

Mini-Symposium: Interventions to Prevent Respiratory Disease

Vaccines to prevent pneumonia in children – a developing country perspective

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EDUCATIONAL AIMS

1. To describe the burden of disease caused by pneumonia and review efforts to reduce this
2. To identify discrepancies in vaccine availability in the developed and developing worlds
3. To review key pulmonary pathogens and assess the evidence base for vaccine prevention
4. To explore indirect effects and economic impact of vaccines
5. To identify priorities for pneumonia research in the developing world

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SUMMARY

Pneumonia accounted for 15% of the 6.3 million deaths among children younger than five years in 2013, a total of approximately 935,000 deaths worldwide. Routine vaccination against common childhood illnesses has been identified as one of the most cost-effective strategies to prevent death from pneumonia. Vaccine-preventable or potentially preventable diseases commonly linked with respiratory tract infections include *Streptococcus pneumoniae*, *Haemophilus influenzae* type-b (Hib), pertussis, influenza, measles, and tuberculosis. Although there have been great strides in the development and administration of effective vaccines, the countries that carry the largest disease burdens still struggle to vaccinate their children and newer conjugated vaccines remain out of reach for many. The Global Vaccine Action Plan (GVAP) has identified priority areas for innovation in research in all aspects of immunisation development and delivery to ensure equitable access to vaccines for all.

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BACKGROUND

Globally, acute respiratory tract infections are the most common cause of both illness and mortality in children. In developing countries, there are approximately 0.22 episodes of pneumonia per child-year with 11.5% progressing to severe disease [1]. Pneumonia accounted for 15% of the 6.3 million deaths among children younger than five years in 2013, a total of approximately 935,000 deaths worldwide (Figure 1) [2,3]. This translates to a

young child dying from an acute respiratory infection every 30 seconds, yet most of these deaths are preventable [3].

Outside the neonatal period, pneumonia and diarrhoea account for approximately 40% of all deaths in young children (Figure 1), [2] which motivated the World Health Organisation (WHO) and the United Nations Children's Fund (UNICEF) to develop the Integrated Global Action Plan for the Prevention and Control of Pneumonia and Diarrhoea (GAPPD) in 2013 [4]. GAPPD aims to ensure access to proven and appropriate preventive and treatment measures for pneumonia and diarrhoea, especially in resource-limited settings where most of these deaths occur [3,4].

Five simple interventions have been recommended to reduce severe pneumonia in childhood: i) exclusive breastfeeding for six months and continued breastfeeding complemented by nutritious solid foods up to age two years; ii) routine vaccination against

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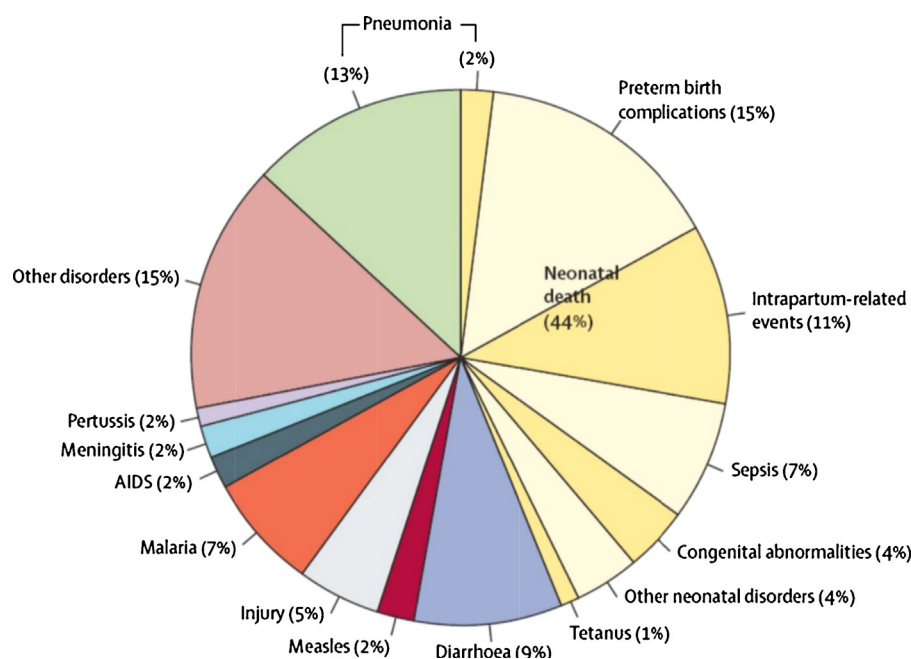


