but the wiser ones build on the experience of others.

We invite you to join us for the IV Congress of SEEMF which will be an excellent opportunity to promote personal and institutional cooperation and friendship for the benefit of physicians and their patients.

The wonderful environment of Portoroz and Slovenia and the traditional hospitality of the local organizer - the Slovenian Medical Association - will be great contribution to that aim.

Prof. Dr. Jovan Tofoski,.
SEEMF Secretary General

Dear colleagues,

Five main topics will be included in the Fourth International Medical Congress– Cardiology, Oncology, Diabetes mellitus, Transplantation related issues in SE Europe and Miscellaneous and two Round tables – Quality and Financing of Health Care and The role of Professional Organizations.

The task of the first topic is to enhance and update the knowledge of the physicians in South-East-Europe in the field of Cardiology. The lectures of high-ranking experts will contribute to this aim, including the new advance in the technology.

The second main topic is Oncology. It is known that cancer is in the second place as cause of mortality in the South-East-European region.

About 350 million people worldwide have diabetes mellitus. The lectures of eminent physicians will help for better understanding the prevention, diagnostics, treatment and common consequences of this chronic disease. There are different issues that need to be discussed in connection with organ donation and transplantation in Southeast European countries. The quality and safety of transplants, infrastructure and financial resources will be taken into consideration. Having in mind the titles of the round tables we must hope for very interesting and fruitful discussion and suggestions.

Acad. Prof. Vladimir Ovcharov
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CARDIOLOGY

MANAGEMENT OF SUPERFICIAL THROMBOPHLEBITIS

M. K. Jezovnik, MD, PhD
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Superficial thrombophlebitis (ST) is a common disease; however, it was long ignored on the assumption that is a benign disease. Recent studies have shown that ST is related to a substantial risk for thromboembolic complications. Therefore, for elucidation of the extension of the disease and the related risk objective diagnostic procedures are needed. Clinical signs and symptoms frequently underestimate the true extension of the thrombus. Further testing is often required to evaluate the presence of deep venous thrombosis. All patients where clinical presentation suggests the involvement of the trunk of the great or small saphenous vein and with the risk factors for venous thromboembolism (VTE) should undergo Duplex sonography with compression test of all deep and superficial venous segments of both limbs. Duplex sonography offers a direct visualisation of the thrombus inside the superficial vein, thrombus relationship to the deep venous system or simultaneous involvement of the deep venous system.

Symptomatic treatment of ST generally includes analgesics, elastic compression, anti-inflammatory agents and ambulation of the leg. Since ST should not be considered as a benign disease, symptomatic and local treatment alone may prove inadequate. Elastic compression of the affected leg relieves the symptoms and speeds up the regression of local signs. However, the effectiveness of compression on thromboembolic complications was not proven. Because of the increased risk for thromboembolic complications in last years, patients with progressed ST are treated with anticoagulant drugs, particularly with low molecular weight heparin (LMWH). Different studies showed that LMWH prevents the local extension of thrombus and its recurrence. However, the evidence on the efficacy of LMWH for the prevention of thromboembolic complications is scarce. The only one large study (CALISTO) showed that treatment with fondaparinux significantly reduced the risk of thromboembolic complications in patients with ST. Therefore, there is the recommendation that patients with ST with thrombosed superficial vein longer that 5 cm should be treated with LMWH at intermediate or therapeutic dosages for at least four weeks. The dosage and duration of anticoagulation depends on the concomitant disease and other risk factors for VTE. In patients with extended ST (> 10 cm) and with additional risk factors for VTE fondaparinux in prophylactic dosage should be considered for six weeks. Routine surgical treatment (ligation) is not advised.

PERIOPERATIVE MORBIDITY IN CARDIAC SURGERY PATIENTS WITH DIABETES MELLITUS

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Objective: Diabetes Mellitus, DM is one of the most common concomitant illness in cardiac surgery patients, with high impact on the early and the late

postoperative period. **Aim**: To study the perioperative morbidity and mortality in limited group of patients with DM, undergoing cardiac surgery.

Methods: Retrospective study of the medical records of all patients undergone cardiac surgery during the year of 2010 divided into 2 groups. First: patients with DM type 1, type 2 or impaired glucose tolerance 511 patients, and Second one without any deviations in the carbohydrate metabolism 1018, NDM. The morbidity was evaluated with the preoperative risk evaluation trough Euro Score, length of the cardio-pulmonary bypass, the operation time and postoperative parameters as length of mechanical ventilation MV, length of ICU stay, support of the hemodynamic and renal function, as well as infectious complications. **Results:** Patients in DM group more often undergo combine surgeries, have longer cardio-pulmonary bypass and need longer support of the hemodynamic and renal replacement therapy. We didn't find any group differences concerning the ES, 6.1 to 6.3, the length of mechanical ventilation and the ICU stay. There is higher rate of infections associated with catheter placement either intravenous 2.9% to 1.6%, $P<0.05$, or urinary 6.3% to 4.8%, $p<0.05$. Mortality rate in DM group is 5.5% compared with NDM group 6.2%, $p>0.1$.

Conclusion: Although the mechanical ventilation and the support of the hemodynamic in patients with DM is longer and the infections associated with vascular and urinary tract catheters are more frequent, the stay in the ICU and the mortality rate are comparable between DM patients and NDM.

CANCER GENETIC COUNSELING AND TESTING – NEW INSIGHTS AND TRENDS

Mateja Krajc, MSc, dr. Srdjan Novaković, dr. Janez Žgajnar, dr. Marko Hočevar

Generally, cancers develop as a result of mutations in cancer genes. These mutations may occur in specific cells during a person's life and are called somatic mutations. Cancers that arise this way are called sporadic cancers and account for the large majority (average 90%) of all human cancers. These mutations are not inheritable. When mutations occur in the germline, they are present in all cells and are inheritable. These mutations create cancer predisposition syndromes, which can be low, moderate or highly penetrant in creating familial cancer syndromes. In these cancer syndromes, mutations usually, but not exclusively, occur in genes that are involved in the regulation of DNA repair and genome stability. Hereditary cancer syndromes might be dominated with a particular cancer type or may produce a heterogeneous pattern of cancer types in the family. Early disease onset, on average, compared to sporadic cancer, is an important characteristic of such families.

There are several hereditary cancer syndromes. The most frequently found and monitored in our population are (i) hereditary breast and /or ovarian cancer syndrome (mainly caused by mutated *BRCA1* or *BRCA2* gene), (ii) hereditary non polyposis colorectal cancer (caused by mutated mismatch repair genes; mainly by *MLH1* and *MSH2* gene), (iii) familial adenomatous polyposis syndrome (caused by mutated APC gene), (iv) and many other, less frequent, such as hereditary malignant melanoma, hereditary thyroid cancer, Peutz-Jeghers syndrome.

Most frequently tested and found in Slovenian population so far is hereditary breast and /or ovarian cancer syndrome. These families are dominated by the occurrence of breast cancer and, less frequently, ovarian cancer. A few other cancer types also occur at a low increased risk. These families account for less than 10 % of all breast cancers. However, a familial aggregation of cancer can be found in up to 25% of all breast cancers, but with a less clear inheritance pattern and disease onset age more similar to the general population of breast cancers. This broader category of familial cancers may be associated with several causes, like chance clustering of sporadic cancer cases within the same family, existence of genetic variation in coincident lower penetrance genes or a shared environmental factor that has impacted on all (affected) relative.

Assessment of an individual's risk of familial or hereditary cancer is based on a detailed evaluation of the family history in which the number of cases and a phenomenon such as anticipation will help decide on which families to screen for the presence of moderate or high risk gene mutations. Advances in molecular genetics have identified a number of genes that are associated with an inherited susceptibility to breast and/or ovarian cancers (e.g. *BRCA1*, *BRCA2*, *TP53, PTEN*, *CDH1*).

Since mutation analysis is relatively expensive due to the complexity genes, clinical inclusion criteria have to be met before starting the analysis. In the first step, blood DNA from an affected family member will be screened for the presence of a mutation. The understanding of the molecular basis of cancer makes it possible to identify families where hereditary breast cancer syndrome may be diagnosed. Individuals who want to evaluate their cancer risk according to their family history search clinical genetics services or familial cancer clinics to receive adequate screening management recommendations. Since the identification of a genetic risk may influence the patient's treatment choices, specialists are also increasingly referring patients for genetic testing. Comprehensive familial cancer clinics, which usually involve multidisciplinary teams, assess the risks and screening options for individuals with a higher cancer risk.

A key step in the cancer risk assessment process is a genetic counseling. Counseling includes education of individuals regarding the genetics of cancer, the likelihood of having a mutation and the likelihood of developing cancer, the benefits and limitations of genetic-susceptibility testing, and the appropriate cancer screening and prevention options. The goal of the counseling process is to educate patients to make informed decisions according to the calculated risks with regard to cancer screening, prevention and genetic testing. During the counseling process, careful attention must be paid to psychosocial issues to ensure effective genetic counseling. The first step for every cancer genetic counselor is the assessment of a detailed family tree with all cancer diagnoses, ages of disease onset and types of cancers.

Typical family trees consist of multiple affected family members in several generations, often with early ages of onset and multiple diseases. Small families and families with a high ratio of men to women in the pedigree may hide the real risk and this limitation should be carefully considered.

Cancer genetic counseling is a communication process that assesses an individual's risks of developing specific inherited forms of cancer. The genetic counseling process helps patients understand and comply with the medical, psychosocial and familial implications of genetic contribution to cancer risk. Genetic counseling

includes interpretation of family and medical histories to assess cancer risk. It also includes education about the genetics and inheritance. At the end of the process the discussion about the options for managing cancer risk and prevention is made. Cancer genetic counseling can lead to genetic testing when the probability of having a mutation is high enough. There are many policy statements, publications and organizational recommendations that propose criteria for when an individual should be referred for genetic counseling, but there are no fixed eligibility criteria for cancer genetic counseling. These include recommendations of the American Society of Clinical Oncology, the NCCN recommendations, the preventive services task force and many others, center specific ones.

The multidisciplinary team of the Cancer Genetic Clinic at the Institute of Oncology Ljubljana has prepared a clinical pathway for the assessment of patients with a positive family history for breast and ovarian cancer and for other frequent hereditary cancer syndromes. In the preparation of the clinical pathway, the patient was our main focus. The main objective is the same as in any other clinical pathway. It represents the basis for equal assessment of patients, the basis for continuous improvement of quality of health care, and the basis for measuring the effectiveness of the patient's assessment.

A safe and high-quality treatment of each patient is of the highest value and priority for all healthcare providers. It is important how health-care providers perform medical assessment; the approach to the treatment of patients should be based on scientific evidence and unified within the healthcare organization. This approach also stimulates the use of clinical pathways.

Health assessment of patients changes continually, according to the clinical guidelines which are considered at multidisciplinary meetings, being constantly updated and improved. The clinical pathway for genetic testing is improving and thus does not represent a static document, but a living substance that is updated daily in favor of a more qualitative assessment of the patient.

Since there is every day more and more knowledge in cancer genetics and its clinical implications in all aspects of cancer management; including prevention, screening and treatments, there is an increasing demand from specialists as well as patients and their families for cancer genetic assessment and clinics have to be prepared with high quality multidisciplinary teams and with appropriate assessment procedures.

CAN ABDOMINAL TUMORS INFILTRATING THE HEART AND INFERIOR VENA CAVA BE TREATED, USING CARDIOPULMONARY BYPASS?

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Background: Most patients with hepatocellular carcinoma and thrombosis of the right atrium have a very short survival. Removal of tumor thrombus is done in order to avoid sudden death from pulmonary embolism. Five to 10% of all patients with

hypernephroma developed renal vein thrombosis, which can proceed in to inferior vena cava (IVC) and right atrium. It was shown that simultaneous radical nephrectomy and thrombectomy of the IVC result in better long-term survival. The aim of this work is to review our experience with on-pump surgical treatment of patients with abdominal tumors, infiltrating the heart and IVC.

Methods: From January, 2009 to December, 2012 seventeen patients, 12 male and 5 female with average age 59 years (from 45 to 78) were treated in our center. Two patients have hepatic mass, one have adrenal mass, 13 have renal mass and one have pelvic mass. All have IVC thrombosis. All patients were operated on-pump from hybrid surgical team.

Results: Radical extraction of the tumor was possible in all patients. ICV thrombectomy was successful in all cases. One patient died during surgery. Among 16 surviving the operation two patients was reexplored for bleeding and three patients required CVVH. In both full recovery of the renal function was observed. One patient died in ICU, because of multi organ failure. No other major complications were observed. All 15 survivors were discharged home. Average hospital stay was 10 days (from 7 to 15 days). Histology revealed hepatocellular carcinoma (1 patient), leiomyosarcoma (1 patient), adrenocortical carcinoma (1 patient), hypernephroma (9 patients), leiomyoma (1 patient).

Conclusions: Our present study shows that patients with malignant diseases and large hepatic, renal, adrenal or pelvic tumors with IVC thrombosis could be operated on-pump, which guarantees radical tumor extraction with acceptable mortality and morbidity.

MARKERS OF PRECLINICAL ATHEROSCLEROSIS AND THEIR CLINICAL RELEVANCE

Prof. P. Poredos, MD, PhD
University Medical Centre Ljubljana, Slovenia

The estimation of risk for atherosclerotic and cardiovascular events based only on the presence of classical risk factors is often insufficient. Therefore, efforts have been made to find markers that indicate the presence of preclinical disease in individual subjects: blood markers of atherosclerosis and preclinical deterioration of the arterial wall. Elevated levels of several inflammatory mediators have been found in subjects with atherosclerosis. Prospective epidemiological studies have found increased vascular risk in association with increased basal levels of cytokines, the cell adhesion molecules P-selectin and E-selectin; and acute-phase reactants such as high sensitive C-reactive protein (hsCRP), fibrinogen, and serum amyloid A. For clinical purposes, the most promising inflammatory biomarker appears to be hsCRP. In the last decade, markers of plaque stability and unstable coronary artery disease have been sought such as myeloperoxidase, soluble CD40 ligand, pregnancy-associated plasma protein A, free fatty acids and placental growth factor. Further, markers of endothelial dysfunction (ED), like circulating molecules as well as indicators of functional deterioration of the arterial wall, that represent a common denominator of harmful effects of risk factors on the vessel wall were identified. It was shown that endothelial dysfunction is closely related

to different risk factors of atherosclerosis, and to their intensity and duration. Measurement of the intima-media thickness (IMT) using high resolution B-mode ultrasonography has emerged as one of the methods of choice for determining the anatomic extent of preclinical atherosclerosis and for assessing cardiovascular risk. A strong correlation between carotid IMT and several cardiovascular risk factors was shown and it has also been found to be associated with the extent of atherosclerosis and end-organ damage of high risk patients. The determination of preclinical atherosclerosis is also important because it enables identification of individual subjects in whom atherosclerotic process is already present and a group of subjects who need intensive management of risk factors.

ROLE OF ECHOCARDIOGRAPHY IN DIAGNOSIS OF PULMONARY HYPERTENSION

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Pulmonary hypertension can be found in multiple clinical conditions, with specific characteristics, which were classified into 5 clinical groups in the new guideline for the diagnosis and treatment of the European Society of Cardiology. These conditions have different epidemiology, pathology, genetics, diagnostic features and treatments.

Pulmonary hypertension is defined as haemodynamic and pathophysiological condition defined as an increase in mean pulmonary arterial pressure (PAP) >25mmHg at rest assessed by right heart catheterization.

Regardless of the pathogenesis of occurrence, PH is progressive processes which lead to right ventricular (RV) overload, hypertrophy, dilatation and RV failure. Rate of progression depend of the obstructive changes in pulmonary microcirculation and the influence of the PH to the RV. The inadequate adaptation of the myocardial contractility is one of the reasons in the progression of the heart failure in a chronically overloaded right ventricle.

Transthoracic echocardiography can give several parameters which correlate with right heart haemodynamics, and should be performed in a case of suspected PH.

Echocardiography can give important information in detection of PH and discovering some of the etiological reasons for PH. Also, echocardiography can give us information about hemodynamic impact of the PH on RV chambers and RV function. Several parameters are important for estimation of right ventricular function: right atrial and ventricular dimensions and volumes, functional area changes (FAC%), D-shape of the LV, tricuspid annular plane systolic excursion(TAPSE), myocardial performance index, inferior vena cava size and collapsibility, S velocity estimated by Tissue Doppler Imaging and additional information gated from the advance echocardiograpic technique, like strain, strain rate, three-dimensional echocardiography. TAPSE and pericardial effusion are parameters which are included for assessing disease severity, stability and prognosis in patients with PH.

The estimation of the systolic pulmonary artery pressure (SPAP) is based on the peak velocity of the jet of tricuspid regurgitation, using simplified Bernoulli equation. Tricuspid regurgitation velocity more than 3,4 m/s, and estimated PA systolic

pressure(SPAP) more than 50 mmHg with/without additional echocardiographic variables is suggestive of PH. Estimation of PH based on Doppler echocardiography measurements is not suitable for screening for mild, asymptomatic PH.

Echocardiography can be recommended tool for screening in the specific diseases and has central position between noninvasive procedures in detection of PH, follow up of PH and assessment when right heart catheterization is indicated.

We can conclude that echocardiography is a noninvasive, easy tool who can help in discovering patients with PH and the influence of PH on the RV function, can estimate severity of PH, discover many conditions which can be responsible for PH, follow up patients during the disease and after some procedures and therapy and can give prognostic information of this patients.

VALVULAR HEART DISEASE IN MACEDONIA-INCIDENCE OR COINCIDENCE

Tager IS

Cardiothoracic Surgery department-Acibadem –Sistina Hospital, Skopje, Macedonia

In this presentation I will try to elucidate some questions that occured since the start of the new Cardiac Surgery Department in Macedonia, 3 years ago. From the meny questions I asked myself, I found few essential above all. What is the spectrum of pathology of cardiac disease to be expected. Functioning for meny years in a very large scale Israely Clinical Center with all the facilities, I was preparing to build as complete service as possible.

The preparations and search for information showed that there is no organized published data. Morover, there is no organized data on the post op follow up and destiny of the patients. Some of the data came from the National Health Insurance, another source where the two existing Centers with Angiolabs in Skopje & Ohrid, and also the published data from a previously existing and active Cardiac surgery department.

They shawed approx 80% CABG and 20% Valvular pathology .

While I expected similar ratio surprisingly I observed 50% valvular pathology, mainly Aortic Stenosis, and approximately one third Mitral Valve Disease. Rheumatic Mitral Disease is almost nonexistent opposite of my expectations.

This presentation will present data and discuss the possibilities why although still not a member in the ECC , the pathology we encounter is very simmilar and with distribution just like in the western world.

OBESITY AND CARDIOVASCULAR RISK

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There is obesity pandemic with increasing prevalence in most developed as well as in developing countries. Obesity is an independent risk factor for cardiovascular disease (CVD), especially central adiposity having detrimental effects on metabolic and vascular health. Abdominal adiposity is strongly associated with insulin resistance, and consequent atherogenic dyslipidemia (high triglycerides, low HDL-cholesterol, highly atherogenic small, dense LDL-cholesterol particles), hypertension, prothrombotic profile, and low grade systemic inflammation, which all play essential roles in the pathogenesis of CVD. Waist circumference (WC) and waist-to-hip ratio are widely used as indirect measures of abdominal or central adiposity. The cutoffs for WC (94 cm for men, 80 cm for women) were recommended by the International Diabetes Federation in 2005. Accumulating evidence indicates that the above measures of abdominal adiposity are significantly and positively associated with risks for chronic diseases such as CVD, diabetes mellitus, and some cancers independently of overall adiposity. The association of these measures with mortality has been recently evaluated. Elevated WC was associated with significantly increased CVD mortality even among normal-weight women. Intra-abdominal or visceral adipose tissue is highly metabolically active releasing abundance of free fatty acids into the portal circulation along with adipokines, disturbing insulin signaling in the liver and muscle tissue, interfering with insulin secretion by damaging pancreatic beta-bells, causing systemic inflammation, endothelial dysfunction, and impairing fibrinolysis. Adipose tissue that accumulates in the heart, skeletal muscle, the liver, and the pancreas, has local toxic effects as it can damage these organs directly in a paracrine-autocrine manner.

Regular physical activity has the most beneficial effects on visceral adiposity reducing it substantially and increasing insulin sensitivity along with the essential improvement of the metabolic profile. Exercising muscles produce and secrete myokines that counteract the proinflammatory adipokines.

Key words: obesity, abdominal adiposity, insulin resistance, cardiometabolic risk, adipokines.

LEFT VENTRICULAR REMODELING AND DIASTOLIC DYSFUNCTION IN TYPE 2 DIABETES MELLITUS

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Previous studies have shown the independent or combined effect of diabetes on left ventricular function. Remodeling of the left ventricle has been shown to be an independent predictor of increased cardiovascular risk in persons with risk factors.

Aim: To evaluate the left ventricular morphology and function in diabetic type 2 patients.

Methods: We studied 236 pts (age 35- 69 years, 55.5% male) with type 2 diabetes mellitus (0-10 years) with preserved systolic function (EF > 50%) and asymptomatic for heart failure. M-mode echocardiographic analysis was performed to determine chambers dimensions, wall thickness, left ventricular mass and left ventricular

mass index. Pulsed Doppler and tissue Doppler evaluation was performed according to standard evaluation.

Results: 66.1%(80/236) of pts had diastolic dysfunction; 55.5% (131/236) of them had diastolic dysfunction of 1 degree, 10.2% (24/236) had diastolic dysfunction of 2 degree and 0.4% (1/236) had diastolic dysfunction of 3 degree. 49.6%(117/236) of pts had normal geometry of left ventricle, 22.7% (56/236) of pts had concentric remodeling of LV, 15.7% (37/236) of pts had eccentric hypertrophy of LV and 9.7% (23/236) of them concentric hypertrophy of LV. Left ventricular index mass was 99.2 gr/m2, LV EDD 48.2 mm and left atrial diameter 37.4 mm. The presence of diastolic dysfunction was strongly correlated with LV remodeling (r= 0.5), and left ventricular index mass had significant correlation with LA diameter (r= 0.65).

Conclusion: Diabetic patients have a high prevalence of subclinical diastolic dysfunction that correlates with remodeling of the left ventricle. Echocardiographic evaluation is important in this population at high risk of developing cardiac heart failure.

ДИСФУНКЦИЯ МЫШЦ КАК ОДИН ИЗ СИСТЕМНЫХ ПРОЯВЛЕНИЙ У БОЛЬНЫХ НА ХРОНИЧЕСКОЕ ЛЕГОЧНОЕ СЕРДЦЕ ПРИ ХРОНИЧЕСКОМ ОБСТРУКТИВНОМ ЗАБОЛЕВАНИИ ЛЕГКИХ

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Современная концепция хронических обструктивных заболеваний легких (ХОЗЛ) основанная на том, что следствием прогрессирующего и затяжного воспалительного процесса в бронхо-легочной системе есть экстрапульмональные проявления, которые определяют тяжесть течения и прогноз заболевания. В последние годы все большего внимания заслуживают метаболические и мышечно-скилетные нарушения, такие как: снижение массы тела, дисфункция скелетных мышц, их гипотрофия и атрофия. Это приводит к нарушению функциональных возможностей и снижению физической активности больных, снижению качества и длительности жизни.

Особеностью дисфункции скелетных мышц у больних ХОЗЛ, осложненным легочным сердцем, является нарушение соотношения сокротительных миофибрил: уменьшение миофибрил I типа (медленных, оксидативних) и рост доли миофибрил типа IIb (быстрых, гликолитических). Уменшение доли миофибрил I типа в скелетных мышцах у больных ХОЗЛ свидетельствует о снижении оксидативной способности мышц.

Рассматривая проблему дисфункции скелетных мышц, стоит уделить внимание дисфункции дыхательных мышц, как один из основных патогенетических состовляющих легечной недостаточности, которая в свою очередь есть одной из ведущих причин смерти больных ХОЗЛ и составляет 38% среди всех факторов летальности.

Патогенетические механизмы, которые лежат в основе развития дисфункции дыхательных мышц связаны с системными восполительными эффектами заболевания, что может приводить к уменьшению массо-ростового

индекса, нарушению энергетического обмена, оксидативного стресса, потери общей массы мышц и нарушению функции скелетних мышц в целом и дыхательных мышц в часности. Таким образом дисфункция дыхательных мышц у больных ХОЗЛ, осложненным легочным сердцем, имеет важные медецинские и социальные последствия. Однако, недостаточно изученым на сегоднящний день есть влияние базисной терапии ХОЗЛ на состояние скелетных мышц и дыхательной мускулатуры в часности, на розработаные методики коррекции функций дыхательних мышц в общем комплексе реабилитации. Все вышеуказанное обуславливает актуальность проведения исследований по этой проблеме.

MEASUREMENT OF BLOOD PRESSURE IN THE FOURTH YEAR OF LIFE

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Introduction: In the fourth year of a child's life is done systematically pregled.Then when it comes to physical examination of the bodies, measured body weight and height, blood pressure, lab work .To is an important indicator of growth and development and screening for disease.

Objective: Monitoring of blood pressure in relation to body mass.

Methods: We observed 70 children in the fourth year of life.We analyzed have their BMI (body mass index) and blood pressure level.

Results: Of 70 children, 34 were boys and 36 djevojčice.5 girls and 3 boys had a BMI above 90 percentile.Od all subjects only one girl had a pressure above 90 percentile.Ona a normal BMI. We ordered it in control when the pressure is still persisted.After monitoring of blood pressure at home, where it was shown that the occasional jumpes of hypertension, the girl was sent for testing. The same has not had a urinary tract infection or other diseases.

Conclusion: The measurement of blood pressure in the 4th age is significantly due to early detection of hypertension. Prevention and timely treatment disease represent the essence of systematic reviews.

СОВРЕМЕННОЕ СОСТОЯНИЕ ПРОБЛЕМЫ АРТЕРИАЛЬНОЙ ГИПЕРТЕНЗИИ В УКРАИНЕ И ПЕРСПЕКТИВЫ ЕЕ РЕШЕНИЯ

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Актуальность проблемы. Артериальная гипертензия является одним из ведущих вызовов общественному здоровью в Украине и мире. Повышенное артериальное давление вносит весомый вклад в общую смертность населения, формирует основу для развития многих болезней системы кровообращения и их осложнений.

Методы исследования. В работе использованы библиографический, статистический и аналитический методы.

Результаты. В Украине зарегистрировано более 12 млн больных артериальной гипертензией , что составляет 32% взрослого населения. Распространенность гипертензии с каждым годом возрастает. Лишь за 2000-2012 гг. она увеличилась на 175%. Доказано, что у лиц с высоким артериальным давлением в 3-4 раза чаще развивается ишемическая болезнь сердца и в 7 раз чаще - расстройства мозгового кровообращения. При наличии гипертензии риск общей смертности повышается у мужчин в 4,5, у женщин - в 2,0 раза. Большинство больных (60%) относятся к группе лиц трудоспособного возраста, от состояния здоровья которых зависит трудовой и экономический потенциал. Однако у части больных гипертензия остается недиагностированной, кроме того, лишь немногим более половины (53%) пациентов выполняют врачебные рекомендации, эффективно лечатся лишь 12% больных. Риск возникновения осложнений и преждевременной смерти возрастает с увеличением числа сопутствующих гипертензии факторов риска. Согласно исследованиям, проведенным в Институте кардиологии имени академика Н.Д. Стражеско, только 1% пациентов с повышенным артериальным давлением не имеет дополнительных факторов риска; у каждого восьмого пациента гипертензия сочетается с одним, у каждого четвертого - с двумя, у 61% пациентов - с тремя и более дополнительными факторами риска. Неконтролируемая гипертензия является одним из наиболее весомых факторов сокращения продолжительности жизни населения. В целях обеспечения эффективного контроля артериального давления среди населения Украины необходимо активизировать усилия медицинского персонала, особенно учреждений первичной медицинской помощи, направленные на своевременное выявление у пациентов гипертензии, а также создание у больных мотивации к длительному, а не эпизодическому медикаментозному лечению и коррекции сопутствующих факторов риска. Совершенствование организации медицинской помощи пациентам с гипертензией с использованием современных принципов стандартизации и доказательной медицины, имеет приоритетное значение для системы здравоохранения.

Выводы. Медико-социальная и экономическая значимость проблемы артериальной гипертензии выдвигает возрастающие требования к совершенствованию ее профилактики, диагностики и лечения.

Первичная профилактика гипертензии сегодня рассматривается с позиции общей профилактики болезней системы кровообращения и заключается в предупреждении, своевременном выявлении и коррекции таких доказанных факторов риска, как курение; гиперхолестеринемия; избыточная масса тела, гиподинамия, а также злоупотребление алкоголем.

Проблема противодействия артериальной гипертензии требует системного подхода и решения на общегосударственном уровне. Новые перспективы дальнейшего противодействия эпидемии гипертензии, как и других социально значимых хронических неинфекционных заболеваний, очерчены проектом Государственной программы «Здоровье-2020: украинское измерение».

EFFECTS OF ESSENTIAL HYPERTENSION ON CORONARY MICROCIRCULATION: CASE REPORT

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Background: Hypertension is one of the most widespread cardiovascular risk factor that underlies the establishment of atherosclerotic deterioration of arterial walls. Microvascular abnormalities can both results from and contribute to hypertension. Heart is organ that may suffer end-organ damage with changes in myocardial microvessel structure and density. This changes of the circulation are associated with chest pain and the reason for ischemia is still found within epicardial vessels (stenosis, coronary spasm, myocardial bridges, endothelial dysfunction), but in some cases none of the suitable causes can be found. In this context we talk about microvascular angina.

Methods: We present a clinical case of 64 years old female patient with chest pain a few days before actual hospitalization and 15 years history of hypertension. This is second hospitalization of the patient; in previous one she had chest pain and coronary angiography was performed but without detection of significant coronary artery lesion. We performed several clinical investigations during actual hospitalization: blood chemistry, electrocardiograms (ECG), 24-hour ECG Holter monitoring, carotid Doppler ultrasonography (CDU), echocardiography (ECHO), myocardial perfusion scintigraphy (MPS), as well as coronary angiography (CA).

Results: Physical examination and biochemical parameters were normal, with pathological ECG detecting Q-wave in anteroseptal leads and left anterior hemiblock. Twenty four-hour Holter ECG monitoring showed rhythm disturbances in terms of single multifocal ventricular extrasystoles with periods of bigeminy and trigeminy, as well as single and pairs of supraventricular extrasystoles. CDU finding was normal. ECHO revealed reduced global left ventricle contractility with impaired segmental kinetics of the middle and apical segment of the interventricular septum and anterior wall with EF 36%. MPS was pathological and showed wide region of perfusion defect (sequela) in multiple segments encompassing 48% of the left ventricle muscular mass including apical aneurysm. At the end, CA was performed but it did not detect any significant coronary artery lesion.

Conclusion: Abnormalities of microvessel structure and microvascular network density often accompany and may be an important cause of primary hypertension. Microcirculatory abnormalities are also likely to be central to many forms of hypertensive end-organ damage including those involving heart, especially coronary artery disease.

CHROMOSOMAL ABNORMALITIES AND CONGENITAL HEART DISEASES DETECTED IN CHILDREN

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Congenital heart disease (CHD) occurs in approximately 1-3% of live births, but in a much higher percentage of those aborted spontaneously or stillborn. 30% of total abnormalities is for CHD. Incidence is varying from 4-50/1000 live births, 10% of spontaneously aborted fetus. CHD may occur as a single isolated malformation or as associated anomaly in 33%. The causes for CHD can be categorized into three major groups such as, chromosomal, single gene disorders (10-15%) and multiple factors (85-90%). With cytogenetic techniques is found that about 0.4 - 26.8% of all CHD are associated with several chromosomal anomalies like numerical and structural variations. Here we report the association of chromosomal variations with CHD in our ordination. For our study we used the documentation of the personal doctor for 13 years (2000-2013), as well as genetic and chromosomal analysis from the Medical Faculty in Skopje. A total of 534 confirmed CHD cases were considered for the present study whose age ranged from 1day to 18 years. 15 from them were with chromosomal abnormalities (2.80%). 12 from them (80%) were with chromosomal numeric abnormalities, 2 with structural abnormalities (20%). In chromosome abnormalities were present 26.67% patients with Tetralogy of Fallot, 20% with VSD, by 13.33% for those with PDA and CoA, by 6.67% for those with TGV, BAV, ASD and single ventricle. The need of early prenatal diagnosis of chromosomal abnormalities is very important for early detection of CHD.

IMPACT OF BODY MASS INDEX IN CLINICAL OUTCOME IN PATIENTS UNDERGOING PERCUTANEOUS CORONARY INTERVENTION

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Background: Previous studies have described an "obesity paradox" with cardiovascular disease, whereby higher
body mass index (BMI) is associated with lower mortality in heart failure, acute myocardial infarction, acute coronary syndrome, atrial fibrillation..

Purpose: We sought to investigate the impact of body mass index (BMI) on morbidity and mortality in patients following first-time elective percutaneous coronary intervention (PCI).

Methods: Were included in the study 191 patients who underwent the first-time elective PCI from September 2011 to August 2012 in University Hospital Center "Mother Teresa" Tirana and were followed for a period of 6 months. We excluded patients who had previously undergone revascularization. Patients were categorized according to BMI groups. BMI 18.5 - 24.9 kg/m2 normal group, 25 - 29.9 kg/m2

overweight group and> 30 kg/m2 obese group. Baseline characteristics of patients across the 3 BMI categories were compared using χ2tests for categorical variables and Student t test for continuous variables

Results: During follow-up there was only one death in overweight group. Compared with normal weight individuals, those overweight had more high risk coronary anatomy (13.6% vs 1.6% p = 0.0241), number of stents per person higher (1.93±1.01 vs 1.63±0.79 p = 0.0429) and were older (60.56±9.94 vs 57.37±10.26) p = 0.042). Compared with normal weight individuals, those overweight had a reduced number of rehospitalizations (7.34% vs 20% p = 0.0186) and total events (8,42% vs 20% p = 0.032). Also compared with normal weight individuals, obese patients had a reduced number of rehospitalizations, but not significant (13.9% vs 20% p = 0.3).

Conclusions: The patients with higher BMI had a better clinical performance. Overweight patients although were older, with more high risk coronary anatomy and a higher number of stents per person, had in all less rehospitalizations and events. "Obesity paradox" seems to be present, even in Albanian patients

ENDOVASCULAR TREATMENT IN PATIENT WITH ADVANCED ATHEROSCLEROSIS CASE REPORT

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This report describes the case of a 79 year-old male after CABG, with stable angina, significant stenosis of the left carotid artery and left subclavian artery,, who underwent implantation of self-expandable stent of the left carotid artery and balloon-expandable stent of the left subclavian artery with excellent clinical outcome.

Key words: CAS –carotid artery stenting, CEA – Carotid endarterectomy.

Introduction: The question that we often ask ourselves these days is when and how CAS is a possible alternative to CEA in the treatment of patients with carotid stenosis.

Over the past 10 years technical progress, new devices for cerebral protection and skills development led to encouraging results in the treatment of symptomatic and asymptomatic severe carotid stenoses.

Going in different vascular territories endovascular techniques allow us to deal with difficult decisions in every day clinical practice regarding high risk patients.

Case: 79 year-old male with risk factors – age, gender, arterial hypertension , dyslipidemia was referred to our hospital for angiographic assessment with stable angina , after CABG and previous stroke. On physical examination, he had blood pressure difference between arms – 20 mmHg. Cardiopulmonary auscultation showed normal pulmonary status and mitral valve systolic murmur. ECG showed sinus rhythm, without ST-T changes in rest The echocardiogram showed a good global left ventricle (LV) ejection fraction (EF) of 64%, with mitral regurgitation – II degree .LA – 43 mm. Echo-sonography showed occluded,right internal carotid artery and 70% stenosis of the left carotid artery. CT scan found prior silent stroke. Diagnostic coronary angiography revealed native coronary arteries – significant distal left main stenosis, RCA- proximal

occlusion, LIMA graft to LAD- patent ,venous graft to RCA - patent, venous graft to Rcx - occluded, preserved EF with MR – II degree, significant subclavian stenosis, severe stenosis of left internal carotid artery, occluded – right internal carotid artery.

