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Conference Report

12th ISNS European Regional Meeting Oral and Poster Abstracts

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Abstract: Due to the impact worldwide of COVID-19, the 12th European ISNS meeting planned to be live in Luxembourg in November 2020 became Luxembourg Going Virtual in November 2021. The conference theme derived from the geographic location of Luxembourg was retained: *Newborn screening—working together in the heart of Europe*. Abstracts of the newborn screening experience and knowledge shared in both oral presentations and posters at the symposium are gathered here to assist in selecting presenters to attend virtually and posters to view online. Some abstract highlights include findings from pilot studies of new screening disorders, the value of screening older previously unscreened children, and benefits of second tier testing.

Keywords: newborn screening; ISNS; Europe

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1. Invited Presentations

I00. Working Together in the Heart of Europe

Jim R Bonham

President, International Society for Neonatal Screening

The last year and a half has been a remarkable time for countries across the world. We moved from an era of normal social contact into the virtual age in one giant leap and sadly almost a quarter of a billion people have contracted COVID-19 with around 5 million tragically dying as a result.

Of course babies have continued to be born and I must pay tribute to the way in which newborn screening programs across the world continued to operate and to the dedication of the staff—all of you, who have made this possible—and the industries, including our sponsors, who have maintained supplies in this difficult time.

During the last 18 months we learned much about mass genetic testing in our populations and this has emphasized the potential for the technology to be applied in public health programs and newborn screening may be a beneficiary of this. We shall hear much more of this during our conference. The months of isolation also reminded us to value one another and the human touch, to make our societies grow and flourish.

In an exciting development on 28 June 2021 saw the first 'International Neonatal Screening Day' which ISNS has helped create, and we look forward to this developing in 2022.

Within Europe itself, we have seen a growing emphasis, supported by on-line meetings, to work with policy makers, MEPs, patient groups, the European Reference Networks and of course ISNS to help develop screening policy and practice. You will be hearing more about this during the meeting.

Ultimately; however, it is science and medicine that delivers life changing benefits for our children and their families and looking at the program we have much to learn and much to celebrate during the coming days of this exciting three day conference, I hope that you enjoy the talks and unlock some of the potential that they contain.

significance when determining cut-off values that maybe considered for newborn screening in the near future.

P27. **Newborn Screening for MCAD Deficiency: Experience of the First Ten Years in Eastern Andalusia, Spain**

Raquel Yahyaoui, Adela Pozo, María José Aguilar, Javier Blasco-Alonso, Carmen Benito, Pedro Ruiz-Sala and Belén Pérez

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Background Medium-Chain Acyl-CoA Dehydrogenase Deficiency (MCADD) is an autosomal recessive fatty acid oxidation disorder with a potentially fatal outcome. It is caused by mutations in the ACADM gene; the most prevalent mutation is c.985A>G. The objective of this study was to evaluate the prevalence, clinical course, and biochemical and molecular phenotype of MCADD cases detected in the first 10 years of newborn screening in our center.

Methods: From April 2010 to December 2020, the acylcarnitine profile, including C6, C8, C10, and C10:1, of 433,614 newborn DBS cards was measured by tandem mass spectrometry. Newborns with screen positive results were referred to physicians for further confirmatory testing (plasma acylcarnitine analysis and identification of biallelic pathogenic variants in the ACADM gene) and follow-up care.

Results: Twenty-six newborns were referred for confirmatory testing for with C8 values above the screening cutoff of 0.17 μmol/L. They had a mean level of 5.72 μmol/L (range 0.90–32.38). All 26 had elevated C6 levels and 18 also had elevated C10 values. 20 of the screen positive infants had an MCADD diagnosis confirmed by plasma acylcarnitine analysis. Molecular testing was available for 21 confirmed cases: 13 were homozygous for the common c.985A>G mutation, four were compound heterozygous for c.985A>G, and five had other mutations. The variant c.199T>C was not found in any patient. The average follow-up period was 3.5 years. Two patients were lost to follow-up during the first year. Two patients had a metabolic crisis; both were homozygous for the c.985A>G mutation. Six patients had at least one episode of hypoglycemia during follow-up. Ten patients required L-carnitine oral supplementation. The estimated prevalence of MCADD is 1:16,677 live births.

Discussion: MCADD frequency in our center is comparable to reports from other newborn screening programs. Early detection and treatment have successfully prevented adverse health outcomes in our MCADD patients.

P28. **Seven Years Experience with Selective Newborn Screening for Inborn Errors of Metabolism in North Macedonia**

Violeta Anastasovska, Mirjana Kocova, Elena Sukarova-Angleovska, Milica Pesevska and Nikolina Zdraveska

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The development of tandem mass spectrometry screening permits increasing the capacity of potentially detectable congenital metabolic diseases by semi-quantitative detection of over 70 metabolites and their characteristic patterns. Although inherited metabolic diseases (IEM) constitute more than 100 different rare conditions, their cumulative incidence reach of approximately 1:1600–2000 newborns.

Neonatal screening for IEM was performed by measuring of 12 amino acids and 13 acylcarnitines (Chromsystems Diagnostics, Germany), in dried blood spot collected 48–72 h after births, using LC/MS/MS method, during the 2014–May 2021.

