Pneumococcal immunization in children - the Hungarian experience

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Agenda

• Country demographics, NIP

• First step – risk based PCV implementation

• Guideline for pneumococcal prevention

• Surveillance systems in Hungary
  – IPD surveillance
  – Pneumococcal serotype changes

• Mini study of „real world effects”
Country background - Hungary

• Key demographics*
  – Birth cohort: 88 050
  – Population: 9 982 000
  – Infant mortality: 4,9%

## National Immunization Plan*

### Hungary

<table>
<thead>
<tr>
<th>Summary chart</th>
</tr>
</thead>
</table>

### The Hungarian Childhood Vaccination Schedule

<table>
<thead>
<tr>
<th>Age</th>
<th>DTaP</th>
<th>IPV</th>
<th>Hib</th>
<th>PCV¹</th>
<th>MMR</th>
<th>HepB</th>
<th>dTap</th>
<th>BCG</th>
</tr>
</thead>
<tbody>
<tr>
<td>At birth</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Yes²</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 months</td>
<td>Yes³</td>
<td>Yes³</td>
<td>Yes³</td>
<td></td>
<td></td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 months</td>
<td>Yes³</td>
<td>Yes³</td>
<td>Yes³</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4 months</td>
<td>Yes³</td>
<td>Yes³</td>
<td>Yes³</td>
<td></td>
<td></td>
<td>Yes</td>
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</tr>
<tr>
<td>15 months</td>
<td>Yes³</td>
<td>Yes³</td>
<td>Yes³</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18 months</td>
<td>Yes³</td>
<td>Yes³</td>
<td>Yes³</td>
<td></td>
<td></td>
<td>Yes</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>6 years</td>
<td>Yes⁴</td>
<td>Yes⁴</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Yes</td>
<td></td>
<td>Yes</td>
</tr>
<tr>
<td>14 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Yes</td>
<td></td>
</tr>
</tbody>
</table>

*The Hungarian Childhood Vaccination Schedule as on 8 October 2010*

1. Non-mandatory vaccination and free of charge for children under 2 years.
2. HepB vaccine is given at this stage to infants of HbsAg positive mothers and to mothers with unknown HbsAg status. Administered in 3 doses, starting within 12 hours post-partum (in case of HbsAg positive mother simultaneously with HB immunoglobulin), second dose, 1 month later and third dose, 6 months after first dose.
3. DTaP, IPV and Hib are given as a combined vaccine.
4. DTaP and IPV are given as a combined vaccine.

*source: www.euvac.net*
PCV implementation in Hungary

- **Registration PCV-7**: Jan 16, 2007
- **PCV for high risk children 70% reimburs.**
- **DRG for high risk reimbursement**
- **Pneumococcus guideline accepted**: Jul 2006
- **PCV-7 into NIP 3+1, voluntary basis**: Apr 16, 2007
- **30 Nov 2008**: PCV-7 into NIP 3+1, voluntary basis
- **1 April 2009**: >80% coverage NIP 2+1, voluntary basis
- **1 April 2010**: PCV-13
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# Risk categories in the pneumococcal prevention guideline

<table>
<thead>
<tr>
<th>Condition</th>
<th>Criteria</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobinopathies/Sickle cell disease</td>
<td>Low birth weight infants (specify weight: (&lt;2500))</td>
<td>X</td>
</tr>
<tr>
<td>Congenital or acquired asplenia</td>
<td>Preterm infants (specify gestational age (&lt;32) weeks)</td>
<td>X</td>
</tr>
<tr>
<td>Splenic dysfunction</td>
<td>Children (&lt;24) mo of age</td>
<td>X</td>
</tr>
<tr>
<td>HIV infection</td>
<td>Children (&lt;36) mo of age</td>
<td>?</td>
</tr>
<tr>
<td>Immunodeficiency</td>
<td>Children attending out of home care</td>
<td>?</td>
</tr>
<tr>
<td>Malignancy/Cancer</td>
<td>Any chronic disease or specify</td>
<td>X</td>
</tr>
<tr>
<td>Immunosuppressive or radiation therapy</td>
<td>* Chronic cardiac diseases</td>
<td>X</td>
</tr>
<tr>
<td>Solid organ transplant</td>
<td>* Chronic pulmonary disease</td>
<td>X</td>
</tr>
<tr>
<td>Bone marrow transplant</td>
<td>* Chronic renal disease</td>
<td>X</td>
</tr>
<tr>
<td>Cerebrospinal fluid leaks</td>
<td>* Chronic hepatic disease</td>
<td>X</td>
</tr>
<tr>
<td>Cochlear implants</td>
<td>* Diabetes mellitus</td>
<td>X</td>
</tr>
<tr>
<td>Asthma</td>
<td>Others (please list): prior IPD</td>
<td>X</td>
</tr>
<tr>
<td>Infants who are not breastfed or limited breastfeeding</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Risk based immunization policy – as a first step for PCV introduction – it did not work for Hungary
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Vaccine recommendations