Procedure: After cannulation of the left common carotid artery using 5 Fr right diagnostic catheter,0,035 Cook wire and 8 Fr Guide long sheath,. Distal embolic protection device – Epifilter wire was used and 7.0/30 mm Carotid-Wallstent was deployed and postdilation with balloon 5,0/17 mm was done with good angiographic result. After that we cannulated the left subclavian artery with 5Fr diagnostic catheter. Lesion was crossed with 0,035 Cook-wire and the same 8 Fr carotid sheath was used as a guide catheter.
Omnilinc-balloon-expandable stent 8.0/28 was deployed successfully

Conclusion: Endovascular treatment of patients with multifocal lesions is an alternative option of treatment especially in patients with high surgical risk .The advance of methodology, indications and operator experience based endovascular treatment in a much better position, which was supported by the results of several randomized trials. Evidence informs our medical decisions, but we also must use the evidence in the context of the patient's situation. The summary findings of large clinical trials must be applied to individual pts with specific characteristics. Good clinical judgment in the present day has evolved into the clinician's ability to appropriately interpret and incorporate available evidence in the day-to -day management of patients.

DIABETES

TREATMENT OF DIABETES MELLITUS ACCORDING TO RECENT GUIDELINES

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Management of patients with Type 2 diabetes mellitus (T2DM) demands a comprehensive approach which includes diabetes education, an emphasis on life style modification, achievement of good glycemic control, minimization of cardiovascular risk, and avoidance of drugs that can aggravate glucose or lipid metabolism, and screening for diabetes complications. Comprehensive diabetes management can delay the progression of complication and maximize the quality of life. Once lifestyle measures implemented, if hyperglycemia persists, above individual HbA1c targets, a medication should be started in T2DM. Metformin remains the first-line treatment for patients with diabetes. If metformin is contraindicated or is not tolerated, any one of the other available antihyperglycemic drugs may be used as monotherapy.

Latter, combination of two oral drugs, now offers several options, mainly the choice to associate a conventional insulin-secretagogues; sulfonylureas, glinide, or a new one belonging the class of "incretin based therapy",such as DPP-4 inhibitors or the injectable GLP-1 analogues which can also be sometimes chosen at this stage. These options are mostly new and have the advantage a neutral or favourable (for GLP-1) effect on body weight in obese type 2 DM patient and the absence of any hypoglycaemic risk in both classes of incretins. But this risk varies depending on the patient profile, much higher if the target HbA1c is low (6 to 6.5 or 7%), or in the elderly, fragile and/or in case of renal insufficiency. These two different situations with a high risk of hypoglycaemia, define best indications of this new class. If dual oral therapy does not achieve the goals we are faced with three options: triple oral therapy: metformin-sulfonylurea-gliptine or one of two approaches with injections, insulin or GLP-1 analogues. The use of GLP-1 analogues is often delayed today and put wrongly in balance with the transition to insulin, a use already delayed in Slovenia and insufficient. The use of incretin based therapy is new and needs to be validated by studies of sustainability on glycemic control, prevention of microvascular and macrovascular complications and after years on the market security of use and lack of long term safety profile. In short, individualization of strategies and HbA1c targets are required. This individualization can easily be done through the handy guide proposed by the experts ADA/EASD statement. A recommendation that for the first time also prioritizes the costs of the strategies. Finally, we must reconsider every treatment after a maximum of 6 months of use, if the results are deemed inadequate substitute rather than adding drugs and the reinforce the lifestyle changes.

COGNITIVE IMPAIRMENT IN PATIENTS WITH DIABETES

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Several lines of investigation suggest a link between diabetes and disorders of cognitive functions. The domains of information processing speed, executive functioning and memory are most often affected. The term executive functions refers to cognitive processes necessary to the successful planning, decision making, judgment and and monitoring goal-directed behaviour. In an environment with changing conditions, the executive functions apparently directs activities that demand novel responses. Besides cognitive symptoms, behavioural, emotional, and motivational disturbances may be observed, such as apathy, indifference, impulsivity, irritability, and disinhibition.

Traditionally, executive dysfunction was exclusively related to damage to the (pre)frontal cortex. More recently however, it has been shown that brain damage distant from the frontal lobes, damage to subcortical structures or interruption of connections between frontal and non-frontal areas, may also impair executive functions.

Structural brain imaging studies in older adults with diabetes show that cerebral atrophy and lacunar infarcts are more common, relative to people without diabetes. In addition, there are clear indications that diabetes is a risk factor for widespread incomplete infarction, which are associated with more chronic, diffuse, and less severe ischaemia. The dysexecutive syndrome observed in these patients probably results from ischaemic interruption of parallel circuits from the prefrontal cortex to the basal ganglia and corresponding thalamocortical connections. Possible risk factors for impaired cognition and subcortical brain imaging abnormalities in diabetes include many factors that are linked to diabetes but are not specific to diabetes, like hypertension and hyperlipidemia.

METABOLIC SET UP AND RISKS IN OBESE CHILDREN

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Obesity is a growing problem around the world with an onset very early in childhood. It affects children of all ages, even infants and babies. American incidence studies show that between age 9 months and age 2 years, U.S. children consistently move toward less desirable weight status, with a different obesity risk across demographic subgroups, suggesting that health policy might focus on those children at greatest risk.

A range of hormones which regulate energy metabolism are secreted by adipose tissue, among which adiponectin and leptin are the main adipokines regulating insulin sensitivity. Insulin resistance, on the other hand, is among the central events and influences metabolic and cardiovascular complications occurring in obese children.

The aim of this study was to present the metabolic set up in obese children and different risks causing morbidity later in life. We are presenting results of several studies in obese children of different ages performed in the Republic of Macedonia.

BMI measurement during a systematic check up at 11-13 years old school children in three urban elementary schools confirmed obesity in 13% of measured children.

Metabolic status in obese children
No validated definition with standardized cut-off values of the metabolic syndrome is available in children.

Insulinemia has been shown to be higher in obese children compared with the lean age-matched controls. In 78 obese and overweight children at the age 13.5±4.1 years with a BMI >85%o the correlation between the BMI, peak insulinemia on OGTT and insulin resistance expressed as HOMA index was analysed. More than half of obese children (53.6%) had a relative with diabetes, obesity, hyperlipidemia and/or hypertension. BMI was higher in the pubertal group and significantly higher in girls. The only significant metabolic difference between the prepubertal and pubertal groups was the peak insulinemia: 87.361±59.3□U/ml versus 57.9±26.3□U/ml ($p<0.01$). The conclusion of the study was that a significant insulin resistance exists in most of the obese children. Peak insulinemia is higher in the pubertal group suggesting that the risk for glucose intolerance rises during puberty.
Adiponectin/leptin. We have studied the correlation of leptin and adiponectin levels with the BMI and insulinemia in obese children and adolescents and compared them with the results in lean controls of matched age. Leptin level in the obese children was 36.1±13.7ng/ml versus 5.7±1.5 in non obese children ($p<0.05$). There was a significant correlation between the BMI and leptin ($p<0.01$). Adiponectin levels were 10.5±4.8 ng/ml average in obese children and 15.2±6.9 ng/ml in controls ($p<0.05$). There was a significant negative correlation of BMI with the adiponectin levels ($p<0.05$). Our study also confirmed that obese adolescents have a more atherogenic lipoprotein profile, associated with increased insulin resistance (IR). Adiponectin was inversely associated with atherogenic lipoproteins in adolescents, even after adjusting for obesity and IR. Glucose intolerance was found in 24% of 158 studied obese children.

Metabolic programming: The concept of metabolic programming has been recognized for many years and focused towards long-term detrimental effects of foetal under nutrition and low birth weight progressing towards obesity later in life.

We assessed in our study the correlation of anthropometric parameters with leptin and adiponectin levels in healthy preterm(N=36), SGA (N=30) and term newborns (N=36) Significant difference was found in leptin (higher) and adiponectin (lower) levels in SGA newborns compared to other studied subgroups.
Leptin and adiponectin levels were positively correlated with all anthropometric parameters: body weight, body length, BW/BL, BMI, and pondered index ($p<0.05$). These results indicate that the stage of body growth maturity is positively correlated to adipocytokines involved in fetal growth regulation.

Conclusions. 1.Significant foetal programming is involved in later obesity in childhood.; 2.SGA newborns are an especially vulnerable group prone to develop metabolic syndrome later in life.;3.Obese children have significant early metabolic parameters such as hyperinsulinemia, high leptin levels and lower adiponectin levels 4.Family risk factor cluster to families of obese children; 5.Glucose intolerance is a frequent finding in obese children and should be monitored closely in order to prevent overt DM2.

Taking together all these risks, health professionals should follow the weight in children starting very early, and screen for obesity in the early age 2-5 years for the possibility of early intervention.

NEW TECHNOLOGIES IN DIABETES DIAGNOSIS AND MANAGEMENT

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The burden of diabetes leads to increase in patient health care costs and is associated with significant morbidity and mortality. New approaches for early diagnosis, treatment and control of the disease are very important to protect from complications and to diminish the health expenses.

EZSCAN is a new technology based on strong association between small nerve neuropathies, sweat gland dysfunction and insulin resistance and increased blood sugar. This diagnostic method is easy to operate, reproducible and not expensive and identifies those with increased risk**.** EZSCAN has the potential to be useful tool in diabetic risk diagnostic and early detecting of complications.

Continuous glucose monitoring (CGM) performs multiple blood glucose measurements and is used for defining the control and changing the treatment regimen in diabetic patients, especially those with varying glucose levels and experiencing frequent hypoglycemic episodes. iPro 2® Professional is forth generation continuous glucose monitoring system, valuable for detecting high and low glucose fluctuations, and is small enough for patient to forget they have it on. iPro2 Professional CGM uses a tiny glucose sensor to record 288 glucose readings over a 24-hour period. Glucose data are captured in the system and is uploaded to CareLink iPro Software. The reports are useful for educating and motivating patients to implement changes in their diabetes management after viewing the effects that specific foods, exercise, stress, and medications have on their glucose levels.

The continuous subcutaneous insulin infusion therapy (insulin pump) is a medical device used for the administration of short acting insulin and is thought to be most physiological way for insulin replacement. Recently it is used not only in type 1, but also in type 2 diabetes. Combining insulin pump technology with continuous blood glucose monitoring system improves real-time control of the blood sugar level. Closing the loop will allow the system to function as an artificial pancreas.

ОСОБЕННОСТИ РАЗВИТИЯ, ДИАГНОСТИКИ И ЛЕЧЕНИЯ ГНОЙНЫХ ЗАБОЛЕВАНИЙ МЯГКИХ ТКАНЕЙ У ЛЮДЕЙ С САХАРНЫМ ДИАБЕТОМ И ОЖИРЕНИЕМ

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Сегодня в мире на ожирение страдает около 30-40% населения. Ожирение также является одним из главных факторов развития сахарного диабета 2-го типа. Целью нашего исследования было установление особенностей развития, диагностики и лечения гнойных заболеваний у таких людей. Под наблюдением было 102 пациента, которые были распределены на 4 группы по индексу массы тела (ИМТ). В 1 группу (ИМТ до 29,9) вошло 34, во 2-ю (ИМТ - 30,0-34,9) – 19, в

3-ю (ИМТ - 35,0-39,9) – 18 и в 4-ю (ИМТ 40,0 и больше) 31. У 33 пациентов были абсцессы, фурункулы были - у 18, карбункулы - у 14, флегмоны и аденофлегмоны были по 10 человек. У остальных 17 - были другие гнойные заболевания мягких тканей. Пациентам проводились все необходимые клинико-лабораторные, морфологические и иммунологические исследования с применением компъютерной томографии. Результаты. В среднем пациенты 1-й группы пребывали в стационаре 8,5±2,34* дня. Пациенты 2,3 и 4-й групп - 10,58±2,77*, 15,67±3,12* и 15,74±3,7* дня, соответственно (* – p<0,01). Количество экссудата в очаге воспаления в среднем в первой группе было 45,44±11,8** мл, во 2-й - 35,32±7,75**, а в 3-й и 4-й - 32,39±10,83** и 91,84±25,33** мл, соответственно (** – p<0,05). Было выявлено, что развитие гнойно-некротических процессов у людей с крайними формами ожирения часто имел замаскированный характер со стертой клинической картиной и с уменьшением болевых ощущений. Большинство этих процессов у таких пациентов имели более разлитой и тяжелый характер.Причины этому были следующие. Во-первых, морфологически, с увеличением ИМТ прогрессивно возрастают дистрофические и компенсаторно-приспособительские изменения в скелетно-мышечной ткани, с чрезмерным разрастанием жировой ткани в мышцах, что является предпосылкой для развития гнойно-некротических процессов. Во-вторых, у людей с гиперожирением значительно возрастает микробное обсеменение кожи и резко снижается бактериальная активность кожи, что способствует постоянной микробной нагрузке на организм. В-третьих, пациенты с ожирением (особено с диабетом) ощущают боль на много меньше, чем люди с нормальной массой тела. Это приводит к тому, что развитие воспаления имеет замаскированный характер и больной обращается за медпомощью поздно. В-четвертых, у пациентов с ИМТ более 40,0 часто наблюдается присутствие нескольких фаз раневого процесса одноновременно, когда в одном углу раны можна наблюдать грануляции а в другом – умеренные гнойные выделения. В процессе наблюдения нами также были обнаружены сложности лечения таких пациентов. 1.У врачей часто прослеживаются элементы полипрагмазии, из-за того, что много препаратов не дают ожидаемого эффекта ((тяжело рассчитать нужную дозу препарата), так как стандартные протоколы или рассчет на кг/массы тела, или на л/крови для больных с ожирением не подходят). 2.Биодоступность препаратов (антибиотиков) к месту гнойного воспаления уменьшается с ростом степени ожирения. 3. Практически нет возможности производить внутримышечные иъекции, так как толщина подкожной клетчатки очень толстая и иглы не достают мышечной ткани. Выводы. У больных с ожирением и диабетом есть много предпосылок для замаскированного и более тяжелого развития гнойно-некротичних процессов мягких тканей. Для топической диагностики очагов поражения при тяжелых гнойно-септических заболеваниях целесообразно применять компъютерную томографию. При лечении, кроме полноценного хирургического вмешательства, коррекции метаболлических нарушений и сахара крови, следует активно проводить местное лечение (антисептики, сорбенты, мази на гидрофильной основе, антибиотики).

LABORATORY MARKERS FOR BLOOD VESSEL DAMAGE IN SOME CHRONIC DISEASES

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Background. Blood vessel (BV) damage is common for some chronic diseases such as diabetes mellitus (DM), chronic renal failure (CRF), and some autoimmune diseases. This damage may cause serious conditions as following: heart failure, stroke, kidney loss, amputation, vision loss, etc. The aim of this study was to optimise some laboratory markers for blood vessel damage in chronic diseases.

Methods. Lipid peroxidation level (LPL), oxidized low density lipoproteins antibodies (LDL-ox Ab), low density lipoproteins (LDL) and high density lipoproteins (HDL) were measured in patients with diabetes mellitus - DM (n=23) and in patients with chronic renal failure - CRF (n=20). The number of 21 volunteers was considered as a control group. For LPL marker the fluorimetric method with thiobarbituric acid was used. For LDL-ox Ab enzyme immunoassay was performed by Biomedica gruppe, Austria. HDL and LDL were measured by colorimetric test (dry chemistry –Johnson-Johnson, USA).

Results. The LPL level was noticed to be increased 5.70±2.3 μmol/L in DM and 5.40±1.0 μmol/L in CRF. Increased level of LDL-ox Ab was found for DM to be 340±144 mU/ml ($p<0.01$) and for CRF to be 356 ±259 mU/ml ($p<0.01$). In both chronic diseases decreased HDL levels were found: 0.96±0.3mmol/L for DM and 0.76±0.3mmol/L for CRF ($p<0.05$) and increased LDL levels: 2.79±1.3mmol/L for DM and 2.43±0.6mmol/L for CRF ($p<0.05$).

Conclusion. The obtained results showed that used biochemical parameters may be important markers to estimate the blood vessel damage in chronic diseases, but also to evaluate the therapeutic effects of these patients.

Key words: laboratory markers; vessel damage, diabetes mellitus.

APPLICATION OF MOLECULAR-BIOLOGICAL TECHNIQUES UPON THE DETERMINATION OF THE GENETIC PREDISPOSITION FOR DIABETES MELLITUS

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Introduction: Diabetes mellitus (DM) is a group of metabolic diseases in which a person has high blood sugar, either because the body does not produce enough insulin, or because cells do not respond to the insulin that goes into bore. It is an autoimmune disease when β cells who secrete insulin, become the subject of a specific attack on its own immune system. Like autoimmune disease is characterized by different long time in patients but at the same time and "quiet" period that does not meet the usual symptoms of the disease.

The goal of this work is: assessing of the extent of the population affected by diabetes mellitus; tracing the presence of diabetes mellitus in the general population;

tracing the clinical course; indicating the diagnostic procedures for diabetes mellitus; complications in diabetes mellitus; role of laboratory technician and monitoring laboratory analysis; how much this disease is hereditary in the population.

Results: Study includes 6000 patients in east part of R. Macedonia, in period of 2005 to 2012. 314 of them are patients with diabetes mellitus and this number has been gradually increasing over the years. As a result of the above analyzes and investigations are coming to the opinion that diabetes mellitus is more and more frequent in general population in Macedonia. **Conclusion:** In diabetes mellitus secondary occur autoantibodies in a few fractions: glutamic acid decarboxlylase, (GAD), islet cell autoantigen, (ICA), islet cell citoplasmatic autoantigen, (ICCA), islet cell surface autoantigen, (ICSA), insulin autoantibody, (IAA) and tyrosine phosphate (IA-1 I IA-2). Diagnosis of antibodies in serum is sufficient indicator of so-called “prediabetes”. For these reasons the determination of antibodies is particularly useful in the early diagnosis of disease Application of molecular-biological techniques (PCR, Real Time PCR, sequencing and hybridization of DNA) that is proving the gene polymorphism (in HLA) are necessary for early diagnosis on diabetes mellitus (especially tip 1) and genetic predisposition of the patient.

ПРОУЧВАНЕ НА РИСКОВИТЕ ФАКТОРИ ЗА РАЗВИТИЕ НА ЗАХАРЕН ДИАБЕТ СРЕД НАСЕЛЕНИЕТО ОТ ОБЩИНА КЪРДЖАЛИ НА ВЪЗРАСТ 25-64 ГОДИНИ

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Увод: Захарният диабет е признат за един от най-значимите здравни проблеми в световен мащаб. Той се дължи на комбинация от генетични фактори и основно на поведенчески фактори на риска, свързани с начина на живот - нездравословно хранене, намалена физическа активност, наднормено телесно тегло и затлъстяване.

Целта на настоящото проучване е да проучи рисковите фактори за развитие на захарен диабет сред лица на възраст от 25 до 64 години от община Кърджали.

Методи: Извадката за изследването е случайна, двустепенна, представителна за населението на възраст 25-64 години. Изследвани са 1600 лица чрез анкетен метод. Използван е унифициран въпросник по програма СИНДИ на СЗО за интегрирана профилактика на хроничните неинфекциозни болести, съдържащ данни за генетична обремененост и основните поведенчески рискови фактори за развитие на заболяването. На всички лица е извършено антропометрично изследване.

За статистическа обработка е използван SPSS, версия 17.0. За сравнение на изследваните по възраст е използван непараметричния критерий на Ман-Уитни (Mann-Whitney Test). За сравнение на постоянни променливи между групите в норма и със захарен диабет е използван Хи-квадрат тест (Chi-square test).

Резултати: Резултатите от проведеното проучване показват, че 6,3% (100 лица) от изследваните са с повишена кръвна захар (диабет) и 93,7% (1500 лица) са в норма.

Средната възраст на лицата с отклонения в кръвната захар е 53,5±7,8 години, а на втората група – 43,9±11,1 години. Тестът показва, че двете групи се различават статистически значимо по отношение на възрастта (P<0,001).

Установява се зависимост между диабет и наличието на други заболявания. Точният критерий на Фишер показва, че има статистически значима зависимост между диабета и хипертонията (P<0,001). В групата на диабетиците 63,0% са хипертоници, докато в другата група този процент е 26,2%.

Взаимното честотно разпределение на лицата с диабет и холестерол показва, че тази група съставлява 42,0%, докато за другата група този процент е 10,6%. Отново се установява статистически значима зависимост между диабета и холестерола (P<0,001).

В групата на диабетиците 3,0% са с инфаркт, докато в другата група този процент е 0,7% (P=0,043). С диабет и стенокардия са 6,0% срещу 1,9% (P=0,019), а със сърдечна недостатъчност 9,0% срещу 2,0% (P<0,0001).

Изследването на зависимостта между фамилната обремененост със захарен диабет и развитие на заболяването доказва, че съществува статистически значима връзка. 14% от лицата с диабет са посочили, че първостепенен родственик (майка) страда от това заболяване срещу 4,2% от другата група (P<0,0001). При 3,0% от изследваните родител (баща) е с диабет срещу 0,7% от втората група (P=0,043).

Анализът на данните за физическата активност на двете групи показва статистически значима зависимост между диабета и честотата на физическите упражнения (P=0,036). Ежедневно правят упражнения 5,0% от първата и 5,7% от втората група; седмично – съответно 2,0% и 4,3%; няколко пъти годишно или по-рядко – 75,0% и 68,3%; не могат поради болест/инвалидност – 7,0% и 2,3%.

При групата с диабет се установява значимо по-висок ИТМ спрямо лицата с нормално ниво на кръвната захар. Процентът на лицата с диабет и наднормена телесна маса и затлъстяване (ИТМ≥25 кг/м^2) е 87,0% срещу 61,5% от втората група. Установява се статистически значима зависимост (P<0,0001).

Изводи: Проучването доказа връзката между генетичните и поведенческите фактори на риска на живот. С висока статистическа достоверност на резултатите е установената наднормена кръвна захар при лица с хипертония, след инсулт, инфаркт, наднормени холестерол и телесна маса. Това налага необходимостта от планиране и разработване на ефективни програми за подобряване начина на живот с цел превенция и контрол на заболяването.

Congress topic: Diabetes

ALTERNATIVES TO PLASTIC RECONSTRUCTION OF POST-TRAUMATIC HEEL DEFECTS

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Introduction. Soft tissue heel defects are special requirements for recovery. The skin of the heel has specific mechanics, which ensures axial loading with no lateral mobility. That stems from the important role, which this specific region plays in the phase of walking and in taking the body weight.

Methods. Nowadays there are different options for reconstruction. Recently the most popular has proved to be the regional fasciocutaneous flaps and the adiposefascial grafts, which are distal vascular based. We present a management of post-traumatic heel defects through a study that includes 16 patients (between 48-65 years old), whose problems are based on vascular insufficiency and decubitus lesions after bedsores.

Results. According to the characteristics of each heel defect we have applied different alternative methods: in 11 patients – distal based sural island flap; in 5 patients – distal based adiposefascial flap. We represent clinical cases.

Conclusion. All of the flaps have lived. The patients were satisfied with the proposed reconstructions. We have discussed some advantages and disadvantages of the applied flaps.

DIAGNOSIS AND MENAGEMENT OF DIABETES MELLITUS TYPE II

in PZU Pro-Medica, Kochani R. Macedonia

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Background:Diabetes mellitus type II is a metabolic disorder that is characterized by high blood glucose in the context of insulin resistance and relative insulin deficiency. Type II diabetes is initially managed by increasing exercise and dietary modification. If blood glucose levels are not adequately lowered by these measures, medications such as Metformin or insulin may be needed. Long-term complications from high blood sugar can include heart disease, strokes, diabetic retinopathy where eyesight is affected, kidney failure which may require dialysis, and poor circulation of limbs leading to amputations.

Methods: Retrospective analyzing method. Medical history of the patients in PZU Pro-Medica Kochani R. Macedonia. Analysis of clinical symptoms, physical and biochemical examinations. Charts separated by patients sex, rural or urban living place and patients age.

Results: The number of analyzed patients is 1554, female 506 and male 1048. In period from 2002 to 2012, 18 patients, 7 male and 11 female were having symptoms of Diabetes mellitus polyuria (frequent urination), polydipsia (increased thirst), polyphagia (increased hunger) and weight lose also a hypertension. These patients were in age of 24 to 75 years. The analysis were positive, fasting plasma glucose ≥ 7.0 mmol/l and with a glucose tolerance test, two hours after the oral dose a plasma glucose ≥ 11.1

mmol/l the urine analysis were negative for acetone and sugar. The prevalence of D.M. type II in Pzo Pro-Medica for 10 years period (2002- 2012) is 1,15%, female 2,17% and male 0,66%. After diagnosed D.M. type II the initial therapy was with Metformin and changes in Lifestyle. 15 patients were responding positive of the therapy with fasting plasma glucose 6-6,8 mmol/L, glucose tolerance test 8-8,5 mmol/L and glycated hemoglobin (HbA1c)<6%. Also after using antihypertensive therapy the blood pressure was under 130/80mmHg. Only in 3 patients, 2 female and 1 male were not responding of the therapy. In those patients to oral anti-diabetic medications was added insulin therapy.

Conclusion: We conclude that in our office, the prevalence of type II is greater in female population. There is not a big difference whether the patients come from rural or urban environment and any genetic factor is not identified. We maintained glycemia at normal levels with treatment prescribed by internists-diabetologists, usually using of Metformin tablets per-os. The only risk factor in our treated patients is hypertension, which we resolves with use of anti-hypertension drugs.

In any case, it's very important that we have a mutual trust between the patient and family doctor, which refers to the fact that patients accept hygiene-dietetic dietary regimen, and increased practicing of physical activity and exercises, also. We perform health control every 3 months, together with internist-diabetologists.

САХАРНЫЙ ДИАБЕТ В УКРАИНЕ: СОВРЕМЕННЫЕ МЕДИКО-СОЦИАЛЬНЫЕ АСПЕКТЫ

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Актуальность проблемы. Проблема сахарного диабета является одной из чрезвычайно актуальных в медико-социальном аспекте, учитывая потребность в постоянном медицинском наблюдении за больными и весомый вклад заболевания в структуру инвалидности и смертности населения.

Методы исследования. Использованы библиографический, статистический и аналитический методы.

Результаты. Численность больных сахарным диабетом в мире превышает 360 млн человек. Преобладающая доля больных приходится на развитые страны, медико-демографическая ситуация в которых характеризуется постарением населения, демографическими перекосами, эпидемией ожирения. Исследования экспертов свидетельствуют о вероятности стремительного роста заболеваемости диабета в ближайшие десятилетия, с распространением болезни не только в экономически развитых странах, но и странах с низким и средним уровнями дохода. Распространенность диабетав Европе составляет 2,7%, однако характеризуется значительными колебаниями от 0,1% в Албании, Греции; 0,3% в Таджикистане и Туркменистане до 6,5% - Португалии, 7,7% - Чехии. В странах ЕС сахарным диабетом болеют 4,1% населения, странах СНГ -1,7%.

Сахарный диабет занимает четвертое место в списке самых опасных хронических неинфекционных заболеваний, ежегодно этим заболеванием заболевают 7 млн человек, умирают около 4 млн человек. Если в следующее десятилетие не будут приняты неотложные меры, то количество смертей от диабета возрастет более чем на 50%. Половина случаев смерти от диабета формируется за счет людей в возрасте до 70 лет, свыше 55% умерших от диабета, составляют женщины. Доказано, что болезнь все чаще диагностируется в молодом возрасте, является веской причиной слепоты у лиц трудоспособного возраста, развития почечной недостаточности, ангиопатий.

Актуальна проблема сахарного диабета и в Украине. В 2011 г. ним болело 1,3млн человек, или 2773,1 на 100 тыс. населения. Диабет обуславливает почти 3% первичной инвалидности взрослого населения страны. В течение двух последних десятилетий его распространенность среди населения увеличилась в 1,7 раза, в том числе за 10 последних лет - почти на треть.

Стремительно растет и первичная заболеваемость сахарным диабетом, о чем свидетельствует ежегодная регистрация более 110 тыс. новых случаев заболевания. В целях обеспечения эффективной профилактики, своевременной диагностики, качественного лечения, реабилитации и улучшения качества жизни больных диабетом в Украине осуществляются комплексные профилактические, лечебно-диагностические и медико-организационные мероприятия в рамках Комплексной программы «Сахарный диабет». Программа направлена на обеспечение раннего выявления больных, стопроцентное диспансерное наблюдение, эффективное лечение, уменьшение частоты осложнений, связанных с диабетом. Большое внимание также уделяется созданию сети школ медико-социальной адаптации больных диабетом. Международный опыт показывает, что если вовремя предотвращать осложнения сахарного диабета и подходить к лечению комплексно, можно сократить уровень инсультов у больных на 85%, ампутаций - на 60%.

Выводы. Проблема сахарного диабета является одной из чрезвычайно актуальных в медико-социальном аспекте, учитывая потребность в постоянном медицинском наблюдении за больными и весомый вклад заболевания в структуру инвалидности и смертности населения.

Поэтому приоритетное внимание должно уделяться мерам комплексной профилактики сахарного диабета, эффективность которых доказана реализацией целевых профилактических программ и проектов во многих странах.

FIRST REPORT OF 'WHITE COAT ADHERENCE' AS A RISK FACTOR FOR HYPOGLYCAEMIA

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Background: 'White coat adherence' is a new term describing a change in behaviour of people with diabetes, while expecting an interaction with diabetes care professionals. This is in particular observed just before the patient's visit to the clinic. In a recent publication it has been concluded, that highly motivated families of children

with diabetes were for ex. performing blood glucose measurements with increased frequency just a few days before the child's visit to the clinic. As we have observed hypoglycaemic episodes occurring to the patients just at the time of their routine clinical care visits, we decided to look at this phenomenon more closely. The aim of this retrospective study was to see, whether 'white coat adherence' had any influence on the incidence of hypoglycaemia in diabetic patients at the time of their visit to the clinic.

Methods: In this retrospective study, we looked at patient charts of all 677 patients with type 1 and type 2 diabetes, who visited the diabetes in the period of 5 months (from Nov 2, 2012 to March 29, 2013). We checked the blood glucose results at the time of the visit to the clinic. If their blood glucose was equal to or lower than 3,9 mmol/l, with or without symptoms described in the chart, they were considered as having a hypoglycaemic episode. Those identified as having a hypoglycaemic episode were interviewed on the phone by one of the staff members in order to discuss the potential reason for this episode, if data on the reason for hypoglycaemia were not available in the chart.

Results: Patient characteristics were: 95 patients with type 1 diabetes – 63 females, aged (mean, SD) 37.3 y. (13,7); 32 men, aged 40,4 y. (15,2). 582 patients with type 2 diabetes – 252 females, aged 63.5 y. (11,3). 330 men, aged 70.1 y. (10,4). among them, there were11 patients (1.6%) identified with a hypoglycaemic episode at the time of their visit: 5 with type 1 diabetes (4 females), 4 on continuous subcutaneous insulin infusion, 1 on multiple daily injections (MDI) and 6 with type 2 diabetes (2 females), 1 on MDI, 5 on oral anti-diabetics. Among patients with type 1 diabetes, the respective reasons (patient-reported or chart) for the hypoglycaemic episode were: a wish to get pregnant, hence taking corrective insulin more often; deciding to go to the clinic on foot instead of by car; having a long walk in cold weather before the visit to the clinic; having eaten more and taking extra unsulin, not to be high at the visit; no particular reason. Among patients with type 2 diabetes, the reasons for the hypoglycaemic episode (patient-reported or chart) were: having eaten less than usually before the centre visit (3 persons), was more active that day (1), no particular reason (2).

Conclusion: There is a relatively small proportion of patients who experienced hypoglycaemia just at the time of their visit to the clinic. However, clinician should be attentive to this phenomenon, as any additional hypoglycaemic episode that may happen due to 'white coat adherence' is redundant. Reasons for hypoglycaemia in our study were multiple and we may only speculate that some were related to 'white coat adherence', not necessarily reported as such. Therefore, patient-clinician relation should be revisited in order to identify barriers, triggering this dysfunctional behaviour change.

CONCENTRATION OF APOLIPOPROTEIN-B_{100} (Apo-B_{100}) AND LIPOPROTEIN (a) [Lp (a)] IN PATIENTS WITH DIABETES MELLITUS (DM)

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Patients who suffer from diabetes have 3 to 4 times higher risk of developing coronary disease compared with healthy people. One of the main risk factors of patients with DM atherosclerosis are abnormalities of apolipoproteins particularly ApoB_{100} and Lp (a). According to the undertaken researches patients who suffer from Diabetes Mellitus (DM) has been proven that there is a high correlation between high concentration of the ApolipoproteinB_{100}, Lipoprotein(a), diabetic nephropathy, micro and macroalbuminuria as well as diabetic retinopathy (1) . One of the most common complications of diabetes are: macro and micro vascular changes. There is verified evidence that patients with insulin-dependent DM or those treated with oral therapy are potential sufferers with the highest risk of coronary diseases, cerebral strokes compared to the healthy population or followed by any other disease etiology. In the plasma of patients with DM are detected (except high concentrations of: glycemia, Apo-B_{100}, Lp (a), LDL-ch, triglycerides and C-reactive protein (PCR) and low HDL-ch concentration and Apoli-poprotein-A_1 (Apo-A_1), which also shows the presence of insidious inflammation in patients with DM, which accelerates the appearance of complications of coronary atherosclerosis, cerebral or peripheral arteries (2).

Key words: Apolipoprotein-B_{100} (Apo-B_{100}), Lipoprotein (a), Diabetes Mellitus (DM, atherosclerosis (Ath), blood glucose (Gl), the glicolised Hemoglobin (HbA1c), lipids profile (LT, TCh, TG, HDL-ch and LDL-ch-ch).

ONCOLOGY

HYPERTHERMIC ISOLATED LIMB PERFUSION (HILP) FOR MELANOMA

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The incidence of cutaneous melanoma (CM) in the white population increased faster than that of any other cancer in recent decades (3-7% annual increase) and it varies at different geographical latitudes. In Central Europe the incidence is 10-14 per 100,000. About 20% of all relapses of CM are in the form of in transit/satellite metastases. In transit metastases are multifocal cutaneous or subcutaneous metastases that spread through lymphatic system between the site of the primary melanoma and the regional lymph node basin. Since about 50% of all melanomas are located on extremities, we can expect about 5-8% of in transit metastases on extremities. Overall 10-years survival of patients with in-transit metastases is 20–40%. According to most national guidelines the treatment of choice for patients with more than 3-5 in transit metastases located on limbs is hyperthermic isolated limb perfusion (HILP). The procedure was first performed back in 1958 by Creech but is technically very demanding and performed only in selected highly specialized centers in USA, Europe and Australia. It is performed in endotracheal general anesthesia with systemic heparinization. Surgical isolation and cannulation of the major artery and vein (iliac/femoral; axillary/brachial) is performed and the limb is connected to the extracorporeal circulation consisting of a roller pump, oxygenator, veneous reservoir and heat exchanger to warm the perfusate. Hyperthermia is used because of a direct tumoricidal effect and because it augments drug cytotoxicity by increasing blood flow, membrane permeability, local metabolism and drug uptake. The most effective cytotoxic drug in HILP is Melphalan (L-phenylalanin mustard) because of its short half-life, limited cell cycle specificity and low vascular endothelium and soft tissue toxicity. The usual dose is 10 ml/l for lower extremity and 13 ml/l for upper extremity. The concentration of Melphalan achieved with such a dose in isolated limb is 4-10 times higher than the maximally tolerated systemic concentration. In patients with a bulky disease (>10 metastases and/or metastases>3 cm) a higher percentage of complete responses can be achieved if Melphalan is combined with a tumor necrosis factor (TNF-α). TNF-α has a selective (tumor- associated vessels) vasculotoxic effect which causes hemorrhagic necrosis and in addition 4–6-fold increases uptake of the cytostatic drugs. However, because of systemic toxicity of TNF-α (sepsis like hypotension) a continuous systemic isotopic leakage monitoring during the procedure is mandatory. Overall response rate to HILP is 65-90% (complete response in 50 - 70% and partial response in 15 - 40% of patients).

Institute of Oncology in Ljubljana started with HILP in 2008 and is since May 2010 one of only 40 centers accreditated for the usage of TNF-α in the world. Our experience with first 50 procedures performed will be presented during the congress.

