

tially in tandem with the increase in the HIV epidemic over the past two decades,” says Professor Shabir Madhi, co-director of the Respiratory and Meningeal Pathogens Research Unit of Witswatersrand University, which is based at Baragwanath Hospital.

“Currently 50% of children who are hospitalized for pneumonia in South Africa are HIV infected, even though they make up less than 5% of the childhood population,” Madhi says, adding: “HIV-infected children have an increased risk of being colonized with pneumococcus and a 40-fold greater risk of developing several invasive pneumococcal diseases.”

The case fatality rate for HIV-infected children with pneumonia in hospital is about 7% compared to about 1.5% for children who are not infected, he says.

Children with HIV generally get worse, more protracted and recurrent pneumonia than those who are HIV negative, according to Dr Tammy Meyers, director of the Harriet Shezi Children’s Clinic at Baragwanath Hospital.

Dr Prakash Jeena, head of Paediatric Pulmonology at the Nelson Mandela School of Medicine, has also seen a marked increase in the incidence of pneumonia among children. About 70% of children at the Durban hospital with “very severe pneumonia”, diagnosed according to WHO criteria, are HIV positive and about one in four or five of them will not survive.

Only 54% of HIV-infected children respond to standard therapy for pneumonia, compared with 80% of children who are not HIV positive.

The paediatric HIV/AIDS service at Groote Schuur Hospital in Cape

Town faces similar challenges, with its inpatients and children attending two community clinics in the outlying townships.

Director of the paediatric HIV/AIDS service, Dr Paul Roux, who is also co-founder of the HIV care and treatment organization Kidzpositive, says that he has seen *Pneumocystis jiroveci* pneumonia almost exclusively in infants who are HIV positive.

Speedy treatment is critical when it comes to treating these infants. “They need to be identified early,” Meyers says. “All babies exposed to HIV should be tested for HIV at four to six weeks. If they are positive they should be started on Bactrim [sulfamethoxazole-trimethoprim] prophylaxis. This can significantly reduce pneumonia and other diseases.” She adds that babies infected with HIV should be put onto live-saving antiretroviral therapy as early as possible. This practice is standard at the Harriet Shezi clinic and other big centres, but less common at outlying clinics with fewer resources.

Jeena says that children with HIV experience more severe bouts of pneumonia that are more difficult to treat. The chief cause of pneumonia among children with HIV is *Streptococcus pneumoniae*. Madhi and his team have evaluated a vaccine which targets this and *Haemophilus influenzae* type b, which can also cause pneumonia. The vaccine helps to prevent hospitalization for severe pneumonia.

Children with HIV are at risk of being infected by a broader range of bacteria, viruses and other pathogens than those who are HIV negative. As a result, Madhi says: “You need to use antibiotics which are broader in their activity. This, in turn, is associated with

higher cost as well as a greater chance of pathogens becoming resistant to the antibiotics.”

Jeena adds that it is currently not possible to diagnose some of these pathogens in rural areas due to their limited access to sophisticated laboratory facilities, so they are developing a diagnostic tool to assist health professionals.

Meyers says it is important to also check for tuberculosis among children with respiratory infections, but that it is hard to diagnose. Roux says doctors also need to look out for the “second wave” of children with HIV, who were well at birth but now, at seven or eight years old, are presenting with complications.

Caring for babies and children with HIV has come a long way since Roux and his colleagues started their paediatric service in 2002; they now have 650 children on antiretrovirals.

“In the old days, all we could offer was care and 24-hour access. If a mother [of a child with HIV] picked up an infection, she had to come straight to us.” Roux urges health-care workers to acknowledge mothers as equal partners in caring for their children.

“It is not just enough to have the staff and the building; the clinic has to be friendly. The mother must want to come and be recognized as a member of the team. They see their child every day. Once a child is on antiretrovirals, we see them once every three months.”

Roux says that the effective treatment of HIV-positive children is not only about access to medicines. “Time and time again in Africa, it is not just about access to antiretrovirals. It is about access to health care.” ■

Controversial funding mechanism to fight pneumonia

New financing methods show promise in fight against pneumonia, the biggest killer of children. Theresa Braine reports from Mexico.

More than two million children aged less than five years die of pneumonia every year worldwide. Most of these deaths occur in the poorest nations where treatment is not always readily available and where vaccines are hard to come by. Now there is a big global push to prevent the infections that cause

pneumonia using unique financing mechanisms to develop and purchase new vaccines.

Vaccines exist against some strains of pneumococcus bacteria, which can cause childhood pneumonia as well as meningitis and otitis media. But these vaccines are often too pricey for

developing countries or they do not protect against the strain prevalent in a given country.

Public health experts and government officials have developed an innovative financing approach, called Advanced Market Commitment (AMC). Under this scheme, donor nations finance the purchase of new pneumococcal vaccines at a pre-agreed price if demanded by countries in need and if the vaccines meet certain product characteristics. The aim is to drive investment into late-stage vaccine development and building

manufacturing capacity. Companies that benefit from AMC financing are obliged to supply the vaccine for a prolonged period of time at a reduced price, to assure long-term sustainability of the scheme.