Total of 36,076 newborns (23.6% of neonatal population for the study period) have been screened for IEM and incidence of 1/2004 have been obtained. In selective metabolic screening in North Macedonia are included neonates born in 12 out of total 27 birth centers all over the country which completely accomplished sample collection criteria. The

newborns with a prolonged stay in intensive care units and indication for IEM were also included in the metabolic screening program. We detected a total of 18 newborns with IEM, of which eight had medium-chain acyl-CoA dehydrogenase deficiency (MCAD), 6 had phenylketonuria (PKU), and single newborn with maple syrup urine disease (MSUD), hypermethioninemia (MET), tyrosinemia type I (TYR I) and carnitine palmitoyltransferase I (CPT I) deficiency, respectively. Additionally, PKU was detected in three more children born in private birth centers which were screened at age 10 months, 18 months, and 2 years at the request of the Department of Neurology at the University Clinic for Pediatrics.

Neonatal metabolic screening is an important diagnostic tool for the diagnosis of various types of IEM, and it can provide substantial benefits to patients and their families. Early diagnosis is important not only for treatment but also for genetic counseling. Activities to cover all newborns in Macedonia are underway.

P29. Expanded Newborn Screening Program in Slovenia Using Tandem Mass Spectrometry and Confirmatory Next-Generation Sequencing Genetic Testing

Barbka Repic Lampret, Ziga Iztok Remec, Ana Drole Torkar, Mojca Zerjav Tansek, Vanja Cuk, Dasa Perko, Blanka Ulaga, Tadej Battelino and Urh Groselj

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Introduction: Expanded newborn screening (NBS) is possible with tandem mass spectrometry, a method used for simultaneous testing of many different metabolites, including numerous acylcarnitines and amino acids on dried blood spots (DBS), which enable detection of many aminoacidopathies, organic acidurias and fatty acid oxidation disorders. To prepare an optimal strategy for the organization of the expanded newborn screening for inborn errors of metabolism, a pilot study was performed analyzing 10,048 NBS cards. The expanded NBS was introduced in Slovenia in September 2018. Seventeen metabolic diseases were added to the pre-existing screening panel for congenital hypothyroidism and phenylketonuria, and the newborn screening program was substantially reorganized and upgraded.

Methods: Tandem mass spectrometry was used for the screening of dried blood spot samples. Next-generation sequencing was introduced for confirmatory testing. Existing heterogeneous hospital information systems were connected to the same laboratory information system to allow barcode identification of samples, creating reports, and providing information necessary for interpreting the results.

Results: By the end of 2020 a total of 39,324 samples were screened. Twelve patients were confirmed positive with additional testing. Among them a unusually high incidence of detected patients with Very long-chain acyl-CoA dehydrogenase deficiency was detected.

Conclusions: An expanded newborn screening program was successfully implemented with the first patients diagnosed before severe clinical consequences.

P30. Retrograde Dried Blood Spot Screening for Tyrosinemia Type 1 in Two Patients

Jaka Šikonja, Barbka Repič Lampret, Jernej Brecelj, Žiga Iztok Remec, Ana Drole Torkar, Mojca Žerjav Tanšek, Tadej Battelino and Urh Grošelj

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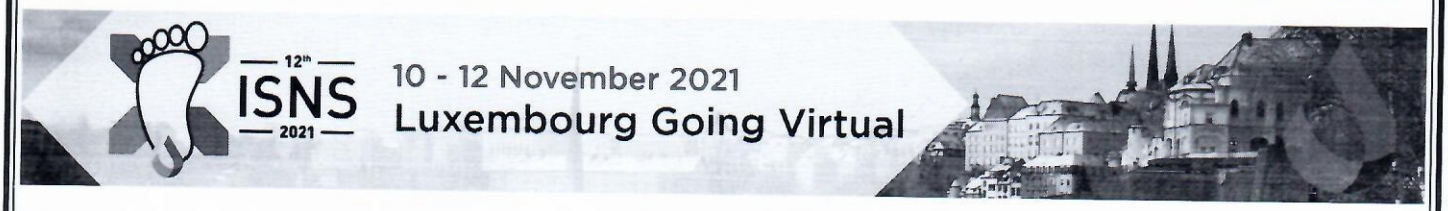
Tyrosinemia type 1 (Tyr1) is an inborn error of tyrosine (Tyr) catabolism which can cause severe liver dysfunction. Most patients present with clinical signs by age three. Timely treatment can be achieved by NBS primarily using succinylacetone (SA) from DBS. NBS-diagnosis is associated with a more favorable outcome with less disease complications compared to a diagnosis after presentation of symptoms. However, in Europe, NBS for Tyr1 is currently being performed in less than half of the countries.

We aimed to perform a retrograde screening in two patients with Tyr1 using DBS taken at birth (both were born prior to the implementation of expanded NBS program using tandem mass spectrometry in 2018 which has included Tyr1). Analysis was done 3.1 and 5.2 years from DBS collection.



CERTIFICATE OF ATTENDANCE

This is to certify that

Prof Violeta Anastasovska

has attended the **12th ISNS European Regional Meeting, Luxembourg Going Virtual,** held online, from 10 - 12 November 2021.

Jim R. Bonham	Kate Hall	Patricia Borde
ISNS President	*ISNS 2021 LOC Chair*	*ISNS 2021 President*