TREATMENT OF HER2-POSITIVE EARLY BC: FROM CLINICAL STUDIES TO DIALY PRACTICE

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Background: Breast cancer (BC) is in the developed world as well as in Slovenia the most common cancer in women. With the evolution of the tumor gene signature the longterm clinical obseravtion that BC is a spectrum of different diseases in terms of prognosis and response to treatment was confirmed. Using this tool as well as classical clinico-pathological paramethers four types of BCs can be differentiated and HER2-positive type is one, representing about 15% of them. It is a distinctive entity, charactherised by overexpression of HER2 receptor and/or HER2 gene amplifiaction with an agressive behaviour. With the introduction of antiHER2 treatment its prognosis has significantly improved. Trastuzumab was the first antiHER2 drug approved for the treatment of patients with metastatic HER2 positive BC at the beginning of this century. Good results in the metastatic setting led to clinical studies with adjuvant treatment. The results of the latter were presented in 2005 and were the basis for the approval of one year adjuvant treatment of patients with HER2 positive BC. A significant improvement in disease free survival in the range of 40-50% was demonstrated and the risk of dying from BC was reduced by one third. This is the range of benefit seldom achieved in oncology. In the proceeding years new antiHER2 drugs became available. Lapatinib was the next approved drug and recently pertusumab and trastuzumab-emtansine.

Adjuvant treatment with trastuzumab became available in Slovenia in 2005 and here we present the outcome of this treatment in routine clinical praxis in our patients.

Methods: With the approval of adjuvant trastuzumab we introduced the Slovenian HER2 registry. The main objective of this project was to evaluate treatment results in our real life patient population with possible additional sub-analysis. Data were collected from patient's records.

Results: In the 5-year period (2005-2009) 313 patients with HER2 positive BC were treated with adjuvant trastuzumab at the Institute of Oncology Ljubljana. Median age of the pateints was 52 years (23 – 76). Median follow-up time was 4,4 years (maximum 6,9 years). The majority of tumors were invasive ductal carcinomas 297 (95%), 6 (2%) were invasive lobulare carcinomas and the rest were other histological types. Seveny percent of tumors were grade 3, 27% grade 2, 1% grade 1 and for 2% data about the tumor grade was not avalable. Fifty-six percent were estrogene receptor and 42% progesterone receptor positive. Only 79 (25%) of patients had axillary lymph node negative disease. Data regarding the adjuvant chemotherapy was available for 95% of patients, 127 (40%) received an anthracycline based and 165 (53%) anthracycline and taxane based chemotherapy. In the univariate model the size of primary tumor, involvement of axillary lymph nodes and tumor grade were found to have a significant impact on progression free survival. In the multivariate model only lymph node involvement retained its significant impact. For overall survival only lymph node involvement showed a significant impact (HR 1,36; 1,05-1,78). Progression free survival rates were 92,3%, 84,2% and 80,8% at 2, 3 and 4 years and overall survival rates 96,6%, 94,4%, and 92,5% at 2, 3 and 4 years respectively.

Conclusion: The prognosis of HER2 positive BC has improved significantly since the introduction of antiHER2 drugs. Our results based on the treatment of real-life BC patients are comparable to the results obtained in international clinical studies.
There are new promising antiHER2 drugs that will probably even improve these impressing results.

PALLIATIVE CARE: THE CHALLENGE TO MAKE ONCOLOGY COMPREHENSIVE

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The term “Palliative” derived from the Latin word “Pallium”, which means the “mask” or “mantle”. This explanation fits exactly the essence of palliative care – to mantle, mask or alleviate incurable conditions.

Palliative care is an approach that improves the quality of life of patients and their families facing the problems associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and different symptoms as well as other problems - physical, psychosocial and spiritual.

The last 3-4 decades of 20th Century attributed palliative care to the patients, in whom the aggressive treatment was not any more indicated, and only. Current approaches (WHO, 2002) deem that palliative care must be attributable to any chronic progressive intractable illness. These changes resulted from the realization of the fact, that problems arisen at the terminal stage can already be envisaged on the early stages of the disease.

Palliative Care focuses on two main tasks: relieving patient’s condition throughout the course of the disease (together with the radical treatment means) and providing multi-approach support in the last months, days and hours of life.

Correspondingly, Palliative care is particularly important for patients with cancer, as the burden of issues that cause suffering is particularly high in these patients. According the WHO data, two-thirds (seven million) of 10 million new patients with cancer each year are not cured and die within a year of their diagnosis; of those living with cancer, 60% will experience significant pain.

With the rapidly aging world population and the associated increase of multiple ‘‘non-communicable’’ diseases, the need for palliative care will increase dramatically over the next 50 years: The incidence of cancer will more than double to an estimated rate of 24 million new cases per year by 2050.

In 1990, the WHO pioneered a Public Health Strategies (PHS) to integrate palliative care into existing health care systems. This included advice and guidelines to governments on priorities and how to implement national cancer control programs where

palliative care would be one of the key components (pillars) of comprehensive cancer care.
In many Countries the planning of National Cancer Control Program was (is) conducted in accordance with the data given in the table presented above. Implementation of Palliative Care in this program implicates to make specialized oncological support comprehensive, covering all stages of cancer – throughout the "Curative" or "Life-prolonging" Treatment to advanced and end-of-life care.

ABOUT THE DIAGNOSTIC AND TREATMENT OF MALIGNANT GASTRIC ULCERS

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The work analyses the research of 548 patients who are suffering from gastric ulcers. The majority of studied patients were men 443 (80.8%). The age of the patients varied from 19 to 78. The ulcers appeared on the side of curvatura ventriculi minor with 472 patients (86,1%), as for the rest, it was placed on the paries posterior. These were 76 patients (13,9%). The first type of ulcers caused suffer of 278 patients, (50,8%), the second type - 227 patients (41,4%), and the III - 43 (7,8%).

427 patients (77, 9%) underwent the X-ray examination. From the given patients, the right diagnostics were provided to 392 people (91, 3%). Only endoscopy research was held with 121 patients (22, 1%), and together with the X-ray research, it counted 337 (61, 5%) people. Consequently, the endoscopy study was delivered to 458 (83,6%) patients. The gastric ulcers were diagnosed to 434 cases (94, 7%).

According to our data malignization diagnosis was made with 29 patients (5.3%), 21 (72.4%) were the men and 8 (27.6%) women. Their age fluctuated from 38 to 77. Ulcer anamnesis duration was from 2-31 years. Among the examined ones 19 people appeared to be diseased by the first type ulcers (by H.D. Johnson classification), as for 10 patients, they had the II type ulcers. In 21 cases disease was localized on the curvatura ventriculi major (72,4%).

According to the shape, there are malignized ulcers of 1 cm in diameter – 2 patients (6,9%), from 1 to 2 cm -5 patients (17,2%), from 2 cm to 3 cm - 8 patients (27,6%), and above 3 cm -14 (48,3%) patient.

X-ray examination was performed on all 29 patients, and 17 of them (58,6% - a) were diagnosed by malignized gastric ulcer or gastric ulcer diagnosed with cancer. 27 patients underwent gastroscopy with biopsy (two refused to research), from them 21 was diagnosed malignization - (77.8%).- 3 of those patients (11.1%) malignization were diagnosed morphologicaly only after second time gastroscopy and biopsy. In 6 cases (20.7%) the malignization signs could not be revealed by biopsy and gastroscopy.

Comprehensive research showed that the gastric ulcer malignization diagnosis were given to 23 (79,3%) before operation, and intra operation counted 4 (13.8%) patients. In 3 cases ulcer excision express technique was used, and in 1 case - macroscopically. 2 patients (6.9%) has not been determined the character of malignant

gastric ulcer and after the operation, the morphological study of the material revealed the right diagnosis.

25 patients (86,2%) underwent gastric subtotal resection (17 – Bilroth I method, 8 –Bilroth II method), 2 - gastrectomy, 1 - the economic gastric resection with vagotomy , 1 - truncal vagotomy, ulcer excision and pyloroplasty.

In 2 cases (when the diagnosis cannot be raised), 1 – economic resection, and after verification of diagnosis was made repeated operation – subtotal resection, as for the second case, was done a truncal vagotomy, ulcer resection and piloroplasty. Patients and his family members refused to repeat the operation.

Most often histological form of cancer was adenocarcinoma - 21 cases, *scirrhous* carcinoma - 6, low differentiate cancer - 2. 1 patient died after surgery (cardiovascular system failure).

Distant results of the study was able to deliver in 24 patients. Among them 19 are stationary investigated, 5 – data based on the clinical cards..

STUDY OF ENDOMETRIAL CANCER WITH OPTO-MAGNETIC SPECTROSCOPY

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Endometrial cancer is the most common gynecological malignancy in the World. Conventional methods for endometrial cancer detection such as hysteroscopy, endometrial biopsy and transvaginal ultrasound are used in everyday practice, but dilation and curettage (D&C) is considered to be the golden standard. However, the use of endometrial sampling methods is increasing lately since those methods do not necessary require anesthesia and can be performed in the office, in an outpatient setting. All methods stated above are time consuming and subjective.

In this work, we investigated samples of endometrial cells with Opto-magnetic spectroscopy. Opto-magnetic spectroscopy is based on light-matter interaction that depends on covalent bonds, ion-ion, ion-dipol or dipol-dipol interaction and takes into account a difference between diffuse light and reflected polarized light. Based on previous investigation of cervical cancer cells with Opto-magnetic spectroscopy, the goal was to apply the same method to detect endometrial cancer. The digital pictures of samples were taken under white light and under polarized white light, 20 times each, and afterwards digital images were processed with convolution algorithm which depicts Opto-magnetic method.

Results were compared to conventional techniques and confirmed with histopathology findings. Results indicate the possibility of Opto-magnetic spectroscopy to categorize samples in several groups, separating cancer from normal samples. This

non-invasive method provides less chance of error occurrence in screening process as well as less time needed for test results.

STEREOTACTIC AND IMAGE GUIDED TECHNIQUES IN TREATMENT OF CENTRAL NERVOUS SYSTEM TUMOURS

Uros Smrdel; Bozidar Casar

Background: Stereotactic techniques are increasingly used in treatment of localized lesions within and without central nervous system (CNS). There are numerous techniques (single shot and fractionated, frame-based and frame-less), that can be used. Our aim is to review those techniques, indications for their use and to evaluate our experience.

Introduction: From beginning of 1960s, stereotactic radiosurgery has been used for treatment CNS metastases and arterio-venous malformations. Since the introduction of thermoplastic masks to stereotactic frame and later frame-less systems, stereotactic radiotherapy and with it the treatment of wider range of tumours has become feasible. With the introduction of image guided techniques, one can dispose of body frame use for stereotactic body radiotherapy (SBRT), thus making procedure more patient friendly and also prone to less errors. As these changes has begun to be widely applied, we must be able, to assure proper quality assurance/control, be sure what we are delivering to our patients (dosimetry) and be able to properly select patients for treatment.

The selection of patients is beginning to be of utmost importance, as SRS/SRT is a powerful tool, but as we know, in most cases, SRS/SRT is palliative treatment and its principal aim is to improve quality of life. In many cases this can be achieved by simpler and for a patient less strenuous procedures. Some decision making aids are discussed and evaluated on our set of patients.

Patients and methods: Since the 2007 190 (appr) patients were treated at Institute of Oncology Ljubljana using SRS techniques, majority being CNS metastases of solid tumours and some acoustic neurinomas. We evaluated survival of those patients, and the effect of tumour type, performance status and number of metastases. We also retrospectively assigned to patients he RPA class and tumour specific Graded Prognostic Assessment. Univariate and multivariate analysis were then performed. We evaluated the effect of SRT as salvage therapy for recurrent gliomas and hypophyseal tumours and SRS as definitive treatment of accoustic neurinomas.

Results: The breast carcinoma patients fared the best, interestingly, the renal cell carcinoma patients fared the worst, with lung cancer and melanoma patients coming in between. But when adjusted for RPA class, the only independent prognostic factor was the patient RPA class, which was far stronger predictor than tumour specific prognostic class. SRT for recurrent gliomas is effective treatment for gliomas patients recurring more than a year after primary treatment. It confers effective palliation, though, it is vital, that irradiated volume remains as low as possible. We are observing normalisation of hormone levels and response in patients with hypophyseal tumours after SRT, while in cases of accoustic neurinomas, there were no progressions, and no significant deterioration of nerve function after SRS.

Conclusion: Stereotactic and image guided techniques are usefull tool in treatment of secondary and some primary CNS tumours. With proper QA/QC protocols they are safe alternative for palliative treatment of seconday tumours, for selected patients. For these patients, survival is same as for surgicaly treated patients, while the procedure is usually outpatient. For the primary CNS tumours, SRS/SRT is effective in treating accoustic neurinomas and hypophyseal tumours, and can be used as palliation for glioma patients.

EPIDEMIOLOGY OF CANCER DISEASES IN DIFFERENT EUROPEAN REGIONS AND THE IMPORTANCE OF RISK FACTORS

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Background: Cancer epidemiology studies the distribution of cancer in populations and its changes over time. It evaluates the associations between different exposures and disease to decide whether the observed relationships are likely to be causal. Its ultimate goal is to identify risk factors that may lead to introduction of effective preventive measures. Many modifiable cancer risk factors have been identified in the recent decades, but cancer continues to affect millions of individuals, their families and society in general, and it is a growing concern for health care systems, because of the human and material resources required to manage it. Inequalities in cancer incidence, mortality and survival, both between and within European countries, represent a major challenge for public health. Factors that contribute to regional differences in the types or burden of cancer include regional variations in the prevalence of major risk factors, availability and use of medical practices such as cancer screening, availability and quality of treatment, and age structure.

Data sources and methods: The published estimates of the incidence of and mortality from cancer overall and at specific cancer sites in Europe in 2012 are presented. The known risk factors that could explain the differences in cancer burden observed are reviewed. Cancer incidence and mortality estimates for 2012 are from the European Cancer Observatory (ECO) database. The regions of Europe follow the geographical definition of the United Nations (World Population Prospects, the 2010 revision). According to this definition, Europe is divided in 4 regions: Northern, Western, Eastern, and Southern. Basic incidence and mortality measures are used to present the cancer burden: absolute numbers, crude and age-standardised rates (per 100,000 population).

Results: There were over 3.4 million new cases of cancer (excluding non-melanoma skin cancer) in Europe in 2012, 53% (1.8 million) in males and 47% (1.6 million) in females. The most common cancer sites were breast (464,000 cases, 13.5% of all cancer cases), followed by colorectum (447,000, 13.0%), prostate (417,000, 12.1%) and lung (410,000, 11.9%). These four cancers represented half (50.5%) of the estimated overall cancer burden in Europe in 2012. The estimated total number of cancer deaths was 1.75 million, of which 56% (976,000) were in males and 44% (779,000) in females. Lung cancer was the most frequent cause of death (353,000 deaths, 20%), followed by colorectal cancer (215,000 deaths, 12.2%), breast cancer (131,000, 7.5%) and stomach cancer (107,000, 6.1%).

After adjusting for different age structure, overall incidence rates in both sexes were the highest in Northern and Western European countries, in males in France (550/100.000) and in females in Denmark (454/100.000). In both sexes, the lowest all-cancer incidence rates were in Southern and Eastern European countries, in Albania, Greece and Bosnia and Herzegovina (around 260 in males and 200 in females). Mortality was the highest among males in Eastern and Central Europe and females in Denmark, while it was the lowest in males from Northern Europe and females from Southern European countries.

Different pattern of cancer incidence and mortality in different parts of Europe reflects differences in distribution of cancer risk factors on one side and differences in availability of screening, timely diagnosis and quality of treatment. With respect to reducing mortality, advances in cancer treatment have not been as effective as those for other chronic diseases; effective screening methods are available for only a few cancers, so primary prevention through lifestyle and environmental interventions remains the main way to reduce the burden of cancer. Among potentially modifiable cancer risk factors, the most important are tobacco smoke, alcohol consumption, diet (deficit in intake of fruit and vegetables), overweight and obesity, physical inactivity, reproductive factors and exogenous hormones, solar and ionising radiation, infections and occupational exposures.

Conclusions: The proportion of new cases or deaths from cancer due to risk factors mentioned varies among populations because of different prevalence of the risk factors and the method of estimation. In 2005, it has been estimated that 35% of cancer deaths worldwide were attributable to potentially modifiable risk factors. The recent study for the UK concluded that the exposure to less than optimum of potentially modifiable risk factors was responsible for 42.7% of cancers in UK in 2010 (45.3% in males and 40.1% in females).

There have been no detailed estimations on the proportion of avoidable cancer for different parts of Europe, but high incidence and mortality from smoking related cancers especially in Central and Eastern Europe and unfavourable distribution of other risk factors in this region support the importance of primary prevention that offers the greatest public health potential and the most cost-effective, long-term method of cancer control. It includes application of effective tobacco control measures, reduction of excessive alcohol consumption, maintenance of healthy body weight and physically active lifestyles, dietary intervention, avoidance of excess sun exposure, reduction in occupational exposure to carcinogens and immunization against or treatment of infectious agents that cause certain cancers. Recommendations on cancer prevention for general population are summarised in the European code against cancer; its last version from the year 2003 is currently under revision.

EARLY DIAGNOSIS-PRIMARY MALIGN TUMOR OF SMALL INTESTINE-CASE REPORT

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Carcinoma of small intestine are rare tumors and make up about 1 to 2% of all primary malign tumors of gastrointestinal system, and therefore it is hard to collect data from the hystory of disease for the purposes of analysis. These clinical sympthoms are characteristic also for other benign diseases of digestive system so they do not raise suspicion and alarm for carcinoma of small intestine. There is no set of clinical sympthoms which are characteristic for certain type of tumor. Carcinoma of small intestine have bad prognosis due to often late diagnosis, because uncharacteristic clinical sympthoms of carcinoma of small intestine can make the early diagnosis very hard to perform, postpone surgical treatment, and make the postoperational prognosis of the patient worse.

Due to late setting of diagnosis the patients are surgically treated in the late stadium of disease, and about 25% of patients are subjected to surgery with picture of acute abdomen (perforation, bleeding, obstruction).

The aim of this study was to show that clinical suspicion for existence of malign neoplasm of small intestine, adequate diagnostic treatment, and setting early diagnosis contributes to fast and accurate choice of therapy, i.e. adequate surgical resection, as method of choice in treatment of this disease.

In this study, using retrospective hystory disease and opeartion protocole, we showed a patient (a woman), 62 years old, with primary malign tumor of small intestine (PH leiomyosarcoma intestini tenui), surgically treated. In the case of this patient, by using the complete diagnostical procedures as well as analysis of clinical parameters, early diagnosis of malign tumor of small intestine was established. After that the adequate surgical treatment was done (operational treatment), as the only correct way of treating and the basic factor connected with survival.

The most important prognostic factor for survival is radical resection of tumor proximal and distal from tumor with regional lymphadenectomy, and in the case of unresectal lesions by-pass procedures and paliative radiation therapy. Inadequate resection contributes to more frequent occurence of recurrent disease and demands radiation therapy and chemotherapy.

THE USE OF TRANSVAGINAL ULTRASOUND POWER DOPPLER IN DIFFERENTIATION OF BENIGN OF MALIGNANT ENDOMETRIAL CHANGES IN WOMEN WITH POST MENOPAUSAL BLEEDING AND ENDOMETRIUM THICKNESS ABOVE 4 MM IN MACEDONIA

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Objective: To evaluate the use of transvaginal ultrasound power Doppler in differentiation of benign of malignant endometrial changes in women with post menopausal bleeding and endometrium thickness above 4 mm

Material and Methods: 42 post menopausal women having metrorrhagia and endometrial thickness above 4 mm, undergone transvaginal ultrasound power Doppler velocimetry and dilatation and curretage as a gold standard in diagnosing hystopathological forms of endometrial changes. Pulsatility Index (PI), Resistant Index (RI), Peak Systolic Velocity (PSV), Multi-vascular, Single vascular and Dispersed pattern of endometrial blood vessels were evaluated.

Results: From the 42 evaluated women, 28,6% had endometrial carcinoma, 47,6% endometrial polyp, 16,6% endometrial hyperplasia, and 7,2% normal endometrium. The Doppler velocimetry showed a significantly lower PI and RI in endometrial vessels and uterine arteries were obtained in endometrial cancer cases than in patients with normal endometrium. But in comparison among different pathologies the Doppler indices were not significantly different. The power Doppler patterns among different pathologies had very high Specificity and Positive Predictive Value, and slightly lower Sensitivity and Negative Predictive Value.

Conclusion: Transvaginal ultrasonography using power Doppler velocimetry and different vessel patterns is a valuable diagnostic method in in differentiation of benign of malignant endometrial changes in women with early endometrial pathologies.

ANDTIDEPRESSIVES AND ANXIOLYTICS AS AN ADDITIONAL THERAPY TO THE TREATMENT OF CANCEROUS PAIN

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Background: Pain is the most frequent cause of the cancerous patient's suffering. Cancer and pain cause fear, depression and anxiety of both the patient and his/her close family. According to the definition of the International Association for studies of pain, it is "an unpleasant sensory and emotional experience connected with actual or potential tissue damage". The aim of this work is to show that antidepressives and anxiolytics have a significant position in the therapy of cancerous pain which is insufficiently used in practice.

Methods: Thirty patients (18 females, 12 males) aged from 35 to 75, who are sick with neoplasma (with different localization and etiopatogenesis) were observed by retrospective analysis in the period of time from 2010. to 2012. All of them were treated

by the psychiatrist in the medical Health Center “Gadzin Han” for having pain and anxious depressive symptomatology in the range of adaption disorder (F43.2).

Results: According to patophysiological mechanisms there are three categories of cancerous pains: somatic, visceral and neuropathic. The intensity of pain increases as the malign decease progresses, partly due to the growth of tumor itself and partly because of the patient’s weaker ability to tolerate pain. In that case it is necessary to predict which remedy would be useful with that “unbearable” pain. Pharmcotherapy can successfully solve the two thirds of pain syndromes with cancerous patients. Modulation of pain signals can be developed on spinal or supraspinal level and in that process the main role is played by different neurotansmitters (dopamine, serotonin). These achievements are used in the therapy. Serotonin activities are increased by antidepressive inhibition of repeated taking serotonin and in that way the activity of descendant inhibitory system for modulation of pain is also increased. Thus the antidepressives can effectively remove neuropathic pain. Anxiolytics don’t have specific analgetic function. In this case, these remedies should be avoided , but they can be used only if the patient’s obvious anxiety can’t be removed in some other way.

Conclusion: The therapy of pain of the patients with advanced malign deceases should provide them the possibilities to do basic life functions and relatively painless dying. Cancerous pain should be completely analysed and pharmacotherapy should be the basic manner of cancerous pain treatment.

THE USE OF TRANSVAGINAL COLOR BLOOD FLOW IMAGING IN PREDICTING CERVICAL MALIGNANCY

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Objectives: To evaluate the usage of transvaginal color Doppler velocimetry in predicting cervical malignancy.

Material and methods: 43 patients were examined, 18 with invasive carcinoma, used as a study group, and 25 patients with proven normal findings used as a control group, by transvaginal color Doppler ultrasound, measuring the resistance index (RI) of tumor blood flow.

Results: The study group showed significantly lower RI 0.48 (0.45-0.52), compared to the controls 0.65 (0.63-0.68) $p<0.0001$. 0.58 RI cut off value or less showed sensitivity of 79% specificity of 94%, a positive predictive value of 94% and negative predictive value of 79%

Conclusion: The use of transvaginal color Doppler velocimetry using the measurements of RI of the cervical tumor blood flow can help in early diagnosis and management of cervical malignancies but their usage as a screening diagnostic program is bounded.

HOW OFTEN ARE PATINETS WITH COLORECTAL CANCER MANAGED ACCORDING TO ENHANCED RECOVERY AFTER SURGERY PROTOCOL?

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Enhanced recovery after surgery (ERAS) protocol is a perioperative patient management model where management process optimizations help shortening patients' recovery time. Application of ERAS protocol in colorectal cancer surgery is a demanding process, challenging our professional and especially organizational perspectives.

A questionnaire regarding acceptance and using of ERAS was sent to all thirteen heads of surgical departments where colorectal cancer patients are operated in Slovenia. Heads were asking to describe usage of ERAS protocol in colorectal patients in 2012. The questionnaire was analyzed using Microsoft Excel.

All departments return the questionnaire. Among all heads of departments there is a strong agreement that ERAS is a relevant clinical concept, which must be used in colorectal cancer patients. Only seven clinical departments have developed a clinical pathway consistent with ERAS protocol, but principles of ERAS are followed at least partly or completely in twelve clinical departments. Obvious is lack of activity before the operation, particularly missing is the educational interview with dietitian and physiotherapist, which is implemented in only one department. Less than half of the patients drink the glucose-drink before the operation, and the prophylaxis of nausea and vomiting is not predominating either. More than two thirds of patients still suffer the mechanical preparation of bowel before the surgery. More than half of them have a central line and are admitted to intensive care unit (ICU) after the operation. In half of departments thoracic epidural for postoperative pain relief and for blockade of sympathetic stress response is used systematically. For normothermia during the operation are mostly used heating pads. In one third of departments there is no intraoperative prevention for postoperative nausea and vomiting. More than half of patients have drainage tubes in place for more then 48 hours. More than 75 % of the patients do not sit up in bed or stand up on the day of the surgery. More than half still have the nasogastric tube on first postoperative day and early verticalization is implemented only in two departments. Patients discharge plan is on seventh day for colon cancer and eighth day for rectal cancer.

We analyzed implementation ERAS concepts in all surgical departments in Slovenia in 2004. If we compare this analysis with the one done in 2004 we can conclude that there is an important shortening of average planned hospital stay. Acceptance of ERAS principles are more on theoretical basis than practical one. Despite understanding ERAS, there is no shift or changes in organizational issues. Nevertheless the majority of patients are still not managed following the ERAS protocol. The implementation of ERAS concept in Slovenia is rather poor, not as we would expect considering evidence based positive effect, but comparative to other's experience.

POSTTRAUMATIC FAT NECROSIS OF THE BREAST - DIFFERENTIAL DIAGNOSIS WITH BREAST CARCINOMA

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Aim: The purpose of this study was to quantitate and describe the clinical, cytomorphological, mammographic and sonographic features in order to evaluate the evolution of posttraumatic fat necrosis in the breast.

Materials and methods: This study is based on a retrospective review of patient records at our breast unit from January 2011 to January 2013. During that period, we identified 28 fat necrosis lesions in 25 patients. The histologic diagnoses were made following surgical excision in the Department Of Thoracic Surgery at the Military Medical Academy in Sofia, Bulgaria.

Results: Clinical findings: Of all patients, 23 presented with at least one palpable mass. In two of the patients there were no palpable masses. In four patients, the palpable mass strongly suggested malignancy. The predominant mammographic features of the 28 lesions (25 cases) apparent in mammograms revealed radiolucent oil cyst (*8 cases*), round opacity (*5 cases*), asymmetrical opacity or heterogenicity of the subcutaneous tissues (*5 cases*), dystrophic calcifications (*6 cases*), clustered pleomorphic microcalcifications (2cases), and suspicious speculated mass-differential diagnosis with carcinoma(2 cases). Sonography was performed by using a 7.5 mHz transducer in 10 cases. Sonograms were solid, anechoic with posterior acoustic enhancement. In 15 cases FNAB was performed, the results from which were consistent with fat necrosis, benign or inflammatory breast features. None of the postoperative histological findings were malignant.

Conclusion: Postraumatic fat necrosis of the breast is a process which results from aseptic saponification of fat by means of blood and tissue lipases. The condition is important because it is often mistaken for carcinoma, both clinically and radiologically.

TRIAGE OF WOMEN WITH ATYPICAL SQUAMOUS CELLS OF UNDETERMINED SIGNIFICANCE (ASC-US) WITH COLPOSCOPY AND HUMAN PAPILLOMAVIRUS (HPV) POLYMERASE CHAIN REACTION (PCR) TEST

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Objective: Up to 15% of women with ASC-US have underlying high-grade cervical intraepithelial neoplasia 2 (CIN2) or CIN3. Although the Papanicolaou test has reduced the incidence of cervical cancer significantly, the test still has some limitations with respect to sensitivity and specificity. False negative rates for cervical premalignant lesions and cervical cancer between 15% and 50% and false positive rates of about 30% have been reported. There are several proposed concepts of triage for these women: to refer women with ASC-US to colposcopy, namely, repeat cytology, immediate referral to colposcopy, and reflex testing of HPV.

Methods: Retrospectively we have reviewed the medical histories of 104 patients that were refered for further investigation (colposcopy and HPV-PCR testing)

and cervical biopsies and endocervical curettage in the last two years for cytological findinng of ASC-US.

Results: Of these, 81 (77,8%) did not have cervical intraepithelial neoplasia (CIN), 14 (13,5%) had CIN1, 9 (8,6%) had CIN2 or CIN3 (CIN2+). High risk (HR) HPV was detected in 41 (39,4%) patients. All of the patients with histologically confirmed CIN were positive on one or more high risk HPV types.

Conclusion: The concept for triage of ASC-US cytoligal findings that first a HPV test should be done and after that a referal to colposcopy and further necessary examinations for the HR HPV positive are performed, has been proven well in practice. Colposcopy is usually useful in patients with ASC-US less than 30 years of age for distinguishing an obvious lesion in a patient and a patient who needs only further follow-up.

USE OF GRANULOCYTE-COLONY STIMULATING FACTOR (G-CSF) IN HEMATOONCOLOGY: WHAT SHOULD A GENERAL PRACTITIONER KNOW

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Neutropenia is a well known risk factor for infections in patients receiving myelosupressive chemotherapy. Despite the advances in the treatment of neutropenic patients, infections are still the most common chemotherapy adverse events.Since late ninetees, based on the recognition that granulocyte colony stimulating factor (G-CSF) stimulates neutrophil production, its recombinant forms (filgrastim, lenograstim and recently pegfilgrastim) are used to support the delivery of chemotherapy.

Here, we summarise the two decade clinical experience with G-CSF, particularly addressing the issue of its rational use.

Randomised clinical trials and meta-analyses investigating administration of G-CSF have shown that primary prophylaxis with filgrastim shortens the time to neutrophil recovery and significantly reduces the incidence of febrile neutropenia in many tumor types. Pegfilgrastim, a pegilated form of filgrastim, which is administered once per chemotherqapy cycle is comparable to filgrsastim in its efficacy. Unfortunatelly, no benficial effect of filgrastim on infection-related mortality was seen, as well as complete remission rate and overall survival. Despite these important uncertainities, the most recent guidelines from three international cancer organisations (EORTC, ASCO and NCCN) indicate the use of G-CSF in certain subgroups of neutropenic patients as those with profound and prolonged neutropenia with documented infections and comorbidities.

In conclusion, G-CSF has enabled development of more aggressive chemotherapy regimens and treatment of a greater number of patients. In the future, because the patient population with neutropenia is very heterogeneous, models of infection risk assessment for neutropenic patients should be developed to identify the patients who will benefit mostly from the treatment with G-CSF. Pharmacoeconomic analysis of prophylactic G-CSF administration are warranted.

РЕАБИЛИТАЦИЯ ПАЦИЕНТОВ С ОНКОЛОГИЧЕСКИМИ ЗАБОЛЕВАНИЯМИ В РЕСПУБЛИКЕ БЕЛАРУСЬ

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В Республике Беларусь во всех её регионах развита и четко функционирует служба медицинской реабилитации, представленная стационарными и амбулаторно-поликлиническими отделениями медицинской реабилитации, как для взрослого, так и для детского населения.

Отделения (центры) медицинской реабилитации имеют методическую базу, основой которой являются протоколы медицинской реабилитации, в которых указаны мероприятия реабилитационно-экспертной диагностики. При проведении реабилитационно-экспертной диагностики оценивается реабилитационный потенциал, устанавливается клинико-функциональный диагноз, определяется реабилитационный прогноз, функциональный класс нарушений, категорий ограничений жизнедеятельности. После проведения реабилитационно-экспертной диагностики составляется индивидуальная программа медицинской реабилитации пациента, в которой отражаются мероприятия физической, психологической реабилитации, необходимая медикаментозная терапия, физиотерапевтические мероприятия, порядок проведения «школ больных».

Много внимания уделяется разработке и практическому внедрению стандартов реабилитации онкологических пациентов.

Важным условием психологической реабилитации онкологических пациентов является выработка и поддержание мотивации на реабилитацию. Это связано с тем, что реабилитация требует нередко изменения жизненных стереотипов (питания, двигательной активности, поведения на работе), активных кинезотерапевтических мероприятий, временных затрат.

Вторым методом медицинской реабилитации является физическая реабилитация. К ней относятся ЛФК, проводимая в группах, индивидуально, массаж, аппаратная физиотерапия, бальнеотерапия.

Показанные физиотерапевтические мероприятия способствуют формированию системной приспособительной реакции, обладают свойством рефлекторно и общего воздействия и стимулируют, таким образом, саногенетические механизмы компенсации и иммунитета.

Важным аспектом медицинской реабилитации является диетотерапия. Суть заключается в том, что на фоне тренирующих реабилитационных воздействий формируются компенсирующие функциональные системы, активируется синтез биологических субстратов, которые нужны для формирования и поддержания увеличивающейся массы замещающих структур.

Медикаментозное воздействие в реабилитационной практике – это, в первую очередь, применение препаратов, обладающих стимулирующим саногенез эффектами. К таковым относят иммуномодуляторы, витамины, антигипоксанты и др. Они принадлежат к ряду «реабилитационных» и при наличии показаний назначаются больному в стационарном отделении медицинской реабилитации.

Особенно важен в реабилитации онкологических больных системный подход, учитывая полифункциональность возникающих нарушений и стойких последствий самого онкологического заболевания и его специфического лечения, а также комплексный характер реабилитационного воздействия, направленный на разные звенья патологических процессов ведущих к формированию стойких последствий и риску инвалидизации.

AGENTS PRESENT IN WORK ENVIRONMENT AND THEIR ASSOCIATION WITH LARYNGEAL CANCER

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Background: The well-established risk factors for development of laryngeal cancer (LarC) are cigarette smoking and alcohol consumption. Other implicated risk factors are asbestos, pesticides, benzenes, as well as different types of dusts.

The **aim** of this study was to perceive the eventual causative associations between occupational exposure and development and distribution of laryngeal cancer.

Methods: The investigation was an analytical type of case-control study. It elaborated 185 patients diseased of LarC, and the same number of persons without malignant disease (control group-CG). Risk analyses were done using unconditional logistic regression, which provides results in the form of crude odds ratio. The odds ratios and their 95% confidence intervals (CI) were computed.

Results: A total of 145 subjects (78.4%) from the group of LarC patients were professionally exposed to carcinogenic agents. Of these, 33.8% were exposed to probable carcinogens (PC) and almost double was the percentage of those exposed to definite carcinogens (DC) (66.2%). A total number of 124 subjects from the CG were exposed to these agents. Of them, 25% were exposed to PC and 75% to DC. Subjects exposed to occupational carcinogens were at a significantly higher risk of developing LarC in comparison to unexposed subjects (OR=1.78; 95%CI, 1.12<OR<2.84). Subjects exposed to DC were at a 1.57 (95%CI, 0.96<OR<2.57) fold higher risk of getting sick in comparison to unexposed subjects. Subjects, professionally exposed to DC and with >20 years of service, were at almost double higher risk (95% CI, 0,91<OR<3,72), and those exposed to PC were at 1.72 (95%CI, 0,50<OR<5,91) fold higher risk to develop LarC in comparison to those who held their occupation <20 years. A significant number of diseased subjects who were professionally exposed were at the same time active smokers (78.8%).

Conclusion: Prevention of LarC encompasses many activities including: complete elimination of the agent from the workplace, reduction of its concentration and decrease of agent exposure.

Key words: laryngeal cancer, occupation, professional exposition.

UROTHELIAL TUMORS AND BALKAN ENDEMIC NEPHROPATHY FACTS AND DILEMMAS

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Introduction: Urothelial carcinomas are the fourth common tumours in human patology after prostate (or breast), lung and colorectal cancers. Despite the fact that urothelium represents histological and functional unit, bladder tumors account 90-95%, of urothelial carcinomas, while upper urinary tract (UUT) transitional cell cancer (TCC) account only 5-10% of urothelial carcinomas. There are differences in the epidemiology and natural history of urothelial tumors in different parts of the world, which is very specific in areas with Balkan endemic nephropathy (BEN). These diseases following the controversy related to the geographic and temporal correlation of onset, and possible links to the etiology. Changes in the incidence and nature of tumors of the proximal and distal urothelium, are extremely present in area with BEN, so expressed to talk about two distinct diseases or disparate twin diseases.

