Global Burden of Pneumococcal Disease in Children under 5

Susan Wang, MD, MPH
Expanded Programme on Immunization

World Health Organization
Streptococcus pneumoniae

- Gram-positive encapsulated diplococcus
- Transmitted by direct contact with respiratory secretions from patients and healthy carriers
- Usual outcome of exposure is transient nasopharyngeal colonization, not disease
- Disease caused either by contiguous spread to sinuses or middle ear, aspiration into the lungs, or invasion of bloodstream with or without seeding of secondary sites
Streptococcus pneumoniae (cont’d)

- Pneumococcal resistance to antimicrobials is a serious and growing problem (penicillins, cephalosporins, trimethoprim-sulfamethoxazole, macrolides, and fluoroquinolones)

- Laboratory diagnosis based on growth in culture media

- Failure to isolate the organism often occurs due to prior antibiotic treatment, improper handling and transport of specimens, use of inappropriate culture media
Diseases caused by *Streptococcus pneumoniae* (Pneumococcus)

- **Invasive pneumococcal disease (IPD):** infection of a normally sterile site
  - Pneumonia
  - Meningitis
  - Febrile bacteremia
  - Arthritis
  - Peritonitis
  - Osteomyelitis

- **Less serious, but more common pneumococcal disease**
  - Otitis media
  - Sinusitis
  - Bronchitis
Invasive pneumococcal disease (IPD)
**S. pneumoniae** is the most common cause of bacterial pneumonia

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**S. pneumoniae** in lung aspirates from children with pneumonia

- **Papua New Guinea** (1): 35%
- **The Gambia** (2): 50%
- **Zimbabwe** (3): 25%
- **The Gambia** (4): 40%

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Pneumococcus is a significant cause of bacterial meningitis

In low-income countries, about 45% of people with pneumococcal meningitis die, compared to 29% with Hib meningitis and 8% with meningococcal meningitis

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Incidence of Invasive Pneumococcal Disease in Children <2 Years by Population

<table>
<thead>
<tr>
<th>Country</th>
<th>Incidence, cases/100,000 pop</th>
</tr>
</thead>
<tbody>
<tr>
<td>Finland</td>
<td>45.3</td>
</tr>
<tr>
<td>Chile</td>
<td>49.1</td>
</tr>
<tr>
<td>USA, multisite</td>
<td>166.9</td>
</tr>
<tr>
<td>Kenya</td>
<td>213</td>
</tr>
<tr>
<td>Gambia</td>
<td>458</td>
</tr>
</tbody>
</table>

Sources: Robinson KA JAMA 2001; Davidson M JID 1994; O’Dempsey TJ PIDJ 1996; Levine MM PIDJ 1998; Eskola J JAMA 1992; Berkley NEJM 2005
Invasive Pneumococcal Disease Incidence, by Age, USA, 1997

Available at: www.cdc.gov/ncidod/dbmd/abcs/survreports/spneu98.pdf.
Children at increased risk for pneumococcal disease

- Children with anatomic or functional asplenia: sickle cell disease, other sickle hemoglobinopathies (hemoglobin S-C disease, S-β thalassemia)
- HIV-infected children have 2.8 and 12.6 times the rate of HIV uninfected children
- Children in out-of-home day care have 2 to 3 times the rate of disease compared to children at home
Burden of disease due to *S. pneumoniae*
Pneumococcal surveillance for laboratory confirmed disease only provides part of the picture. Additional cases preventable with vaccination can be identified by surveillance for invasive disease.
Role of Surveillance for Pneumococcus

- Surveillance data alone does not accurately measure burden of disease
  - Low sensitivity of culture based methods, esp for pneumonia
  - Low specificity of non-culture based methods (PCR, UAg)
  - Representativeness depends on many factors
  - Poor quality surveillance may hurt evidence-based policy making

- Surveillance is important for monitoring the impact of vaccination
  - Changes in disease pre- and post- vaccine introduction

- Modeling is essential to establish disease burden
VHO Disease Burden Estimation Process

- **Goal:** produce estimates of cases and deaths for global, regional, and country levels for children < 5 years of age with 2000 as base year

- **Database of evidence**
  - Systematically collected
  - Publicly available

- **Methods for estimation**
  - Transparent methods
  - Communication of uncertainty of estimates
  - Public dissemination

- **Independent expert group**

- **Country consultation prior to release of country-level estimates**

- **Clearance through WHO-EIP**
  - Compatibility with burden estimates for other diseases
Outline of General Analytic Methods

- Literature
- Meta-analyses (country specific parameters)
- Adjustments
- Models

- Incidence
- CFR
- VE
- Access to care, HIV, Hib vaccine use
- Meningitis
- Invasive NPNM
- Pneumonia

PAHO Regional Symposium of New Vaccines, Lima
1-3 December 2009
Global burden of disease due to *S. pneumoniae* in 2000 (children < 5 yrs)

- 14.5 million episodes (range, 11.1 – 18.0 million) of invasive pneumococcal disease
  - Americas: 713,000 (range, 551,000 – 950,000)

