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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.

P11. **Introduction of Neonatal Screening for Cystic Fibrosis in the Republic of North Macedonia**

Violeta Anastasovska, Milica Pesevska, Stojka Fustik and Ana Stamatova

Department for Neonatal Screening, Faculty of Medicine, Ss. Cyril and Methodius University in Skopje, University Clinic for Pediatrics, Skopje, North Macedonia

The newborn screening for cystic fibrosis (CF) in North Macedonia was started as a pilot study in 2018, and become national program from April 2019. Because early testing and treatment of CF can lead to improved health, the screening test must be conducted as soon as possible.

Immunoreactive trypsinogen (IRT) was measured from dry blood spots collected 48–72 h after birth on filter paper using the DELFIA method (referent value 70 ng/mL). Second IRT test was preformed after 21 day of birth (referent value 45 ng/mL). After positive second IRT test a sweat test was proceed. Final diagnosis is done by molecular testing on CFTR gene.

In the period from 2018 to May 2021, a total of 48,315 newborns were screened and CF incidence of 1:2842 was obtained. During this period, 225 newborns were called for second IRT test (0.47%) from which 160 had normal IRT levels and sweat test was done on 65 newborns. False positive were 48 (0.1%), and cystic fibrosis was detected on 17 (0.04%) newborns. CF diagnosis in newborns with positive sweat test was confirmed by molecular CFTR analysis, and F508del mutation was found as most frequently (70.6%). Among the CF newborns 11 were males and six females. According to ethnicity, Albanians newborns (70.6%) compared to Macedonians (29.4%) were dominant probably as a result of consanguinity marriages.

These results put into sharp importance of newborn screening for CF. It is equally important to ensure that programs are established with careful consideration of the implications for the population.

P12. **Cystic Fibrosis: Full CFTR Sequencing for All Hypertrypsinemic Infants in Norway**

Emma Lundman, Asbjørg Stray-Pedersen, Janne Strand and Rolf D. Pettersen

Oslo University Hospital, Norwegian National Unit for Newborn Screening, Oslo, Norway

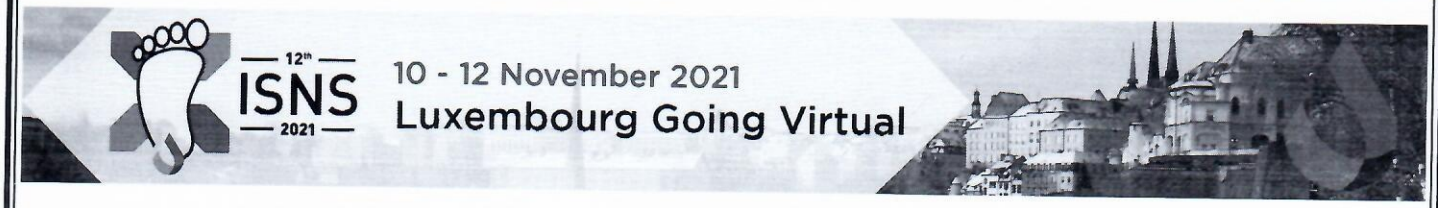
The Cystic fibrosis patient population of Norway has long been known to have a lower frequency p.Phe508del homozygotes compared to other parts of Europe. Thus, when implementing CF newborn screening in 2012, a survey of the most common patient variants indicated that it would be beneficial to use a large variant panel (Luminex CFTR 71 variants assay) with additional Sanger analysis of common Norwegian patient CFTR variants (Lundman, Gaup et al. 2016). As new technological advances allowed for a more extensive variant evaluation, a three tier NGS workflow was adopted from 2015. Second tier MiSeqDx CFTR 139 variants analysis was followed by another NGS method, full gene sequencing of the carriers using IonAmpliSeq CFTR panel. However, the costly and time-consuming workflow gave long lead times for infants carrying rare variants. (manuscript in preparation)

As of 2021, a two-tier workflow was implemented to improve timeliness and comprehensiveness in the screening program.

All infants are offered newborn screening after 48 h of age. The first-tier test screen for elevated IRT (Immunoreactive trypsinogen), using the GSP (Perkin-Elmer). The cut-off at 38 ng/mL captures approximately 5% of samples. As a second tier, DNA is extracted from the same dried blood spots and sequenced over the whole CFTR gene using MiSeqDx and TruSight Cystic Fibrosis Clinical Sequencing Assay as a second tier.

This new era with full variant visibility combined with high sample throughput is expected to yield valuable insights into the spectrum of CFTR variants that can be observed in a population.

The results of the first months of full gene screening will be presented with regards to response time, variant interpretations and insights.



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*