Decision makers in Hungary

• NIP – budget financed
  • National Institute of Epidemiology/ National Institute of Public Health
    • Vaccine Advisory Board
      • Epidemiologists, experts, primary care doctors representative

• Guidelines – Relevant medical Boards (Infectology, Pediatrics)
  • Issued/accepted by the Ministry of Health

• Marginal role
  • Hungarian Society of Infectious Diseases
  • Hungarian Society of Pediatrics
Pneumococcal disease, guidelines for prevention

- Accepted and published by the Ministry of Health in 2006
  - Prepared and submitted by the Board of Infectologists – me
  - Updated in 2008: 3+1 schedule PCV 7
  - Updated in 2009
    - 2+1 vaccination scheme, surveillance, new clinical data
    - PCV-7 coverage reached 83% within 6 months
  - Updated in 2011 – adult indication for PCV-13

- Available vaccines:
  - PCV-7 (Prevenar7/Wyeth) followed by PCV-13 (Prevenar13/Pfizer)
    - NIP 2-24 mo
      - on a voluntary basis – first time ever, NIP is obligatory...
    - 2-5 y olds: reimbursement (70%) in certain risk groups (DRG, no social issues)
  - Pneumovax’23- MSD, Pneumo’23 -Sanofi-Aventis
    - Private market
    - Prescription – partial (‘normative’ :25%) reimbursement
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Blood sample from a sterile site

Microbiology Laboratory

- Hospital
- Private
- NCE
- Regional

Positive, Pneumo Strain

To NCE Lab

- PCR
- Sero-typing

NCE Dept. of Infectious Diseases

NCE IPD DATABASE „EFRIR” capture-recapture

Reporting data

Local ANTSZ

Reporting
Data collection on pneumococcal disease burden in Hungary

- **Hungarian IPD study** (Oct. 2002 - Nov. 2004)
  - 95 IPD cases /2 y
    - 66 *Streptococcus pneumoniae* isolates
    - 17 meningitis
    - 5 deaths - 4/5 meningitis
  - Incidence - IPD
    - 14,92/100 000 <5 y
    - 12,49/100 000 <2 y

- ASPECT study – IPD+pneumonia – terminated in 2010.

- National database on pneumococcal meningitis
  - Notifications – DRGs in hospital charts

- **Pneu surveillance initiated** Q4 2008
Serotype distribution in Hungary before NIP
(age group < 5 years, No of isolates: 66
Zs. Mészner, ESPID, 2005 p)

Leading PCV7 serotypes: 14, 6B, 19F
Non-Prevenar serotypes
Pneumococcal meningitis in Hungary 2001-2006*