Objective: Evaluation of epidemiological, clinical and histopathological characteristics of urothelial tumors in areas BEN.

Patients and methods: Retrosepective analysis of the tumors in patients residing BEN areas (patients treated at Department of Urology of the General Hospital Doboj and patients suffering from BEN treated on hemodialysis in HD centers, Samac and Doboj), in the period from 2003. to 2012. Epidemiology of cancer include: localization and tumor incidence, average age, patients gender. Clinical characteristics were evaluated by history and diagnostic procedures: signs and symptoms, association of proximal and distal urothelium tumors, tumor invasiveness, associated renal failure. The histopathological grade of malignancy of the tumor-determined in biopsy or operational material. Data were compared with the findings of urothelial tumors from the areas without BEN.

Results: In ten-year period (2003-2012). In Doboj region was 281 diagnosed urothelial tumors (incidence 104,1/100,000 inhabitans). From areas with BEN there were 103 patients with urothelial tumors, with the incidence of 299,4/100 000 inhabitans, (85 Bladder cancer - incidence of 247,1, proximal urothelial cancer 18 - incidence of 52.3.) Ratio male/female in area with BEN was 1,6:1. Average age of patients was 74.4 year. Chronic renal failure Terminal stage of chronic renal failure (hemodialysis) had 30,1% of patients.

Association of bladder cancers and UUT-TCC (at the time of primary diagnosis or in history of disease) had 21,6% of patients, and only 1,9% of patients from non endemic areas.

Non-invasive urothelial cancer was 86,2%, while 13,8% of patients had an invasive form. Histological grade was: G1(55.4%), G2(33,9%) and G3(10.7%).

From the area without BEN, there were 178 tumors with incidence of 75.5/100,000 inhabitans Bladder cancer-Inc. 75.1, proximal urothelial tumor-Inc.0,42). Ratio male/female was 4,4:1. Average age of patients was 69.3. Histological grade was:G1 (65.7%),G2(19,79%), G3 (14,6%).

Conclusions: The nature of urothelial tumors in the area of Balkan endemic nephropathy in recent years is variable and specific.

Dominant changes are: increase in the general incidence of tumors, enormous leap incidence of bladder cancer, paradoxical decline in the incidence of upper urinary tract of urothelial tumors, invasive growth forms and increase of histological malignancy, association of urothelial tumors of the both upper and lower urinary tract, high percent of chronic renal failure.
Geographic and temporal correlation of urothelial tumors and Balkan endemic nephropathy is confirmed by the epidemiological facts, but is followed by many dilemmas, especially in the etiology and pathogenesis, which maintain decades long mystery of complex interrelationships.

ОНКОЛОГИЧЕСКИЕ ЗАБОЛЕВАНИЯ КАК ГЛОБАЛЬНАЯ ПРОБЛЕМА ЧЕЛОВЕЧЕСТВА

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Актуальность проблемы. Одной из глобальных проблем XXI ст. являются онкологические заболевания, вследствие которых в мире ежегодно умирает почти 8 млн человек. По оценкам Всемирной организации здравоохранения, 40% всех случаев рака можно предотвратить. Вместе с тем, прогнозные данные свидетельствуют, что без принятия эффективных мер борьбы с онкологическими заболеваниями в течение 2005-2015 гг. умрет еще 84 млн человек.

Методы исследования. Использованы библиографический, статистический и аналитический методы.

Результаты. В структуре смертности от онкологических заболеваний первые места занимают рак легких (17,1%), желудка (13,5%), печени (8,7%), толстой кишки (8,6%) и молочной железы (6,6%). Существуют половые различия в заболеваемости злокачественными новообразованиями : среди мужчин наиболее распространенными формами являются рак легких, желудка, ободочной и прямой кишки, предстательной железы, у женщин преобладает рак молочной железы, легких, желудка, шейки матки.

Онкологические заболевания более распространены в экономически развитых странах мира. Так, раком болеет 1,6% населения Европы, 0,4% населения центральноазиатских стран. Только 4% населения в Африке умирает от рака, в то время как в Европе - 19%. Показатель смертности от рака варьирует в диапазоне от 30% в западной части Европейского региона до 10% - в восточной. Рак является причиной значительной доли потерянных лет жизни, прожитых с инвалидностью. В европейских странах онкологические заболевания - это вторая, наиболее распространенная причина смертности после болезней системы кровообращения. Он обуславливает 11% лет жизни, прожитых с инвалидностью. Средний коэффициент смертности от рака у лиц трудоспособного возраста в странах ЕС составляет 79, в странах Восточной и Центральной Европы – 104 на 100 тыс.

населения. У мужчин рак легких является причиной 27% всех смертельных случаев от рака в Западной Европе и 33% - в новых независимых государствах. У женщин рак легких наблюдается с меньшей частотой по сравнению с мужчинами.

В течение 1990-2009 гг. заболеваемость раком увеличилась в Европе на 18,2% и достигла 396,6 случая на 100 тыс. Высокие ее уровни характерны для стран Европейского Союза (475,5 на 100 тыс.). Лидируют по уровням заболеваемости онкологической патологией Венгрия (816,5), Чехия (759,4), Ирландия (697,7). Сравнительно невысокие показатели выявлены в Таджикистане (36,6), Туркменистане (67,6) и Кыргызстане (83,1).

Выводы. Онкологическая ситуация в мире свидетельствует о необходимости совершенствования борьбы с раком, которая должна учитывать как национальный, так и международный опыт в этой сфере, ориентироваться на стратегические приоритеты, определенные Глобальной стратегией борьбы с раком, Парижской Хартией борьбы против рака и другими документами международного уровня.

Международный опыт, в частности европейских стран, показывает, что благодаря применению на практике имеющихся сегодня знаний можно предупредить возникновение четверти всех случаев заболеваний раком в регионе и успешно вылечить более трети больных.

CHROMOSOME 15 BREAKAGE: A STRONGLY POSSIBLE CAUSE OF BOTH ATRIAL SEPTAL DEFECT OSTIUM SECUNDUM AND ACUTE PROMYELOCYTIC LEUKEMIA IN A 22 YEAR OLD FEMALE.- CASE REPORT

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Chromosomal aberrations that involves DNA breaks result in structural chromosomal instability, massive loss of genetic information and chromosomal rearrangements. They lead in chromosomal translocations, inversions or sequence deletions and drive through a tumorigenesis and a increased predisposition to leukemia and other cancers. We report the finding on the cariotype of a chromosomal breakage on the chromosome 15 involving the genomic regions 15q14-22 in a 22 year old female diagnosed in 2009 with isolated Atrial Septal Defect Ostium secundum 5mm developing in January 2013 an Acute Promyelocytic Leukemia . There are many genetic conditions related to changes on the chromosome 15 and Acute Promyelocytic Leukemia is one of them caused by the the translocation t[15;17][q22;q21] in which the PML gene localized on 15q22 provides the material for the PML protein that block cell growth and proliferation and induces apoptosis in combination with other proteins. Mattson et al [2008] mentioned the importance of the chromosomal aberrations in the chromosome 15 and suggested the gene locus ACTC1 [ASD5] [Phenotype MIM 612794], located on 15q14, as very important for the cardiac septal formation. The reduced levels or impaired function of this gene at some crucial stage of development leads to a delayed looping of

the heart preventing so the normal septal development and resulting in ASD5. This strongly suggests the chromosome breakage 15q14- 22 we founded, as the possible cause of an isolated ADS 5 in our patient, triggering a chromosomal instability and generating so the start point of the Acute Promyelocytic Leukemia. Further genetic reseaches are still on going and we are waitig for the results.

TRANSPLANTATION

PEDIATRIC HEMATOPOETIC STEM CELL TRANSPLANTATION (HSCT) AND THE EXPERIENCE OF TURKEY

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Pediatric HSCT activity was started in 1990's in Turkey. Pediatric HSCT differs from adult HSCT in terms of the indications, procedures, follow up and complications. So, this complex medical treatment option is more difficult than the adult procedure. The main indications in pediatric age group is non malign diseases including hemoglobinopaties, inherited immune deficiency syndromes, bone marrow failure syndromes, inherited metabolic disorders. The half of the transplantations (53,6%) are in non malign diseases in Turkey. Pediatric HSCT has been performed to more than 2000 patients by the 16 transplantation centers and teams in Turkey. One of these team from Adana, Turkey carried on nearly 100 transplantations in pediatric age group. Acibadem Adana Pediatric Stem Cell Transplantation center was established this year and carried out 12 transplantations from February.

MONTENEGRO – DEVELOPMENT OF THE KIDNEY TRANSPLANTATION

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Background: In Montenegro there was no transplantation program until the September of 2012. On the other hand, there was 89 patients with transplanted kidney until this period and all of these transplantations were performed abroad. 15% of these transplantations were performed in areas of black organ markets such as India and Pakistan. Beside the ethical problems, these transplantations carried high risk of medical complications. Patients who underwent the kidney transplantation in areas of black markets usually came back or developed afterwards a lot of complications which has to be treated in our center. On the other side, outr health system had to ensure the solution for patients with terminal organ failure, for whom the organ transplantation is the only suitable way of medical treatment. It has been started with preparing of all neccessary conditions for the beginning of transplantation program in Montenegro since 2006 with different activities including public, legal, medical, educational and international cooperation aspects.

Methods: these data refer to the activities brought on the development of organ transplantation in Montenegro.

Results: It has been started with a lot of public campaigns focusing on the importance of organ donation and transplantation in our own health system since 2006. The law about organ donation and transplantation was conducted in 2009. Since that it has been hardly worked on obtaining of all medical conditions for the beginning of the program. The best support was brought throw collaboration with international groups and societies as RHDC (Regional Health Development Center) and SEEHN (South-Eastern Europe Health Network) and excellent collaboration with medical centers and

colleagues from Clinical Center Zagreb, Croatia. The memorandum about collaboration in the filed of transplantation medicine between Montenegro and Croatia was signed between two ministeries od health in April of 2012. Medical stuff from Clinical Center of Montenegro underwent education in Clinical Center of Zagreb during the 2012. All necessary resources and medical equipment has been provieded before the begginnig of the program. The first kidney transplantation from living donors in Clinical Center of Montenegro were preformed on 25th and 26th September 2012 under the supervision of doctors and medical stuff from Clinical Center Zagreb Croatia. Five more kidney transplantations from living donor were performed on until now and we have prepared other pairs for living kidney transplantation until the 2013. First transplantations were accompanied with a lot of attention from European transplantation community. We received many congratulations from WHO (World Health Organization), Eurotransplant and ERA EDTA (European Renal Association – European Dialysis and Transplantation Association). All of seven kidney transplantation performed until now, went without any complication in recipients, neither in kidney donors.

Conclusion: Ensuring the development of transplantation program allowed controlled transplantation and the safety of our patients. The development of transplantation system improved many medical fileds in our health system and improved continious education of medical staff. We are working on the development of transplantation of the other organs and deceased donation program as our major aims in the next period.

THE INFLUENCE OF DONOR'S HEMODYNAMICS ON THE QUALITY OF THE ORGAN INTENDED FOR TRANSPLANTATION

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One of the first important moments in organ donation is early recognition of a potential donor. Starting with aggressive therapy on time is crucial. On one hand, a potential donor can sometimes became a patient with good chance for survival. On the other hand if there is brain damage incompatible with life, our efforts go directed towards saving the quality of the organ intended for transplantation.

Today, we still have a progressive increase in the gap between the number of organs available and the number of patients requiring a transplant. Early recognition of potential donors can minimize this gap.

Prompt actions are clearly associated with the increase in the number of quality organ availability for transplantation, and a decrease in the number of donors lost due to cardiovascular failure. They also increase post transplant survival of the graft and the recipient.

After brain death (BD) is diagnosed and after the consent of family , we must continue providing hemodynamic stability, correct oxygen deficits (our main goal is aggressive maintenance measures in providing oxygen to the tissues (DO2), delayed DO2 is associated with inflammatory responses, and can cause serious damage to organs), treat bacterial infections (blood and urine cultures should be collected for all donors), reverse hypothermia (ideal body temperature between 36ºC and 37.5ºC), watch

for and correct metabolic disorders (especially hypernatremia), treat endocrine, renal and hepatic changes, correct coagulation disorders and correct any other reversible organ dysfunction.

Laboratory tests mast include blood typing, blood count, electrolytes, renal and liver function tests, amylase, cardiac enzymes, arterial blood gas, coagulation studies and serology. Abnormal levels of sodium, potassium, magnesium, calcium and phosphorus must be regulated immediately because they lead to organ damage.

It is recommended that CVP is monitored in every deceased donor because hypovolemia is the primary cause of hemodynamic instability in potential donors, and aggressive volume replacement is the first measure to be adopted. Insufficient replacement can result in inadequate tissue perfusion, systemic inflammatory activation, organ dysfunction and reduced quality of transplant organs, but unnecessary fluid administration may cause acute lung edema. Therefore, both insufficient and excessive fluid infusion may harm transplant organs and impact post-transplantation survival of transplant organs.

In the initial stages, hemodynamic monitoring should include an arterial line, an assessment of fluid-responsiveness and tissue perfusion. If minimal blood pressure (BP) is not reached following appropriate volume expansion, vassopresor or inotropic drugs should be started. Infusing these drugs without appropriate volume replacement may result in arrhythmias and worsened hypotension. However, following the initial volume expansion, doubts concerning actual myocardial function and the donor's ability to tolerate additional volume infusion remain.

In addition, the empiric use of inotropic drugs can cause damage to the lungs for transplantation and may be disastrous for the patient. Sometimes we use the esophageal Doppler monitoring (EDM) during optimization of organ donors before organ procurement. The EDM technology is noninvasive, technically easy and less expensive than the traditional pulmonary artery catheter. EDM is most beneficial to hemodynamically instable organ donor patients.

It is easy to acquire many different guidelines to properly managing hemodynamic support, but the most important message is to act before the catecholamine storm causes excessive damage to organ systems.

IMMUNE SYSTEM AS A SERIOUS REASON FOR INFERTILITY AND RECURRENT PREGNANCY LOSS

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The problem with infertility and recurrent pregnancy loss is growing between young fertile age generations. Many reasons have focus to immune problems, but still the patients are trying to find solution mostly with gynecologists. In the past decade the immunological problems took over a serious part of reasons for fertility problems.

Immunology of reproduction is developing branch with many “cross reactions” with transplantation immunology, especially in immune tolerance and fetus/graft rejection, based to alloimmunity. Many researches have been made to clear mysticism of controlling alloimmunity, but in practice few test are used

withundefinedsignificanceto clarifyand solve the problem:shared human HLA-A and DQ antigens between spouse, soluble HLA-G, antipaternal blocking or cytotoxic HLA antibodies, cross-matching between spouses, reproductive immunophenotype, Th1/Th2 cytokineprofile. NK cells number and activation assay (NKa), regulatory T-cell (T-reg) in peripheral blood or in endometrium (biopsy) are promising tests with practical importance.

The parts of autoimmunity that affect reproductive processes are often subclinical and most of the women who have recurrent pregnancy loss are otherwise well. This is the reason to get wide and deep anamnesis which will determinate the spectrum of autoantibodies that should be tested. Organ-specific antibodies such as anti-thyroid antibodies (aTPO, aTG), and organ-nonspecific antibodies, including antinuclear antibody, anti-ssDNA, anti-dsDNA, anti-histone antibody etc., as well as antiphospholipid antibody, anticardiolipin antibodies, lupus anticoagulant, could be easy detected in many laboratories. Anti-TSH and anti-FSH are added to autoantibodies test panel in recent time. The presence of autoantibodies could diminish the organ or cell function, or to influence the endocrine or coagulation system and involve them as a secondary immunological reason for fertility problems.

Finally, Thrombophilia (Inherited and Acquired) is anindivisiblepart of investigation of fertility problems, close connected with immune system activation. Resistances to activated Protein-C, natural anticoagulant blood levels, screening hemostasis and fibrinolysis, and gene mutations of coagulation factors arenecessary analyses to complete the investigation of fertility. It is recommended to perform those coagulation analyses before pregnancy, because it is shifted to procoagulant state during pregnancy. Freely blood flows through placenta nourishes the baby and is prerequisite factor for successful pregnancy.

Finally, solving the problem with infertility and recurrent pregnancy loss is team work and the place of reproductive immunologist in this team is necessary for recognizing the immune problems, determination the analyses for testing, interpretation the results and prescribing the imunomodulatory and/or anticoagulant therapy.

RELIGION AND ORGAN DONATION-WHERE DO WE STAND TODAY

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The religious view on organ donation are veryimportant for transplantation. Certain religious group have different views of the current brain death criteria. All major religious accept organ donation or accept the right of individual members to make their own decision. Roman Catolic Churchare in favour of organ donation as acts of charity and as a means of saving a life. Jehovah’s Witnesses require that organ be drained of any blood due to their interpretation of the disallowance of blood transfusion from the Bible. Muslims require that the donor have provided written consent in advance. Orthodox Judaism considers it obligatory if it will save a life, as long as the donor is considered dead as defined by Jewishlaw, but it is a matter of debate among different rabbins. Shinot’s group disfavor organ donation or transplantation and those who follow the folk

customs of the Gypsies. Positive views on organ donation also have Buddhism and Hinduism and other Indian religious.

We need to beteter understand and explain donation criteria and to learn about the Spanish model of organ donation. All religions may help us do havebetter organ donation.

CHANGING PATTERNS IN THE UROLOGICAL POSTRANSPLANT CARE FOR AN INCREASED TURNOVER OF KIDNEY GRAFT RECIPIENTS IN R. MACEDONIA

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The living donor kidney transplant (LDKTx) program in Republic of Macedonia has been initiated in 1977 but without a real continuum in the following years. Then, the education of transplant professional abroad (1985-87) was shown as a successful step for improvement and 15 cadaveric kidneys have been transplanted in 1987-1989 while another 7 were allocated to the other centers of former Yugoslavia. This successful period may be explained also by the exceptional work of a dedicated procurement person – neurosurgeon, complementary funeral expenses covered by the University hospital and in general and the enthusiasm of the whole transplant team involved as achievements in our country showing their competence in the field. However, there was no established organisational infrastructure and it could not have continued for a longer period.

In the period of 1996-2011 there was a regular living kidney transplant program (average of 13 transplantation per year) performed at the University Department of Urology mostly by 1 urologist. In addition, 18 LDKTx were performed in patients from Kosovo. Looking for the reason of such a small number of transplants even in the presence of prepared LD pairs we have focused on 2 essential problems. First, a very low reimbursement per transplant procedure allocated according to the DRG code at the Urology Department, and second, the insufficient number of dedicated professionals to the field of kidney transplantation (1 urologist and 1 nephrologist in charge for the whole program). However, this assessment was possible only after our involvement into the South-eastern Europe Health Network (SEEHN) initiative operating under the Regional Cooperation Council, as successor to the Stability Pact for South-eastern Europe (SEE). In fact, all Balkan countries involved were supported by the newly created Regional Health Development Centre (RHDC) on Organ Donation and Transplant Medicine established in Croatia (Zagreb) as a competent regional resource centre assisting SEEHN countries to create or improve their own donation and transplantation programmes.

Thus, at the very first professional meeting (27-28 May 2011 in Skopje, Macedonia), the organ donation and transplantation needs of each country within the SEE geographical region were addressed. Since SEEHN operate in a close coordination with the Ministries of health (MOH) they become quite aware of the current situation and accomplished a few steps for further improvement of the transplant program.

Thus, the budget per transplant procedure DRG code was increased from 3.500 to 10.000 Eur generating a positive budget at the Department of Urology. Second, the surgical team was composed from a combination of 3-4 urologists and a vascular surgeon. The third problem was the capacity of our transplant center that was enlarged for 1 bed (in total 5 beds) with a changed practice that donors may be hospitalized at the regular word apartments. In order to speed up the turnover in the transplant center and prevent graft hypoperfusion and related consequences of acute tubular necrosis, delayed graft function and prolonged hospitalization, we modified the anesthesiological treatment during the procedure with mean arterial pressure (MAP) of at least 85 mmHg. In addition, we also agreed for an urocatheter removal at 5-7 days as regular practice whenever possible. Finally, we did assume as early as possible hospital discharge with a frequent outpatient visits in the following weeks at the Departments of Nephrology & Urology.

At the end of the year 2012, after 24 successfully performed LDKTx procedures over the period of only 7 months we are pleased to report that all these maneuvers have led towards the 4-fold improvement as compared to the year 2011. As for the first half of the year 2013 we have already performed 28 LDKTx, awaiting 40 KTx at the end of the year and start of the deceased donor transplant program once bylaws from the Ministry of health are enacted and infrastructure established. We are eager to implement it for the good of our patients, so, be it!

LIVER TRANSPLANTATION EXPERIENCE AFTER 300 CASES.

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Success rates after liver transplantation increased due to the better surgical techniques and the newly developed surgical instruments. We have been doing liver transplantation since 1998. During this period we performed 302 cases. 162 cases were from living donors and 140 cases were from cadaver donors. The most common indications were viral hepatitis and cholestatic liver diseases with 63 and 48 cases respectively. The donors were mostly mother in 45 cases, father in 37, and sibling in 24 cases and other relatives in the remaining patients. We did not have Clavien Grade IV or V complications in our living donors. In all series the recipient patient survival rate was %83. The most common complications were biliary leak and arterial thrombosis in 36 (%16) and 30 (%10) cases respectively. Most of the complications were treated by interventional radiology and in only 15 cases we needed reoperation. Today surgical technique is standardized and with the new surgical instruments and microsurgery the success rates within the first year after liver transplantation reached to approximately %90 percent

ТРАНСПЛАНТАЦИЯ ОРГАНОВ В РЕСПУБЛИКЕ БЕЛАРУСЬ

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Трансплантация органов является одной из самых сложных отраслей современной медицины, определяющей уровень оказания высокоспециализированной медицинской помощи.

Цель исследования: оценить реализацию программы трансплантации органов в Республике Беларусь.

Методы: Для реализации программы трансплантации органов при финансировании из двух источников (муниципальный и республиканский бюджет) был создан Республиканский научно-практический центр трансплантации органов и тканей. В состав центра вошло Республиканское отделение по координации органного донорства, координирующий работу региональных отделений органного донорства и «Единый регистр трансплантации», содержащий сведения о лицах, заявивших о несогласии на забор органов для трансплантации после смерти и о лицах, которым проведена трансплантация. Центр осуществляет свою деятельность на основании Закона Республики Беларусь «О трансплантации органов и тканей человека» 1997г., с редакциями от 2007г. и 2012г., в котором закреплена правовая норма - «презумпция согласия».

Результаты: Создание стройной государственной системы оказания трансплантационной помощи населению Республики Беларусь позволило в период с 01.01.2008 по 01.06.2013г. освоить и впервые выполнить трансплантации печени, сердца, комплексов почка-поджелудочная железа, печень-почка, сердце-почка и существенно расширить спектр высокотехнологичных оперативных вмешательств. Общее количество выполняемых трансплантаций увеличилось почти в 35 раз (с 8 - 0.8 на 1млн. в 2005г. до 274 - 29 на 1 млн. в 2012г.). За этот период времени выполнено 1082 органных трансплантации. Из них: 796 трансплантации почки (трехлетняя выживаемость трансплантата: от живого родственного донора - 92%, от донора со смертью мозга - 80%) , печени – 196 (госпитальная летальность - 5,4%,однолетняя выживаемость - 92,1%),сердца -90 (однолетняя выживаемость - 85,4%), поджелудочной железы -6. Количество эффективных доноров со смертью мозга увеличилось с 0.4 на 1 млн. в 2005г. до 11,2 на 1 млн. в 2012г. Это позволило Республике Беларусь войти в число 50-ти ведущих стран мира в области трансплантации органов.

Заключение: Реализация программы трансплантации органов обеспечила население Республики Беларусь высокотехнологичной трансплантационной медицинской помощью, позволила подготовить высококвалифицированные медицинские кадры, существенно расширить спектр высокотехнологичных оперативных вмешательств, укрепить авторитет белорусской медицины и расширить международное сотрудничество.

KIDNEY TRANSPLANTATION IN TURKEY

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End stage renal disease (ESRD) is a serious public health problem in Turkey. Acoording to CREDIT (Chronic renal disease in Turkey) study (more than 10 000 people) , the prevalence of ESRD in Turkey is %5-6 per year. We are estimating over 100.000 ESRD patient in 2016. Kidney transplantation is the best solution for ESRD patients. Approximately 3000 kidney transplantation were performed in 2011 and 2012. Our center is one of the leading center performing almost 200 kidney transplantation. We are the only center in Turkey where donor operation are performed with NOTES (Natural Orifice Transluminal Endoscopic Surgery) technic in female donors. More than 60 female recipient donated their kidneys via vaginally. In this presentation, we would like to share our experience with other Balkan Countries.

SURVEY OF RENAL TRANSPLANTATION IN SLOVENIA OVER FORTY-TWO YEARS

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Background. Renal transplantation is the treatment of choise for many patients with end-stage renal disease. Successful renal transplantation improves length of life and quality of life and costs less than chronic dialysis.
Method. This is brief survey of renal transplantation in Slovenia, a country with a population of 2 million, which has one renal transplant center. The emphasis is on the Eurotransplant (ET) period (2000 – 2012). The establishment of an appropriate national transplantation organization resulted in an increase in transplantations and the acceptance of Slovenia into ET at the beginning of 2000. Current prevailing immunosuppression is composed of cycloporine microemulsion (Neoral), mycophenolate, methylprednisolone, and anti-interleukin-2 receptor monoclonal antibody (basiliximab).

Results. By the end of 2012, 979 renal transplantations had been performed. From 1970 to 2009, 126 patients had been transplanted from living related donors, only two of them in ET era. From 1986 to 1999, 239 patients received renal grafts from deceased donors. From 2000 to 2012, 614 patients were transplanted from deceased donors. In 2012, 62 renal transplantations were done; this was the highest number of transplantations per year. Three hundred and fifty-one (57%) renal grafts were shipped from other ET countries. The HLA-antigen mismatch of 2.7 ± 1.1 was not significantly different to that before 2000. From 2000 to 2012, the one- and five-year patient survival rates were 98.0% and 94.4%, respectively. The concomitant deceased donor graft survival rates were 94.0% and 87.8%, respectively.

Conclusions. In the ET era, the number of deceased donor renal transplants per year was 2.8 times higher than in the 14 years before. Short- and medium-term results of

the last 13-year period have been very good and even better than those presented in large reports.

CAN WE IMPROVE THE GRAFT FUNCTION BY THE USE OF EARLY PROTOCOL BIOPSY?

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Protocol allograft biopsy (PB) has been introduced in many centers over the world in past years, to determine the presence of acute and chronic lesions, drug nephrotoxicity and virus nephropathy (NP), in stable, well-functioning allografts. The information provided by PB studies suggests that acute lesions tend to reach their maximum during the initial months after Tx, and the incidence of chronic lesions is low during the first month, progressively increasing thereafter. Treatment of early subclinical acute rejection (SAR) found at BP performed at 1-3 months after transplantation has been associated with: decrease in late clinical rejection episodes, decrease of early chronic allograft nephropathy (CAN), lower serum creatinine at 24 months, and an improvement of long-term graft function.From the results of our protocol study we come to the conclusions that a protocol 1-month biopsy may be valuable to determine a high prevalence of SAR and to individualize the treatment of these subclinical condition in stable allografts. Further more we demonstrate that untreated SAR at 1-month biopsy showed greater susceptibility for acute histological deterioration on the 6 month biopsy, accelerating the progression of CAN. A beneficial effect of the treatment of SAR should be confirmed by long-term follow up of the graft function at 1 or 2 years. These results suggest that the persistence of chronic active inflammation may be responsible for the histologic progression of CAN. PB have aided research and provided insights into the pathogenesis of early and late allograft injury. PB role is evolving from research to a clinical management tool aimed to detect subclinical pathology requiring treatment adjustment. PB frequently reveal unexpected findings in stable allografts, thereby influence therapy in the majority of pts. Detection of SAR in PB remains important despite declining prevalence with triple therapy, the evidence favors treatment, if found. Individualization of therapy in high-risk pts and safe reduction of immunosuppression in standard risk individuals becomes possible by performing PB. Other potentially reversible chronic pathologies that may be detected by PB: BK virus-associated NP, if/ta and CNI nephrotoxicity, allow modifications of therapy to limit ongoing graft injury. Biopsy is safe and inexpensive compared with costs of earlier graft failure and return to dialysis.

INCREASING USE OF THERAPEUTIC APHERESIS IN KIDNEY TRANSPLANTATION

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Apheresis removes harmful substances mainly antibodies or immune complexes in immunological diseases from the patients´ plasma. In kidney transplantation plasma exchange or immunoadsorption plays an important role in patients with acute antibody mediated (humoral) rejection, in patients who are highly sensitized before transplantation and in patients with recurrence of focal segmental glomerular sclerosis (FSGS) in transplanted kidney.
In the Department of nephrology, University medical Center Ljubljana the first kidney transplantation was performed in 1970 and the first centrifugal plasma exchange in 1980 and membrane plasma exchange in 1982. Since then Apheresis unit at our department became the only therapeutic apheresis unit in Slovenia performing in the last years around 1,000 procedures per year. The apheresis treatment of recurrence of FSGS in transplanted kidney began in 1998 and acute antibody mediated (humoral) rejection since 2005.

Antibody mediated rejection was considered only when therapy of the (cellular) rejection (mainly pulses of metilprednisolone) was not successful. Hallmark in diagnosis of humoral rejection were donor specific antibodies in the serum of the recipient and histologically, fragments of complement C4d in peritubular capillaries with neutrophil and monocyte infiltration of peritubular and glomerular capillaries. When clinical criteria (rapid decline of renal function, usually antidonor antibodies) met with histologic findings, the diagnosis of acute humoral rejection was established. The main, graft saving therapy was apheresis. It is important to begin with apheresis as soon as possible and to apply appropriate volume of plasma which should be processed. Mostly 5 plasma exchange procedures are performed (1 plasma volume) in the first week and every other day thereafter until improvement occurs (improvement of renal function, disappearance of donor specific antibodies). After each plasma exchange low dose of CMV hyperimmune immunoglobulin (0.2-0.4g/kg BW) was administered. Immunoadsorption is usually performed 3 times (2-3 plasma volumes) in the first week and 2-3 thereafter until graft function improved. Hyper immune globulins have not been given although it might have been useful.

In the Transplant Center of the Department of Nephrology we have evaluated 23 antibody mediated acute rejections between 2005 and 2011 in 23 transplanted patients which have been treated with plasma exchange as explained above. Ten of 23 were men, mean age 41±16 years, in 78% there was concomitant T-cell mediated rejection. The highest serum creatinine during rejection was 349±155µmol/L. Immediate success of therapy was achieved in 19/23 (83%) patients, advanced graft dysfunction was observed in 1/23 (4%) and graft failure occured in 3/23 (13%) patients. After 3 months serum creatinine was 182±98µmol/L. One year patients´ survival was 95% and graft survival 62%, respectively. Serum creatinine was 144±52µmol/L at the end of the first year. Results are comparable to the data from the literature.
In kidney graft recipients, with biopsy proven focal segmental glomerular sclerosis (FSGS) as primary kidney disease, 30 % recurrence of primary kidney disease occurred

after transplantation. Both plasma exchange as well as immunoadsorption are relatively efficient therapies for recurrence of FSGS in transplanted kidneys. Three to 5 plasma exchange or 3 immunoadsorption procedures per week are suggested at start of the treatment, followed by 3 and 2 procedures, respectively in the second and third week. Proteinuria which is suspicious for recurrence of FSGS is between 0.5-1.0 g/day and is threshold for the beginning of apheresis therapy. Graft biopsy is useful and should be performed. Sometimes several cycles of apheresis therapy are needed to achieve remission. In our group of 25 transplant patients with FSGS in native kidneys (biopsy proven), 11/25 (44%) recurrence of FSGS occured in transplanted kidney, 8 women, age 9-61 years. They were treated with plasma exchange or immunoadsorption, remission was achieved in 7 (in 1/7 after 9 years of chronic, every 3 weeks plasma exchange), loss of graft in 2/11 patients, while 2//11 (women) are still on chronic plasma exchange for 3 (in the meanwhile she delivered a child of 900 g) and 15 years. The former had recently proteinuria 6.5g/day and serum creatinine 152μmol/L and the letter had proteinuria 5.15g/day and serum creatinine 294μmol/L. Both were taking also galactose, 15 g twice a day, for 3 and 6 months, respectively, without clinically relevant effect.

Transplantation of highly sensitisized patients is very demanding, requiring pretreatment before transplantation and strong immunosupression after it. Plasma exchange should be performed (1 volume of plasma) on days -4, -3, -1, 0; Immunoglobulin 0.1g/kg BW should be given after each plasma exchange, splenectomy is suggested at time of transplantation, rituximab 375mg/m2 on day -4. Induction therapy with Thymoglobuline, plasma exchange on days 1 and 3 after transplantation. Suggested maintainance immunosupression are steroids, tacrolimus and mycofenolat mofetil.

In the conclusion, apheresis therapy, either membrane plasma exchange or immunoadsorption, is important mode of treatment of acute antibody mediated rejection which significantly improved graft survival after such rejection episodes. Apheresis is still efficient tool in the treatment of the recurrence of FSGS in transplanted kidney. Our own experience revealed that nearly 15 years of chronic apheresis could preserve graft function, which would be otherwise, without apheresis, lost. Highly sensitisized patients are a great challenge and need meticulous treatment and more intensive immunosuppressive therapy.

BOSNIA AND HERZEGOVINA - CURRENT SITUATION IN THE FIELD OF TRANSPLANTATION

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Summary: Bosnia and Herzegovina is a country with two Ministries of Health from the two Bosnian entities, Federation of Bosnia and Herzegovina and Republic of Srpska and one Health Department in Brcko District. Ministry of Civil Affairs, on the country level, although limited, must coordinate activities between these Ministries. Availability of data related to organ transplantation in Bosnia and Herzegovina is scarce. These data are mostly available to a small number of people concentrated in medical

centers. Therefore importance and awareness of organ transplantation in Bosnia and Herzegovina society doesn't exist. Bosnia and Herzegovina has three Transplant Centers: Tuzla, Sarajevo and Banja Luka. Bosnia and Herzegovina doesn't have potential donor identification system developed as well as potential recipients system. Certain steps regarding public awareness have been done by Donor Network of Bosnia and Herzegovina and Donor Network of Canton Sarajevo. We have 9000 signed Donor cards in Canton Sarajevo, but they are not obligatory.

Cadaveric kidney transplant waiting list in Federation of Bosnia and Herzegovina exists from 2006. List has 180 registered patients from Federation of Bosnia and Herzegovina. According to Bosnia and Herzegovina Renal Registry 600 patients are candidates for cadaveric renal transplantation in 2011.

There were 2892 patients that have continued or started dialysis in Bosnia and Herzegovina in 2012. From that number 2264 patients were already on chronic hemodialysis (HD) and 79 patients on peritoneal dialysis (PD). Total number of patients with functional graft was 182 and total number of patients who died was 387 in 2012. Total number of patients who already were on HD was 2217 and 92 on PD in 2011. If we compare these data to the data in 2012 we can conclude that the number of patients on HD has increased but the number of patients on PD has decreased. We must also considerate that 31 patients have been transplanted in 2012. In Bosnia and Herzegovina. In Federation of Bosnia and Herzegovina have been 17 kidney transplantation and 2 liver transplantation.

Potential donor identification, their approval or their families' approval is the key element for organ transplantation. Increasing the number of brain deaths identifications elevates chances for higher number of organ transplantations. Appointing brain death coordinators in the hospitals is the first step in this process. Constant public education and awareness as well as health care professionals' education must be included in the process. Bosnia and Herzegovina needs better organization and central coordination as well as Central Transplantation Body.

Key words: kidney transplantation, legislation, Renal Registry of Bosnia and Herzegovina

CMV RELATED PROBLEMS IN RENAL TRANSPLANTATION AND HOW TO DEAL WITH.