AMC also has its critics, who believe the scheme to be cumbersome, inefficient and not flexible enough to incorporate innovations, and that better vaccines may come down the pipeline during the 7 to 10 years that AMC will be subsidizing prices. At stake is the health of millions of children worldwide and the attainment of the fourth of the eight UN Millennium Development Goals (MDGs), to reduce by two-thirds the mortality rate among children less than five years of age.

Just a few years ago childhood pneumonia was barely on the public health radar, says Hans Kvist, a spokesperson for the GAVI Alliance, which is heading the AMC pneumococcal vaccine initiative. But over the past few years, health officials have begun to recognize the toll that pneumonia takes and look for ways to finance large-scale vaccinations. In Mexico, for example, pneumonia is the second-leading cause of hospitalization, says Dr Silvia Lule, who heads the paediatric services unit at the National Institute of Respiratory Illnesses (Instituto Nacional de Enfermedades Respiratorias, or INER).

Elsewhere, the figures are starker because Mexico is one of the few developing nations to have implemented wide-scale vaccination in high-risk populations. Any child with a respiratory condition or HIV is automatically vaccinated against pneumococcal disease, says Lule.

Countries with fewer resources than Mexico may be able to rely on AMC. In 2007, several countries agreed to provide US\$ 1.5 billion to finance the AMC pneumococcal programme. The AMC for pneumococcal vaccine is scheduled to be launched later this year as a pilot project with the hope that, after it is successful, the same model can be applied to malaria, tuberculosis and perhaps even clean water projects.

The idea behind AMC is to create a level playing field for poorer nations that need vaccines and to compensate for the fact that the developing-world market for such vaccines is often small and risky

from the manufacturer's perspective. If poor countries can't afford to pay prices high enough to cover the manufacturers' investment costs, and thus cannot guarantee a demand for the product, the company will lose money. Under these circumstances, AMC steps in and subsidizes prices to make it viable for pharmaceutical companies to develop and produce the vaccines, while guaranteeing a price that developing countries can afford to pay, thus ensuring a continuous demand for the vaccine.

“The aim is to drive investment into late-stage vaccine development and building manufacturing capacity.”

The money for a pneumococcal vaccine has been secured, with pledges from Canada, Italy, Norway, the Russian Federation and the United Kingdom, as well as the Bill & Melinda Gates Foundation, says Kvist of the GAVI Alliance, a public-private sector consortium, which promotes and funds vaccines for developing countries. In February 2007, the GAVI Alliance – formerly known as the Global Alliance for Vaccines and Immunization – promised US\$ 1.5 billion towards the AMC effort. In Latin America, for example, Nicaragua will be the first of 30 countries to benefit from support for pneumococcal vaccines, says Kvist, while Guyana and Yemen have been shortlisted to receive AMC support. “This US\$ 1.5 billion would be absolutely crucial in achieving the MDGs,” says Kvist.

The AMC for pneumococcal vaccine is being run as a pilot programme that, if successful, could be used to support other initiatives in the future, such as development of vaccines for malaria, tuberculosis and other ailments, says Kvist.

The GAVI Alliance estimates that the AMC pneumococcal vaccine programme will save five million lives overall by 2030, including between 500 000 and 700 000 of those lives

during the 10 years the AMC is scheduled to run. A 2006 document, prepared by the GAVI Alliance and the World Bank to explain the AMC mechanism, estimates that each dose will cost US\$ 5–7, with developing countries contributing a co-payment of about US\$ 1 per dose, although Kvist says price negotiations continue. The first AMC payments would begin in 2010 and last for nine to 10 years.

However, the AMC plan has been criticized, most notably by Andrew WK Farlow, Donald W Light, Richard T Mahoney and Roy Widdus, in their Center for Global Development (CGD) 2005 report to the WHO Commission on Intellectual Property Rights, Innovation and Public Health. The authors expressed several concerns, including the fear that the long-term nature of the financing method could exclude companies that want to join the scheme later, even those with better vaccines. AMC is currently considering some measures to extend the benefit of AMC to late-coming companies. The report also considers the possibility that the AMC's promise of a contract to the first company that comes up with a vaccine that meets the minimum specifications could lower quality and efficacy.

It's telling that the four authors of the report were part of the initial advisory committee that came up with the AMC idea. “After a careful review of the CGD report and of its earlier drafts – indeed, all of us advised on it – we conclude that the CDG model for these vaccines is unworkable, inefficient and inequitable towards the wide range of potential developers and suppliers of such vaccines,” they wrote in their 2005 report.

Whether AMC is the solution or not, the fact remains that vaccines are pricey, and mechanisms do not exist to force companies to drop their prices or to make a vaccine or drug for which there is a public health need. Global health organizations and experts are turning more and more to public-private partnerships to try to reduce the time lag between the moment a vaccine is introduced in the developed world to the day it reaches the developing world. ■