<table>
<thead>
<tr>
<th>Age y</th>
<th>Case No</th>
<th>Morbidity/100 000 inhab.</th>
<th>Death No</th>
<th>Letality (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>23</td>
<td>4,1</td>
<td>8</td>
<td>34,8</td>
</tr>
<tr>
<td>1-2</td>
<td>11</td>
<td>1,0</td>
<td>3</td>
<td>27,3</td>
</tr>
<tr>
<td>3-5</td>
<td>22</td>
<td>1,2</td>
<td>5</td>
<td>22,7</td>
</tr>
<tr>
<td>6-9</td>
<td>9</td>
<td>0,3</td>
<td>1</td>
<td>11,1</td>
</tr>
<tr>
<td>10-14</td>
<td>13</td>
<td>0,4</td>
<td>1</td>
<td>7,7</td>
</tr>
<tr>
<td>15-19</td>
<td>5</td>
<td>0,2</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>20-29</td>
<td>12</td>
<td>0,1</td>
<td>3</td>
<td>25,0</td>
</tr>
<tr>
<td>30-39</td>
<td>38</td>
<td>0,4</td>
<td>6</td>
<td>15,8</td>
</tr>
<tr>
<td>40-49</td>
<td>52</td>
<td>0,6</td>
<td>18</td>
<td>34,6</td>
</tr>
<tr>
<td>50-59</td>
<td>84</td>
<td>1,0</td>
<td>31</td>
<td>36,9</td>
</tr>
<tr>
<td>60-</td>
<td>114</td>
<td>0,9</td>
<td>57</td>
<td>50,0</td>
</tr>
<tr>
<td>all</td>
<td>383</td>
<td>0,6</td>
<td>133</td>
<td>34,7</td>
</tr>
</tbody>
</table>

*Source: National Centre for Epidemiology
Pneumococcal meningitis
(cases per 100,000 inhabitants in Hungary)

Source: National Centre for Epidemiology, Annual epidemiological report, 2008, 2009
Pneumococcal meningitis
(cases per 100,000 inhabitants in Hungary)

Data collection on pneumo disease burden

Negatives:
- No data on AOM
- No data on pneumonia—ASPECT study!!
  - Not even on death related to pneumonia
  - No data collection on IPD in different age groups
- No routine serotyping of circulating pneumococcal strains

Problem:
- Disease awareness is less than optimal, due to lack of adequate information on pneumococcal disease burden
*S. pneumoniae* isolates (N= 765) by origin sent to the Central lab (OEK) between 2008-2011.

Source: T. Tirczka NCE Hu
Changes in *Streptococcus pneumoniae* serotypes after the introduction of PCV 13 vaccine (from 01-04-2011) to 5 years age groups

Before the introduction of PCV13 (number of isolates = 54)

After the introduction of PCV 13 (number of isolates = 26)

Source: T. Tirczka NCE Hu
Vaccine coverage between 2008-2012 among IPD isolates

Source: T. Tirczka NCE Hu
Vaccine coverage by age after the introduction of PCV 13 vaccine among IPD (from 01-04-2011)

Source: T. Tirczka NCE Hu
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According to WHO:

• Age is the most important risk factor for IPD

• They highly recommended the incorporation of the conjugated pneumococcal vaccines into NIPs for all children

• 39% less all cause pneumonia hospitalizations could be expected
the proof is in the pudding...
Study of a medical student (Varga Gabriella, Semmelweis University, Faculty of Infectology, 2011).

XR verified pneumonia in a tertiary care Hospital for Children (Heim Pál) in Hungary in children below 2 prior and after the introduction of PCV.
Tertiary care pediatric hospital (Heim Pál): all cause pneumonia hospitalization before and after PCV implementation in children less than 2 y - age
Tertiary care pediatric hospital (Heim Pál): all cause pneumonia hospitalization before and after PCV implementation in children less than 2 y- LHS*
DRG data – whole country - on pneumococcal admissions
2007.10 – 2008.04 vs. 2009.10 - 2010.04*

All cause pneumonia cases – not only XR confirmed

2007.10 - 2008.04: 2710 cases
2009.10 - 2010.04: 2536 cases

-6.4%

*Source: National Centre for Epidemiology
To sum it up….

- PCV implementation into the Hungarian NIP has already beneficial results on
  - pneumococcal meningitis data

- Pneumococcal surveillance data
  - prove the effect of the PCV7
  - there are early signs of the PCV13 benefits

- The „mini study”
  - showed marked decrease in XR confirmed pneumonia hospitalisation
  - pneumococcal surveillance data are needed for further evaluation
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