Pneumococcal Disease in the Era of Pneumococcal Conjugate Vaccine

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KEYWORDS

- Pneumococcal disease • Pneumococcal conjugate vaccine
- Invasive pneumococcal disease • Pneumococcal meningitis
- Pneumococcal pneumonia

KEY POINTS

- Universal immunization of infants and toddlers with pneumococcal conjugate vaccines has resulted in decreases in invasive pneumococcal disease, all-cause pneumonia, empyema, mastoiditis, acute otitis media, and complicated otitis media.
- The impact of pneumococcal conjugate vaccine extends beyond those immunized to children too young to be immunized, children unable to respond to the vaccine, and adults in the community as a result of herd effect.
- Children with comorbid conditions have higher rates of pneumococcal disease and increased case fatality rates compared with otherwise healthy children.
- Treatment of pneumococcal disease requires an approach that considers site of infection, antimicrobial susceptibility patterns in the community, and severity of illness.

The universal immunization of infants and toddlers with pneumococcal conjugate vaccine (PCV) in the United States beginning in 2000 heralded a new era for pneumococcal disease prevention. Conjugate vaccines were immunogenic in young infants, prevented vaccine type invasive pneumococcal disease (IPD), pneumonia and otitis

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media, and decreased nasopharyngeal colonization with vaccine serotypes leading to a herd effect that affected all age groups. However, new challenges emerged that would eventually lead to second-generation conjugates that included a larger number of serotypes to address both replacement disease (increases in disease owing to nonvaccine serotypes) and providing more expansive coverage for the global community. Postlicensure studies provided new insights into the importance of serotype distribution among carriage isolates and how the event-to-carrier ratio for a specific serotype permits us to understand the substantial decline in IPD in the absence of a decline in overall pneumococcal colonization. The limitation of current diagnostic tools for pneumococcal pneumonia became apparent from the discord between the prevalence of diagnosed pneumococcal pneumonia in studies of pediatric pneumonia compared with the observed decline in all-cause pneumonia associated with pneumococcal vaccine uptake in the community.[1,2] Despite the progress in prevention, pneumococcal disease continues to disproportionately impact children in low-income countries and those with comorbid conditions (in high-income countries) and remains a major cause of mortality and morbidity.

EPIDEMIOLOGY

Nasopharyngeal colonization with *Streptococcus pneumoniae* is an initial step in the pathogenesis of pneumococcal disease. Asymptomatic carriage is common with reported prevalence ranging from 11% to 93%; carriage varies with age, environment, the presence of upper respiratory infections, and population studied.[3,4] Risk factors for pneumococcal carriage include age younger than 2 years, exposure to overcrowding and household smoking, attendance at out-of-home child care, winter season, and lack of breast feeding.[5] Initial acquisition of pneumococci occurs earlier in low-income countries, (as early as the first month of life) compared with high-income countries and peaks at 2 to 3 years of age.[4,6] Among school-age children, 20% to 60% may be colonized, whereas only 5% to 10% of adults are colonized. The duration of carriage also varies and is generally longer in children than in adults.[6] The relationship of carriage to the development of natural immunity is poorly understood, but the prevalence of nasopharyngeal carriage declines over time, suggesting that colonization elicits protection.[7] The impact of conjugated vaccines on pneumococcal carriage has been dramatic; vaccination has resulted in near elimination of vaccine serotypes and increased prevalence of nonvaccine serotypes, with little change in the overall rate of pneumococcal colonization. Changing serotype distributions in the nasopharynx has led to a subsequent reduction in IPD, as most nonvaccine serotypes have a lower likelihood of causing disease once colonization has been established, and decreased transmission of vaccine serotypes to under- or unimmunized children and adults, also resulting in lower rates of IPD in under- or unimmunized children and adults.[8]

Most *S pneumoniae* serotypes are found to cause serious disease, but of the 92 known pneumococcal serotypes, 10 serotypes account for nearly 62% of invasive disease worldwide.[9] The rank order and serotype prevalence differ over time, by age group and by geographic area. In the United States, before widespread use of 7-valent pneumococcal conjugate vaccine (PCV7), serotypes 4, 6B, 9V, 18C, 19F, and 23F were the most common serotypes isolated from blood or cerebrospinal fluid (CSF) and were responsible for 80% of the invasive infections in children younger than 5 years.[10] Serotypes 6B, 9V, 19F, and 23F also accounted for approximately 80% of penicillin-nonsusceptible isolates. Pneumococcal disease is mostly episodic; however, pneumococci are transmitted from person to person by respiratory droplets, and