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Cytomegalovirus (CMV) is one of the most important infections in kidney transplant (KTx) recipients. Detectable levels of IgG anti-CMV antibodies in the plasma as witness of exposure to the virus increase with age in the general population and so in the majority of donors and recipients prior to transplantation. In this regard, the use of induction therapy and immunosuppressive drugs in KTx patients increases the risk of clinically relevant CMV disease. CMV is also a significant factor associated with increased morbidity, mortality and overall costs of treatment in the renal transplant setting.

The distinction between CMV infection (based on laboratory findings) and CMV disease (clinical findings - fever, leukopenia, or organ involvement) is important. By quantitative polymerase chain reaction (PCR) it was determined that the patients with CMV DNA levels of ≥500 copies/µg of total DNA in peripheral blood had clinical evidence of disease although PCR results may vary significantly by laboratory.

In the past, when the treatment was only administered once CMV disease occurred the overall incidence of CMV disease was approximately 20 to 60 percent. Subsequently, preventive strategies have significantly lowered the incidence of CMV disease, which is approximately five percent with modern approaches. Valganciclovir has been prophylactic therapy of choice for CMV infection and/or disease among transplant recipients.

A multicenter trial (IMPACT trial) compared 200 days versus 100 days of valganciclovir prophylaxis (900 mg daily) among 326 high risk (D+/R-) renal transplant recipients. At 12 months, fewer patients in the 200-day group developed CMV disease compared with those in the 100-day group (16 versus 37 percent, respectively) suggesting that duration for CMV prophylaxis of 100 days may be insufficient for CMV D+R- transplant recipients.

The highest risk of infection is in CMV-positive donor and CMV-negative recipient. Because of these difficulties, some centers had previously avoided the placement of CMV-positive kidneys into CMV-negative recipients. Transplant recipients with CMV-negative donor and CMV-positive recipient may have reactivation of latent CMV infection due to the administration of immunosuppressive drugs. Finally, CMV-positive donor, CMV-positive recipient are at risk for both reactivation of latent virus and superinfection with a new viral strain and have the worst graft and patient survival at three years post-transplantation. No treatment with antiviral prophylaxis therapy has been recommended only in CMV-negative donor, CMV-negative recipient.

The optimal duration of prophylaxis is unknown, although compared with 100 days of therapy, prophylactic therapy for 200 days was associated with a significantly lower incidence of confirmed CMV disease. However, it depends partly upon the institution and available resources. The current recommendation may be to provide prophylaxis with valganciclovir for 6 to 12 months in the D+/R- patients and for 3 months for D+/R+ or D-/R+ patients who receive lymphocyte-depleting induction or rejection therapy. Concerning the maintenance immunosuppressive regimen it is prudent to temporary ir permanently permanently discontinue the antimetabolite drugs (azathioprine or MMF). It is particularly important to do that in the cases of a developed disease with gastrointestinal bleeding.

CHANGING PATTERNS IN RENAL REGISTRY DATA IN MACEDONIA IN LINE WITH THE INCREASED NUMBER OF KIDNEY TRANSPLANTATIONS

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The purpose of the study is to give an overview of end-stage renal disease (ESRD) and renal replacement therapy (RRT) and its changing patterns in the Republic of Macedonia in a period of the last 10 years (2002-2011).

Data are collected by questionnaires for individual patients that are distributed to 19 hemodialysis centers in the country. Incidence, prevalence, mean and median age, primary renal disease, established therapy, number of renal transplants per year and mortality are assessed and analyzed.

There is an increase of incident patients on RRT over the years, from 75,5 in 2002 to 154,5 per million population in 2011, on day 91, adjusted for age and gender. Mean age of incident patients is also increasing, from 55,2±14.0 at day 91 in 2002, to 59,3±14,2 in 2011. Diabetes and hypertension are increasing and have become the leading cause of renal failure in incident patients at day 91, unadjusted, in 2011 (23,3 and 29,8%, respectively). Prevalent counts on RRT are also increasing, from 559,2 per million population in 2002, adjusted for age and gender, to 949,4 in 2011. Glomerulonephritis, hypertension and unknown cause of renal failure are the leading cause of ESRD in prevalent patients. Hemodialysis is the predominant RRT modality in Macedonia either for incident, or prevalent patients, and is around 90%. The crude death rate on dialysis is relatively low, 11,6% in 2011.

Incidence and prevalence on RRT are continuously increasing, and nowadays, diabetes and hypertension are becoming the leading cause of ESRD. Kidney transplantation is underrepresented over the years with an average of only 14 transplanted patients per year. However, a sudden change in regard of substantial increase in transplants from living donors took place in the country in 2012 and we sincerely hope it will maintain with the same success in the forthcoming years.

RENAL TRANSPLANT IN ALBANIA: RISK FACTORS FOR GRAFT FAILURE

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Introduction: Many studies have demonstrated a logistic relationship between serum cholesterol levels and the incidence of coronary-vascular diseases. In patients with a renal graft hyperlipidaemia occurs in 60-80% and cardiovascular death in 40-60% of the patients. In patients with a renal graft, myocardial infarctions occur 25 times more often compared to the normal population. In spite of this, there is still discussion whether renal transplant patients with high serum cholesterol levels should be treated, as there is no conclusive evidence of a direct relationship between serum cholesterol level and cardiovascular death in this multi-risk patient population.Our aim of the study is to

evaluate the effect of serum cholesterol, as a continuous variable, on long-term graft, patient and over-all graft survival.

Materials and Methods: All transplanted patients having at least 5 years of follow-up were included in the study. To evaluate the long-term risk factors, we studied those patients that were alive with a functioning graft, one year after transplantation (n=100). Serum cholesterol, creatinin and data regarding the presence of proteinuria and hypertension between one and two years after transplantation were gathered. Hypertension was defined as a diastolic blood pressure above 95 mm Hg and/or a systolic blood pressure above 140 mm Hg at two or more visits, or the use of antihypertensive medication. Proteinuria was defined as urinary protein excretion above 0,15 gr per 24h at more than 2 visits. Patients were not routinely treated with cholesterol lowering medication.

Results: In the Cox proportional hazards analysis serum cholesterol at one year after transplantation turned out to be an important, independent variable influencing all end points (adjusted for all other variables in the model}. The infiuence on graft failure censored for death was log-linear and there was interaction with serum creatinine at one year. The adverse effect of elevated serum cholesterol levels on the graft failure rate decreased with increasing serum creatinine levels. The influence of serum cholesterol on the rate ratio (RR) for patient failure was linear and there was interaction with recipient age. The negative influence of serum cholesterol on the RR for patient failure decreased with increasing recipient age. Increasing serum cholesterol levels influenced the risk of over-all graft failure and there was interaction with recipient age. As recipient age had interaction with donor age and serum creatinine the influence of all four variables together on the RR was estimated. It is shown that the RR for over-all graft failure in young recipients of a renal transplant significantly increased with higher cholesterol levels, whereas there was hardly any inftuence on the RR for elderly recipients. The risk increased proportionally with increasing serum creatinine levels.

Conclusion: Serum cholesterol levels have an independent influence on graft, patient and over-all graft failure.

CURRENT SITUATION AND PERSPECTIVES FOR RENAL TRANSPLANTATION IN ALBANIA

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Background: During the last decade Albania has undergone under deep political and economic changes. An enormous support of the nephrology community by central authorities has resulted in gradual increasing number of patients treated with renal replacement therapies (RRT) (hemodialysis, peritoneal dialysis and renal transplantation), though not in equally manner. Recently, different chronic dialysis units are gradually established at several public and private hospitals in Albania. As a result the total number of dialysis patients and dialysis centres of the country steadily increased.

Methods: This is a multicenter, cross-sectional study. From January 2007, all patients with end stage renal disease were included in the analysis.

Results: There were a total of 592 patients [368 (62.2%) M and 224 (37.8%) F] treated for end stage-renal disease. Four hundred four (68.2%) patients were treated with hemodialysis (HD), 51 (8.6%) with peritoneal dialysis (PD) and 137 (23.1%) with renal transplantation. The increase in the number of patients treated with renal replacement therapies (RRT) during the last decade correlated very closely with the increase in healthcare spending per person. Most renal transplantations have been performed in Turkey (45.2%), less in Greece (22.0%), Albania (18.2%), Italy (8.4%), Pakistan(3,2%), Austria(2,1%) and Hungary (0.5%). Most recipients received the transplanted kidney from a living donor [131 (95.6%)], only 6 (4.3%) from a cadaveric donor. Among living donors 86.7% were consanguineous, and 13.3% were not.
Since the first renal transplantation in Albania performed on 2008, it has been an impressive increase in the number of renal transplant procedures.

Conclusions: The nephrology reality in Albania is still expanding, but certainly inadequate to the real needs of the population. The model based on national electronic registry is perhaps the best suited to systematic, longitudinal surveillance of chronic disease. Based on this surveillance program it should be possible to adopt future national disease prevention strategies.

RENAL INVOLVEMENT IN LIVER TRANSPLANT PATIENTS

Mihai Voiculescu, *Romania*

In the last years important progresses have been made in liver transplant. Nowadays, the life expectancy at 5 and 10 years after transplantation is better than in the early 1990s. Both the patients and graft of survival rates at 1 and 5 years are now higher (95% and 70% vs. 80% and 50%), mostly due to improvements of surgical skills and intensive care assistance.

Longitudinal epidemiological studies demonstrate that the kidney failure is one of the most important causes of morbidity and mortality in liver transplant patients. Recent data have shown that many factors could affect kidney in liver transplant patients. Pre-transplant factors include: previous renal dysfunction hepatorenal syndrome, high bilirubin levels, hypoproteinaemia, hypoalbuminaemia, APACHE II scores, hypertension, diabetes, HCV infection, serum creatinine, MELD score, increasing age, female gender. Intra-operative factors include: haemodynamic instabilit, intra-operative bleeding,surgical technique, and the conventional risk factors. Post-transplant factors are: CNI immunosuppressive therapy, HCV infection, tubular necrosis, delayed graft function, post-reperfusion syndrome, contrast nephropathy, drug-induced nephritis, dopamine/vasopressors usage, infection, relaparotomy, volume of transfused products, polypharmacy.Prospective studies demonstrated that 60% of the liver transplant patients have proteinuria and GFR less than 60 ml/min. Multivariate analysis emphasized that all the patients with HCV chronic infection and high level of calcineurin inhibitors are more prone to develop kidney failure and proteinuria.

KIDNEY TRANSPLANTATION IN TURKEY

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End stage renal disease (ESRD) is a serious public health problem in Turkey. Acoording to CREDIT (Chronic renal disease in Turkey) study (more than 10 000 people) , the prevalence of ESRD in Turkey is %5-6 per year. We are estimating over 100.000 ESRD patient in 2016. Kidney transplantation is the best solution for ESRD patients. Approximately 3000 kidney transplantation were performed in 2011 and 2012. Our center is one of the leading center performing almost 200 kidney transplantation. We are the only center in Turkey where donor operation are performed with NOTES (Natural Orifice Transluminal Endoscopic Surgery) technic in female donors. More than 60 female recipient donated their kidneys via vaginally. In this presentation, we would like to share our experience with other Balkan Countries.

OUTLINE OF TRANSPLANTATION DEVELOPMENT IN BULGARIA

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There is a government recognized authority - The Bulgarian Executive Agency for Transplantation (BEAT) under MoH subordination responsible for organizing and supervising all transplant activities, including: donation and transplantation of organs, tissues and cells; preparation and maintenance of recipient waiting lists; preparation and maintenance of the Organ Donors' Register; authorization of transplant institutions and teams; implementation of quality standards regarding organs, tissues and cells; traceability of organs, tissues and cells; monitoring and verification of the results of transplant procedures.

Current situation in Bulgaria is characterized by increasing number of patients in need of organ transplantation, increasing the morbidity and mortality in the waiting list and slowly increasing number of potential donors.

Problems faced in transplantation fields:

- Insufficient knowledge of transplant legislation by the majority of state-owned institutions, medical opinion, citizens, church etc.
- Negative mass-media image on the transplant service
- Inadequate organization and administrative structures for transplantation activity at national level
- Lack of education and public information
- Inadequate financial support.

Goals for the future

- To establish and approve the National program for transplantation and action;
- To Implement of a program according the EU Directives;
- To establish the National Committee on Transplantation;
- To develop the national program for continued training of staff;

- To review all governmental decrees, minister orders, regulation and guidelines in the transplantation field;
- To define the special budget for Transplant Activities;
- To develop the national program for education and public awareness about organ donation and transplantation.

The hope is to foster a new vision for deceased organ donation and transplantation, translated into shared national objectives and cooperation and collaboration among countries to be encouraged.

PREEMPTIVE KIDNEY TRANSPLANTATION – PRO AND CONTRA

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Preemptive kidney transplantation (transplantation before the beginning of dialysis) is widely considered as the best form for renal replacement therapy (RRT) for many patients with advanced chronic kidney disease (CKD). It is suggested that that the patients with CKD stage 4 or a glomerular filtration rate (GFR) less than 30 ml/min/1.73 m^2 should be referred to a transplant program (1). Grams et al. have shown that trends in the time of performing preemptive kidney transplantation has been moved towards higher levels of GFR in the last years, with no improvement in survival in patients who had been transplanted earlier (2). In parallel with this finding, recent study in pediatric kidney graft recipients did not show superior survival in preemptively transplanted patients (3).

Preemptive kidney transplantation – pro: There are many arguments in favour of performing preemptive kidney transplantation compared to transplantation after initiation of dialysis: better patients and graft survival (4), less delayed graft funtion, better quality of life, avoidance of vascular access surgery, easier return or continuation of work, less cost because of dialysis avoidance, ameliorating the effects of uremia (5). One of the main obstacles for preemptive transplantation is organ shortage, so it is not surprising that main source of donors in preemptive kidney transplantation are living donors. However, preemptive transplantation from deceased donor is significantly contributing to a pool of preemptively transplanted patients.

Preemptive kidney transplantation – contra: In parallel with many advantages of preemptive transplantation, there are also concerns:

a) The lifespan of the kidney graft is limited, and in the case of preemptive transplantation its consumption begins before it is truly needed.

b) The ability of the patients to consume toxic immunosuppresive regimens is limited and serious complications occur both in short and long-term, reinforcing the point that consumption should not began before it is truly needed.

c) The preemptively transplanted patient is exposed to the premature operative risk.

d) In an individual patient with GFR 20 ml/min/1.73 m^2 or so, one cannot predict how long he will live without a need for RRT. He may well for a long period at the given level of kidney function. In addition, if transplantation turned to be less than ideal, he might end up in severe CKD, and with toxic immunosuppresion regimen on the top of that, potential antirejection treatment, possibly leading to serious opportunistic

infections, potential for malignancy and other complications in the following years. We have experienced much of these problems with an adolescent a few years ago and have lost some of the enthusiasm for preemptive transplantation.
e) Waste of the native kidney function of the recipient may be a consequence of surgery and calcineurin and other toxicity.
f) The cost of transplantation, especially in the first year, is relatively high, even in the absence of serious complications, so postponing it may reduce total RRT cost.

Problems with outcome measurements: *Lead-time bias (6*). In preemptive transplantation the kidney is transplanted into the patient that does not need either dialysis or transplantation. Indication for transplantation is based on arbitrary criteria, like GFR 20 ml/min/1.73 m^2, without a real clinical problem that requires introduction of RRT. Many papers advocating preemptive transplantation did not address lead-time bias for preemptively transplanted patients. When kidney is put in the patient with GFR 20 ml/min/1.73 m^2, survival is counted from the day of transplantation, and compared to the survival time of the patients that started dialysis at the level of GFR 5-6 ml/min/1.73 m^2 or who were transplanted after they began dialysis (survival in that cases is usually counted from the day of transplantation and not from the day of the first dialysis). The true comparison between patients' survival with preemptive and classical transplantation (after dialysis) would be a comparison in survival from the start of RRT (and not from the day of transplantation) at the same level of GFR, or adjusted for that. The idea of early dialysis (a kind of parallel to preemptive transplantation) and its potentially beneficial influence on survival, modern some time ago, was abandoned after addressing lead-time bias (7, 8). However, addressing lead-time bias may be very demanding or even impossible.

Delayed graft function (DGF). Lower incidence of DGF after preemptive transplantation was reported. DGF is defined as the need for dialysis in the first week after transplantation. However, preemptively transplanted patients did not need dialysis before transplantation anyway. So it is possible that trasplanted kidney may have »true« DGF that is masked by the residual function of the native kidneys.

Additional problem wiht interpretation of preemptive transplantation result is that it is not *clear* ***to what extent native and transplanted kidney contribute to the global kidney function after transplantation***. At the day of preemptive transplantation the patient has significant own kidney function that can actually stay stable or even improve after immunosuppressive therapy, hydration, diuretics etc, depending on original kidney disease. Interventions used to enhance graft function may actually improve the function of the native kidneys. However, patient's independence from dialysis from the day of preemptive transplantation is attributed completely to the transplanted kidney. Of course, native kidney function after transplantation may be affected in other direction. Already fragile kidneys may be adversely affected by calcineurin-based immunosuppression. Ishani et al have shown that posttransplant kidney function in preemptively transplanted patients is independent of the level of pretransplant kidney function and suggested that preemptive transplantation should be delayed as long as possible, provided that patient does not have uremic symptoms and that dialysis can be safely avoided (9).

Preemptive work-up for transplantation enrollment : Preemptive work-up for enrolling the patient for transplantation while approaching dialysis has obvious advantages. It reduces time needed to enroll on the waiting list. There might be also other

benefits. The patients in advanced CKD, approaching dialysis, can be under great psychological stress. This period (just before starting dialysis) may be psychologically the most vulnerable period during the long course of CKD and RRT. From personal experience, preemptive work-up for transplant list enrollment may serve as a kind of »psychoterapy«. Patient may really see and feel that he has alternative to dialysis. During performing various diagnostic or correction procedures to become a transplant candidate the patient may be preoccupied in the manner that may be benefitial, avoiding focusing on the »horror« of rising creatinine level and approaching dialysis. **Preemptive kidney (re)transplantation in the patient with failing kidney graft:** Patients with failing kidney graft seem to be neglected when promoting preemptive transplantation. Such patients already receive immunosuppressive therapy and are often very distressed to go back to dialysis. Putting another kidney will help them avoid dialysis, vascular access surgery, a need for transplant nephrectomy (which is a demanding surgical procedure) after stopping immunosuppresion. Continuation of immunosuppressive therapy can also help in avoiding further sensitization.

Preemptive transplantation – summary of pros and cons: Taking all pros and cons into account, preemptive transplantation is the excellent RRT approach for many patients with advanced CKD. It seems that there is no advantage of performing transplantation earlier (compared to late) in the course of CKD. Preemptive work-up for enrollment for transplantation is advisable for patients with advanced CKD that are potential kidney transplant candidates. Although neglected, preemptive (re)transplantation should be considered in patients with failing kidney graft.

DONOR COMPLICATIONS IN LIVER TRANSPLANTATION

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Background. End stage liver diseases are considered as indication to liver transplantation in many cases. Many studies show that results of living donor liver transplantation (LDLT) do not significantly differ from cadaver donor transplantation. Careful approach to LDLT is mainly explained by risk of biliary complications in donors.

Material and methods. 600 LDLT cases were carried out in Inonu University Liver Transplantation Institute 2007 through 2012. Mean age of donors was 31 (18-65) years, body mass index 27.4 (24-36) kg/m2, follow-up period 39 months (2-58). 538 donors underwent right hemihepatectomy, 19 donors left hemihepatectomy, and 43 donors left lateral sectorectomy. Mean remnant liver volume for donors was 37% (26-87%), duration of operation - 327 min (205-440 min), intraoperative blood loss - 310 ml (105-800 ml) and hospital stay was 7.2 days (5-13 days).

Results. 116 donors totally developed 187 postoperative complications (19.3%). 1st degree complications were noted in 91 donors, 2nd degree complications in 20, 3a degree in 32, 3b degree in 43, and 4a degree in 1 donor (T92-Dindo classification). Most of complications were not severe and managed conservatively. Bile leak, bilioma, and

strictures occurred in 10.6% cases. Repeated surgery was applied to 34 donors. There was no mortality.

Conclusion. Donor complications in LDLT are presented mostly by biliary disorders and can be managed successfully.

IMPROVED HEMODYNAMIC AND GRAFT FUNCTION THROUGH BYPASS SURGERY IN A LIVING DONOR KIDNEY TRANSPLANT RECIPIENT

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Introduction: Kidney transplantation (KTx) is the best option for renal replacement therapy. A pretransplant diagnostic work-up excludes any organ damage or failure. However, sometimes, a rare complication could jeopardize the graft function of the recipient, requiring a new surgical procedure in order to either save or improve the graft function.

Here, we do report a first case to the best of our knowledge for an improved hemodynamic in a living donor KTx patient through an autologous saphenous vein graft bypass surgery between the renal and iliac external artery.

Case report: A 28-year-old female patient with a juvenile diabetes mellitus and diabetic nephropathy as a primary cause of end stage renal disease was initiated on dialysis treatment since 2011. She was prepared for potential living donor kidney transplantation from her mother. Because of her long-term diabetic illness she also performed a CT angiography of her iliac blood vessels which didn't show any substantial hemodynamic problem.

At the transplantation the disproportion of the diameters of the renal and iliac internal artery was ameliorated by a surgical technique. However, after the declamping of the vessels, the kidney got a pink color but was not as hard as it should have been supposed to be. However, there was an initial urine output on the table, and it was assumed as correctly done transplantation.

Postoperatively, there was a slow decline in the serum creatinine in the following days, but it remained around 300 mcmol/l and the patient gained some excess of fluid and edema in the lower legs. The Doppler signal showed hypoperfusion in the renal artery of 64.8 cm/sek and a low parenchymal RI of 0.57. A new CT angiography of the graft was performed finding a kinking of the renal artery before the anastomosis. In addition, there was a lower blood flow in a narrowed lumen of the internal iliac artery immediately after the bifurcation from the common iliac artery.

So, the patient has undergone a second surgical intervention with shortening of the renal artery in order to omit the possibility for another kinking. Since, there was no sufficient flow to increase the consistency of the kidney which was pink but soft again, another blood supply was required. Hence, a venous autologus graft from saphena was

obtained and latero-lateral anastomosis was bridged over between the renal and iliac external artery.

The Doppler flow was now showing an improved blood flow in the renal artery of 102 cm/sek and the RI over the parenchyma was 0.61-0.63. The serum creatinine normalized within the following days and she was dismissed from the hospital at 10 days after the second surgery.

Conclusion : In cases with insufficient renal blood flow through the kidney allograft an improved perfusion could be obtained by latero-lateral anastomosis as bridging vascular technique between the renal and iliac external artery with an autologus vein graft from saphena.

ADVANCED FEATURES FOR SURGICAL PENIS ENLARGEMENT

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Introduction: Cosmetic surgery for penis enlargement known as phalloplasty, gaining popularity in the early nineties. Although similar techniques have undergone a certain evolution and improvement over the years, they still remain controversial method.

Various urological associations and experts in plastic surgery still question the safety and effectiveness of certain methods.Extension of the penis known classical method is achieved by cutting the suspensor ligament of penis which supports the penis to the pubic bone. In such surgery can be prepared some serious complications.

Material and Methods: For a period of 12 years / 2000 to 2012/ 29 men were operated to extend the penis. They used a single - stage surgical technique:

1. Interruption and extending the frenulum breve of the penis. This allows the head of the penis to rise, especially in patients with congenital short frenulum breve and gain valuable centimeter.
2. Transposition of the angle between the scrotum and penis for removal or return of the anatomical angle back.
3. VY plastic in the base of the penis with or without lipectomy around the pubic bone, depending on the level of accumulated fat. At weak patients do not need to be done lipectomy.

Results:- The method is safe and does not violate the anatomical and functional structure of the penis. Saving anatomical connection to the penis to the pubic bone, which stabilize it and maintain an erection pointing up.

- The method is non-invasive than traditional surgery and does not give serious complicated in the postoperative period. Two weeks after surgery, the patient can lead a normal sex life without any interference erections. The penis is extended from 4-5 cm, compared to the initial size of the penis before surgery.

- The method allows deeper penetration of the penis into the vagina of the woman and the very sense of a more favorable character.

TO INDIVIDUAL SENSITIVITY TO THE NEUROTRANSMITTERS OF EXCITATORY AND INHIBITORY ACTION IN THE PREDICTION OF COMPLICATIONS OF BURN PROCESS

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Regulating mechanisms a stress - realizing and a stress of limiting systems define features of a clinical course of any pathological process [4]. Features of an individual adrenergicimmunoreactivity of an organism have pathogenetic value to development of complications of a burn disease of eyes [2,5,6]. Individual sensitivity of an organism of the patient to neuromediators of braking action at a burn process wasn't investigated yet. We have the basis to consider that the activity ratio a stress - realizing and a stress - limiting systems of rather individual reactivity of the patient with a burn injury of eyes will be possible to have predictive value for timely forecasting of complications of burn process.

The purpose of researches was determination of value of a ratio of individual sensitivity of an organism of the patient by a heavy burn injury of eyes to neuromediators of raising and braking action of the patient for forecasting of complications of burn process.

Material and methods. Clinic-immunological researches are conducted at 32 patients with burns of eyes of IV degree of weight for 14-21 days from the moment of a burn with application of standard immunological techniques, and also by means of load dough "active" E-RUL with adrenaline and oxybutyrate sodium [1,3]. Noted character of a clinical current of a burn disease of eyes taking into account development of their complications. Foranassessmentofdivergencesused x2 – Pearson'scriterion.

Results. Assessment of level of an adrenoretseption of "active" T-lymphocytes at 32 patients, for 14-21 days from the moment of burn injury of eyes allowed to define that at all patients the dezadaptive type an organism stress reactivity on a burn injury of eyes is observed. Misinformation the adaptive type of reactivity represents overdue activation of simpato-adrenal system on action a stress of a factor and thus its realization in gipergic option (R. Chalanova, 2011) is feature of an individual adrenergic immunoreactivity.

By results of own researches it is established that level of reception of "active" T - lymphocytes to oxybutyratesodium at patients with a heavy burn injury of eyes, same, as well as level of an adrenoretseption of "active" T – lymphocytes, was ranging from 2% до28%. The obtained data testify that for the most part of patients with burns of eyes of heavy degree (2/3 surveyed patients) inherent the raised indicator of reception of "active" T - lymphocytes to oxybutyrate sodium.

The carried-out clinic-immunological analysis allowed to come to a conclusion that for forecasting of a current of a burn disease the index of a ratio of indicators of an individual adrenergic immunoreactivity of an organism of the patient to neuromediators of raising and braking action has values. The complicated current of a burn disease of eyes was observed at an index of a ratio of these indicators at balance, or is lower (≤) 1,0. The raised index (<) 1,0 was observed at an uncomplicated current of a burn disease of eyes.

Thus, clinic-immunological researches at patients with heavy burns of eyes established that definition of an index of a ratio of neuromediators exciting and braking action gives the chance to predict complications of a current of a burn disease, namely a cornea ulcer, uveits, melting corneal transplant, the complicated cataract, secondary glaucoma.

LIVING DONOR KIDNEY TRANSPLANTATION IN JEHOVAH'S WITNESS PATIENT

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Introduction: There are many ethical dilemmas and yet current controversies for organ transplantation in Jehovah's Witness (JW) patients since none of the patients would agree to receive transfusion of blood either before or after transplant. However, these are even more prominent ethical issues when there is a pair for living donor kidney transplantation (LDKTx). There are reports for a similar safety and efficacy of renal, pancreas, liver and heart transplantation in JW patients, compared to non-JW patients for the graft and patient's survival. Here, we do report a first case to the best of our knowledge for a LDKTx in a JW recipient.

Case report: A 25-year-old male patient with chronic glomerulonephritis as a primary cause of end stage renal disease was initiated on dialysis treatment since 2004. He was a couple of times refused for potential kidney transplantation from a living donor, his mother. His case was reviewed once again and with an argument that his belief will never chang, and both the donor as well as the recipient will never be in a better condition for transplantation than it is at present, he was accepted and put on the waiting list for a LDKTx.

A plan for preparation of this elective surgery consisted from an increase in his blood count by erythropoietin therapy (up to 140 g/L of hemoglobin level), hemodilution within the transplant procedure if needed and careful surgical inspection and hemostasis at the operative field for all eventual small postoperative bleedings.

The mother was a bit more obese since she couldn't decrease her body weight more than 10 kg. Second, the right kidney was selected for donation because of the single renal artery. During the procedure it appeared that the kidney was tightly connected to the lower part of the liver and the kidney underwent a small damage with a blue zone while nephrectomised. Under the perfusion there was no problem and the graft was safely transplanted with an initial urine output on the table. While performing the uretero-bladder anastomosis, all of sudden an abrupt bleeding occurred from the kidney rupture on the spot it was injured. The patient was immediately hemodiluted with a 1,5 l of cristaloids in a fast infusion manner and an appropriate surgical intervention was performed. Namely, the ruptured area was stitched, and then sealed up by means of a layer of a collagen preparation and with fibrin adhesive, and finally the parenchymal

space was enveloped in a vicryl mesh that was fastened under slight tension to the capsule. The field was surgically checked for a small vessels hemostasis.

Postoperatively, there was a decrease in the blood count and hemoglobin level was reduced up to 66 g/l immediately after the surgery. However, the patient was not in a need for a blood transfusion, and with an appropriate cardiovascular compensatory function. The graft function was excellent and after this initial surgical problem the clinical course after transplantation went completely uneventful and he was discharged from the hospital at 10 days after the surgery with normalized serum creatinine.

Conclusion: The professional responsibility in LDKTx in JW patients is greater and the procedure more critical compared to any deceased donor transplantation. If recipient's blood count sufficiently increased it may overpass eventual bleeding problems as occurred in our case. Hemodilution is partly saving the blood, and finally, its important to preserve any further surgical blood loss from the operative field with a patience inspection of the field and appropriate hemostasis from all small blood vessels. Finally, it's also important that the pre-operative evaluation confirms a good cardiovascular function in order that any unforeseen event with an excessive anemic episode could be sufficiently tolerated.

RENAL FUNCTION IN LIVING KIDNEY DONORS

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It is now evident that the annual number of available deceased donors will not resolve the ongoing organ shortage. The significant mortality that occurs for those patients awaiting an organ transplant necessitates the consideration of every possibility of live organ donation.

Nevertheless, the needs of transplant recipients however, do not outweigh the priority of the long-term health of organ donors. The consensus statement of the Amsterdam Forum elaborated in 2005 the principles of care of the live kidney donor, and stated that all donors should have standard tests performed to assure donor safety that address the risk of immediate and long-term negative health consequences for the live donor. Regarding the medical suitability of live kidney donors, all candidates should be evaluated for renal function, blood pressure, presence of cardiovascular risk factors like diabetes, obesity, dyslipidemia and smoking. Complete urinalysis should be performed, including assessment for the presence of erythrocytes, protein and bacteria in the donors urine. Medical criteria which preclude live kidney donation include: GFR less than 80 ml/min/1,73m2, hypertesnion with organ damage, obesity with body mass index over 35 kg/m2, diagnose of diabetes or fasting blood glucose over 126 mg/dl, proteinuria over 300 mg/day, persistent microscopic hematuria which has not have been evaluated by urine cytology and complete urlogic work-up, urinary tuberculosis and cancer. Apart from the medical evaluation, the psychosocial suitability and willingness to donate must be assessed for the living kidney donor.

Looking for the long term consequences of living kidney donation, the questions to be answered are: what percent of donors develop proteinuria? what percent of donors

develop CKD? do the donors present higer proteinuria compared to control population? do the donors present higer rate of CKD progression and loss of GFR compared to control population?

Evaluation of the data from DONOR NETWORK (36 studies, 3529 donors, mean follow-up 6 years) showed that: mean survival is very good in living kidney donors; compared to other single kidney patients, renal function is well preserved on long-term periods (20 – 30 years); microalbuminuria and proteinuria have higher incidence and values compared with control population, without reaching significant values; high Blood Pressure prevalence is similar with control population.

EVALUATION OF POSTOPERATIVE COMPLICATIONS DONORS FOR CLAVIEN CLASSIFICATION IN LIVER TRANSPLANTATION.

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We analyzed on the survey results 250 donors who was operated on hepatectomy for liver transplantation from a living donor from January 2012 to May 2013. Right-sided hepatectomy performed 226 (90%) donors, left-sided hepatectomy 7 (2.8%) (2, 3, 4 segments), the lateral hepatectomy (segmental) 17 (6.8%) donors. The average age of donors was 32.1 years. In 48 (19.2%) of 250 donors were found in a total of 76 different events, with the same donor and there is one more complication. Mortality among donors were not noted. Various kinds of complications were observed in 44 donors (19.5%) underwent right-sided hepatectomy, 2 donors (28.5%) with left hepatectomy and 2 (11.7%) on the left lateral segmentectomy. Among the noted 76 complications Clavien classification 38 (50%) referred to the degree I, 5 (6.6%) to the II degree of severe complications of 14 (18.4%) of IIIa, 17 (22.4%) of IIIb and 2 (?) to IVa degree. Complications IVb and V degrees were recorded. Re-operations were needed in 5.4% of cases. More common complications of the biliary tract (n = 27, 35.5%). Wound infection and accumulation of fluid in the pleural cavity occupied in the following turn by frequency of occurrence (n = 24, 31,6%, n = 7, 9.3%).

Key words: liver transplantation from a living donor, the donor hepatectomy, Clavien classification

VARIA

ALLERGEN IMMUNOTHERAPY OF ATOPIC ALLERGIC DISEASES

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The allergen specific immunotherapy /SIT/ has been long and widely applied in the complex therapy of atopic allergic diseases. The main mechanisms of the SIT leading to correction of immune reactivity by stimulation of CD4+CD25+ Treg cells and the released by them IL-10 and TGF-ß in the switch from Th2 to Th1 cytokine type is discussed. The contemporary understandings about conditions and reasons for SIT, the obtained clinical results and its preventive efficacy are analyzed according the latest international consensus documents. The new approaches in this field based on the development of the molecular immunology and genetic engineering are presented. The author shares his more than 40 years experience with allergen specific immunotherapy in the control of some respiratory allergic diseases on the basis of 618 patients with bronchial asthma and/or allergic rhinitis followed up to 3-5 years after accomplishing of the treatment.

THE COMBINATION OF EXHIBITION AND SCIENTIFIC CONGRESS - A MEANING FOR THE PROFESSIONAL ORGANIZATION AND THE INDUSTRY

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Introduction: Exhibitions are market events, characterized by a specific duration, at which a large number of companies present their products, sell them or spread information in order to promote sales. The exhibitions are also perceived as a social service activity that delivers and exchanges information in accordance with the social needs so as to allow viewers to make purchases, investment decisions, or to update their knowledge. The trade show is something of a mix between direct selling and advertising. Trade shows can play a cost-effective role in the communications mix, especially in the early stages of the process-need recognition, development of product specifications and supplier search. There are specific types of exhibitions that are combined with other events such as seminars, special events and congresses. This combination raises visitor interest, driven by the high demand for information exchange and the availability of experts.

Methods: Literature review of 60 articles, found in Scopus, MEDLINE/PubMed, Web and own research regarding the trends, associated with the performance of Bulgarian Pharmaceutical Days – the biggest exhibition and educational forum for the pharmacists in Bulgaria.

Results: There is shift in the sources of pharmaceutical information, used by physicians - from mail or journal advertising to meetings and conferences. At the same time, sales calls with healthcare professionals are becoming more and more challenging

because of limited time. This further enhances the role of trade shows held in parallel with scientific conferences and healthcare professionals 'meetings.
Bulgarian Pharmaceutical Days forum is visited by more than 1500 pharmacists, which represent approximately 30 % of the registered pharmacists in Bulgaria. An important part of the event is the educational program which presents academic achievements in various fields of science related to pharmaceutical knowledge and public health. The main topics of 6th edition of Bulgarian Pharmaceutical Days (2012) are: „Influence of political and legal environment on access to medicine products and pharmaceutical care", „Health and economics benefits of pharmaceutical care" „Iatrogenic diseases – the role of pharmacist in their prevention", „European vision of pharmacies, pharmacists and pharmaceutical practice", „Analysis of pharmaceutical market" „Falsified medicines", „Patient's role regarding access to medicine products and drug policy decisions" „The price of health – the significance of pharmacoeconomics in health systems" „Pharmaceutical care as a source of financial benefit for the pharmacy" „Workplace violence in pharmacies". During the period 2008-2012 it is observed a noticeable increase in the scientific value of the conference part, which reflects also in the credit valuation that the event receives by the Quality Committee of Bulgarian Pharmaceutical Union.

