



Editorial

## Childhood pneumonia in Sub-Saharan Africa: Still a challenge

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Pneumonia is the leading killer of children under five years globally yet most deaths are preventable. In 2017, there were approximately 808,920 pediatric pneumonia associated deaths and more than 100 million childhood pneumonia episodes estimated worldwide, with low- and middle-income countries (LMICs) being disproportionately affected particularly those in sub-Saharan Africa.<sup>[1]</sup> Improved socioeconomic and living conditions, strengthened strategies to reduce pediatric HIV and anti-retroviral therapy provision, and new improved conjugate vaccines such as pneumococcal conjugate vaccine (PCV) and *Haemophilus influenzae* type b (HiB) have significantly improved the incidence and severity of pneumonia in children. Further, substantial reductions in pneumococcal pneumonia in adults have been achieved through immunization of children, which interrupts transmission of disease-causing serotypes from the nasopharynx of children to susceptible adults. However, pneumonia still remains common, although disease may be mild.<sup>[2]</sup> Further, pneumonia and especially recurrent disease may impair lung function, setting a trajectory for the development of chronic respiratory disease.<sup>[3]</sup>

Increasing evidence shows that multiple pathogens are associated with pneumonia etiology. Organism interactions and dysbiosis of the nasopharyngeal microbiome are likely to be important in pneumonia pathogenesis. In the context of high coverage for new conjugate vaccines, viruses, especially respiratory syncytial virus (RSV), are increasingly emerging as key pathogens. In the Pneumonia Etiology Research for Child Health multicountry case-control study, a cross-sectional study of children hospitalized with severe or very severe pneumonia, RSV was the predominant pathogen across all seven sites in LMICs.<sup>[4]</sup> Similarly, in the Drakenstein Child Health Study, a South African birth cohort study, RSV was the predominant pathogen identified in ambulatory pneumonia and severe pneumonia up to 2 years of age, occurring in around 25% of pneumonia episodes.<sup>[5]</sup> Viruses such as SARS-CoV-2, the novel coronavirus that causes COVID-19, have been responsible for pandemics, due to emergence of strains to which humans have no immunity. However, globally children have been largely spared and only mildly affected with fewer SARS-CoV-2 infections, asymptomatic or mild disease, and much lower mortality than that occurring in adults.<sup>[6]</sup> Coinfection with several organisms is common in pneumonia, with mixed bacterial-viral, viral-viral, mycobacterial-viral, or mycobacterial-bacterial occurring. *Bordetella pertussis* is an important cause of LRTI in unvaccinated or partially vaccinated infants or those with HIV infection or exposure. *Mycobacterium tuberculosis* is an important cause of acute childhood pneumonia in countries with high tuberculosis (TB) prevalence. *Pneumocystis jirovecii* and cytomegalovirus are important opportunistic

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infections to be considered in children with an underlying immunodeficiency.

Recent advances include molecular diagnostics, such as polymerase chain reaction for respiratory viruses, and TB like Xpert® MTB/RIF Ultra, which have improved the understanding of the etiology of pneumonia. Lung ultrasonography for the diagnosis of pneumonia and its complications such as pleural effusion, is safe, repeatable, low cost, point of care, more sensitive than chest radiography, correlates with chest computed tomography, and has no radiation.<sup>[7]</sup>

Risk factors for pneumonia and severe disease include child, maternal, environmental, pathogen, and health system factors, with opportunities for prevention, promotion, and control of childhood pneumonia, particularly for modifiable risk factors. Child factors which increase susceptibility to pneumonia include male sex, preterm birth, malnutrition, lack of breast feeding, HIV infection/exposure, or impaired immunity. Optimal nutrition including supplemental Vitamin A that lowers mortality from measles infection by 23%;<sup>[8]</sup> prophylactic zinc which reduces the incidence of pneumonia by 13%, especially in malnourished children;<sup>[9]</sup> and Vitamin D which may reduce pneumonia severity, TB disease, or severity of COVID-19.<sup>[10]</sup> Maternal factors include young age, low maternal education, and physical or mental illness. Good antenatal care, optimal maternal physical and mental health, and control of HIV in HIV-infected mothers are important as these impact on birth outcomes, risk of pneumonia, and child health. Environmental exposures include crowding, poverty, tobacco smoke, or air pollution. Good ventilation in the home should be encouraged; infants should not be kept on their mothers' backs when cooking and clean cooking fuels should be promoted.

Pulse oximetry to monitor hypoxia and aid in timely oxygen supplementation is now more widely used in Africa, however, regular use could be further improved. Innovative oxygen supplementation and non-invasive ventilation strategies are increasingly being used on the continent. In Uganda, a low-pressure oxygen storage system can continuously provide oxygen equivalent to the treatment of one child for 30 days despite power cuts have been piloted and is ready for clinical field trials.<sup>[11]</sup> Physicians in Malawi have found low-cost bubble continuous positive airway pressure systems to be useful in the management of children with respiratory distress including pneumonia.<sup>[12]</sup> Regarding treatment of pneumonia, antibiotics remain the corner stone of treatment with prompt referral of severe illness for oxygen and other supportive management. New interventions to prevent RSV disease in children are well underway with Phase 3 trials of a maternal vaccine or a long-acting monoclonal antibody given to infants showing much promise.<sup>[13,14]</sup>

Intersectoral collaboration to strengthen poverty alleviation strategies, improve living conditions, optimize child

nutrition, and ensure all children have access to clean running water are essential to reduce the burden of illness. Pathogen factors include virulent organisms, high exposure levels, or infection with multiple organisms which may lead to more severe disease. Timely diagnosis, antimicrobial prophylaxis (for TB infection, HIV exposure, and pneumocystis pneumonia), and appropriate definitive and supportive pneumonia treatment are key. Health system factors include lack of access or affordability of effective preventive (such as immunization) and management (such as timely access to appropriate antimicrobial therapy and oxygen).

Current immunizations contained in the WHO EPI programs to prevent pneumonia include diphtheria, pertussis, measles, *HiB*, and PCV. Influenza vaccine is recommended for high-risk children older than 6 months of age or their household members and is given yearly, however, it is not on most EPI programs in Africa. These public health interventions, including immunization programs, nutritional rehabilitation, zinc supplementation, exclusive breastfeeding, and water, sanitation, and hygiene strategies, have all contributed toward marked reductions in mortality. Despite the availability of these effective and cost-effective interventions to end preventable childhood deaths from pneumonia, coverage is low in many LMICs, particularly in Africa.<sup>[15]</sup> Successful implementation of the WHO/UNICEF Integrated Global Action Plan for the Prevention and Control of Pneumonia and Diarrhea<sup>[16]</sup> to monitor the protection, prevention, and treatment of pneumonia and diarrhea in children under 5 years of age, and ensuing mortality, will need strong commitment from national governments, health-care professionals, private sector, and other stakeholders.

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