- About 826,000 (range, 582,000 – 926,000) deaths in children aged 1-59 months; of these, 90,000 (range, 60,000-100,000) among HIV+ children
  - Americas: 33,100 deaths (range, 23,600 – 39,500)

- *S. pneumoniae* causes around 11% (range, 8-12%) of all deaths in children aged 1-59 months (excluding pneumococcal deaths in HIV-positive children)

S. pneumoniae incidence rates globally
(per 100,000 children < 5 yrs)
10 Countries with Highest Incidence of Pneumococcal Disease in AMRO Region

Disease Incidence per year (Per 100,000 children under 5)

- Haiti
- Guyana
- Saint Lucia
- Honduras
- Nicaragua
- Paraguay
- Guatemala
- Trinidad
- Suriname
- Antigua

Source: Hib/SP GDB June 15, 2009 Final A
10 Countries with Greatest Number of Pneumococcal Cases in AMRO Region

<table>
<thead>
<tr>
<th>Country</th>
<th>Total Case per Year (Thousands)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brazil</td>
<td>180</td>
</tr>
<tr>
<td>Mexico</td>
<td>120</td>
</tr>
<tr>
<td>USA</td>
<td>60</td>
</tr>
<tr>
<td>Colombia</td>
<td>40</td>
</tr>
<tr>
<td>Haiti</td>
<td>30</td>
</tr>
<tr>
<td>Guatemala</td>
<td>20</td>
</tr>
<tr>
<td>Venezuela</td>
<td>20</td>
</tr>
<tr>
<td>Argentina</td>
<td>20</td>
</tr>
<tr>
<td>Peru</td>
<td>10</td>
</tr>
<tr>
<td>Honduras</td>
<td>10</td>
</tr>
</tbody>
</table>

Source: Hib/SP GDB June 15, 2009 Final A
Distribution of *S. pneumoniae* Deaths by Syndrome, Globally

89% Pneumonia

4% other IPD

7% Meningitis
S. pneumoniae mortality rate
(deaths per 100,000 children under age 5)

Burden of disease caused by Streptococcus pneumoniae in children younger than 5 years: global estimates

Lancet 2009; 374: 85
Greatest Proportion of Global Pneumococcal Deaths are in Africa and Asia

- AFR: 51%
- SEAR: 23%
- EMR: 12%
- EUR: 2%
- WPR: 5%
- AMR: 1%

Source: Hain & Emeis, June 15, 2009, Final A

PAHO Regional Symposium of New Vaccines, Lima
1-3 December 2009
Countries with Greatest Pneumococcal Deaths are all in Africa and Asia
10 Countries with Greatest Number of Pneumococcal Deaths in AMRO Region

- Brazil
- Mexico
- Haiti
- Bolivia
- Peru
- Guatemala
- Colombia
- Honduras
- Ecuador
- Venezuela

Total Deaths per Year (Thousands)

Source: Hib/SP GDB June 15, 2009 Final A
SP pneumonia case fatality rate
(Children under age 5)

Case Fatality Rate (%)

- <5
- 5 - <10
- 10 - <20
- ≥20

Source: Hib/SF GDB June 15, 2003 Final A
SP meningitis case fatality rate
(Children under age 5)
Summary

- *Streptococcus pneumoniae* is a major cause of morbidity and mortality among children < 5 years in developing countries. Annually for this age group, the Americas are estimated to have
  - 713,000 invasive pneumococcal disease cases
  - 33,100 deaths

- 73% of deaths are due to pneumonia, 14% to meningitis, 13% to other invasive pneumococcal disease
Acknowledgements

Thomas Cherian
Hope Johnson
Kate O'Brien
Carsten Mantel
Extra slides
SP incidence rate: PAHO region
(per 100,000 children under age 5)

Source: H/HSP/ERB June 15, 2009 Final A
Comparison of *Streptococcus pneumoniae* disease burden estimates for PAHO using different models

<table>
<thead>
<tr>
<th>Disease</th>
<th>WHO</th>
<th>Sabin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pneumonia</td>
<td>595,000 (463,000-741,000)</td>
<td>327,000</td>
</tr>
<tr>
<td>Meningitis</td>
<td>8,400 (6,000-11,500)</td>
<td>4000</td>
</tr>
<tr>
<td>Deaths</td>
<td>33,000 (23,000-39,000)</td>
<td>18,000</td>
</tr>
</tbody>
</table>
Comparison of Disease Burden Estimates

- Geographic scope: Sabin – limited to Latin America and Caribbean; WHO – included North America


- Diseases: WHO case definition included more NPNM while Sabin case definition included only sepsis for NPNM cases

- Modeling strategies: WHO – adjusted for access to care and HIV prevalence
SP mortality rate: PAHO region
(deaths per 100,000 children under age 5)
SP pneumonia case fatality rate: PAHO region (Children under age 5)

Source: Hib/SP CDC June 18, 2009 Final A
SP meningitis case fatality rate: PAHO region
(Children under age 5)
What drives pneumococcal deaths? Population size, or pneumococcal mortality?

[Graph showing population size vs. pneumococcal deaths per 100,000 children under 5 years for various countries such as India, China, Nigeria, Pakistan, Ethiopia, DR Congo, and Afghanistan.]