Pneumococcal disease: Global burden, epidemiology, scope for vaccine prevention

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Pneumococcal Carriage and Disease

- Ear infections
- Nose and throat (Healthy persons)
- Pneumonia
- Blood stream infections
- Meningitis
Principales Causas de Muertes por Enfermedades Infecciosas (estimados)

Deaths (millions)

- < 5 years old
- ≥ 5 years old

S. pneumoniae: ~1.6 millones muertes, incluyen ~800,000 muertes en niños

Fuente: WHO, 2000
WHO estimates 2.7M childhood deaths from vaccine preventable illnesses.

Pneumo, Hib & Rotavirus account for ~60% of vaccine preventable deaths in children.
WHO Global Disease Burden Project

- **Objective:** to generate country-specific Hib and Pneumo burden estimates
- **Database of evidence**
  - Systematically collected
  - Publicly available
- **Methods for estimation**
  - Transparent methods
  - *Communication of uncertainty of estimates*
- **Independent expert committee review x 2**
- **Clearance through WHO-EIP**
  - Compatibility with other disease burden estimates
- **Country consultation prior to release of country-level estimates**
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<th>Estimate</th>
<th>Uncertainty Range</th>
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<td><strong>Pneumonia</strong></td>
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<td>Incidence Rate**</td>
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<td><strong>Meningitis</strong></td>
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<td>Incidence Rate**</td>
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<td>§ Deaths in HIV -</td>
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<td><strong>Other non-pneumonia, non-meningitis invasive disease</strong></td>
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<td>Incidence Rate**</td>
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Timeline of Disease Burden Project

• Country Consultation Letters: August 2007
• Responses due by September-October (6 weeks)
• Final numbers by October-November 2007
• Publication in Fall-Winter 2007
• Website with numbers
• Tool for calculating disease burden in other years/evaluating impact of implementing vaccination programme
Pneumococcal Epidemiology: Invasive disease basics
Incidence and Case Fatality Ratio by Age Group
Invasive Pneumococcal Disease
ABCs 1998

Robinson et al JAMA 1998
Invasive pneumococcal disease in healthy adults and adults with selected comorbidities
United States, 2000

Cases per 100,000 persons

- Healthy: 11
- Chronic heart: 43
- Diabetes: 48
- Chronic lung: 59
- Heavy drinker: 92
- Solid cancer: 294
- HIV/AIDS: 341
- Blood cancer: 432

Kyaw M et al JID 2005
Risk Factors for Invasive Pneumococcal Disease

- Nuorti et al. NEJM 2000
- J Watt et al, CID 2003
Invasive Pneumococcal Disease in Navajo and White Mountain Apache Apache vs. White and Black Persons in the General U.S. Population, 1997-8

J Watt et al, CID 2003
Epidemiology of Serotypes

- Over 90 different pneumococcal serotypes
- Pneumococcal serotypes causing invasive disease vary
  - Geographically
  - With age
  - With immune status
  - Between some racial/ethnic groups
  - In ability to be carried
  - In invasiveness
  - In disease manifestations they cause
  - In amount of resistance to antibiotics
Pneumococcal disease prevention and treatment

• Case-management
  – antibiotics, oxygen, supportive care
• Improved nutrition
  – breastfeeding, micronutrients, improved feeding
• Risk factor reduction
  – indoor air pollution, hand washing, HIV prevention
• Immunizations
Pneumococcal Conjugate Vaccine (PCV7)

- Prev(e)nar (Wyeth Lederle) 7-valent vaccine
- Poly- or oligosaccharides of serotypes 4, 6B, 9V, 14, 18C, 19F, 23F
- Conjugated to CRM197
Considerations for PCV

Introduction

• Disease burden
  – Serotype coverage: *Just a part of the story*
  – Absolute burden of vaccine-type disease

• Cost effectiveness

• Feasibility
Serotype coverage with 7-valent vaccine* in the US and Australia

Based on serotype coverage alone, Australia would get the “highest priority” for vaccine introduction, and Navajo would get “lowest priority”
“Preventable incidence” rate is the important measure.

Preventable incidence = ST coverage \times Incidence of disease

Navajo should be “highest”, not lowest priority.
National Programs Using Conjugate Vaccine

• National programs
  – USA, Canada, Australia, Luxemburg, Qatar
• Routine introduction announced for 2006
  – UK, Holland, Norway, Greece
• Countries with moderate vaccine use
  – France (broad “at risk” program)
  – Italy (universal recommendation in 15 / 20 regions)
  – Spain, Portugal (private markets with high coverage).

Source: Wyeth
Status of national programs and licensure of 7-valent (Apr 2006)

Red = Registered and universal infant use or equivalent recommendation (n=13)
Blue = Registered but no universal use recommendation (n=61)

Map source: www.preventpneumo.org June, 2006
Vaccine Supply Environment

**Pneumococcal vaccine pipeline**

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<th>Development Stage</th>
<th>Pre-clinical stage</th>
<th>Clinical trial Phase I</th>
<th>Clinical trial Phase II</th>
<th>Clinical trial Phase III</th>
<th>Launched</th>
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<tr>
<td>Multi-national</td>
<td>~20 vaccines in research/Pre-clinical stage (includes conjugate &amp; protein-based vaccines)</td>
<td>9-valent</td>
<td>13-valent</td>
<td>Expected launch 2008 (US, Europe)</td>
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<td>Emerging suppliers</td>
<td>&gt;4 multi-valent conjugate vaccine projects</td>
<td>GSK¹ 10-valent</td>
<td>11-valent</td>
<td>Prevnar (7-valent)</td>
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¹Completed first Phase III trial; results announced in Jun05

Source: BCG Global Supply Strategy 2005
PneumoADIP team analysis
Pneumo vaccine supply outlook

- 2000-2007: 7-valent, single dose syringe
- 2008-2010: 7 valent and 10 valent, single and multi-dose syringe
- 2011-2015: 10-13 valents, single and multi-dose syringe
- 2016-2020: >3 suppliers, multi-nationals and emerging

- 2-3 Suppliers
  - Multi-nationals
  - + Emerging later

- 4-14 valents
  - Single and multi-dose
  - ?Proteins?
Surveillance as a cornerstone of vaccine introduction

- Provides baseline data before vaccine introduction
- Provides local disease burden data and where possible serotype data
- Pneumococcal surveillance poses challenges
  - Multiple syndromes (some very common)
  - Limited diagnostics
  - Importance of serotypes
Global Framework on Immunization Monitoring and Surveillance (GFIMS)

WHO and CDC joint vision

• By 2010, a strengthened and more integrated epidemiological and laboratory network for vaccine preventable diseases (VPD) surveillance

• Network that provides high quality information to measure disease burden and impact of vaccines

• Link with seasonal/pandemic influenza & emerging threats