NEWBORN SCREENING (NBS) IN SLOVAKIA – NEW APPROACH

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NEWBORN SCREENING CENTRE SK (NSC)
BANSKA BYSTRICA SK

2013 JOINT MEETING NBS&GTS and ISNS
ATLANTA May 5 - 10 2013
WHERE ARE WE FROM?

Czechia

Slovakia

5 million inhabitants
1.3 million children 0-18 y.
60,000 newborns / year
<table>
<thead>
<tr>
<th>DIS.</th>
<th>START</th>
<th>TEST</th>
</tr>
</thead>
<tbody>
<tr>
<td>CH</td>
<td>1985</td>
<td>$T_4_{RIA} \approx TSH_{RIA}$</td>
</tr>
<tr>
<td></td>
<td>2001</td>
<td>$TSH_{ILMA}$</td>
</tr>
<tr>
<td>PKU</td>
<td>1978</td>
<td>Guthrie</td>
</tr>
<tr>
<td></td>
<td>1995</td>
<td>Phe Fluoromet.</td>
</tr>
<tr>
<td>CAH</td>
<td>2003</td>
<td>$17OHP_{ILMA}$</td>
</tr>
<tr>
<td>CF</td>
<td>2009</td>
<td>$IRT_{ILMA}$ IRT – Cl⁻</td>
</tr>
</tbody>
</table>
SPECTRUM OF SCREENED DISORDERS NSC SK

PKU, CH, CAH, CF
MSUD, GAI
IVA, MCAD, LCHAD, VLCAD, CPTI, CPTII, CACT,

RED = ms/ms method
ORGANIZATION NBS SK

RC = REGIONAL RECALL CTRs
RCW – West   SK
RCC - Central SK
RCE - East    SK

69 nurseries

RCW

RCC

SCN

EAST

CENTRAL

WEST

SEA

SEB

CA

TN

RCE

RS

PP

VV
### RESULTS OF NBS SK 1985 - 2012

<table>
<thead>
<tr>
<th>DISORDER</th>
<th>SINCE</th>
<th>No.SCREEN.</th>
<th>No.POSITIVE</th>
<th>SCR.PREVAL.</th>
</tr>
</thead>
<tbody>
<tr>
<td>CH</td>
<td>1985</td>
<td>1,760 390</td>
<td>441</td>
<td>1 : 3 992</td>
</tr>
<tr>
<td>PKU</td>
<td>1995</td>
<td>983 109</td>
<td>166</td>
<td>1 : 5 922</td>
</tr>
<tr>
<td>CAH</td>
<td>2003</td>
<td>498 125</td>
<td>54</td>
<td>1 : 9 225</td>
</tr>
<tr>
<td>CF</td>
<td>2009</td>
<td>219 784</td>
<td>32</td>
<td>1 : 6 868</td>
</tr>
</tbody>
</table>

**CH INCIDENCE**

- 1 : 7 210
- 1 : 2 419
BEFORE INTRODUCTION OF THE SCREENING:

**TOTAL**

27 974

100%

**IRT1 +**

87

0,31%

**IRT1+++**

10 / 0,04%

**IRT2+**

8 / 0,03%

**IRT Esc**

18 / 0,06%

**IRT2-**

51 / 0,18%

**Sweat Cl- negat**

18 / 0,07%

**posit**

8

**CAUCAS**

60 / 68,9%

**GYPSY**

27 / 31,1%

**NO GYPSY**

SCF PILOT STUDY

May 5th – Oct 4th 2007
There was the real risk of false CF positivity in even 30% newborns of Gypsy origin,

In order TO AVOID THE UNACCEPTABLE STRESS OF FAMILIES and

INAPPROPRIATE MEDICAL & ECONOMIC BURDEN

WE REALISED THE STUDY COMPARED OF NBS IRT1\textsubscript{DBS} IN NEWBORNS OF CAUCASIAN AND GYPSY ETHNIC ORIGIN
METHOD

PROSPECTIVE COMPARATIVE STUDY OF THE IRT_{DBS} LEVELS IN CAUCASIAN (MAJORITY) AND GYPSY (MINORITY) DURING REGULAR NBS IN SLOVAKIA

1st MARCH – 31th MAY 2010

GYPSY PHENOTYPIC ETHNICITY WAS Assigned AS „R“ ON THE DBS SAMPLE CARD IN THE NURSERY

LABELING OF ETHNICITY WAS APPROVED BY ETHICAL COMMITTEE OF THE HEALTH GOV.& NBSC SLOVAKIA
INDIVIDUAL DATA WERE ASSIGNED AS CONFIDENTIAL
THE NUMBER AND ETHNICITY IN THE CF STUDY
1st March – 31th May 2010

Caucasians     8 742
Gypsies           1 500
Total               10 242

Percentage of Gypsy Newborns - 15% is higher than percentage of the whole Gypsy population - 10%

NATALITY RATE IN GYPSY POPULATION IS HIGHER THAN IN CAUCASIAN POPULATION
<table>
<thead>
<tr>
<th></th>
<th>No. Newborns</th>
<th>Mean value</th>
<th>95% confidence interval</th>
<th>99% confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gypies</td>
<td>1500</td>
<td>26.92</td>
<td>26.20</td>
<td>27.66</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>25.98</td>
<td>27.90</td>
</tr>
<tr>
<td>Caucas.</td>
<td>8742</td>
<td>20.77</td>
<td>20.45</td>
<td>21.13</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>20.36</td>
<td>21.25</td>
</tr>
</tbody>
</table>

**MEAN VALUES OF IRT1 ARE OF 23% HIGHER IN GYPSIES THAN IN CAUCASIANS**
MEAN VALUES OF IRT1 IN CAUCASIANS AND GYPSIES

Bootstrap Mean Intervals of Confidence 95% = Solid Line, 99% = Dashed Line.

