The Remaining Risk of Pneumococcal Disease in Children

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Agenda

• Epidemiology of *Streptococcus pneumoniae* infections
• High risk conditions and serotype distributions
• *S. pneumoniae* vaccines
• Experience with PCV7 and PCV 13

• Summary
S. pneumoniae: causative agent of IPD and Mucosal Disease

- Gram-positive diplococcus \(^1,^2\)
- Polysaccharide capsule \(^3-^5\)
  - Virulence factor
  - Defines serotype
  - Vaccine target
- >90 serotypes \(^6\)

Background

- A Gram positive encapsulated diplococci and normal inhabitant of the nasopharynx\(^1\)
- Capsule: virulent factor, specific polysaccharide = basis for vaccine
- Global nasopharyngeal (NP) colonization/carriage ranges:
  - 10% - 85% in children <5 years of age\(^2,3\)
  - 4% - 45% in adults\(^2-4\)

Acute Otitis Media
Sinusitis
Pneumonia
Bacteremia
Meningitis
Spread to other individuals


Highest incidence and mortality rates of IPD at extremes of age

Incidence of IPD and associated mortality rates (USA, 2009)

Cases
Deaths

Cases of invasive disease (per 100,000)

Deaths associated with IPD (per 100,000)

Effect of Risk Factors on Incidence of IPD Among Children 2-15 Years of Age, UK (2008-2009)

Higher IPD rates in patients with underlying clinical risk conditions

Incidence Rates and Risk Ratios for All-Cause Pneumonia: Healthy, At-Risk, and High-Risk Persons

• **Research Design**
  – Retrospective cohort analysis using U.S. healthcare insurance claims

• **Data Source**
  – 2 large longitudinal electronic insurance claims databases representing >25 million persons annually from 2007-2010

• **Study Population**
  – All persons ≥5 years of age enrolled on January 1 in one or more study years

• **Outcomes**
  – Cases of IPD and all-cause non-bacteremic pneumonia were ascertained from inpatient and outpatient claims data

Rate Ratios for IPD and CAP: Asthmatics vs. Healthy Persons

• Epidemiology of *Streptococcus pneumoniae* infections
• High risk conditions and serotype distributions
• *S. pneumoniae* vaccines
• Experience with PCV7 and PCV 13

• Summary
Historic milestones: more than 100 years of pneumococcal immunization

1911
- Wright: Whole cell vaccine

1945
- MacLeod, et al: 4-valent PPV

1976
- Merck: 23-valent PPV

1983
- Wyeth: 7-valent PCV

2000
- GSK: 10-valent PCV

2009
- Pfizer: 13-valent PCV

A polysaccharide (ps) is chemically linked (conjugated) to a protein carrier. 

<table>
<thead>
<tr>
<th>Differences between PPV 23 and Conjugated vaccines (PCV 13)</th>
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<table>
<thead>
<tr>
<th></th>
<th>Polysaccharide vaccine</th>
<th>Conjugate vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Minimum age of vaccination</strong></td>
<td>&gt; 2 years</td>
<td>6-8 weeks</td>
</tr>
<tr>
<td><strong>Immune response</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>. at 2 months of age</td>
<td>Absent to weak</td>
<td>Strong</td>
</tr>
<tr>
<td>. at 2 years of age</td>
<td>Moderate to strong</td>
<td>Strong</td>
</tr>
<tr>
<td><strong>Duration of immunity</strong></td>
<td>Short term</td>
<td>Long term</td>
</tr>
<tr>
<td><strong>Vaccine efficacy</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>. children &lt; 2 years of age</td>
<td>None</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Nasopharyngeal carriage</strong></td>
<td>No effect</td>
<td>Reduction</td>
</tr>
<tr>
<td><strong>Indirect protection</strong></td>
<td>Unlikely</td>
<td>Yes</td>
</tr>
</tbody>
</table>
### CRM 197 S. pneumoniae conjugate vaccines

<table>
<thead>
<tr>
<th>PCV-7</th>
<th>Carrier: CRM\textsubscript{197}</th>
<th>4</th>
<th>6B</th>
<th>9V</th>
<th>14</th>
<th>18C</th>
<th>19F</th>
<th>23F</th>
</tr>
</thead>
</table>

| PCV-13 | Carrier: CRM\textsubscript{197} | 4 | 6B | 9V | 14 | 18C | 19F | 23F | 1 | 5 | 7F | 3 | 6A | 19A |
Efficacy Versus Effectiveness

• **Efficacy:** Results from controlled clinical trials

• **Effectiveness:** Results of the vaccine in real life (when the vaccine is used in the population)
PCV-7 Effectiveness Data