Conclusions: From the perspective of their organizers, Bulgarian Pharmaceutical Days are perceived as scientific and educational forums, where pharmacists and other participants exchange ideas, and not as trade shows. Bulgarian Pharmaceutical Days would be organized in a high probability even without sponsors and exhibitors.
In fact, an event of such scale is essential for fiscal stability of the organization. So involvement of the pharmaceutical industry, without affecting the scientific program is an important element of the management of the organization.

CHANGES OF C-AMP LEVEL DURING OESTRUS CYCLE IN NORMOTENSIVE AND SPONTANEOUSLY HYPERTENSIVE RATS

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Background. The mammalian pineal gland is under adrenergic control; however, the physiological oscillations of gonadal steroids could strongly affect the melatonin synthesis and secretion by acting on the pre- and postsynaptic levels and by modulation of the target cells replay. The aim of this study was to determine the basal levels of cAMP in the pineal gland during the various phases of oestrus cycle in normotensive (NTR), Wistar rats and spontaneously hypertensive (SHR) Okamoto and Aoki rats and to describe the histological finding of the pineal gland tissues.

Methods. Two hundred female mature rats (100NTR and 100SHR) were investigated. They were divided in 4 groups according to the phases of the oestrus cycle (diestrus, proestrus, estrus and metaestrus). The phase of oestrus cycle has been determined by microscopic analysis of the vaginal smears. The level of cAMP (RIA) in

the pineal gland was parameter of its intracellular activity. The pineal gland tissues were stained on HaEo.

Results. In SHR there is a slight shortening of the oestrus cycle. In NTR there was an increase of the cAMP level from proestrus to metaestrus, contrary to the dramatic decrease in SHR. Histological findings of pineal glands showed the presence of many changed pinealocytes with picnotic nucleuses, while the neuroepithelial cells, in the upper parts of the glands, were separated in gland-like islets. There was a normal pineal histology in NTR.

Conclusion. This study indicated signigicant neurohormonal differences between NTR and SHR. The changed adrenal activity in SHR correlated with histological findings in the pineal gland.

Key words: cAMP; oestrus; rats.

ОПИТ ОТ ЛЕЧЕНИЕТО НА ЧЕТИРИ СЛУЧАЯ С ТЕЖЪК ОСТЪР ПАНКРЕАТИТ В УСЛОВИЯТА НА ОБЩИНСКА БОЛНИЦА

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Тежките деструктивни форми на острия панкреатит се проявяват драматично с много остра болка в епигастриума и в последствие целия корем, гадене, повръщане, висока температура и клиника на остър перитонит.
Най-често генезата се свързва с употребата на повече алкохол и заболяване на жлъчния мехур и жлъчните пътища.

За периода септември 2009 год. – април 2013 год. в стационара на хирургично отделение са приети за лечение 40 болни с клиниката на остър панкреатит. От тях посочваме четири случая с тежък остър панкреатит при двама мъже на възраст 46 г. и 50 г. и две жени съответно на 67 г. и 74 г. И при четирите случая имаше симптоматика на холецистопанкреатит с развитие на остър перитонит. След подготовка с вливания, антибиотици, НГС, H_2 блокери и спазмолитици всички болни са оперирани до 12-ия час от приемането им в стационара. При всеки от тях се намери хеморагично-некротичен панкреатит с голям излив с развитие на илеус-перитонит. След холецистектомията през ductus cysticus в холедоха се въвеждаше дренаж по Вишневски за дебарсиране на жлъчни пътища и за последваща холангиография. Бурза оменталис се ревизира и се оставиха два широки дренажа през форамен Winslowi и един дренаж през ligamentum gastrocolicum.

През двойния дренаж се започва лаваж със силно охладени разтвори на Рингер и физиологичен серум. Лаважирането трае постоянно по 12-14 банки за 24 часа в продължение на 3-4 дни. Такъв лаваж въведен от Beger е провеждан, но с разтвори с нормална стайна температура. Хипотермията след лаважа доведе до бързо възстановяване на общото състояние на болните, снижение на амилазата в кръвта, подобрение в коремния статус, възстановяване на чревния мотилитет. Болните се изписват на 10-11 ден. Една от тях на 28-ия ден пристигна с данни за болки в корема, гадене и температура 39,7 ^{0} C, повръщане и с голям абсцес до

панкреаса. След дрениране на абсцеса се подобри и изписа клинично здрава. Другите болни следоперативно имат данни за псевдокисти с размери 3, 4 и 6см/д.

Следоперативно се проведе трансдренажна холангиография на 14-ия ден с цел проверка на пасажа на жлъчката през Papilla Vateri.

Извод: Ролята на лаважа с охладени разтвори е от голямо значение в комплексното лечение на ТОП за добрия изход от заболяването.

ЭКСПРОРТ-ИМПОРТ МЕДИЦИНСКИХ УСЛУГ В РЕСПУБЛИКЕ БЕЛАРУСЬ. СТРАХОВАЯ ЗАЩИТА ВРАЧЕЙ.

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В настоящее время в Беларуси работают 16 республиканских научно-практических центров и более 600 больниц. Наиболее перспективными с точки зрения экспорта медицинских услуг являются такие направления, как трансплантология органов и тканей, кардиология, косметическая хирургия, стоматология, травматология, реабилитация, спелеолечение с использованием паров солей для пациентов с хроническими бронхитами и бронхиальной астмой и др.

В рамках государственной программы экспорта медицинских услуг и с увеличением числа предоставляемым высокотехнологичных операций хотелось бы обратить сегодня внимание на две связанные между собой категории:

Качество медицинской услуги и врачебная ошибка.В современных условиях развития белорусского страхового рынка, сферы медицинских услуг одной из наиболее актуальных и, в то же время, сложных проблем во взаимоотношениях врач-пациент является создание четкого механизма правового регулирования гражданской и уголовной ответственности. На примере Республики Беларусь можно наблюдать стремительное развитие и совершенствование многих видов медицинского страхования, в том числе и страхования ответственности медицинских работников. В сфере здравоохранения Беларусь готова к диалогу со всеми странами.

INTRA- AND EXTRACRANIAL EMBOLIZATION

Dr. Sirakov , assoc.prof. Penev, prof. Bosnjakovic

Endovascular embolization is a nonsurgical, minimally invasive procedure performed by an interventional radiologist and interventional neuroradiologist. It involves the selective occlusion of blood vessels by purposely introducing emboli.

Embolization is used to treat a wide variety of conditions affecting different organs of the human body.

Endovascular treatment of brain aneurysm and AVM’s is minimally invasive method performed to block or stop blood flow into the pathological vessels and to

prevent main complications. In these procedures are used different technical devices like platinum coils, stents, occlusion ballons, liquid embolization agents and etc.

The last 15 years endovascular technics shown significant progress and development in treatment of vascular malformations.

ВЛИЯНИЕ НА НОЦИЦЕПТИНОВАТА СИСТЕМА ВЪРХУ БОЛКОВАТА ПЕРЦЕПЦИЯ ПРИ МОДЕЛ НА ПАРКИНСОНОВА БОЛЕСТ СЛЕД 6-ХИДРОКСИДОПАМИНОВА ЛЕЗИЯ НА ПЛЪХ

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Ноцицептин/Орфанин FQ (N/OFQ) представлява ендогенен лиганд на опиоидния пептиден ноцицептинов рецептор (NOP), който повлиява различни биологични ефекти, имащи значение в модулацията на болковата перцепция, локомоторната активност и др. През последните години вниманието на учените е фокусирано върху аналгетичните ефекти на някои синтезирани ноцицептинови аналози модифицирани с β^2-триптофан в 4та и 5 та позиция.

Паркинсоновата болест е невродегенеративно заболяване, което в 75% от случаите се придружава с болка. Известно е, че базалните ганглии са тясно свързани с ноцицепцията и двигателния контрол. Двигателните пътища се повлияват от ноцицептивната аферентация, а изходът от базалните ганглии повлиява ноцицепцията. По този начин възниква мултидименционална мрежа, която е свързана със сензорно-дискриминативните, афективни, когнитивни и двигателни компоненти на болката.

Обработката на ноцицептивна информация е свързана с енкефалин в стриопалидарните неврони, динорфин и субстанция Р в стрионигралните неврони и допамин в нигрострарните пътища. Базалните ганглии изпращат еферентация към области свързани с обработката на болката.

За нас представляваше интерес повлиява ли ноцицептивната система болковата перцепция при модел на болестта на Паркинсон (БП) у плъхове?

За целта бяха изучени аналгетичните ефекти на: ноцицептин, два нови синтезирани аналози и JTC-801 (антагонист на ноцицептиновия рецептор) върху аналгезията при плъхове с модел на БП.

Опитите бяха проведени върху мъжки бели плъхове порода Wistar (180-200g) при цикъл 12ч тъмно/12ч светло със свободен достъп до храна и вода, след експериментално индуцирана БП. Всяка група бе от 6 животни. Всички опити бяха проведени между 9.00 и 12.00ч.

Животните бяха предварително третиране с desipramine (25 mg/kg, i.p.) и pargyline (25 mg/kg, i.p.), след което бяха анастезирани с ketamine (50mg/kg, i.p.). След въздействието на упойката се поставяха на стереотаксична рамка и се инжектираха със 6-hydroxy-DOPA в доза (8 μg/животно) в левия фронтален лоб на мозъка по средата.

След инжекцията, животните се групираха в две серии в зависимост от продължителността на периода на преживяемост след образуване на лезии: 7-10 седмици и 17-18 седмици. Беше проведена микроскопска верификация на лезиите.

Беше използван метод с прилагане на механично дразнене paw pressure (PP) тест. Всички вещества бяха разтворени във физиологичен разтвор и инжектирани интраперитонеално. Ноцицептинът и двата аналози бяха въвеждани в доза 10 μg/kg, а JTC-801 бе въвеждан в доза 0.5 mg/kg и бе прилаган 10 мин. преди въвеждането на всеки един от пептидите.

Опитите бяха извършени съгласно изискванията на Международната асоциация за изследване на болката и ЕКНМ към МУ- София.

Резултатите са обработени с ANOVA.

Измерванията започваха 10 мин след инжектиране на изследваните пептиди. При въвеждане на антагонистта JTC-801, както и на двата аналога стойностите на болковия праг бяха съизмерими с тези на контролата.

Ноцецептинът и JTC-801 понижиха по-слабо болковия праг при животните с 6-hydroxy-DOPA-аминова лезия, водеща до развитие на експериментална болест на Паркинсон.

Животните с експериментална БП показаха статистически достоверен забавен отговор в сравнение с контролните стойност и с тези без БП в ляво.

Двата аналози имаха по-слаб ефект върху болковия праг в сравнение с тези на ноцицептина и JTC-801 при животните с експериментална БП.

Получените резултати показват, че ноцицептиновата система участва в болковата перцепция при модел на Паркинсонова болест у плъх.

Ключови думи: ноцицептин, JTC-801, болка, модел на Паркинсонова болест

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ВЪРХУ НЯКОИ ОСОБЕНОСТИ НА ЛОКАЛНИЯ ИМУНИТЕТ В БЕЛИТЕ ДРОБОВЕ

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В процеса на еволюционното развитие в дихателната система (ДС) са се изработили механизми, които да поемат нейната защита от действието на различните биологични,физични, механични и химични нокси, с които тя влиза в контакт непрекъснато през целия индивидуален живот- от първото вдишване, до последният дъх. От другата страна на бариерата обаче и микроорганизмите в процеса на своята еволюция са се „научили” да я преодоляват и да използват ДС за „входна врата”.

Към факторите обуславящи локалния имунитет (ЛИ), върху които ще се спрем в това експозе са: морфологично-функционалните особености на ДС, клетъчния и секреторният имунитет. В ограничения обем, с който разполагаме не може да се обхване цялото многообразие и сложност на структурата и

функционирането на местния имунитет в ДС. Подобна е защитата и на всички лигавици, които имат контакт с външната на организма среда.

В белите дробове (БД) има две основни бариери осигуряващи защитата им от различни патогенни агенти: 1.бронхиалната (бронховаскуларна) и 2.алвеолокапилярната. В структурата на бронхиалната бариера влизат: епитела, базалната мембрана, колагенни, еластични и ретикулни влакна, много клетъчни елементи (макрофаги, мастоцити, лимфоцити, плазматични клетки), субмукозата, където са бронхиалните жлези. Много важно значение за осигуряването на местната защита има бронхиалният епител и особено ресничестите клетки. Те осигуряват очистване с постоянното си трептене (като вълните в житна нива залюляна от вятър) с до 1500 колебания в минута. Под въздействието на ресничките всяка вдишана частичка преминава 10 клетки за 1 сек. Ресничките и слузта образуват слузно-ресничести повърхности. Под въздействието на редица фактори двигателната активност на ресничките намалява или спира (тютюнев дим, прахови и химични субстанции от околната среда и токсичните продукти от размножаването на бактериите и репродукцията на вирусите в епителните клетки).

Въпреки съвършеното си устройство морфологичн-функционалните особености на бронхиалната бариера не са в състояние сами да осигурят ефективна защита на ДС от патогенното действие на вирусите и бактериите. Повишената устойчивост на организма при повторно заразяване с един и същ причинител вече се осигурява от придобия имунитет, който има значително по-голямо защитно действие отколкото факторите на неспецифичната местна защита. От синхронното действие и взаимно допълване на естествената устойчивост с факторите на специфично придобия имунитет се осигурява пълната тъканна защита на лигавиците и белодробния паренхим.

Местният секреторен имунитет бива: неспецифичен и специфичен. Секреторните неспецифични фактори за местна защита на ДС са: интерферона и инхибиторите. Интерферона е определящ фактор за неспецифичната устойчивост на ДС към вирусни инфекции. Основни негови продуценти са лимфоцитите и макрофагите, които се намират в голямо количество в лигавицата на горните и долните дихателни пътища, а също и от алвеоларните макрофаги. Инхибиторите са друг съществен фактор за местната неспецифична устойчивоост на дихателните пътища.

Секреторните специфични фактори на ЛИ са имуноглобулините синтезирани в лигавиците на ДС. Възпалителните заболявания от бактериална и вирусна природа водят да рязко увеличаване на клетките продуциращи имуноглобулини (ИГ) в стените на засегнатите органи. На първо място това се отнася до клетките продуциращи IgA, а също така и IgG, IgM IgE. Лимфоцитите, които са предетерминирани за продукция на IgA селективно се „заселват" в тъканите на ДС. Намиращите се близо до епителната покривка на лигавиците клетки, контактуващи с външната среда синтезират местно ИГ предимно от клас А и с това осигуряват местния секреторин имунитет на лигавиците. IgG се намира в дисталните участъци на ДС, а IgE редовно се наблюдава в секретите от ДС. Последният е свързан с алергичните заболявания.

В строежа на секреторния IgA, влиза и гликопротеид известен като секреторна компонента" (СК). Неговият синтез е независим от продукцията на

полипептидните вериги на димера на IgA. В синтезата на антителата принадлежащи към секреторната форма на IgA вземат участие 4 клетъчни системи: макрофаги, плазматични клетки, Т-клетките и епителните клетки, които синтезират СК. Най.важният ИГ на външните секрети IgA, със своя уникален строеж съществено се отличава от своя серумен аналог и проучванита върху имунобиологичните му свойства позволиха да изкристализират представите за дълбокия биологичен смисъл на формиралата се в процеса на еволюционното развитие уникална структура на този ИГ. СК определя едни от най-важните му имунобиологични свойства: антигенната структура, стабилността към различните въздействия, асоциацията с другите секреторни белтъци.

И ИГ от класовете: G, M и E имат важно значение за местната защита на ДС. В долните отдели на ДС има по-голямо количество IgG, именно тук се намират много макрофаги, представляващи основата на устойчивостта на БД към бактериите. Секреторните антитела от клас IgG стимулират функцията на макрофагите. IgE участва в реализацията на свръхчувствителност от бърз тип, като при абсорбцията на антителата IgE върху мастоцитите се освобождават от тях фармакологично активни медиатори: хистамин, брадикинин, SRS-A и други.

Секреторните антитела имат голямо значение и добре очертаната автономност за: предпазване от различни заболявания, контрол върху „нормалната" микрофлора, ограничаване на проникването във вътрешната среда на различни антигени и пр. Способността им да аглутинират бактериите и така да ограничават размножението им, както и да препятствуват тяхната фиксация върху епителната тапицировка на тъканите е много важна в местната защита на ДС.

ЛЕКАРНАТА В СТАРАТА БЪЛГАРСКА СТОЛИЦА - МИСИЯ ЗА СПАСЕНИЕ НА ИСТОРИЧЕСКОТО НАСЛЕДСТВО СВЪРЗАНО С МЕДИЦИНАТА И ФАРМАЦИЯТА В БЪЛГАРИЯ.

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Увод: Докато врачките и баячките практикували масово, а медицината била по-скоро занаят отколкото наука, д-р Марко Павлов написал първите страници от историята на съвременната медицина и фармация по български земи. След участие във Френската революция и гръцката завера д-р Павлов продължава борбата за светло бъдеще, този път в името на родната България. Само че вместо пушка и сабя използва френските учебници от Медицинския университет в Монпелие, хавана и пестика. През далечната 1824г. във Велико Търново той създава „Лекарната" – едновременно лекарски кабинет и аптека. Докато лекувал обикновените хора от народа, ги убеждавал да съхранят българския дух и традиции. Въпреки това спасил живота и на турския паша и неговото семейството, като техен личен лекар. След него, синът му фармацевтът Георги Марков продължил делото на баща си. Историята на Лекарната не е само ретроспекция на първата аптека в България, а символ на хуманизма и патриотизма.

Основната цел е да се очертаят и изследват възможностите Български фармацевтичен съюз да участва в запазването на историческото наследство свързано с практикуването на фармацевтичната професия в България

За постигането на целта са реализирани следните задачи: Изследване на историческото наследство по отношение на Лекарната; Критичен анализ на фактическото състояние на историческия обект; Изследване на възможностите на съсловната организация за запазване и популяризиране на историческото наследство.

Метод: исторически подход, анализ на документи и артефакти, сравнителен анализ, експертна оценка.

Резултати: Годините, през които българските граждани се опитваха да се отърсят от хватката на тоталитарното управление и да въведат принципите на демокрацията в обществения и политически живот са били пагубни за първата Лекарна в страната.

Реституцията на сградния фонд, приватизацията на предприятието отговарящо за стопанисването на обекта, липсата на средства и заинтересуваност в институциите са на път да заличат следите към историята на аптечното дело в България.През 2011 група фармацевти от – гр. Велико Търново започват да търсят възможности за възстановяване на историческия обект.

Заключение: Български Фармацевтичен Съюз и регионалната колегия в гр. В.Търново трябва да се превърнат в двигател на процеса на запазване и популяризиране на историческото наследство, свързано с практикуването на фармацевтичната професия.

Съсловната организация трябва да използва всички възможности за популяризирането на професията и промяна на визията на обществото чрез първата Лекарна и превръщането ѝ в един от най-посещаваните обекти в старата столица на страната и исторически град Велико Търново.

РОЛЯ НА СЪСЛОВНАТА ОРГАНИЗАЦИЯ В ЗАКОНОДАТЕЛНИЯ ПРОЦЕС - РЕАЛНОСТИ И ЦЕЛИ

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Увод: Правните системи на държавите – членки на ЕС са среда на взаимодействие на източници от два правопорядъка – международни, включително на правото на ЕС, и национални, които са създадени по вътрешнодържавен ред. Законодателният процес в РБългария се осъществява от Народното събрание въз основа на Конституцията и на приет от него правилник. Право да внасят законопроекти имат народните представители и Министерския съвет.

Законопроектите се внасят заедно с мотиви към тях, в които вносителят дава становище по очакваните последици от прилагането на проектозакона, включително финансови. В мотивите на законопроектите, които са свързани с членството на Република България в Европейския съюз, се посочва конкретна част от правото на Европейския съюз, която налага съответното регулиране.

Българският Фармацевтичен Съюз (БФС) представлява законова съсловна организация, чиято функция е представителство и защита на правата и интересите на магистър-фармацевтите. Наличието на професионални организации на магистър-фармацевтите със задължително членство е характерно за почти всички държави от ЕС.

Метод: Обзор на законодателния процес в РБългария в периода 2006-2012 година.

Резултати: Публичната природа на БФС – неговото възникване по силата на закона и задължително членство, намира израз в делегиране от страна на държавата на определени регулативни правомощия. Концепцията за съществуване на професионална съсловна организация е същата да изпълнява функции по регулация на професията, като държавата се разтовари от намесата в съсловната сфера.

БФС няма право на законодателна инициатива по приемане на актове от Народното събрание, но практиката е да представя своите проекти на законодателни актове на МЗ или на народни представители, които да поставят началото на нормотворческия процес като легитимни носители на това право.

По силата на Закона за съсловната организация на магистър – фармацевтите (ЗСОМФ) на БФС е предоставено правомощие да издава подзаконови нормативни актове, каквито са Правилата за добра фармацевтична практика и Кодекса за професионална етика на магистър-фармацевтите.

Двата акта имат за предмет уредбата на правила за поведение на магистър-фармацевтите при упражняване на професията им.

Законът е предоставил гаранции за спазването на тези нормативни актове, издадени от БФС чрез правомощията на Комисиите по етика и качество на РФК на БФС да налагат административни наказания, включително лишаване от право да се упражнява професия.

С изменение на Закона за здравното осигуряване през м.декември 2009г., БФС придоби правомощие за участие в системата на управление на здравното осигуряване като един от субектите, които издават условията и реда за сключване на индивидуални договори на всички аптеки в страната с НЗОК. Тези условия и ред, съдържат правилата за сключване на договорите между НЗОК и аптеките, както и съдържанието на самите договори, които са еднообразни по съдържание и се явяват един от двата основни подзаконови акта, които определят системата на лекарствоснабдяване от обхвата на задължителното здравно осигуряване.

БФС притежава и вътрешно съсловни правомощия по определяне на Устава на БФС, на уставите на РФК на БФС и на други актове, определящи организационната структура и дейности. ЗСОМФ е предоставил на БФС възможността да уреди множество въпроси, касаещи функционирането на съсловието.

БФС притежава и функции по участие в органи на управление на управление на системата на здравеопазването, които имат предимно консултативни, но и определени управленски правомощия – Висш съвет по фармация, Висш медицински съвет, Обществен съвет в здравеопазването и други. Правомощието на БФС по закон е да участва и дава становища относно

нормативни актове в областта на Фармацията също представлява форма на участие в процесите на управление на здравеопазването

Заключение: Предизвикателства пред законодателния процес в здравеопазването са формирането на дългосрочна и средносрочна национална лекарствена политика, въз основа на диалогичност и при зачитане позициите на всички участници в сферата на фармацията, имплементиране на добрите практики от страните членки на ЕС и отчитане на експертните оценки на съсловните организации в здравеопазването

Пред БФС съществуват редица възможности да участва в законодателния процес. Същевременно са налице и множество недостатъци.

Отчита се пренебрегване на законовото правомощие на съсловната организация да участва в изготвянето на нормативни актове в областта на фармацията, като избирателно се създават работни групи за определени актове, което е превратно прилагане на принципите на общественото начало.

ИНОВАЦИИТЕ В СФЕРАТА НА ФАРМАЦИЯТА - ХАРАКТЕРИСТИКИ И ЗНАЧЕНИЕ ЗА ИКОНОМИЧЕСКОТО И СОЦИАЛНО РАЗВИТИЕ

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Увод: Иновация (нововъведение) е приложението на нов или значително подобрен продукт (материален продукт или услуга), процес, нов маркетингов или организационен метод в бизнес практиката, в организацията или техните взаимоотношения с външната среда.От гледна точка на обществения интерес и медицинската наука, значение имат преди всичко продуктовите, а не процесните иновации или маркетинговите иновации.

Редица автори поставят ясна разделителна линия между новост и иновация. Създаването на едно ново лекарствено вещество или нов механизъм на действие, сами по себе си не са доказателство за увеличаване на възможностите за лечение.

Отричането на стойността, която притежават тези лекарства, е приемливо за хуманитарните дялове на науката, но не и за икономическите. Тези продукти имат съществено значение за развитието на фармацевтичния пазар. Конкуренцията между лекарствените продукти е предпоставка за създаване на ползи за отделния потребител и обществото като цяло. Същевременно, това е свързано със значителни разходи от страна на производителите и отделяне на огромни финансови и времеви ресурси от страна на обществото за оценката им, а това води до намаляване на възможностите за развитие на истински иновации, т.е. за създаване на качествено нови терапевтични възможности.

Метод: Литературен обзор на 89 публикации в базите данни на Scopus, MEDLINE/PubMed и интернет. Търсенето е извършено по следните ключови

думи: innovation, pharmaceutical innovation, R&D, pharmaceutical industry, pharmaceutical company, pharmaceutical marketing, business model и обхващат периода 1993-2013

Резултати: Измерването на иновационните процеси във фармацията е един от най-трудните практически проблеми при изследването на нововъведенията. Не съществуват хармонизирани европейски изисквания за определяне на степента на допълнителната терапевтична стойност, която новото лекарство осигурява в сравнение с наличните терапии.

Фармацевтичните иновации могат да се декомпозират на последователни, съществени и радикални, в зависимост от значението, което имат нелечимите до момента на създаването им болести и степента, до която успяват да подобрят съответния здравословен проблем.

До средата на 90-те години на XX век преобладаващата част от радикалните фармацевтични иновации и тяхната комерсиализация(реализиране на печалба от въвеждането им на пазара) са дело на малък брой фармацевтични предприятия. В същото време анализа на характеристиките на новите лекарства достигащи до фармацевтичния пазар в края на миналия и началото на настоящия век прави впечатление непрекъснато растящия брой на биофармацевтичните продукти. Тези продукти се разработват, както от големите фармацевтични гиганти, така и от научни колективи или по-малки биофармацевтични компании. Иновациите вече не са плод само на усилията на водещите по отношение на продажбите фармацевтични производители. Дори напротив съвременните научни източници посочват корелация между размера на компанията и вида на иновация, като ясно се посочва че големите компании са добри по отношение създаването на съществени иновации, а малките фирми са по-добри по отношение радикалните иновации.

Заключение: Нашият литературен преглед показва, че по-голяма част от активностите в сектора са насочени към развитието на продукта или към маркетинг-активностите. Така, по-голяма част от иновациите в сектора се оказват търговски, а не фармацевтични. Съществува несъответствие между тежестта на заболяванията и областите на медицината, в която са насочвани средствата на фармацевтичните компании за развитие и внедряване. Такова се установява и между разпределението на средствата за създаването на продукта и разходите за реклама в развитите страни, по отношение на продукти нямащи или имащи незначителни терапевтични предимства в сравнение с наличните на пазара.

С цел да се гарантира развитието на фармацевтичната индустрия като един от ключовите за европейската икономика сектори и същевременно да се защитят интересите на обществото е необходимо, на общностно ниво е да се изгради единна рамка за оценка на иновациите в сферата на фармацията, а на национално да се използват в по-висока степен възможностите на оценката на здравните технологии.

ИНОВАЦИИТЕ В ЛЕКАРСТВООСВОБОЖДАВАЩИ СИСТЕМИ КАТО ЕЛЕМЕНТ НА УСПЕШНОТО БИЗНЕС РАЗВИТИЕ НА ФАРМАЦЕВТИЧНИТЕ ПРЕДПРИЯТИЯ

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Увод: Във фармацевтичната индустрия не съществува бизнес модел, за който може да се твърди, че гарантира успеха на прилагащите го компании. Въпреки това съществуват два основни модела, които предприятията следват с цел да си осигурят превъзходство пред конкурентите.Blockbuster-модела е доминантен по отношение на научноизследователската и развойна дейност и на него се основава бързият ръст на продажбите на тези лекарствени продукти през деветдесетте години на 20-ти век. Като „blockbuster drug" се определят лекарствени продукти достигащи годишни продажби в размер на 1 млрд. USD, а „super-blockbusters" достигащи годишни продажби в размер на 2 млрд. USD. Понастоящем съществуват около 100 продукта притежаващи характеристиките на „blockbuster drug", като само пет могат да се определят като „super-blockbusters". Икономическите реалности днес обаче създават възможности за развитие пред нов тип фармацевтични компании, чиято бизнес концепция се основава на агресивно използване на съществуващите терапевтични възможности, като същевременно се прилагат търсените от пазара стойностно-ефективни решения. Съществено място в тази концепция намират приложението и развитието на лекарство-освобождаващите системи (ЛОС).

Метод: Литературен обзор на 68 публикации в базите данни на Scopus, MEDLINE/PubMed и интернет. Търсенето е извършено по следните ключови думи: pharmaceutical industry, blockbuster, specialty, pharmaceutical marketing, business model, drug delivery system и обхващат периода 2003-2012 година

Резултати: През последните няколко години се наблюдава изтичане на патентите на някои от лекарствата, обозначени като блокбъстъри. Това от своя страна подейства като катализатор за развитие на нови ЛОС и внедряването им в нови продукти, както от страна на притежателите на изтичащите патенти, които виждат в тях възможности за повишаване на ефикасността на съществуващите продукти, увеличаване на привързаността на пациента към предписаната терапия и разширяване на патентната защита чрез препозициониране и преформулиролиране, така и от страна на компаниите, разработващи подобрения на базата на генеричното производство.

Наблюдава се значителен ръст на пазара на ЛОС. Общия пазар на ЛОС е 142.5 млрд. USD за 2012 година, . Лекарствените форми за перорално приложение заемат най-голям пазарен дял от общия пазар на ЛОС

Необходимостта от продължаващото развитие на неинвазивните ЛОС се определя от ниската привързаност на пациентите към предписваните досега терапии,

ограниченията на съществуващите пазари, в съчетание с високата стойност за управление на лечебната дейност.

Заключение: Лекарствоосвобождаващи системи (ЛОС) са стратегически инструмент за разширяване на пазари / показания, удължаване на жизнения цикъл на продуктите и генериране на възможности.

Големият риск, съпътстващ процеса на създаване и навлизане на пазара на нови лекарствени молекули, поражда необходимостта от търсене на бизнес модели, които предоставят възможността за създаване на по-атрактивни от търговска гледна точка продукти, които се характеризират с по-висока вероятност за получаване на разрешение за достъп до пазара, по-кратко време за разработване и по-ниски разходи за развитие.
Съществено предимство на този модел е свеждането до минимум на риска от провал на процеса за разработването на продукта, особено в началните му етапи.

Не само фармацевтичната индустрия извлича полза от развитието на ЛОС. Обществото като цяло получава солидна възвращаемост от инвестициите. Повишеното придържане към терапията при пациентите в резултат на приложението на новите неинвазивни ЛОС може да доведе до понижение на броя на манипулациите при лечението на симптомите, при приложение на инжекционни лекарствени форми. Още повече, че разходите по прилагане на неинвазивни ЛОС са по ниски от тези при инвазивните, поради отпадане на необходимостта от участие на медицински специалист при процедурата.

COGNITIVE PERFORMANCE IN YOUNG ADULTS RELATING TO THE LEVEL OF PHYSICAL ACTIVITY

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Background: Physical activity has been promotes as factor which affect cognitive functioning besides well-known positive effects on somatic health. Electrophysiological and psychological evaluation of cognitive processes: attention, concentration and learning, were assessed in healthy young adult population relating to their level of physical activity.
Material: 90 participants were divided into three groups, (each group consisted of 30 subjects, mean age 20.9 years): sedentary group (low level of PA), recreational group (moderate level of PA) and athlete's group (high level of PA).
Methods: We used classic paper and pencil psychological test, Trial Making Test to evaluate the psychomotor processing and original electrophysiological method EXG – electroexpectogram's paradigm to evaluate capability to response to cognitive demands of investigational milieu.
Results: The participants from physically active group had significantly better electrophysiological parameters of cognitive processes during EXG paradigm. They generated oscillatory EXG curves with certain features of successful cognitive adaptation. Results from TMT- A testing showed that sedentary individuals finished the task

in 31.98 ± 10.14 seconds. For the group with moderate level of PA average total time was 26.37±9.45 seconds. The athletes had the best result: 25.30±5.12 sec. The second part of TMT, part B is more challenging and sedentary individuals solved it for average 79.7±22.33 sec; recreational participants needed 68.23±22.39 sec and the athletes were significantly faster with 60.67 ±14.24 sec.

Conclusion: Young adults who participated in moderate and intensive physical activity showed better cognitive performance on electrophysiological and TMT testing than their sedentary siblings. These results maintained the hypothesis that regular physical activity might be beneficial on cognitive functions in young adults.

THE ANALYSIS OF THE COURSE OF RHEUMATOID ARTHRITIS DEPENDING ON THE CLIMATIC AND GEOGRAPHICAL ZONES OF UZBEKISTAN

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Background. Rheumatoid arthritis (RA) remains a highly topical issue of modern medicine due to its direct connection with social, genetic and emotional as well as psychological factors. However, the results of recent studies suggest that human health is a reflection of environmental changes (Revich BA, 2005). In this regard, the organization of high quality care to patients with RA and arrangement of its preventive measures are impossible without the knowledge and consideration of environmental factors, life circumstances and traditions of the population. Therefore, the evaluation of RA course according to the climatic and geographical zones of Uzbekistan is a significant task, because the republic is distinctive by its geographical location, climatic zones as well as industrial and agricultural development. Thus, the aim of the current study was to analyze retrospectively the situation, the level and structure of RA in Namangan, Khorezm and Surkhandarya regions of Uzbekistan.

Materials and methods. For the retrospective analysis out-patient cards and extracts from clinical records of RA patients were used. The analysis included questions reflecting birthplace and the place of residence, specification of a place of emergence and character of a course of a disease, reproductive health, risk factors, and features of treatment of each specific patient concerning the need for hospitalization over the last 5 years. According to the analysis three groups of patients were selected depending on the place of residence. Their clinical and epidemiological analysis was conducted and regions were divided conditionally into three geographical zones: zone I - Namangan, zone II - Surkhandarya and zone III - Khorezm region.

Results. The conducted retrospective researches showed that RA course in three various climatic and geographical zones have a certain distinction. So, in zone III, indicators such as the tendency to progression of the disease over the past 3 years was dominated with figure 83.4%; while the frequency of cases with a need for hospitalization in one year was 67% and there was a high rate on existence of seropositive results with the point of 75%. At the same time, in this zone, patients with

clinically manifested (visceral form) course - 42% and with the need for aggressive methods of treatment (cytostatics) - in 74%, also prevailed. In zone II manifestation of the disease in the majority of patients had an earlier age - 48% of all cases, changes in reproductive system, i.e. the women with RA within a year most often addressed with the problems associated with a menstrual a cycle violations– 65%, while this figure was only 17% and 28% for zone III and zone I, accordingly. According to the records from out-patient cards in zone II - in 36.4% of women spontaneous abortion occurred, whereas 26.7% of female patients registered with secondary amenorrhea, when in 73.3% of women a various types of menstrual irregularities were the case. In contrast, zone I distinguished itself by a relatively low (positive) performance compared with other zones. However, in this zone, at the majority of patients (59%) the manifestation of the disease was characterized by a gradual deterioration of a patient's condition against the background of accompanying diseases.

Conclusions. The retrospective analysis demonstrated that clinical and epidemiological parameters of RA are different in the three zones of Uzbekistan, which does not exclude the probability of the impact of climatic and geographical factors on the course of a disease. This calls for a more focused and detailed studying of influence of environmental factors on the development and progression of RA.

THE FREQUENCY OF PATIENTS WITH INJURIES TO THE SPINE AND SPINAL CORD

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Introduction: Every job that we do, especially physical, you should have enough concentration and alertness in order to avoid injuries. The goal: The frequency of patients with injuries of the spine and spinal cord treated at the University Clinic for Traumatology, type of injury, treatment and consequences (physical disability) for the period of 2011-2012 years.

Material and Methods: The entire documentation is presented through descriptive method of distribution of patients according to the male and female, age, presence / absence of neurological deficit, type of treatment (conservative / operative).

Discussion: It is assumed that male patients with spinal injuries the backbone and spinal cord are outnumbered in terms of female.It is assumed that the incidence of injury is greatest in the group of 16 to 30 years. It is assumed that spinal injuries resulting in neurological deficit indication for surgical intervention.