(t (10240) = 13.89, p < 0.0001).
FIRST CONCLUSIONS & TASKS

1./ TO ADJUST THE CUT-OFF LIMIT OF IRT1 AND IRT2 (ng/mL) IN GYPSY NEWBORNS

<table>
<thead>
<tr>
<th></th>
<th>CAUCASIAN</th>
<th>GYPSY</th>
</tr>
</thead>
<tbody>
<tr>
<td>IRT1</td>
<td>72</td>
<td>84</td>
</tr>
<tr>
<td>IRT2</td>
<td>60</td>
<td>72</td>
</tr>
</tbody>
</table>

2./ REGULAR LABELING OF THE ROMAN ETHNICITY IN DBS SAMPLE - „R“


4./ CONTINUOUS EVALUATION OF THE INCIDENCE OF CF IN GYPSY POPULATION
THE DISTRIBUTION OF THE GYPSY NATALITY IN SLOVAKIA
Percentage of Gypsy Newborns from Total Liveborn Infants - 2009

SOUTH-EAST DISTRIBUTION

1 – below 1,0%
2 - 1,1 – 5,0%
3 - 5,1 – 10,0%
4 - 10,1 - 20,0%
5 – 20,1 – 30,0%
6 - 30,1 – 50,0%
7 - 50,1 – 60,0%
8 - over 60,0%
Nd – no data
EVALUATION OF THE CF RECALL-RATE (RR) AFTER CHANGE OF GYPSY’S CUT-OFF LIMIT
1st March 2010 – 29th February 2011

Even after improving the cut-off level, Gypsy’s RR remained twofold to Caucasian’s one.

<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>Total</th>
<th>RR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gypsy</td>
<td>8428</td>
<td>209</td>
</tr>
<tr>
<td>Caucas.</td>
<td>51159</td>
<td>626</td>
</tr>
<tr>
<td>Total</td>
<td>59587</td>
<td>835</td>
</tr>
</tbody>
</table>

EVEN AFTER IMPROVING THE CUT-OFF LEVEL, GYPSY´S RR REMAINED TWOFOLD TO CAUCASIAN´S ONE
# Detailed Results of Cystic Fibrosis Screening 2009 - 2012 Years

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value / Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Number of Screened Newborns</strong></td>
<td>219,784</td>
</tr>
<tr>
<td>Of them Gypsies (since 2010)</td>
<td>21,115 / 9.6%</td>
</tr>
<tr>
<td>RR Caucasian</td>
<td>0.58%</td>
</tr>
<tr>
<td>RR Gypsy</td>
<td>0.63%</td>
</tr>
<tr>
<td><strong>Number of Confirmed CF</strong></td>
<td>32</td>
</tr>
<tr>
<td>(Only Caucasians)</td>
<td></td>
</tr>
<tr>
<td><strong>Incidence of CF</strong></td>
<td>1:6,868</td>
</tr>
<tr>
<td><strong>Mean IRT1 CF</strong></td>
<td>333.91 ng/mL</td>
</tr>
<tr>
<td><strong>Mean IRT2 CF</strong></td>
<td>143.30 ng/mL</td>
</tr>
<tr>
<td><strong>Mean Sweat Cl- CF</strong></td>
<td>94.47 mmol/L</td>
</tr>
<tr>
<td><strong>Genotype ΔF508del hom/het/other</strong></td>
<td>13/12/6</td>
</tr>
<tr>
<td><strong>Mean Time of Def. Diagnosis</strong></td>
<td>19.13 Day a.b.</td>
</tr>
</tbody>
</table>
SLOVAK GYPSIES HAVE AN ELEVATED IRT LEVEL IN NBS, BUT CYSTIC FIBROSIS IS EXTREMELY RARE.

ELEVATED IRT LEVELS HAS BEEN DESCRIBED IN AFRO - AMERICAN INFANTS IN USA AND IN FRANCE IMMIGRANTS FROM NORTH AFRICA

ALTHOUGH A LOT OF STUDIES HAVE BEEN CONCERNING TO ETHNIC DIFFERENCES OF GENETIC MARKERS OF THE CF, WE HAVE FOUND NO STUDY PRESENTING THE ELEVATED IRT LEVEL IN GYPSY NEWBORNS

IN CONTRAST THIS, NO CASE OF ROMAN CF HAS BEEN DETECTED DURING NEWBORN CF SCREENING IN SLOVAKIA SINCE 2009. ONLY TWO CASES OF GYPSY CF ARE REGISTERED IN THE SLOVAK CF REGISTER ( MORE THAN 30 YEARS OF EXISTENCE ).

WE SEEN THIS FINDING AS A CONTRIBUTION TO THE KNOWLEDGE OF SPECTRUM OF THE GENETIC CHARACTERISTICS OF SLOVAK GYPSY POPULATION
THANKS FOR YOUR KIND ATTENTION