Vaccination to reduce antimicrobial resistance

Pneumonia remains the leading infectious cause of death in children worldwide, and how best to reduce this burden is worth consideration on World Pneumonia Day on November 12. Antibiotics are effective in treating bacterial pneumonia and access to appropriate antibiotics can be lifesaving. Universal provision of antibiotics to children younger than 5 years could prevent an estimated mean of 445,000 deaths per year due to community-acquired pneumonia—a 75.4% reduction across 101 countries.1 Antibiotics need to be available and accessible to effectively treat pneumonia; however, inappropriate use of antibiotics can lead to the emergence and progression of antibiotic resistance, a serious public health threat.

Barriers to rational use of antibiotics for pneumonia include a scarcity of point-of-care diagnostics appropriate for use in low-resource settings to identify pneumonia in children and to determine causative pathogens. Consequently, health-care providers, particularly those in low-resource settings, are guided to overtreat respiratory symptoms and signs that are not actually pneumonia with antibiotics. At the same time, many children still have little access to treatment and pneumonia mortality is high.

Consequences of inappropriate treatment with antibiotics are profound. Overuse of antibiotics is well known to lead to the development of antibiotic resistance to multiple antibiotic classes.2 Amoxicillin is the recommended first-line treatment for pneumonia because of widespread resistance to co-trimoxazole. Pneumococcal resistance to amoxicillin is low in African countries; however, prevalence of bacterial resistance to other antibiotics used to treat pneumonia is on the rise.3 Many common pathogens causing childhood respiratory infection, diarrhoea, and sepsis are resistant to virtually all first-generation antibiotics as a result of decades of extensive use.4 For example, 89–96% of Streptococcus pneumoniae is now resistant to co-trimoxazole in patients receiving treatment in hospitals in Malawi.5 Malawian surveillance studies6,7 have identified multiple other antibiotics with appreciable antimicrobial resistance prevalence. As the use of oral amoxicillin increases, good antibiotic stewardship is increasingly important for amoxicillin to remain a long-term solution for treating childhood pneumonia. An additional and urgent consideration is the emergence of extended-spectrum β-lactamase and carbapenemase-producing Gram-negative pathogens as a major threat to the treatment of neonatal sepsis.1

Reducing the development of antimicrobial resistance is a key factor for consideration in the prevention and treatment of childhood pneumonia. Diminishing the need for antibiotics by decreasing the incidence and burden of pneumonia is a first step. Prevention measures, such as nutrition, safe water, hygiene and sanitation, and reduction of household air pollution, all play a role; however, vaccination to reduce antimicrobial use and resistance might be an easier alternative in most countries. Antibiotic-resistant bacteria confound management choices, produce treatment failures, and increase health-care costs. Decreasing antimicrobial resistance through a strategy of expanded vaccination has shown promising results. For example, in northern California, introduction of a pneumococcal conjugate vaccine prevented 35 antibiotic prescriptions per 100 vaccinated children, suggesting that 1.4 million antibiotic prescriptions per year are preventable with pneumococcal conjugate vaccine in the USA.8

Vaccination strategies targeting S pneumoniae and Haemophilus influenzae type b have reduced the overall prevalence of invasive bacterial diseases (ie, pneumonia, meningitis, and sepsis) most associated with mortality. Clear direct benefits of the pneumococcal conjugate vaccine include the reduction of invasive pneumococcal disease among vaccinated young children; indirect benefits include reduction of disease in older children and adults. Most antibiotic-resistant pneumococci are of serotypes included in the pneumococcal conjugate vaccine; therefore declines in overall incidence of invasive pneumococcal disease include that due to multiple antibiotic-resistant strains.9,10 In the USA, after the introduction of pneumococcal conjugate vaccine into the routine childhood immunisation programme, incidence of penicillin non-susceptible invasive pneumococcal disease decreased by 81% in children younger than 2 years.9 Interruption of the transmission of antibiotic-resistant vaccine type strains also led to reductions in incidence in older children and adults. With all age groups considered together, the estimated number of cases of invasive pneumococcal disease caused by strains with reduced susceptibility to
penicillin or multiple antibiotics decreased by half after introduction of the pneumococcal conjugate vaccine. Within 4 years after introduction of the pneumococcal conjugate vaccine in children younger than 2 years in South Africa, reductions of greater than 80% were recorded in incidence of invasive pneumococcal disease caused by penicillin, ceftriaxone, and multidrug non-susceptible serotypes.10 Similarly, prevalence of invasive disease due to *H influenzae* type b has all but vanished after introduction of the *H influenzae* type b conjugate vaccine.11

Pneumococcal and *H influenzae* type b conjugate vaccines have reduced the burden of antibiotic-resistant bacterial disease globally. However, the continued use of antibiotics induces selection of replacement antibiotic non-susceptible strains among the remaining non-vaccine serotypes.4 This replacement disease has the potential to erode some of the gains vaccination has shown against resistant infections. Viral vaccines, such as influenza and measles vaccines, might also reduce antibiotic use.12,13 There is an urgent need to search for vaccines or monoclonal antibodies to protect neonates from antibiotic-resistant Gram-negative infections. Widespread vaccination against both bacterial and viral respiratory pathogens should be the first line of defence against antimicrobial-resistant respiratory pathogens, and novel vaccines are required.

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We declare no competing interests.

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