

Pneumococcal vaccination in developing countries



WHO estimates that about 1.6 million people, including up to 1 million children under 5 years old, die every year of pneumococcal pneumonia, meningitis, and sepsis.¹ In populations with high child-mortality rates, pneumonia is the leading infectious cause of mortality and accounts for about 20–25% of all child deaths.² In these populations, *Streptococcus pneumoniae* is identified consistently as the leading cause of bacterial pneumonia, and pneumococcal bacteraemia is an important cause of child mortality.^{3–5} HIV infection increases risk for pneumococcal disease 20–40-fold, and antibiotic resistance makes treatment difficult and expensive.⁶ Thus pneumococcal disease is a major global-health issue.

Clinical trials in Africa have shown that pneumococcal conjugate vaccines improve child survival and protect the most vulnerable children. A trial with nine-valent vaccine in The Gambia reduced all-cause mortality in vaccinated children by 16% (95% CI 3–28%), all-cause hospital admissions by 15% (7–21%), and radiography-confirmed pneumonia by 37% (27–45%).⁷ In South Africa, the same vaccine's effectiveness against invasive pneumococcal disease due to vaccine serotypes was 65% (24–86%) in HIV-infected children and 83% (39–97%) in HIV-uninfected children.⁸ In that trial, vaccination reduced the incidence of lower respiratory tract infections in HIV-infected children by 2566 per 100 000 children a year.⁹

Pneumococcal conjugate vaccines can prevent most serious pneumococcal disease. Although the ranking of individual pneumococcal serotypes causing serious disease varies from country to country, the seven to 13 serotypes included in conjugate pneumococcal vaccines are expected to prevent 50–80% of all paediatric pneumococcal disease worldwide.^{10–12} A licensed seven-valent vaccine is available now. Vaccines with ten and 13 serotypes (including serotypes 1 and 5) might be licensed between 2008 and 2010. With more than 20 pneumococcal vaccine candidates in the pipeline, including common protein vaccines and vaccines from manufacturers in developing countries, the outlook for vaccine supply is good.

Pneumococcal vaccination can be delivered through existing immunisation systems. Adding such a vaccine to the routine immunisation schedule will require training health workers, expanding cold-chain capacity,

and an additional injection, but not more clinic visits. Studies are underway in developing countries to establish whether fewer than three doses can be used for primary vaccination.

A seven-valent pneumococcal conjugate vaccine is licensed in more than 70 countries and is used routinely in several industrialised nations. Surveillance data from the USA indicate that routine childhood vaccination was associated with: large rapid declines in overall and vaccine-type invasive disease in children younger than 2 years old; reductions in vaccine-type disease in unvaccinated children and adults; elimination of racial disparities in disease incidence; significant drops in the frequency of antibiotic-resistant infections; and increases in non-vaccine serotype disease that are small compared with the overall reductions in vaccine-type disease. The decline in disease in unvaccinated people is accounted for by the reduction in colonisation in vaccinated children and thus decreased transmission to unvaccinated contacts. In the USA, this herd immunity effect prevents twice as many cases as the direct effects of vaccination alone.^{13,14}

The potential for serotype replacement to arise after widespread vaccination has been a concern since pneumococcal conjugate vaccines were first developed. In the USA, the frequency of non-vaccine-type disease has risen (about 4000 cases in 2003) but the increase has been small compared with the overall decline in vaccine-type disease (about 30 000 cases in 2003).¹⁴ Findings in Native American children are especially reassuring because vaccination has reduced disease rates substantially, although the epidemiology is similar to that in developing countries—ie, high overall incidence and more non-vaccine serotype disease than in the general US population.¹⁵ These data reinforce the importance of implementing strong sustained surveillance to monitor the effect of vaccination.

Although more data are always helpful, there is a compelling case for giving pneumococcal vaccination in developing countries now. In view of the high burden of pneumococcal disease, consistent proof of conjugate-vaccine protection against vaccine-type pneumococcal invasive disease, pneumonia, and meningitis, and the impressive reduction in all-cause mortality in The Gambia, use of pneumococcal conjugate vaccines—

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beginning with the available seven-valent product—should be started as soon as possible in developing nations. Countries that might be candidates for seven-valent vaccine introduction include Bangladesh, The Gambia, and Kenya, which have a high burden of childhood pneumonia mortality, a great burden of invasive pneumococcal disease attributable to vaccine serotypes, and surveillance to monitor the vaccine's effect.

Disease surveillance is essential for any vaccine programme, particularly for pneumococcal vaccine schedules, in which vaccination is restricted to specific serotypes and increases in the incidence of non-vaccine-serotype disease are expected concomitant with beneficial indirect effects of vaccination. Countries that introduce pneumococcal vaccines should, at least, implement surveillance to monitor the frequency of vaccine-type and non-vaccine type invasive pneumococcal disease in different age groups. Operational assessments of vaccination in the first countries that adopt pneumococcal vaccination will provide important information to guide policy locally and in other countries.

Pneumococcal vaccination in developing countries will need commitment from manufacturers, donors, and the governments of developing countries. The supply situation of the seven-valent vaccine has improved and the manufacturer has indicated its willingness to supply the vaccine to developing countries.¹⁶ The past 5 years have seen major advances in financing of immunisation, including creation of the GAVI Alliance (Global Alliance for Vaccines and Immunization) fund, the International Finance Facility for Immunization, and progress towards establishing the G7 Advance Market Commitment plan. These mechanisms will provide the GAVI Alliance with billions of dollars of flexible, predictable, long-term financing to procure pneumococcal vaccine for the next 10 years. National governments in countries that meet the GAVI Alliance's eligibility criteria are increasing their budget allocations to immunisation. However, vaccines remain undervalued compared with curative services and substantial financing challenges lie ahead. These could be viewed as a reason for inaction on pneumococcal vaccination, but to do so is simply to put off steps that could save lives now.

We urge international donors—especially the GAVI Alliance—and industry to negotiate sustainable affordable pricing of vaccines for developing countries. We call

on the governments of developing countries and their partners to establish pneumococcal disease surveillance and begin preparations for vaccine introduction. By taking these steps, we can make this the year for action to improve child survival in developing countries by using pneumococcal vaccines.

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