Figure 1. Causes of death in children under 5 years of age (2013)

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pertussis, measles, *Haemophilus influenzae* type B (HiB) and pneumococcus; iii) safe drinking water, sanitation and hand washing facilities; iv) improved cooking stoves to reduce indoor air pollution; and v) effective treatment including amoxicillin dispersible tablets and oxygen [4]. We provide an overview of vaccine preventable respiratory infections, current implementation status and novel developments, with a specific focus on the developing world.

CURRENTLY AVAILABLE VACCINES

The first vaccine was developed against smallpox in 1796, but it was not widely used until the 20th century (Figure 2) [5]. Since then vaccination has proven to be one of the most cost-effective health interventions available, leading to the global eradication of small pox in 1980. It is also a key intervention to reduce the unacceptably high mortality associated with childhood pneumonia [6,7]. Uptake of vaccination against important childhood infections, especially in the developing world, increased greatly after the creation of the Expanded Programme of Immunisation (EPI) and the Global Alliance for Vaccination and Immunisation (GAVI) [8]. It is estimated that by 2013, GAVI-led immunisation efforts had averted six million deaths from vaccine preventable diseases [6]. However, progress beyond the core EPI set of vaccines has been relatively slow and the "Expanded Programme of Immunisation (EPI)" term has become a bit of a misnomer with the exclusion of key conjugate vaccines. The WHO estimates that 1.5 million children continue to die every year from vaccine-preventable diseases, accounting for 17% of all under-5 deaths [9]. Delayed introduction of conjugated vaccines against *Haemophilus influenzae* type-b (Hib) and pneumococcus in developing countries is mostly attributed to high cost and lack of political will; resulting in widening vaccine schedule gaps in developed and developing countries (Figure 3) [10].

The WHO lists 27 vaccine-preventable or potentially preventable diseases; [11] those commonly linked with respiratory tract infections include *Streptococcus pneumoniae*, Hib, pertussis, influenza, measles, and tuberculosis. *Streptococcus pneumonia*

and Hib are considered to be the leading causes of child pneumonia deaths worldwide and universal use of conjugated Hib and pneumococcal vaccines should prevent approximately 1 million child deaths per year [12]. It has been argued that with the expected decline of bacterial causes of pneumonia due to increasing vaccine coverage, viral causes may be emerging as commoner causes of pneumonia in children. A study done in Pakistan found that of children admitted with WHO-defined severe pneumonia, up to 36% had at least a viral cause identified; human metapneumovirus was detected in 24 (14.2%), influenza A virus in 9 (5.3%) and respiratory syncytial virus (RSV) in 30 (17.8%) [13].

Pneumococcal disease

Pneumococcal disease is caused by the gram-positive encapsulated bacterium *Streptococcus pneumoniae*; over 90 different strain types have been recognized [14]. *Streptococcus pneumoniae* is a common coloniser of the nasopharynx, but clinical disease mainly presents as pneumonia, sinusitis, otitis media and invasive pneumococcal disease (IPD). IPD occurs when the infection spreads into the bloodstream or to a normally sterile site such as the brain, resulting in bacteraemia and/or bacterial meningitis that are associated with significant morbidity and mortality. Global estimates indicate that pneumococcal disease is responsible for approximately 500, 000 deaths in children annually [15].

The first pneumococcal vaccine was licensed in 1977. This polysaccharide vaccine protected against 14 different strains and expanded to protect against 23 strains in 1984 [16]. The vaccine was found to be effective in adults, but did not generate adequate protective immunity in children younger than two years of age [16]. An enhanced conjugate vaccine for young children (PCV-7) was licensed in 2000. The 7 strains included in this vaccine represented those causing the highest disease burden in the United States of America (USA) and other developed countries, with little consideration of common strains in resource-limited settings. Initial studies demonstrated that PCV-7 was highly effective, reducing IPD caused by vaccine serotypes by more than 90% in

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