Results: analyzed 168 patients with injuries of the spine and spinal brain.126 men (75%) and 42 women (25%) have statistically significant difference, the male population 75% are scored as three times the risk group of women for this type of injury.

Conclusion: This representation is interpreted by the fact that representatives of males frequently engaged in risky activities, both professional and recreational, greater participation in traffic, in addition is the fact that men are more frequently consumed alcohol, which undoubtedly contributes to occurrence of such injuries. The majority of these patients the injury leads to permanent disability leading to major cost

financially and hiring staff for care or hiring family members. Accepting this situation is very difficult by patients because their lives are getting a completely different dimension where and responsibilities are changing.

Key words: spine and spinal cord injury, permanent disability.

SERUM LIPID PROFILE IN WOMEN DURING MENOPAUSE

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Background. Menopause is often accompanied by degenerative processes such as arteriosclerosis that suggest an acceleration of aging triggered by estrogen lack. Diseases of the cardiovascular system, especially of the coronary blood vessels, are among the leading causes of death in menopausal women. The present study was designed to evaluate serum lipids level (HDL-CH, LDL-CH, LDL-CH/HDL-CH index of arteriosclerosis, triglicerydes, and total cholesterol) in women duringmenopause.

Matherial and methods. The study comprised a number of 80 women divided into three groups. The control group included 26 healthy women in their reproductive period. The perimenopausal group consisted of 32 women, with FSH level under 25mU/ml, and with anamnestic data of irregularity of menstrual cycle. The postmenopausal group encompassed 22 women, regarding lack of cycle for more than 12 months. Hormone level was determined with RIA method. Lipid concentration was determined with standard colorimetric-spectrophotometric method.

Results. Statistical analysis has shown that there was a significant increase of total cholesterol, triglycerides, LDL-CH, LDL-CH/HDL-CH index, and significant decrease of HDL-CH and estradiol in both perimenopausal and postmenopausal examines in comparison with the control group($p<0,001$).

Conclusion. This study favours the view that decrease in estradiol level and associated increase in LDL-CH, LDL-CH/HDL-CH index, triglycerides, total cholesterol and decrease of HDL –CH seen in perimenopausal and postmenopausal women may be responsible for the increased risk of atherosclerotic complications in women during menopause.

Key words: menopause; lipid profile.

THE EFFECT OF CHRONIC STRESSES ON THE STRUCTURE OF SKIN.

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Objectives: The scientist study of the psychic stresses effects on the destruction and premature senility in the structure of skin cells directly and indirectly.

Method: During the fetal period. Skin and nerves have a common origin causing by the fetal texture called ectoderm a this closeness causes that many diseases of the skin and nerve are related. Considering the nerves and skin (dermal) diseases , one of the most

important points can be the relationship between stress and its role on the destruction of dermal cells.

Stress influences the skin from several aspects.

These effects can be as follows.

1. Directly: contraction of the face skin muscles upon the nervous disorders and in long – term the spasmodic.

Contractions creates some lines around the lips and the eyes. In the stressful conditions , the people resort to some materials like alcohol and cigarette for comforting them from the emotional and psychic problems which these toxic materials are the main source of free radicals. The negative effect of these toxic materials on the skin cells has been proved for several years.

2. Indirectly: In this stressful state, the biologic factors cause the most damage on the skin. For example when the body lies in the stressful conditions, a material called cortisol is released in the body. Increasing the plasma level of this material is concordant with:

a) Catabolism of the face muscles, collagen and of the skin and consequently the thinness, wrinkles and subsidence of the skin.

b) Upon increasing the cortisol plasma level, the inflammatory like prostaglandins increase in the skin and then the skin capillaries are destroyed and the rate of receiving oxygen is reduced.

c) The recent studies indicate that the enhancement of the cortical is concordant with the cell telomere. This reduction then reduces the cell division and the rate of cell density in the skin textures.

Clearly there is a relationship between the beginning of the dermal diseases like psoriasis eczema and albinism mostly in the stressful situation. All of the three mentioned diseases are the autoimmune deceases caused mostly by the negative function of the body immune system. There is a close relationship between the negative function of the body immune system and the secretion of cortisol.

In this paper, it has been tried that the physical and chemical effects of the stress and its role in the destruction of the stress dermal cells is discussed.

In other works, stress is one of the factors of premature senility in people.

Conclusion: The mental stresses have a direct effect on the dermal cells physically and chemically. Undoubtedly, the various studies performed in the valid medical centers indicate the direct relationship between the chronic stresses and the premature senility of the skin.

HOW TO PREVENT AGING; HOW TO MAKE ANTI-AGING DRUGS

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In all private and non-private labs, scientists are seeking to find a drug can increase our age? It seems that, research on limiting the calorie, to be a good and better purpose. According to scientist, there is no anti ageing drugs can postpone (suspect) the aging of human beings, before may 2002. the aim of anti-aging is that, the development of our boy decreases due to molecular abilities.

It seems that, by using of a low-calorie diet, the health and body in most animals incredibly increase. Research show that the limitation of calorie can postpone aging process in human beneficially. Unfortunately, people have to decrease their calorie from 2500 to 1750 for limiting the calorie in which it is about 30 percent daily calorie. however some people can't do this hard condition of dietary especially in their final ages, but if they can get study for that will be more usable. Therefore, we are crony to produce a drug can mimic the effects of two-eating physiological without one needs to tolerate starving. Question is that, could this combination called caloric restriction mimetic, guarantee the health of people long? And could it postpone the disorders of ageing such as diabetes, sclera, coronary disease, and cancer?

This question was studded in the middle of 90s after meeting with a chemical material that made limitations in rodents. Then, researchers are seeking to find a drug that can affect the same advantages on humans, but they have not been successful but these failures can be a better bridge for making restriction mimetic in the future.

Scientists are taking steps on this subject. Weather these changes in glucose metabolism can have some advantages in limiting calorie or no. glucose that consists of digesting carbohydrates, is the first source of energy for cells as well as the most vital material for producing ATP(the molecule that need for applying cellular activities).

According to researches were carried out between 1940s and 1950s, (2DG) was attracted by some researchers. This was useful for treating cancer in mice of vital enzyme, that is, among the metabolism of glucose in cells. this molecule id similar to glucose structurally: therefore, it is entered in to cell easily and changed to glucose by some useful enzymes, but in the later phase, it is influenced just by glucose and controlled from 2DG medias. Therefore this cell makes a little production of glucose. Now, why the decreasing of mitochondria function for making ATP causes to postponement of ageing? This question is unanswered yet, but scientists stated some hypothesis in this case. One of them stated that, there are molecules that responsible for ageing (they called radical molecules) and they might be destroyable for most cells. it is proved that, controlling the metabolism of glucose can make some limitation in our body. But unfortunately, due to poisonous of high degree of doses (2DG), we can not use that as a wonderful or interesting drugs. However it is safety in low degree of doses, but makes poisoning in some animals. Unfortunately, there is a little safety restrictions between effected dose and the degree of poison; however it is harmful for human beings, in the other hand scientists believe that, there is promising issues on it in the future. So, we are going to study an other way that it is more stable and useful. Researches show that by using of three ways, we can decrease the rate of aging that they are including:

1- Nutrition therapy

2-the use of vitamin and mineral ointments

3-the use of hormone therapy

These researches were found by more struggles, scientific and medical centers as well as, god helped to gather all of these information. This science is very simple and inexpensive, and in this section we tried to focus on nutrition therapy. Researchers wanted to treat and prevent the following items: wrinkling or folding: inner sides such ac cardiovascular disease, cancers, bone cave, Alzheimer, arthritis,…

Nowadays, free-radicals can cause to ageing that can attack to healthily cells such as skin cells and heart cells, inflammation these tissues and finally collapse these parts of body; but we are going to decrease or prevent of them as soon as possible.

AN INVESTIGATION OF AGING RELATION WITH CHRONIC STRESSES

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Since years ago the relationship between chronic stress and premature aging has been distinguished, though without identifying it's action mechanism. Increase in blood cortisol level which can be observed in chronic stresses can lead in telomere(which is effective in our young staying condition) length reduce in different ways. It's first influence is that of increase in inflammations resulted from cortisol which can by itself result in destructing white corpuscle physical and chemical mechanism, and this, at last will result in disorders in their function. Other case is that inflammation resulting from cortisol trough directly influencing related enzymes to telomere results in telomere destruction. Both these factors along with each other result in reducing telomere length. So telomere length shortens earlier. On the other hand, inflammations themselves, as free radicals, are destructing lipids, proteins and carbohydrate layers of cells mechanism without influencing telomeres length and will result in cell death or at least reduce in professional function of cells. In spite of progress in molecules medicine, above mentioned factors were unknown for more than 50 years. On the other hand reduce in endorphin levels, especially serotonin dopamine, *adrenaline* in brain which can bee seen in chronic depressions. Perhaps in addition to_*Cortisol* factor, through reducing excretion during chronic stresses, they themselves can result in immunity system function reduce during normal life time. Through increase in hopefulness, spiritual beliefs, and receiving awards, we achieve to an increase higher, than normal extreme of these materials, at last we observe immunity system function increase of body. But in chronic stresses where amount of these materials decrease, influencing way of these materials on reducing immunity system function is controversial. Dose this influence is resulted from cortisol function influenced by reduce in endorphin level or not this reduce in function appears directly? These factors are sufficient to premature aging appeared by chronic depression. On one hand depressed people can reduce effects of this mechanism, through daily use of advised amount of anti inflammation foodstuffs including: ginger, olive, fishes living in cold waters, nuts, turmeric, cinnamon and mushroom. On the other hand they can compensate reduce in body immunity power function resulted from chronic stresses in a way through regular and completely professional use of vitamin A, C, D found in green tea, zinc sulfate, onion, pro biotic yogurts, aerobic exercises.

Depression and relation with aging process:

1.inflammation,

2. cortisol,

3. unknown factors (materials produced in the time of stress but we don't know them presently).

1.Inflammation:indirectly influencing immunity system, it will cause to reduce in telomere length.
1.influencing related enzymes, it will cause to reduce in telomere length, directly.
2. influences tissues and genes directly.
Cortisol:
1.influencing body immunity system without anti effect_*Cortisol* cause reduce in telomere length.
2.causes reduce in telomere length directly and in addition to influencing body immunity system, leads to disorders related enzymes of telomere.

Key words; aging. chronic stress..

RELATIONSHIP AMONG SERUM LIPIDS, FIBRINOLYTIC ENZYMES AND FACTOR VII IN WOMEN DURING MENOPAUSE

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Background. Hypercoagulability and reduced fibrinolytic capacity, often seen in menopausal women, are associated with hypertriglyceridemia. The important role of thrombogenesis in coronary artery disease (CAD) is supported by the fact that initial high levels of coagulation factor VII (VIIc), and plasminogen activator inhibitor (PAI-1) are all independent risk factors for CAD.The mutual correlation among serum lipids, fibrinolytic enzymes: tissue type plasminogen activator (t-PA), plasminogen activator inhibitor type 1 (PAI-1), and factor VII in women during menopause was studied.

Material and methods. Study comprised a total number of 76 women divided into two groups: group of women in perimenopause (n= 36) and group of women in postmenopause (n=40). Lipid level (HDL-CH, LDL-CH, TG, total cholesterol) was determined with colorimetric-spectrophotometric method, fibrinolytic enzymes were determined using immunoenzyme sandwich method and factor VII of coagulation with the method of deficiency plasma. Data were entered into a data-base and were statistically analyzed. Correlation analysis (Pearson's coefficient) was used for assessing the relationships between the examined parameters.

Results. Fybrinolytic activator (t-PA) was in poor negative correlation with fibrinolytic inhibitor (r = - 0.18), factor VII of coagulation (r = - 0.28), total cholesterol (r = - 0.17) and triglycerides (r = - 0.35), but in weak positive correlation with HDL-CH (r = 0.73) as well. There was a positive correlation between PAI-1 on one hand and factor VII (r = 0.18), triglycerides (r = 0.245) and total cholesterol (r = 0.14) on the other hand, but there was also a weak negative correlation between PAI-1 and HDL-CH (r = - 0.048).

Conclusions. These data suggest that serum lipids, particularly triglycerides have a close relationship with thrombogenesis as evidenced by activated f. VII in the extrinsic coagulation system and also by elevated PAI-1 activities in fibrinolysis.

Key words: menopause, serum lipids, fibrinolysis

CLINICAL MANAGEMENT OF INSECT-VENOM ANAPHYLAXIS

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Anaphylaxis is an acute and potentially life-threatening allergic reaction that can be caused by numerous allergic triggers as food, medications, and insect stings. Reactions to insect stings are common. While most are self-limited, some induce systemic allergic reactions or anaphylaxis. Unfortunately, anaphylaxis continues to be underappreciated and undertreated especially in regard to insect sting anaphylaxis. Prompt recognition, diagnosis, and treatment of these reactions are important for improving quality of life and reducing the risk of future sting reactions. This review focuses on the current recommendations to treat sting induced allergic reactions. This includes the appropriate use of inject epinephrine as the primary acute management tool. Patients with insect venom allergy are at higher risk for development of a recurrent systemic reaction after re-sting. This risk significantly decreases with venom immunotherapy.

COMPARATIVE ANALYSIS REGARDING DIFFERENT VASCULAR ACCESS IN HEMODIALYSIS PATIENTS

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Background. Vascular access (VA) for hemodialysis (HD) enables extra corporeal blood flow with appropriate inflow and outflow pressures, concerning two modalities: catheter and fistula. While the arterio-venous fistula (AVF) is usual VA, central venous catheter (CVC) is used in emergency situation such as thrombosis of AVF, infection or any other situation contraindicated usual access. The aim of the study was to analyze the patient's condition undergoing HD using both, AVF and CVC.

Method. The study was performed on 26 HD patients at age of 54±12 years (43% male and 57 female%) undergoing HD treatment for 113±120 months. Patients with diabetes mellitus were considered 12% and with hypertension 62%. The comparative analyze was performed for 2 periods: HD with AVF, 2 months before the thrombosis, and HD with CVC, after the thrombosis of AVF until functional AVF is applied. Following parameters were compared: systolic blood pressure (SBP) (mmHg), body weight (BW) (kg), heparin (IU), heparin/BW (IU/kg), the blood flow rate to the dialyzer - Qb (ml/min), realized ultrafiltration volume - UF (L/h), time (h), and kt/V (number to quantify HD treatment adequacy, concerning urea clearance to dialysis time and volume of urea distribution in total body fluids). For laboratory parameters, blood cell count, ferritin (mg/L), CRP (mg/L) and Epo (IU) were analyzed.

Results. Significant difference was found for: Qb in AVF period, 280±11 ml/min and in CVC period 258±19 ml/min ($p<0.002$), UF realized in AVF period, 3.23±0.97 L/h and in CVC period 3.03±0.95 L/h ($p<0.02$). For laboratory analyzes: CRP showed significant difference for AVF period 4,94±4.9 mg/L and for CVC period 9.74±9.97 mg/L ($p<0.01$). Other parameters did not show any difference.

Conclusions. Due to impaired Qb rate in CVC, urea removal and HD adequacy decreased, as well as UF as a fluid pulled out from the patient. Increased CRP value may show increased infection risk. These results give overview of the patient's condition in both VA types, which gives an important contribution to patient's health expectation and prevention, respectively.

Key words: vascular access; fistula; catheter; hemodialysis.

КЛАПАНЫ ИСКУССТВЕННЫЕ СЕРДЦА (КСИ) И ПРОТЕЗЫ – КОРРЕКТОРЫ КЛАПАНОВ СЕРДЦА (ПККС) – 25 ЛЕТ В КАРДИОЛОГИИ РЕСПУБЛИКИ БЕЛАРУСЬ

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Работы по созданию искусственных клапанов сердца, предназначенных для имплантации в сердце человека вместо пораженных аортальных и митральных естественных клапанов, начаты в Республике Беларусь более 25 лет назад.

В марте 1987 года министерствами здравоохранения и электронной промышленности СССР были утверждены первые медико-технические требования на разработку клапана сердца искусственного «ПЛАНИКС» после большой работы по их разработке и согласованию их с медицинскими соисполнителями – институтом сердечно сосудистой хирургии им. А.И. Бакулева, Бел НИИ кардиологии и организацией - соисполнителем НПО

Кроме ИКС на предприятии разработаны и освоены протез-корректоры клапана сердца (ПККС) для выполнения реконструктивных операций на клапанном аппарате, позволяющие создать опорный каркас и обеспечить адекватную функцию восстановленного клапана без его замены.

С 1991 по 2013 годы в Республике Беларусь созданы и освоены в производстве четыре модели отечественных ИКС: “Планикс”, “Планикс – Д”, “Планикс – Т”, “Планикс – Э” и протез-корректоры клапана сердца “Планкор” и «Планкор А».

ИКС “Планикс – Э” изготавливают пятнадцати следующих типоразмеров:
Аортальный от АДМ-17 до АДМ- 27
Митральный от МДМ-19 до МДМ-33

ПККС “Планкор” (кольца для вальвулопластики) предназначены для хирургического лечения клапанного аппарата сердца человека, с целью возвращения створок клапана в нормальное положение, которое было до приобретенного порока сердца. Протезы-корректоры выпускаются двух типов: митральные и трикуспидальные 12-ти типоразмеров, обеспечивающие антропометрические возможности сердца человека.

Митральные от М – 26 до М – 36
Трикуспидальные от Т – 26 до Т – 36.

ROUND TABLE

MAIN DETERMINANTS OF BURNOUT SYNDROME (BOS) AMONG GPs IN BULGARIA.EFFECTS OF BAS ON DOCTORS' HEALTH AND QUALITY OF PROVIDED HEALTHCARE.

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BOS is a condition, defined as a sequel of an irresistible stress, caused mostly by work environment factors (stressors), focused on the appropriate psychological personality type, which predisposes to manifestation of BOS. BOS deteriorates the quality of physicians' life. Although burnout in physicians does not differ from that in other professions, physicians' reactions may be unique in some respects, in part because burnout in physicians can have devastating consequences for delivered medical care and patients, respectively.

Doctors' BOS is caused by high levels of persisting professional stress, which acquired the characteristics of psychological distress. Undoubtedly, personality type of doctors should not be undervalued as a very important prerequisite for the occurrence of BAS. But the results of our research show that factors outside that personality even outside the work environment (inappropriate decisions of politicians; hostile public opinion, manipulated by TV, Radio, etc.; aggression; family relationships, etc.) are much more important, because they influence or directly change the work environment factors, turning them into powerful stressors, leading to BOS.

We defined and explored 4 groups of factors connected to high levels of professional stress and hence to BOS occurrence. We measured their strength of impact on GPs by four grade scale as follows: no effect; mild; moderate; strong. These factors are: organizational; economic; psychological, others. All of these factors have apparently resulted in a marked increase in physician stress levels.

Economic factors were assessed by responders as most stressful. 77 % of the participants defined their strength of impact as ''strong". Most numerous but in second place by strength of impact defined as ''strong''- 61% of respondents, are the organizational factors, followed by the other two groups.

Factors, included in these four groups are predominantly determined by the organization of the health care system, i.e. they do not have causal relation with doctors' personality.

Considering these results we have good reason to state that the main reasons for BOS occurrence in GPs evolve in the main from the type of organization of the health care system defined by politicians not from the doctors' personality type. And the most successive way to cope with the BOS in the profession is to improve the health care system first.

DOCTORS' CAREER IN GENERAL PRACTICE: RESULTS FROM AN EMPIRICAL STUDY

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Background: Human resources in health care are central to the achievement of health objectives. Unfortunately, often they are seen as a constant burden instead of a capital asset and a future investment.

Primary care is the foundation of any Public health care system. At the level of Primary health care is where it is possible to use the limited financial resources in the most effective way to achieve better results in protection and improvement of human health. Our attention to human resources in the Bulgarian healthcare system is focused on doctors in general practice in view of the fact that the general practitioner (GP) is a key figure in the health system.

The Purpose of this work is to study characteristics of general practitioners as workforce and to investigate their careers' paths in order to identify factors and barriers that promote opportunities in career of general practice.

Materials and methods: Empirical comprehensive study was conducted – structured interview with 235 GPs from the region of Stara Zagora, Bulgaria for the period of July - December 2012. The interview was devoted to the career development in the general medical practice. In this material we present part of the results, directly related to the goal pointed above. The interview questionnaire was developed by the authors of the study.

Other source of information is the official database of the National Health Insurance Fund, Stara Zagora branch office.

Results: The largest number of GPs are aged between 45 and 54 years. Women predominate, and in the age group of over 54 years female GPs are three times more than the male. In the study area there is only one doctor in the age group under 35 years. The obtained results also demonstrate the characteristics of the medical practices. Most practices are concentrated in big town and villages; the practices are mainly solo-practice. Almost 50% of the solo-practices contain between 700 and 1500 people in their patient list.

The group practices are 3.5% of all practices. They are concentrated in cities and are mainly of two doctors. The average number of patients in a group practice is 3694.

Other aspects of the medical practices are also discussed in the interviews such as preferences for commercial registration (either as Limited Liability Company or sole trader), working place conditions and occupational safety and health.

In the interview doctors described their careers' paths and their motivation for career development. Many of GPs shared that they have met obstacles and barriers to their career development - specialization and continuing education.

Conclusions: The prospects for professional career of today's General Practitioners influence the future of this profession group. Presented age and sex structures focuse on policy decisions and activities with an especially concerning on

women and young doctors. The problem of the career is particularly acute for young doctors.
This in-depth study in all aspects in doctors' career development can serve as effective policies for professional growth and initiation of actions to promote career opportunities in general practice: urgent measures that could make work in general practice more attractive and satisfying.

Keywords: general practitioners, human resources, professional career, interview

THE CLINICAL PATHWAYS – BUREAUCRATIC "HIGHWAYS" OF INEFFECTIVE HEALTH FUNDING

Dr. Stefan Konstantinov, obstetrician – gynecologist, master of public health and health management, ex Minister of Health of Bulgaria

The presentation is a critical analysis of the use of clinical pathways in Bulgaria that came with the creation of the National Health Insurance Fund (NHIF). According to the official definition of the Ministry of Health "clinical pathway" is a set of requirements and guidelines for the conduct of different medical specialists in diagnostic and therapeutic procedures for patients with certain illnesses requiring hospitalization". Since 2001 when their introduction in practice began until 2013 however, clinical pathways have become the primary method of financing hospital health care in Bulgaria. Their structure has changed. From guidelines and management tool for assessment of quality they turned into a system of requirements to contract with NHIF and prices of groups of diseases giving impact on the development of the whole health care.

Usage of the clinical pathways is accompanied by an overall increase in hospitalizations, and the price of each of them is a positive or a negative incentive to development of different hospital sectors. Pricing of clinical pathways is not based on any estimates of the cost of delivered services of medical institutions and is subject of conjunctures reasons and lobbying. As clinical pathways do not take account of the severity of disease and the presence concomitant pathology, their use as a method of financing encourages hospitals to treat mild and fast recovering conditions. The attempt to ensure quality by requiring hospitals to perform a number of tests, procedures, and imposing a minimal hospital stay for the patient bureaucratized the medical activity and their use for the payment of hospitals has become one of the main causes of inefficient and non-transparent spending in Health. Clinical pathways are associated with distortion of medical statistics and formalization of treatment, which has negative consequences for patients and contributes to their low satisfaction with health care in Bulgaria. The author draws conclusions and recommendations necessary for future hospital management in Bulgaria.

РЕГИОНАЛНИ ПРОБЛЕМИ И НЕРАВЕНСТВА В БЪЛГАРСКОТО ЗДРАВЕОПАЗВАНЕ

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В настоящата презентация са разгледани съществуващите неравенства в системата на болничното здравеопазване в България, които са причина за силното компрометиране на солидарния здравно осигурителен модел и препятстват достигането на целите на здравеопазването.

Изследвания и проучвания на общественото мнение показват, че независимо от увеличаване на използваните средства за здравеопазване в последните десетина години, все по-голяма част от пациентите не получават необходимата им медицинска помощ, а част от тях загиват поради затруднен достъп до лечение. Създава се усещането, че е нарушен общественият договор в здравеопазването, който регламентира както задължения за гражданите (да плащат осигурителните си вноски), така и задължения за държавата и публичните институции (да осигурят качествена здравна помощ на всеки нуждаещ се, независимо от местоживеенето му).

Налице са тежки териториални диспропорции в разходването на публични средства за болнична помощ, несъответни на здравните потребности на населението. В резултат на различната обезпеченост с лечебни заведения и с медицински специалисти, както и на остарели методи за регистрация и отчитане, се стигна до сериозно изкривяване на медицинската статистика и фрапиращи разлики в заболеваемостта от определени заболявания и в някои други здравни показатели за отделните региони или в различни години за един и същи регион.

Поради неравнопоставеност по отношение на финансирането и въвеждането на свръхзавишени и ресурсно необезпечени изисквания към малките лечебни заведения за болнична помощ, в рамките на последните 3-4 години редица клинични структури, а на места и цели болници преустановиха дейността си. Това на практика предпостави проявата на дискриминация спрямо около 2,4 милиона български граждани, живеещи в периферните райони, които потребяват болнична помощ в пъти по-малко от средната за страната. Очевидно действащите към момента медицински стандарти не са средство за постигане и поддържане на качество, а инструмент за осъществяване на болничното преструктуриране (ликвидиране на малките болници). Използваната методика на НЗОК за формирането на лимитите или така наречените задължителни прогнозни стойности на разходите, допълнително задълбочи съществуващите неравенства.

Голяма част от функциите на съсловните организации по защитата на професионалните права и интереси на медиците и саморегулацията на медицинската професия бяха отнети с нормативни промени, а друга част се реализират формално поради организационни и вътрешносъсловни проблеми. Контролът над медицинската практика, участието в ценообразуването на здравните услуги, договарянето с финансиращите органи и с правителството, контролът на нормите на медицинската етика и други присъщи на съсловните

организации ангажименти се изпълняват формално. Това е допълнителна предпоставка за задълбочаване на неравенствата и дискриминацията на здравно осигурените български граждани по отношение на достъпа до болнична помощ на географски и социален признак.

В презентацията са представени данни за нееднаквия относителен дял на средствата за болнична помощ, които се разходват на глава от населението в отделните административни области спрямо средния за страната. Представена е и таблица, показваща тенденциите към задълбочаване на неравенствата по отношение на достъпа до публичен ресурс за болнична помощ.

За илюстрация на глобалните негативни ефекти спрямо здравето на нацията са представени сравнителни данни за здравните показатели на България спрямо останалите европейски държави по т.н. Европейски пациентски индекс за 2009г. и 2012г., откъдето е видно, че България е на 33-то последно място и че здравните показатели показват тенденция към влошаване.

Представени са и данни за парциалната покупателна способност (ППС) в долари на разходите за здравеопазване в България и общо за Европейския съюз за периода 2005 – 2010г., откъдето е видно, че съвкупния здравен продукт, потребяван от едно лице в страната е над 3 пъти по-малък от средния за Европейския съюз. Посочени са още 3 много неблагоприятни момента.

Първо - разликата в стойностите на ППС$ в годините нараства. Докато България за 5 години е успяла да добави 228$, то Европейския съюз добавя цели 732$.

Второ – налице са противоположни тенденции по отношение на държавните разходи за здравеопазване. Докато в Европейския съюз относителния дял на държавните разходи нараства с 1,28%, то в България те намаляват с цели 6,44%.

Трето – през 2010г. ППС$ в България намалява под нивото на 2008г.

Като се вземе предвид, че първите публикувани данни за ППС$ са към 1995г. и за Европейския съюз стойността е 1446.41 е съвсем очевидно, че България е на доста повече от 20 години разстояние след ЕС по отношение финансовата обезпеченост на здравеопазването.

В заключение се предлагат мерки за преодоляването на създадените неравенства, между които законодателни и други нормативни промени за гарантиране на равнопоставеност на лечебните заведения за болнична помощ по отношение финансирането, вкл. на спешната медицинска помощ и интензивното лечение; регламентиране на ясни правила и процедури за изработването и утвърждаването на медицинските стандарти (*стандарт за писане на стандарти*), ресурсно обвързване на изискванията в съответните стандарти и постигане на общо съгласие по базовите изисквания на отделните специалности с оглед гарантиране интегритета на системата; възстановяване на принципите на реално договаряне с финансиращите фондове (вкл. НЗОК) на цените и обемите на медицинската дейност; въвеждане на буферни механизми за преодоляване на значителни териториални диспропорции в потреблението на медицинска помощ и др.

LEADERSHIP - AN UNDERVALUED RESOURCE OF THE HEALTH REFORM

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Modern healthcare reform necessarily require the creation of a new organizational culture, which in turn would cause effective leaders of change. From a strategic management perspective leadership is crucial for the success of health reform. The leader is the one competent, respectful and responsible warranty gives motion to the general strategic direction of any change in the health system. The role of the leader is to guarantee to overcome chaos and spontaneous changes to the implementation of targeted, well-informed and well-prepared changes. Therefore the need for a new type of health system leaders is very relevant.

The mentioned need is particularly clearly illustrated in the process of health reform in Bulgaria. This reform, which started in 2000, has not been finalized, as occurs very controversial and faces many difficulties.

One of the main problems and reasons for the failure of health care reform that is deficit of real leaders in the health system at various levels. Shortage of effective leaders correlates with lack of good teamwork in the process of health policy and strategic management of health care. In particular, the shortage of effective leadership and teamwork is currently severe barrier to the functioning and development of the professional organization of the Bulgarian physicians (Bulgarian Medical Association - BMA). The report authors justify the idea that the professional organization of the physicians should be adequate place and "nest" for the growth of the leaders of the national health system - but not false leaders with bureaucratic attitude and a real highly effective leaders of the new organizational culture and successful change in health care.

JUSTICE AND EFFECTIVENESS OF THE FUNDING OF THE HOSPITALS.

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The funding of hospitals, which takes up 60% of the total financial resource for health, warrants the attention of politicians, the medical profession and society as a whole.

The ever increasing costs of hospitals raise primarily two questions – to what extent the funds are distributed fairly, i.e. accessibility to adequate and quality care for every citizen is guaranteed and to what extent the funds are spent efficiently i.e. results meet expectations. In the search for an answer to these questions the financial macroframe of hospital care in the last five years is reviewed, as well as the distribution of insurance payments by NHIF.Data are presented on the structure of the hospital sector, territorial distribution, financial condition and operations of hospitals. Specifically reviewed are hospitalizations, which are currently an unregulated process, and sometimes lead to many negative consequences such as ‘induced needs’ and "cream-skimming".

Reviewed are the health and demographic results that are negative for our country compared with the EU countries.
It is concluded that the funding of hospitals in our country is neither effective nor fair. Indicated are possible approaches and impact measures directed towards a better result.
Key words: hospitals, funding, justice, results inequality, hospitalizations, regulatory process, regulated market.

THE ROLE OF MEDICAL ASSOCIATION IN PROFESSIONAL AUTONOMY

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All physicians with the authorization for medical work in Slovenia must be members of the Medical chamber (MC). Indeed the Ministry of health (MH) empowered MC to regulate and continuously implement statutory control of the medical profession. Because of this hierarchical relationship MC is at least a little politically influenced by the government.

The role of the Slovenian Medical Association (SMA) is on the contrary based on the voluntary membership. It was founded by 13 regional Medical societies from all Slovenian regions. According to the Statute it is organized in the manner of the political bicameralism with the representation of regional societies in one board (Main board) and almost 80 professional associations and sections in the other(Main panel of experts).All the medical specialties are voluntarily connected with appropriate international professional associations. Basic medical specialties like internal medicine, surgery, paediatrics, etc. have established Joint Councils of Experts (JCE) among their sections. These JCEs take decisions about professional guidelines, recommendations, national programmes of education, curricula for specialization, etc. They take into account exclusively international standards and current scientific data without any political influence from the politicians, government, lobbies, etc. They provide total professional autonomy; do not respond to the pressure of the financiers and political cost-effectiveness. JCEs offer the government scientifically-based guidelines and recommendations representing total autonomy of the profession from health policy.

EVIDENCE BASED COSTING OF PALLIATIVE CARE – THE PRINCIPLES OF CALCULATION

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The population of every Country hypothetically can be divided into three main groups: “Healthy People”, “Potentially Curable Patients” and “Advanced Chronic Patients”. Taking into account the above-mentioned groups, obviously, the health care system must also have three principal directions: Preventive (directed at healthy people), intending to maintain the health status and decrease morbidity; Curative (for potentially curable patients), directed at the patient convalescence and rehabilitation and Palliative (for Advanced Chronic Patients), intending to maintain the maximally available quality of life.

If any of the listed directions is omitted, the health care system can not be considered as perfect, for in this case, the corresponding part of the society turns out to be deprived of health care service. Therefore, Palliative Care is gradually becoming the integrated part of National Health Care System in many Countries.

Comprehensive Palliative Care represents the very tool to relieve pain and different distressing symptoms (nausea, vomiting, cachexia, bedsores and pressure ulcers, constipation or diarrhea, etc) and achieve maximal comfort. It enables the advanced patient to make the rest of his life biologically and socially active, encompassing him by the atmosphere of not only medical but also the social and spiritual support.

In 1996, the World Health Organization introduced several measures required as the foundation for developing palliative care through public health approach. Development of the services and financing were among the key issues.

According to the conventionally accepted idea, the palliative care in the end-of-life costs significantly less than the active “treatment” of these patients. Herewith, the costing of palliative care is not as standardized as e.g. surgical procedures or interventional therapy. The costing of palliative care is now being done in many countries of Europe.

The costing of palliative care in Georgia was performed by the initiative group. The project was funded by “Open Society Georgia Foundation”.

The following were determined:

1. The required capacity for implementing palliative care (number of beneficiaries; human resources; number of beds; number of mobile teams providing home care)
2. The types and the volume of services of palliative care;
3. Costing of the services;

The measurement methods by Higginson, McNamara, Van der Velde, Lynch, Gomez, Stjernsward, Higginson and others, also the recommendations developed by WHO, IAHPC for implementing such measurements were applied.

It was established, that Georgia has:

- Up to 30 000 patients needing palliative care annually;
- Up to 500 cancer patients requiring everyday palliative care;
- The need of around 240 beds to provide inpatient palliative care
- The need of up to 100 multidisciplinary mobile team to implement home-based palliative care, each team consisting of 1 physician, 3 nurses, 0.5 social worker and 0.5 psychologist (considering that traditionally, the role of caregivers is taken by family members and relatives in Georgia);

- The number of home visits of mobile team members counts up to 18;
- The expenditure per patient per month counts up to around 310 GEL (~ 140 EUR);
- The average cost of one visit counts up to 17 GEL (~ 8 EUR) - including the staff salary, medications, medical items, transportation, electrocommunication, administrative and other unintended expenses, etc;
- The cost of one hospital bed day in inpatient palliative care setting counts up to 87 GEL (~ 40 EUR) – including the staff salary, medications, medical items, diagnostics, electrocommunication, communal, meal, administrative, amortization and reinvestment expenses, etc.

THE LEADING ROLE OF PROFESSIONAL MEDICAL SELF-GOVERNANCE IN THE MANAGEMENT OF PUBLIC HEALTH SYSTEMS

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Today we are witnessing attempts to monopolize of many governments in the managing of public health systems. Governments unilaterally canceled certain powers of independent corporate organizations of professionals working in this systems. Therefore, the question of balanced and progressive the management of public health system is extremely important.

In our opinion for the best health of citizens, and hence for the security of the state, equal and mutually must be all players of public health system, as a public authority and all citizens (consumers of health services) and professionals who working in the system (physicians, pharmacists, nurses). More than a century of international experience indicates, that by the professionals in the management of public health system must be submitted their own corporate professional organizations, endowed with the functions of the professional self-governance. Professional self-governance in a legal context is viewed as the provided by law system of regulation of relations between all members of a certain profession, designed to consolidate the efforts of representatives of a profession in its relations with the government, the society and each other. That is, as a rule, the special law give the management powers of system to the successful operation of a profession for the benefit of society. Professional self-governance realized through their own representative organizations, based on the principles of decentralization, and which is under the supervision of the state. This organization, in case if there is a law that regulates its activity, in the legal sense is an organization of public law.

That is why in the public health system, if the purpose of its existence is the interests of society and every citizen, it is important to manage this system it on partnership principles. On one side are government bodies and local authorities (ministry, department or the appropriate department in the region), on the other side this is corporate professional medical association. This organization is concerned by all problems with relating to direct activities of physicians, their interaction with government agencies and patients, to perform the function of consolidating between all players of the public health system.

