Childhood Pneumonia: A Global Perspective

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Pneumonia kills children. 2008 data published by Black et al in Lancet (2010; 375:1969-1987) reported approximately 1.6 million children less than five years of age died due to pneumonia, making it the leading cause of death in this age group. Greater than 50% of the annual new cases are in just six countries where it is estimated that greater than 40% of the world's children less than five years of age live: India, China, Pakistan, Bangladesh, Indonesia, and Nigeria. By global regions established by WHO, the estimated clinical pneumonia incidence is highest in Southeast Asia. Childhood pneumonia is caused by a combination of exposure to risk factors related to the host, the environment, and the microorganism; malnutrition, lack of immunizations, and indoor air pollution are to name a few. The leading bacterial causes are Pneumococcus and Haemophilus influenzae type b, both vaccine-preventable diseases. RSV is the leading viral cause and the primary risk factor for secondary bacterial pneumonia. Recognition of the impact of pneumonia on the world's children and the present means to minimize the morbidity and mortality should spur action from those in positions who implement lifesaving interventions.

What's New in Pediatric Enteric Infection?

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Despite reduction in mortality worldwide, diarrhea still accounts for more than 2 million deaths annually. The morbidity and mortality in children under age 5 is significant in both developed and developing countries. The most common bacterial pathogens affecting young children are Salmonella, Campylobacter, Shigella and E. coli O157:H7. In a recent FOODNET surveillance study from CDC, USA in children younger than 1 year, Salmonella had the highest rates at 134/100,000 followed by Campylobacter at 33.5/100,000. The disease burden is much heavier in the developing countries. Recent studies indicated that Shigella is the most common bacterial pathogen causing dysenteric diarrhea in children in developing countries. Antibiotic treatment is indicated for dysentery caused by Shigella species, but Shigella are becoming increasingly resistant to most antimicrobial agents commonly used in the treatment of diarrhea. Among the four species, S. dysenteriae 1 is generally the first to develop resistance to a new antibiotic, but then the other Shigella species follow. Rarely does susceptibility reappear once resistant strains have become endemic in a region. From this perspective, the recent appearance of resistance in Shigella to third-generation cephalosporins is worrisome. In order to ensure appropriate treatment, continual surveillance is required to determine which antibiotics are still active. This strategy of “trying to keep one step ahead” implicates the continual development and testing of new antibiotics, which inevitably are more expensive. As another example, the emergence of Campylobacter that are resistant to ciprofloxacin as well as azithromycin has threatened to undermine the effective treatment of travelers’ diarrhea. Non-typhoid Salmonella are another common enteric pathogen in the developing countries; such infections can generate a substantial mortality or morbidity, depending on the host factors and serotypes of causative organisms involved. The prevalence of the illnesses in the pediatric population and the need to treat severe Salmonella infections in this age group with antimicrobial agents impacts on the escalating antimicrobial resistance that is being seen globally.

Antimicrobial treatment is essential for children with systemic infections caused by Salmonella.
For uncomplicated *Salmonella* gastroenteritis in normal hosts, our recent studies showed that patients with high C-reactive protein (CRP) were more frequently put on empirical antimicrobial therapy and had more complications (CRP ≥ 100 mg/L) than those without. These patients usually became afebrile within 2-3 days after initiation of adequate antimicrobial treatment. Cases receiving antibiotics that were inactive in vitro did not have more complications than those receiving antibiotics active in vitro. The results suggest that antibiotics may be clinically beneficial to a subset of patients with high CRP and longer duration of fever among children with *Salmonella* gastroenteritis. In recent years, gastroenteritis outbreaks caused by viral agents, such as rotaviruses, adenoviruses, astroviruses, and previously un-characterized noroviruses, associated with gastroenteritis, have been widely reported. The clinical manifestations of these viral infections are similar but still show subtle difference. One of the most important but unusual manifestations associated with norovirus infection is convulsive disorder in children, particularly in young infants. The features of infantile seizures associated with norovirus infection included seizures in cluster and recurrence within 24 hrs without focal signs and high fever. Besides, most of the episodes of convulsion occurred within 1 week (mean 2.8 days, range 1–6 days) from the onset of gastroenteritis symptoms. The convulsions associated with norovirus were benign, although some patients still required short-course anticonvulsant therapy. None of these patients reported developed any neurological sequelae. By virtue of the great importance of rotaviruses in pediatric gastroenteritis, epidemiologic studies of infection in young children with rotavirus gastroenteritis following the use of live-attenuated rotavirus vaccines have been carried out. A large scale national US surveillance study conducted by Centers for Disease Control and Prevention showed that the number of rotavirus positive tests immediately after RotaTaq approval and moderate vaccine effectiveness has exceeded what could be predicted based upon the coverage rates, indicating a probable herd immunity effect. There have been a number of studies of Rotarix and RotaTeq conducted in low-income countries. The effectiveness of these vaccines has been less than that observed in high-income populations. Despite the reduced effectiveness in developing, low-income countries, the overall impact of rotavirus vaccines will still be substantial as 85% of all rotavirus-related deaths occur in these countries. Based upon the effectiveness data and the significant potential impact upon the health of the world’s children, the World Health Organization recommended in 2010 that either one of the two vaccines be given to all children.

Acute otitis media (AOM) is the main cause for antibiotic prescriptions in infants and young children. In the last 15 years, antibiotic resistance has been dramatically increasing among the 2 most important pathogens of AOM: *S. pneumoniae* (Pnc) and nontypeable *H. influenzae* (NTHi). A great part of the increasing resistance among Pnc isolates can be attributed to the wrong antibiotic choice, when use of resistance-promoting antibiotics is frequently practiced. On the other hand, the introduction of the 7-valent pneumococcal vaccine (PCV7) was shown to decrease diseases caused by the serotypes included in the vaccine, which cover most of the commonly resistant and multi-resistant strains, except serotype 19A. The co-selection of the Pnc strains by antibiotics on the one hand, and the vaccine on the other hand has promoted some non-vaccine serotypes that are somewhat non-susceptible to antibiotics and could cause problems in the future. As for NTHi, its increasing rate of resistance to various antibiotics in mechanisms other than β-lactam production is alarming. The presence of NTHi component in the PCV10 (PHiD-CV) raised hope of reducing NTHi AOM, but the concept that this indeed is occuring still needs to be proven.

At the present time, it is important to proceed with the widespread use of extended spectrum PCV vaccination and to reinforce judicious use of antibiotics through ongoing training program and appropriate messages to the population. Various examples of such campaigns will be presented.