

## Can the burden of pneumonia among HIV-infected children be reduced?

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Of the approximately 2.1 million children who are infected with human immunodeficiency virus type 1 (HIV-1),<sup>1</sup> more than 80% will develop a respiratory illness sometime during the course of their disease.<sup>2</sup> The prevalence of HIV-1 infection among African children admitted for very severe pneumonia (under the WHO case definition) varies from 55% to 65% and is associated with a case fatality rate of 20% to 34%; three- to six-times higher than children who are not infected with HIV.<sup>3,4</sup> In infancy, pneumonia caused by *Pneumocystis jiroveci* is often the first HIV/AIDS indicator disease that prompts HIV testing and, consequently, early antiretroviral treatment for those infected.<sup>5</sup>

Approximately 2 million children less than 5 years of age die of pneumonia each year in countries with a high prevalence of HIV. The standard case management guidelines for pneumonia recommended by WHO for use in areas with low HIV burdens are less effective in areas where HIV burdens are high.<sup>6</sup> Modifications to these guidelines have been suggested, but their use, as reported in a recently published study of children with very severe pneumonia, resulted in a 45% treatment failure rate among HIV-infected infants in tertiary care settings.<sup>4</sup> Polymicrobial infections with *Staphylococcus aureus*, nontyphoidal *Salmonella* spp. and other Gram-negative pathogens, *Mycobacterium tuberculosis*, *P. jiroveci*, cytomegalovirus and other viruses were commonly seen among the treatment failures and carried a greater than 10-fold risk of a poorer outcome. Randomized controlled studies of alternative antimicrobial agents that are active against some of the pathogens identified among these treatment failures are urgently required.

A second major challenge for standard case management in the HIV era is to develop a management guideline

to care for the largest group of HIV-affected children: HIV-exposed but HIV-uninfected children, who are at increased risk of acquiring pneumonia. Such children, who live in close contact with HIV-infected persons who persistently harbour a multitude of different pathogens, are at higher risk of pneumonia treatment failure than HIV-unexposed control children; however, the risk of an adverse outcome is lower than for HIV-infected children.<sup>7</sup> Studies on the impact of pneumonia on HIV-exposed but HIV-uninfected children are essential.

The other major intervention to reduce pneumonia-related morbidity and mortality among HIV-infected children requires the implementation of preventive strategies. Routine immunizations against *Streptococcus pneumoniae*, *Haemophilus influenzae* and varicella are safe and effective in HIV-infected children, even though their primary immunological response is inferior and they experience faster decay in immunological memory. Despite the lower efficacy of the conjugate pneumococcal (65% versus 83%) and *H. influenzae* type b vaccines (55% versus 91%) against invasive disease in HIV-infected and HIV-uninfected control children, respectively, introduction of these vaccines would considerably reduce the 1.6 million pneumococcal and 300 000 *H. influenzae* deaths that occur each year.<sup>8–10</sup> Other preventive strategies, such as the provision of co-trimoxazole prophylaxis against bacterial and *P. jiroveci* infections, improvement in the provision of prevention of mother-to-child transmission (PMTCT) interventions and early use of highly active antiretroviral therapy (HAART) require urgent scaling-up. In a randomized controlled study of co-trimoxazole prophylaxis versus placebo in HIV-infected older Zambian children, a significant reduction in the hazards ratio for death

of 0.57 (95% confidence interval: 0.43–0.77) was seen in the treated group.<sup>11</sup> Although there is undoubted benefit in providing co-trimoxazole prophylaxis to HIV-infected children, its widespread implementation does carry risks such as development of resistance to a drug used for treating *P. jiroveci* pneumonia. This needs to be studied urgently as ineffective treatment of these conditions could increase mortality substantially. The effective implementation of PMTCT programmes, involving at least dual antiretroviral therapy and effective nutritional advice, will help to reduce to less than 4% the incidence of transmission of HIV to newborns and infants.<sup>12</sup> Such a reduction is likely to have a significant impact on cutting the prevalence of pneumonia among HIV-infected children. Furthermore, use of HAART with HIV-infected children has been associated with a fourfold reduction in the rate of opportunistic infections and a threefold reduction in hospitalizations.<sup>13</sup> The role of nutritional interventions, such as exclusive breastfeeding and zinc supplements, in the prevention of pneumonia among HIV-infected children needs to be explored more thoroughly.

In conclusion, significant attention has to be paid to revising the standard case management guidelines for HIV-infected children with pneumonia through properly conducted randomized controlled studies. The implementation of preventative strategies that include co-trimoxazole prophylaxis, pneumococcal and *H. influenzae* type b vaccinations, PMTCT programmes and early introduction of HAART carry the greatest immediate hope for helping these children. There is a need to rapidly scale up these measures globally. ■

### References

Available at: <http://www.who.int/bulletin/volumes/86/5/08-053223/en/index.html>

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