Institutions of medical self-governance, in one form or another, exist in all developed countries and in most countries of the "third world". In almost all the countries of Europe organization of medical self-governance it is a organizations of public law and therefore their activity is regulated by legislation passed by Parliaments in these countries. Importance and necessity of introducing of medical self-governance as a prerequisite for the independence of the medical profession and optimal functioning of public health systems in each of the countries indicated in the many declarations, resolutions and statements of leading world medical organizations: WMA, SEEMF, EFMA/WHO, WFUMA, CPME, ZEVA etc.

It should be noted that recommendations of Council of Europe offered by national governments indicate to them create favorable conditions in the legal and tax systems for financing and activities of non-government health organizations, and government budget of health care as possible should include an article for the support of such organizations.

On the way to organize of medical self-governance today has become most post-Soviet countries, where state organs have total control's in health systems, and therefore these systems are very weak. However, government bureaucracy most of these countries still have many signs of totalitarism and the desire of monopoly control.

Out the described of above, historical and ours experience, we can draw the following conclusions:

- the medical profession has full historical right to be free profession,
- professional medical self-governance is the best form of association of doctors for the best execution of the mission entrusted to the medical profession,
- medical self-governance is the best form of relations between professionals who work in health care, and other participants in the system - government agencies and patients,
- medical self-governance that eliminates the monopoly managements in the system, becomes a condition as the best development of public health system,
- the existence of medical self-governance gives doctors the legal ability to take on additional responsibilities relating to moral and ethical spheres of their activity,
- public health systems, who including the effective medical self-governance, proved to be much more efficient than a system where it is absent,
- safety and quality of health of citizens has a direct correlation with effective medical self-governance,
- activity medical self-governance ensure for physicians the most effective professional development, legal and social protection, moral and professional support,
- integration of national medical associations in joint interstate and international organizations, enable more effective protection of the medical profession and produced an effective common policy on approval medical self-governance in each individual country,
- intervention of government agencies in medical self-governance is unacceptable both from a legal signs, and through the consequences of an extremely negative influence of such interventions on the functioning of the public health system and the safety and health of all citizens.

We trust that leading role of professional medical self-governance in the management of public health systems has a new perspective and further positive development for the benefit of our citizens, physicians and countries.

KAZAKHSTAN PHYSICIANS AGAINST THE METHADONE PROGRAM

Sadykova A.B., President of the National Medical Association

In 2013 there are ten years since that moment as in Kazakhstan serious attempts to legalize of narcotic “methadone” were undertaken in the framework of the implementation of substitution therapy for drug addiction. Substantiate it is plausible purpose - to fight HIV/AIDS epidemic.

Methadone is a synthetic drug, which is recommended to take by lobbyists of the program. In the framework of the pilot program methadone is purchased at the expense of state budget.

Now opioid substitution therapy introduction occurs simultaneously in all the countries of the world. In some countries of the former USSR and Central Asia the implementation of this program started at the beginning of 2000s and has a uniform pattern.

Synthetic drug methadone was developed in Germany in 1937 at the initiative of the American pharmaceutical company Eli Lilly, which owned the patent for its production and which imported it to the USA in 1947, getting permission of USA Food and Drugs Administration (FDA). Eli Lilly is the biggest corporation of the production of the strong psychotropic preparations.

Since the late 90-ies in Kazakhstan and in neighboring Central Asian countries, the introduction of a programme for the prevention of HIV/AIDS begins. The introduction begins with the fact that countries are encouraged to use a special therapy, recommended by the WHO (World Health Organization). The recommendation has incorrect information, the patient may have a normal life, constantly taking these drugs in their lifetime.

In 1997, Soros Foundation (a public name of the Institute «Open Society», founded in the USA by the financier George Soros, is associated with scandals about the legalization of drugs), UNAIDS (joint United Nations programme on HIV/AIDS) and several other areas of the UN allocate money through a number of public and state organizations of Kazakhstan on prevention of AIDS. Work on prevention is aimed at the following groups: injecting drug users, sex workers, men who have sex with men.

Instead of searching for cause-and-effect relations and solutions to the existing problems, these groups are strongly supported under the guise of AIDS prevention.

In 2001 the new idea for the prevention of HIV/AIDS introduced. It is recommended that drug users take the drug orally (that is, through the mouth). For this we introduce the notion of an opioid substitution therapy (OST). Drug users, who use injected opioid drugs (opium, heroin and other drugs produced from poppies themselves), are recommended to take a synthetic drug methadone, which must be issued to them free of charge in units of issue. This non humane program was the first step towards legalization of drugs and the maintenance of drug addiction at the expense of the state.

WHO has issued the instruction, that this method of treatment is safe and the most effective, and through other organizations makes the UN member countries to implement the program. The essence of the program is the first of its implementation provide the United Nations funds, and later should provide the state. WHO begins to publish the statistics, indicating the widespread AIDS epidemic, especially in the countries of the former USSR and recommends that the OST is an effective method of treatment. Lobbyists of the methadone program often refer to WHO reports.

The Global Fund to Fight AIDS, Tuberculosis and Malaria (GF) was established by UN in Kazakhstan in 2002, and it is the main sponsor of HIV prevention among the risk groups mentioned: RIN, RS, MSM. In 2003, GF provided Kazakhstan with the first disbursement of USD 6,502,000 to be spent during two years. The disbursements are made through 'Republican Center for Prevention and Fight Against AIDS' established by the Ministry of Health of the Republic of Kazakhstan. Currently, USD 120,130,475 have been paid to Kazakhstan. Officially, these funds are received by the Ministry of Health of the Republic of Kazakhstan. GF provides similar funds to other countries: USD 349,167,952 have been paid to Ukraine (as for introduction of methadone program, Ukraine is now a leader among former Soviet republics), and USD 95,946,952 have been paid to Kyrgyzstan. In Russia, the methadone program is prohibited by Government.

Introduction of methadone program was not fluent in Kazakhstan. In 2003, 'Narconon' Public Organization engaged in rehabilitation of drug addicts started to resist the program, and was supported by some governmental officials, physicians of the Ministry of Health, and police officers. 'National Medical Association' Republican Public Association, takes active part in opposing introduction of methadone program.
On December 8, 2005, resolution No. 609 of the Ministry of Health of the Republic of Kazakhstan 'About introduction of maintenance therapy' was issued. In fact, it was the first official resolution introducing the program, at first, as a pilot project, and then, if it is successful, as routine practice.

Due to opposition from a number of governmental officials and public organizations, the program was not actively introduced. As a result, new public organizations were established to promote the program. For example, in 2006, World Bank established the Central Asian Regional AIDS Fund. The fund includes a coordinating committee consisting of officials of ministries and members of public organizations.

Methadone program lobbyists issue new reports of WHO and UNODC and other 'respectable' organizations stating that methadone maintenance therapy is successfully introduced in such countries as the Czech Republic, Lithuania, and Poland.

Alternatively, religious organizations are involved to prepare Moslem coaches for prevention of AIDS. Such conferences and seminars are held under the support of UN and the Central Asian Regional AIDS Fund.

I n October 2008, the Central Asian Regional AIDS Fund launched pilot projects in Pavlodar, Temirtau, and later, in Ust-Kamenogorsk. 25 patients were chosen in each of these cities. Methadone is given by narcological dispensaries controlled by the Ministry of Health.

In 2010, 'National Medical Association' RPA applied to the Ministry of Health of the Republic of Kazakhstan for establishment of a committee for independent assessment of

results of introduction of pilot project. Such committee was established, and produced negative conclusion on the program, and claimed that it was a false treatment method aimed at promotion of methadone abuse in our country.

In addition, independent experts (narcologists and psychiatrists) state that patients being treated become more dependent on daily dosage of methadone, and they show outbursts of aggression and suicidal thoughts, and 60 % of methadone consumers become impotent, and 75 % of women have affected or absent menstrual cycles. In addition, introduction of the program is accompanied by strong violations of legislation of the Republic of Kazakhstan regulating narcotic substance circulation.

However, lobbying of the program is increasing.In November 2010, Civil Committee on Human Rights (CCHR, public non-commercial organization) started to work in Kazakhstan, and was involved in fight against introduction of methadone maintenance therapy. CCHR involved the public, mass media, and public organizations in its activities, and held some public actions. The fighters against methadone maintenance therapy program were supported by a number of governmental officials, orthodox Church activists, Moslem leaders, youth organizations and common people. Every week, people send letters to President of the Republic of Kazakhstan (sometimes, up to 100 letters per week), and every month a few conferences and actions are held, and overall reviews are prepared for governmental bodies, and regular articles are published in mass media.

In November 2010, 'National Medical Association' RPA, on behalf of physicians, narcologists and psychiatrists sent an open letter to President of the Republic of Kazakhstan against introduction of methadone maintenance therapy program. The letter was signed by 293 physicians from various cities of Kazakhstan. Then, this movement involved more and more medical officers. Currently, the declaration against methadone program was signed by more than 500 people.

US Embassy is ready to take any measures to introduce methadone program in Kazakhstan. It wrote a threatening letter to the Minister of Health.

"I strongly urge you to expand medication assisted therapy activities. Reversal of the initial decision to scale–up medication assisted therapy activities in Kazakhstan will have considerable public health consequences for the citizens of Kazakhstan and will endanger the approval of any future grants from the Global Fund."

The letter may be very interesting for Government of Kazakhstan from the viewpoint of state sovereignty. Intervention, i.e. interference of one state in internal affairs of the other state with violation of rights of the latter is prohibited by a number of international legal acts including UN Charter.

As a whole, in Kazakhstan, methadone maintenance therapy and other programs against HIV/AIDS are lobbied by at least 80 organizations. Main international organizations lobbying and funding these lobbying efforts include GF, UNAIDS, UNODC, USAID (United States Agency for International Development), World Bank, WHO, Soros Foundation. The total amount provided under all these programs was at least USD 500 million.

Non-governmental organizations may and must support the closing of the methadone program.

In 2011, at least, in two former Soviet republics, methadone maintenance therapy programs were almost stopped due to fierce resistance and lobbying by anti-methadone

maintenance therapy groups. In Kazakhstan, in response to government's plans to extend the methadone maintenance therapy to more patients, a group of medical officers launched a campaign against methadone maintenance therapy and requested to close the program. One of key figures standing behind the campaign was chief medical officer of a narcological clinic treating drug addicts by complete abstinence from any drugs.

The plans of extension of the program in Kazakhstan were frozen. In Kyrgyzstan, Administration of President received about 30 letters against methadone maintenance therapy, and many of these turned out to be false. Then, in October 2011, a popular Kyrgyz film-maker shot documentary film titled 'Trap' against methadone maintenance therapy.

'National Medical Association' RPA calls to international medical community for protection, and:

1. Stopping introduction of methadone maintenance therapy in both Kazakhstan, and all over the world because it is a false treatment.
2. Suspension of the activities of the organizations lobbying introduction of methadone maintenance therapy in the territories of countries.
3. Elaboration of efficient measures against drug dealing and abuse.
4. Introduction of efficient measures of drug abuse prevention.
5. Introduction of efficient medical and social programs of treatment, and social and psychological rehabilitation of drug addicts.

AUTOREGULATION (SELF-REGULATION) IN HEALTH CARE SYSTEM AND WORK OF DOCTORS IN MACEDONIA

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Autoregulation in the country can be connected with the reestablishment of the Doctors Chamber of Macedonia in 1992. The initiative to restore the Chamber came from the Macedonian Medical Association, the only association of physicians of Macedonia then. The beginnings of the formation of the new Chamber went along with the disintegration of the former Yugoslavia and the establishment of Macedonia as an independent state, and were also a result of demographic changes and in accordance with the new Health Care Law passed on November 7, 1995.

It took eight years, Doctors Chamber to get the first public authorization as introducing of Powers to license and passing a Medical exam, on February 24, 2004. In 2011 was made the first extension of licenses (Powers of licence) of all doctors.

With the upgraded Health Care Law, Doctors Chamber of Macedonia Chamber on January 17, 2013 gets new public-oversight authority over the professional work of healthcare facilities and other institutions that provide health care and health care workers and associates. This authorization was given to the Chamber in order to provide control of professional work, implementation of professional guidelines assessment as well as assessment of the conditions and manner of provision of health care.

Under the Law, professional associations within the Macedonian Medical Association, organized various forms of professional training of health workers,

participate in drafting guidelines for professional work in certain specialties and suggest measures for improving the professional work of health professionals.

However, lately, probably as a result of retrograde movements in the area of self-regulation in the world, such movements are observed in Macedonia, as well. They consider especially the internal organization of the Medical Chamber, which with the new Act (Health Care Law) is treated almost as a state institution; changes in the CME with which the state takes over part of the credentials of the professional associations, and amazing short period of the public powers and the possibility these to be taken off by the Minister of health etc.

Concerning Macedonian Medical Association, lately there are attempts from Health Insurance fund and MOH to interfere, unauthorized and opposition to the Law, in the process of KME. Macedonian Medical Association opposed very strong to this attitude, and for the time being good positive result.

HEALTH PROFESSIONALS SELF-GOVERNMENT AS THE BASIS OF PUBLIC HEALTH IN UKRAINE

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The critical state of the public health and medical care system in Ukraine is known to all and in fact is recognized by the government. It is also known that though de jure and de facto the centre of decision-making in Ukraine is at the state level, the lion's share of health care services is provided at the regional and local levels, and the role of the public sector in health care is not legally defined. Since 2012 on the basis of a special law a pilot project to reform the system of health care is carried out in the Donetsk, Dnipropetrovs’k, Vinnitsa oblasts and Kyiv. This year the reform process started all over the country and has encountered significant defects that include among others excessive centralization, corruption mechanisms for licensing and accreditation and administrative dependence of most doctors, lack of freedom of professional organizations.

Despite the long-term preparation and learning neighbours experience, particularly in Poland and Russia, the reform implementation is extremely difficult and many issues are facing rejection of the population and physicians. There are many mass protests, a wave of discontent filled the Internet. the Ministry of Health and local authorities is Responsible for the implementation of these reforms. However, so far they are not capable to responsibly and effectively solve the problems.

The health care system that was established in the Soviet era today is totally inadequate, incapable and inefficient. Today’s health care system in Ukraine is a growing threat to social and economic development of the state and its security, and violates the fundamental right of citizens - the right to health care. However, only the administrative reform of health care without the simultaneous development of civil society institutions that are directly involved in the health care, the effective public health system is not achievable. A key component of public health care is the health professionals' self-governing. The physician is a central figure in the any health system. Unfortunately, in Ukraine, the doctors are actually removed from the development of health care policy

and the decision-making. We need to strengthen both the medical organizations and their positions in the reform on the European (democratic) principles, according to EU-Ukraine Association Agenda.

There are about 190,000 physicians in Ukraine. Their rights to a proper income, opportunities for professional growth are neglected and the vast majority of them are pushed into the shadow economy and a priori accused of corruption. In many ways the doctors themselves belong to vulnerable groups. The economic rights of doctors are not protected despite their formal membership in trade unions. An average physician's salary is 50% lower than the average in Ukraine on the whole. The level of self-organization of physicians is low. Less than 10% of physicians are members of national medical organizations (UMA). The law about medical self-government is blocked over a decade; despite that, it is a fundamental need for Ukrainian doctors. The physician is the central persona in public health therefore other health professionals- may follow the example of physicians in protecting their rights. The poor and deprived of rights physician is the main threat to the patient. Medical ethic, implementation of best professional practices, continuous training, and professional honour are the main components of prevention of the medical errors, professional negligence and wrongs. Because of that, the development of medical associations and the professional self-government are in the interests of patients.

Over the last decade, our association performed or participated in several national projects. All these projects meet the basic objective of the European strategy of "Health for All in the 21st Century", approved by the European Regional Committee of WHO. We will be continue our research and analytical activities. Now the actual research aims for our association are:

- determine public opinion on important aspects of health care reform using public survey, focus groups or surveys with in-depth interviews.
- conducting the analytical studies on: (a) national and regional policies in the organization of medical care; (b) medical services market and health insurance; (c) rights and interests of the patient and the doctor.
- studying the experience of professional self-governments of physicians in Europe.

We will also continue the monitoring of the activities of deputies of Verhovna Rada and officials of the Ministry of Health, deploying "positive pressure", preparing the requests and suggestions to the government to correct the process of reform of health care and lobbying for the enactment of the medical self-government.

The creation of UMA teaching centres in regions (west, centre, east and south) for training of the activists of the regional associations of physicians; preparing for the introduction of self-government, the introduction of remote consultation and training leaders of regional and local physicians communities are target goals for us.

Strengthening the capability, technical and political skills of self-governing doctor's organizations is crucial for the promotion of accountability, integrity and transparency of the public health care system on the national and regional levels. UMA is sufficiently prepared to move to another level of activity – performing functions of self-governing. This requires movement into two different levels: the revision and lobbying of the project "Physician's self-governing" (national and legislative levels) and the development of the regional associations and their branches in the rural and remote

regions, especially in the Eastern part of Ukraine, some southern and central regions (regional and institutional levels). The experience of the most active UMA organizations in Lviv, Odessa and Kiev are very important for this process. We expect close cooperation between doctor's, patient's and other organizations that are dealing with health care and creations (with the initiative and participation of the doctor's organizations) the regional associations or coalitions of the health care. The utmost goal of such associations will be reconciling the interests of different groups and more effective control on the implementations of the reforms.

European experience, the experience of Ukrainian Diaspora physicians, exchange of experience between doctors from different regions of Ukraine will encourage the activity of medical community to overcome passivity and exclusion of doctors from social processes. The collaboration with the World Federation of Ukrainian Medical Associations, uniting Ukrainian doctors from 14 countries and South-East European Medical Forum, which brings together 17 national medical organizations, including Ukraine is very important for our development.

Our aims are essential for strengthening and expanding the geography and impact of the health professional organizations, their collaboration with other civil society groups and patients organizations, including them in the process of health care reform, increasing their influence through the creation of the regional coalitions and lobbying the legislature self-government of physicians.

РОЛЯ И ОТГОВОРНОСТИ НА БЪЛГАРСКАТА АСОЦИАЦИЯ НА ПРОФЕСИОНАЛИСТИТЕ ПО ЗДРАВНИ ГРИЖИ ЗА БЪДЕЩОТО РАЗВИТИЕ НА СИСТЕМАТА НА ЗДРАВЕОПАЗВАНЕ

М.А.Василева

Българска асоциация на професионалистите по здравни грижи, България

Увод: Българската асоциация на професионалистите по здравни грижи (БАПЗГ) е съсловната организация на медицинските сестри, акушерките и асоциираните медицински специалисти, създадена и регламентирана със закон, приет от Народното събрание на 03.06.2005г. Това я натоварва със сериозни очаквания от страна както на професионалистите по здравни грижи, така и от обществото като цяло. За да изпълнява своята роля в условия на финансова криза и сериозен недостиг на кадрови потенциал, Активът на БАПЗГ полага неимоверни усилия за издигане и утвърждаване на професиите, за активно представителство пред управленските органи на всички нива, където се вземат решения, да дава становища и предложения по важни законопроекти, касаещи здравеопазването, да повлиява здравните политики и да бъде гарант за високо качество на предоставените здравни грижи с основен фокус върху етичното професионално поведение и на безопасността на пациента. Основна цел на БАПЗГ е да представлява своите членове и да се грижи за професионалното им израстване, продължаващото обучение и социалния им статус. Важна задача на БАПЗГ е да убеди управляващите, че инвестициите в сестринството са печеливши и политиката на задържане на здравни специалисти в страната е от съществено значение за бъдещото развитие на здравеопазването.

Методи: Приложени са документален, анкетен и социологически методи. Направени са проучвания сред медицински сестри относно мнението им за ролята им в условията на съвременното здравеопазване и тяхната удовлетвореност. Представени са данни от проучвания чрез анкети на нагласите за миграция и анализ на получените резултати.

Резултати: Осъзнава се новата роля на професионалистите по здравни грижи както по отношение на здравето, така и по отношение на болестта. Днес все по-ясно става колко е важно участието ни в цялостния комплекс от здравни грижи и възприемането на пациента като биосоциално същество - с неговия бит, култура, етнос и религия. Разширените умения и компетенции са предпоставка за адекватен отговор на нуждите от здравни грижи на българските граждани, за професионална удовлетвореност, но и за повишени очаквания за добро заплащане и възможност за кариерно израстване. Хроничното недофинансиране на здравеопазването е основна причина за нагласа към миграция. В същото време новата реалност налага изисквания за по-висока квалификация, разработване на иновативни и интегрирани по-добри практики, справяне с нови задачи в мултифункционалния екип. Обществото очаква от нас да посрещнем предизвикателствата на Европейската стратегия „Здраве 2020“, въпреки неблагоприятните условия на професионалната ни среда.

Изводи: БАПЗГ е един от основните фактори в българското здравеопазване и ясно осъзнава своята ключова роля и отговорности за правилното му функциониране и развитие. Като изразител на позицията на професионалистите по здравни грижи, Асоциацията провежда научни форуми по здравни грижи и е катализатор на идеи за рентабилни, ефикасни и ефективни практики. Усъвършенстването на сестринския модел в болничната помощ и развитието на модела на здравни грижи по типа на интегрираните здравно-социални услуги ще доведат до сериозен напредък при предоставяне на здравни услуги и ще утвърдят значението на автономните функции на професионалистите по здравни грижи.

ФИНАНСИРОВАНИЕ И КАЧЕСТВО ОКАЗАНИЯ МЕДИЦИНСКОЙ ПОМОЩИ; НАУЧНЫЕ ОСНОВЫ ФОРМИРОВАНИЯ СОВРЕМЕННОЙ СТРАТЕГИИ РАЗВИТИЯ ЗДРАВООХРАНЕНИЯ

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Актуализация проблемы хронических неинфекционных заболеваний, являющаяся одной из новых угроз для мирового сообщества, приводит к повышению прогнозируемого риска увеличения глобального бремени болезней, медико-социальных и экономических потерь. Преодоление проблемы требует не только повышения доступности, качества и эффективности медицинской помощи путем совершенствования деятельности отрасли, но и решения всего спектра

социально-экономических проблем, усиления профилактики, формирования здорового образа жизни, улучшения качества жизни населения.

Методы исследования: библиографический, аналитический, статистический.

Результаты. Современные демографические процессы в Европейском регионе Всемирной организации здравоохранения характеризуются постарением, сокращением рождаемости, уменьшением общего коэффициента фертильности, а также снижением уровней общей, младенческой и материнской смертности, стабилизацией и определенным увеличением средней ожидаемой продолжительности жизни населения. На фоне территориальной дифференциации индикаторов здоровья в ряде стран наблюдается негативная динамика отдельных показателей.

В Европе 86% всех смертей и 77% бремени болезней вызваны хроническими болезнями, имеющими общие факторы риска. Почти 60% общего бремени болезней обуславливают 7 ведущих факторов: артериальная гипертензия, табакокурение, злоупотребление алкоголем, гиперхолестеринемия, избыточная масса тела, недостаточное потребление фруктов и овощей, гиподинамия.

В Украине, как и в других европейских странах, болезни системы кровообращения, злокачественные новообразования, хронические обструктивные болезни легких и др., значительно распространены и являются причиной повышения уровней заболеваемости, инвалидности и смертности населения. Их распространению способствуют курение, злоупотребление алкоголем, наркомания и другие факторы риска. Вызывают беспокойство преждевременная смертность мужчин трудоспособного возраста, отставание средней ожидаемой продолжительности жизни от среднеевропейского показателя на шесть, от показателя в странах Европейского Союза – на 10 лет, сохранение естественной убыли населения (-3,5 на 1000). Рост демографических потерь, весомые экономические убытки, обусловленные неблагоприятной медико-демографической ситуацией, создают реальную угрозу национальным интересам государства, что требует разработки и реализации новых стратегий здравоохранения.

С учетом международного опыта, основных положений новой европейской политики в сфере здравоохранения, в Украине в 2011 г. была утверждена Концепция государственной программы «Здоровье-2020: украинское измерение», а в 2012 г. разработан ее проект. Стратегические ориентиры Программы нацеливают на сохранение и укрепление здоровья, профилактику заболеваний, снижение заболеваемости, инвалидности и смертности, повышение доступности, качества и эффективности медицинской помощи, обеспечение социальной справедливости и защиты прав граждан на охрану здоровья.

Выводы. В Украине, как и других странах Европейского региона наблюдается актуализация проблемы хронической патологии, что приводит к повышению прогнозируемого риска увеличения глобального бремени болезней, медико-социальных и экономических потерь.

Реализация Государственной программы «Здоровье-2020: украинское измерение» обеспечит сокращение распространенности хронических болезней,

что будет способствовать улучшению здоровья, увеличению трудовых ресурсов и экономического потенциала страны, повышению качества жизни населения.

REPRESENTATION OF ETHICS IN MEDICAL EDUCATION

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Introduction: The word "doctor" means 'to teach: A teacher is someone acknowledged as a guide or helper in processes of learning. Teaching is a necessary professional attribute for doctors. The General Medical Council (GMC), stated in its 2010 version of the document Good Medical Practice that all doctors should be willing to contribute to teachingand those doctors involved in teaching should adopt the skills, attitudes and practices of a good teacher. Commitment to ongoing education is one of the principles of professionalism which are specific to family medicine.

Object: The aim of this presentation is to discuss the challenges, clues and future projections of ethics education for general practitioner/family physicians through different aspects of the matter.

Methods: This is a literature review about medical ethics education in general practice/family medicine from past to the future.

Results: As medical educators family physicians have a lot of responsibilities such as being a information provider in the clinical context, being a role model on the job and being a resident assessor etc. Besides, medical ethics education in family medicine needs some different dimensions beginning from self awareness to analytical approach to obligations and law.

Conclusions: We can begin to teach residents about what the term "profession" means.

With our professional role modeling residents and students can see equity, clinical wisdom and ethical values in action.To teach and evaluate social part of the medicine like ethics and professionalism presents the most challenging part of education. Have notes the great conflict of the young physicians between humanistic values and dehumanizing features of the health care system.The profession we should have standards of education in ethics also.

Key words: Medical ethics, education, professionalism, general practice, family medicine, primary care

HOSPITAL AND HEALTHCARE IN STARA ZAGORA DEPARTMENT (DISTRICT) AFTER THE RUSSO-TURKISH WAR AND UP TO THE EARLY XXth CENTURY – EMERGING, ISSUES AND PERSPECTIVES

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Introduction: The Ottoman conquest of Bulgaria at the end of the XIVth century deprived Bulgarian ethnicity of high range structures such as: state, religious hierarchy, aristocracy and educated circles for a period of almost five centuries. The medieval aristocracy and the intellectual elite of the Second Bulgarian Empire were eradicated physically and morally. In this context, the basic level institutions (family, kinship, patriarchal community as well as some rudimentary institutional elements from the old system e.g. local churches and monasteries) assumed the functions of the destroyed structures.

The Ottoman governments issued almost no sanitary legislation or arrangements. As late as 3th of December 1852, the Ottoman authorities passed a special law for the establishment of a Sanitary Board, managing the health care in the empire. This date marked the beginning of the organized health care in the Ottoman Empire that encompassed up to 1878 also the Bulgarian lands. The same regulation put the basics of the local health administration – area doctors, paid by the state and city doctors, paid by the municipalities. The Sanitary Law of 1852, the Statutes of Bulgarian Exarchate from 1871 and the establishment of the first hospitals in the cities of Shumen, Ruse, Pleven, Veliko Tarnovo and Varna mark the beginning of hospital and healthcare on Bulgarian territories, included in the Ottoman Empire.

The Treaty of Berlin (1/13/ July 1878) altered significantly the status of the lands between the Balkan and the Rhodope Mountains that formed the autonomous Ottoman province of Eastern Rumelia. It was under the political and military power of the Sultan, but it had administrative autonomy. Stara Zagora Departement (District) was an important administrative and economical centre of this province after the Liberation. These special features predetermined the directions in the development of hospital and healthcare at Stara Zagora Departement (District) after the Russo-Turkish War.

The aim of the following study is to present a general picture of the health system in the Bulgarian lands before and after the Liberation. The study uses comprehensive documentary materials in order to do a thorough analysis of Eastern Rumelia (incl. Stara Zagora Dept.) administrative features and focuses on the conditions and problems, affecting the hospital and healthcare development in Stara Zagora Department (District) after the Russo-Turkish War in 1878 and up to the early XXth century.

Material and methods: The study surveys official historical documents from this period, among them *Organic Statute of Eastern Rumelia*, *Regional Collection of Laws in Eastern Rumelia since 1880*, *Summaries and Reports of Stara Zagora District Governors about the State of Stara Zagora District for the Period 1888-1908*, as well as recollections by contemporaries.

Results and conclusions: The comprehensive documentary materials allow to trace the social, economic, and political processes and to determine the significance of prominent individuals and charities after the Liberation that influenced the health system development in the department. This analysis supports the view that hospital and healthcare development in Stara Zagora Department (District) since 1878 up to the early XXth century was not a single step but a lasting process that resulted from continued efforts, directly dependent on economic conditions, maturity and medical experience of the Bulgarian society after Liberation.

Keywords: historical method, History of Medicine, hospitals, Stara Zagora Department (District), Bulgaria.

UNINTENDED PREGNANCY PREVENTION IN GENERAL PRACTICE: ATTITUDES OF GENERAL PRACTITIONERS WITH PRACTICES IN A BIG CITY

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Introduction: Unintended pregnancy is a serious reproductive health problem and clarifying the roles and responsibilities on the level of primary care and providing general practitioners (GPs) with state-of-the-art tools and training is important for solving this challenge. Preventive activities related to the reproductive health of women are a part of the multidirectional practice of the general practitioner (GP) from the start of the reform in primary healthcare in our country. Their legal regulation has undergone changes which we can generally summarize as facilitating access to specialized obstetric and gynecological medical care.

The aim of the following study is to present and discuss the place of GPs with practices in a big city according to the unintended pregnancy prevention as a part of activities for reproductive health prevention through studying their attitudes, behavior and motivations.

Materials and methods: A pilot study was conducted: an individual semi-structured interview with 25 general practitioners working in individual practices since the introduction of the institution of GP in the town of Stara Zagora: a regional and university center.

Results and discussion: The interviewed 25 GPs have the following characteristics in common: work as GP from the start of the reform; their practices are large, well-established, individual, in a big regional center; they have a specialty in general medicine, internal medicine or pediatrics. All GPs carry out the activities for prophylactic examination of women in full scope, as stated in the Program: according to Appendix 13 Prophylactic examinations of mandatory health insured persons above the age of 18, forming of risk groups among mandatory health insured persons above the age of 18. They express responsible behavior and engagement in conducting these activities. The majority of GPs (20) express the need of particular guidelines on

unintended pregnancy prevention in general practice and activities in this direction that to be a part of their work in the health insurance system. They discuss this problem from the viewpoint of their abilities to contribute to reproductive health, as standing the closest and knowing the needs of their patients the best that eases and contributes to an effective process of communication and consultation, which requires full trust in an especially delicate sphere of human life and relationships. The other 5 GPs express doubt about the usefulness of such directions, assess their abilities and responsibilities on the background of the other multidirectional activities they do. For example: "Health education is needed in school. GPs cannot replace all other institutions. We in some way promote health and give advice to the youth"; or "This (counseling and prescription of contraceptives) does not occur in my office, but directly in the pharmacy".

Conclusions: The majority of GPs with established, large practices in the university city express the need of particular guidelines on unintended pregnancy prevention in general practice and activities in this direction that to be a part of their work in the frame of the contract with the national health insurance system. They discuss this problem from the viewpoint of their abilities to contribute to reproductive health, as standing the closest and knowing the needs of their patients the best.

Key words: general practitioner, reproductive health, unintended pregnancy prevention, activity, interview.

HEALTH CARE FOR CHILDREN IN THE STATE POLICY OF BULGARIA (1878-2008)

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Background: Health reform in Bulgaria has posed major challenges to child health, particularly to the organization of prevention in early childhood. This directed us to analyze the preventive care for mothers and children in an extended period of time in order to identify strengths and weaknesses in the context of public health policy and reform up to today.

The aim of this study is to analyze and evaluate policies for health care for children in Bulgaria for the period from 1878 to 2008.

Methods: Historical method and analysis of the content of the laws and regulations of the examined period are used in the study.

Results and discussion: The first health legal acts adopted in the restored Bulgarian State: 1879-1888 did not give any special treatment to problems related to children health. The Public Health Act 1903 - regulated the Rural Health Division as a mandatory organizational form, where district doctor or paramedic should work. According to the Public Health Act of 1929 in the activities of the district doctors was included a new progressive element - health care for infants and children.

In the 20s and 30s of the 20th century hard work for the benefit of Child Health was carried out by nongovernment organizations, among which the Union for the Protection of Children in Bulgaria. The Union accomplished many activities in the field of prevention by creating a health advisory stations which undertake ongoing monitoring of the health status of children and extensive health education of mothers. The Union managed to bring together the activities of all government agencies, companies and individuals who had a bearing on the question and thanks to their joint activities it was able to build orphanages, children's dining rooms, summer kindergartens, summer resorts and other socio-medical activities for children.
Turning point in the organization of child care occurs after the establishment of a new type of state system in Bulgaria in 1944 and with the adopted in 1946 the Law on Health Protection of Mothers and Infants. With this act and the subsequent legislation health care for children became one of the priorities of the state policy.

Children medical care was carried out mainly by pediatricians on the principle of the pediatric division and working as a team with nurses. This work was based on the principle of dispensary observation. Patronage nurses became involved in the pediatric section and they have greatly contributed to preventive work. Manifestation of this teamwork was the good results - successful immunization program, reduction of infectious diseases and child mortality reduction.

With the health care reform in 2000, the system of pediatric health divisions was destroyed and child health activities became responsibility of the newly created institution of general practitioner. Currently in Bulgaria there is a very good legislation in the field of child protection, but preventive care is not well realized in the contemporary circumstances. The place and the role of the nurse is not regulated, thus this remains an unutilized resource in caring for the child.

Conclusions: The historical review of the health legislation in the field of child health reveals to us valuable practices in the recent past: child consultation as a separate divisional structure and patronage nurses could be a model of good practice today.Tracing the historical development of the child care system for a long historical period could be a source of ideas for practices in various socio-economic conditions.We consider the study of best nurses' practices and opportunities for their introduction in our health system as important for the achievement of better health results.

Key words: Bulgaria, health care policies, child health, historical review, nursing.

SEEMF STATEMENT ON THE INTEGRITY OF THE NATIONAL PUBLIC HEALTH SYSTEMS

Adopted by the Third International Medical Congress of SEEMF, September 2012, Belgrade, Serbia

The participants of the Third International Medical Congress organized by the Southeast European Medical Forum (SEEMF), which brings together organizations of physicians from Albania, Belarus, Bulgaria, Georgia, Greece, Kazakhstan, Macedonia, Republic of Srpska - Bosnia and Herzegovina, Slovenia, Serbia, Ukraine, Uzbekistan, with representatives from Russia and Romania – a region in which there are about 500,000 practicing physicians, following the basic principles and objectives of WHO and WMA, as well as the priorities of SEEMF and the organizations of physicians in our countries, declare that they:

- Recommend to join the efforts of the public health sector, NGOs, academia, citizens, private companies and government agencies and to recognize that health is a priority for the development of each country and to provide adequate financial resources in order to guarantee achievement of high quality modern healthcare, as well as the priorities and goals of WHO Strategy 2020.
- Believe that the main feature of a democratic and socially responsible government should be its responsibility for the health of the population and the guarantee of equal access to health care for all citizens, regardless of their ability to pay for health care.
- Believe that the fundamental principles of the functioning of national health systems are those that are based on the recognition of independence, professional autonomy and self-governance of the medical profession.
- Believe that a crucial problem of health systems in the region are young doctors. Their career and development prospects should be subject to special analysis and effective management decisions aiming at long-term improvement of the quality of medical care.
- Call on the competent national authorities of the countries to adopt as mandatory for the operation of national health systems the principles defined in the WMA statements and declarations on professional autonomy, self-regulation and independence of National Medical Associations.
- Condemn attempts and actions by government agencies that intervene and restrict the activities of both national independent organizations of physicians and the physicians themselves, thereby causing harm not only to the medical profession, but also directly to its citizens and express support to the WMA Council resolutions on the problems experienced by physicians in different parts of the world.

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