Global Burden of Pneumococcal Disease in Children under 5

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**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

![Bar chart showing the percent of aspirates containing S. pneumoniae, H. influenzae, and other bacteria from children with pneumonia in Papua New Guinea, The Gambia, and Zimbabwe.](chart)


Ikeogu MO. *Arch Dis Child.* 1989; 64(8):1207.

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;
vine 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-ß 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.

Culture positive disease

Culture negative meningitis and pneumonia

Can be identified by surveillance for invasive disease

Additional cases preventable with vaccination
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
WHO 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
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, 60,000-100,00) 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

Source: Hib/SP GDB June 15, 2009 Final Analysis

(*) deaths included
10 Countries with Greatest Number of Pneumococcal Cases in AMRO Region

Brazil
Mexico
USA
Colombia
Haiti
Guatemala
Venezuela
Argentina
Peru
Honduras

(*) deaths included
Distribution of *S. pneumoniae* Deaths by Syndrome, Globally

- **Pneumonia**: 89%
- **Meningitis**: 4%
- **other IPD**: 7%
**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: 893-902
Greatest Proportion of Global Pneumococcal Deaths are in Africa and Asia

(+) deaths included

Source: H1b/SP GDB June 15, 2009 Final Analysis
10 Countries with Greatest Pneumococcal Deaths are all in Africa and Asia

Proportion of Global (%)
10 Countries with Greatest Number of Pneumococcal Deaths in AMRO Region

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

Case Fatality Rate (%)

- <5
- 5-<10
- 10-<20
- ≥20

Source: Hib/SP GDB June 15, 2009 Final Analysis

(+) deaths included
SP meningitis case fatality rate
(Children under age 5)

Case Fatality Rate (%)

Source: Hib/SP GDB June 15, 2009 Final Analysis
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)

Number of cases per 100,000 children <5
- <1000
- 1000-<2000
- 2000-<3000
- ≥ 3000

(+) deaths included

Source: Hlib/SP GDB June 16, 2009 Final Analysis
Comparison of *Streptococcus pneumoniae* disease burden estimates for PAHO using different models

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

- **Geographic scope:** Sabin – limited to Latin America and Caribbean; WHO – included North America
- **Literature reviews:** Sabin – 1990-2006 and nonpublished data; WHO – 1980-2005 with global databases
- **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)

Number of deaths per 100,000 children <5

- <10
- 10-<100
- ≥100

Source: Hlb/SP GDB June 15, 2009 Final Analysis

(+): deaths included
SP pneumonia case fatality rate: PAHO region (Children under age 5)

Case Fatality Rate (%)
- <5
- 5 -<10
- 10 -<20
- ≥20

(+ ) deaths included

Source: H1b/SP GDB June 15, 2009 Final Analysis
SP meningitis case fatality rate: PAHO region (Children under age 5)

Case Fatality Rate (%)

- <20
- 20 - <40
- 40 - <60
- ≥60

(+ deaths included)

Source: Hib/SP GDB June 15, 2009 Final Analysis
What drives pneumococcal deaths? Population size, or pneumococcal mortality?

- India
- China
- Pakistan
- Bangladesh
- Uganda
- Nigeria
- Ethiopia
- DR Congo
- Angola
- Afghanistan

Pneumococcal deaths per 100,000 children under 5 years

Under 5 population (million)