- **IPD**
- **Carriage**
- **Indirect Effect**
- **OM**
- **Pneumonia**
- **Office Visits**
- **Antibiotic Resistance and Use of Antibiotics**
- **Cost-effectiveness**

OM=otitis media.
IPD=invasive pneumococcal disease.
Situation: 10-years Post-Introduction of PCV7

- Need to improve *S. pneumoniae* vaccine coverage in developing countries (serotypes 1 and 5)

- Emergence of new serotypes in invasive and non-invasive infections

19A, 6A, 3 and 6C (among others)

Bender JM, et al. CID. 2008;46:1346-1352
Gerts RE, et al. JID 2010:201 (1 March)
PCV 13: Pediatric Effectiveness data (2013)

- French data on nasopharyngeal colonization
- Israeli data on NP colonization and Otitis Media
- Uruguay data on invasive disease
- UK data on invasive disease
- USA data on invasive disease

Pirez M et al. ISPPD 2012, Foz Iguacu, Brazil.
http://www.hpa.org.uk/Topics/InfectiousDiseases/InfectionsAZ/Pneumococcal/EpidemiologicalDataPneumococcal/CurrentEpidemiologyPneumococcal/InPrevenar7/pneumo01Cumulativeweeklyunder2INPrevenar7vacc/
Early Trends of Pneumococcal Infections in Children after PCV-13 Introduction in the USA


Overall decline: 42%
< 24 months of age decline: 53%
# Global Asthma Prevalence by Age and Region

**International Study of Asthma and Allergies in Childhood (ISAAC)\(^1\)**
**Cross-Sectional Questionnaire Conducted 2000-2003**

<table>
<thead>
<tr>
<th>Region</th>
<th>6-7 Years of Age (388,811 participants / 61 countries)</th>
<th>13-14 Years of Age (798,687 participants / 97 countries)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Current wheeze (%)</td>
<td>Asthma, ever (%)</td>
</tr>
<tr>
<td>Africa</td>
<td>10.0</td>
<td>3.4</td>
</tr>
<tr>
<td>Asia-Pacific</td>
<td>9.5</td>
<td>10.9</td>
</tr>
<tr>
<td>E. Mediterranean</td>
<td>9.4</td>
<td>7.0</td>
</tr>
<tr>
<td>Indian subcontinent</td>
<td>6.8</td>
<td>4.5</td>
</tr>
<tr>
<td>Latin America</td>
<td>17.3</td>
<td>11.2</td>
</tr>
<tr>
<td>North America</td>
<td>19.1</td>
<td>20.0</td>
</tr>
<tr>
<td>N. and E. Europe</td>
<td>8.7</td>
<td>4.0</td>
</tr>
<tr>
<td>Oceania</td>
<td>21.7</td>
<td>29.2</td>
</tr>
<tr>
<td>W. Europe</td>
<td>9.6</td>
<td>9.7</td>
</tr>
<tr>
<td><strong>Global total</strong></td>
<td><strong>11.5</strong></td>
<td><strong>9.4</strong></td>
</tr>
</tbody>
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\(^1\) Global Asthma Prevalence by Age and Region.
Among children 5-17 years of age, the presence of asthma resulted in a 4x higher risk of IPD.

The cumulative excess risk of IPD over 10 years in persons with asthma is 10-30 cases per 10,000 persons.
Is there a role for Prevenar 13 in this age group?

13-Valent Pneumococcal Conjugate Vaccine (PCV13): > 5 to <18 years of age

Immunogenicity and Safety clinical trials in Children > 5 to < 18 years of age were completed

**US**

PCV 13 naive children and adolescents, 6 to 17 years of age, for the prevention of Invasive Pneumococcal Disease caused by the 13 serotypes included in the vaccines

**EU**

PCV 13 naive children and adolescents, 6 to 17 years of age, for the prevention of Invasive Pneumococcal Disease, Pneumonia and Otitis Media caused by the 13 serotypes included in the vaccine

**Asia**

Philippines and Thailand

The use of Prevenar 13 in this age group is not approved in South Korea
Summary

- Pneumococcal disease is the #1 vaccine-preventable cause of death worldwide¹
- Certain conditions, such as asthma, increase the risk of IPD and pneumococcal pneumonia
- Children aged > 5 to < 18 years of age are at risk for IPD and pneumonia
- PCV 7 proved to be a very efficacious vaccine against invasive and mucosal disease
- Worldwide, an emergence of new serotypes such as 1, 3, 5, 6A, 7F and 19A have followed PCV-7 implementation
- The addition of this emerging serotypes in the new conjugated vaccine (Prevenar 13) improve vaccine coverage
- Effectiveness data for PCV13 have proven the added value of additional serotype coverage