Nasopharyngeal Carriage of Pneumococcal Pediatric Serotypes: A Risk for Acute and Recurrent Otitis Media in Children and for Invasive Disease in Susceptible Adults

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(See the article by Libson et al., on pages 1869–75.)

Otitis media represents a vast disease burden and is the leading indication for the administration of antibiotics in children [1]. Various studies have linked pneumococcal nasopharyngeal colonization with increased risk of acute and recurrent otitis media [2–5]. In this issue of The Journal of Infectious Diseases, Libson et al. [6] extend these observations to show that children in whom pneumococci have been eradicated from the middle ear yet who continue to harbor pneumococci in the nasopharynx at the end of antibiotic treatment are at increased risk of subsequent episodes of otitis media. This study strengthens the argument, as pointed out by the authors, that the impact that antibiotics have on nasopharyngeal carriage should be considered during the evaluation of new and existing drugs. To date, few studies of new or existing drugs have evaluated their impact on nasopharyngeal carriage. Most drugs that are used to treat upper respiratory tract infections have little ability to eradicate colonization in the nasopharynx and are therefore likely to select resistant strains in the flora, either by selection of spontaneous mutants harbored in small numbers among the susceptible flora or by enhancement of the proportion of pre-existing resistant strains in the carried population [7–9]. Thus, isolates from both the nasopharynx and the middle ear in patients with recurrent otitis media show increased antibiotic resistance [10]. Fluoroquinolones are used to eradicate nasopharyngeal carriage of meningococci, but an initial study in children showed only a 55% reduction—and not an eradication—of nasopharyngeal carriage of pneumococci, despite 10 days of treatment with these drugs [11]. The relationship between carriage and otitis media is complex, and host susceptibility and concurrent viral infection [12] are probably critical to the pathogenesis of both acute and recurrent otitis media. The current strategy to interrupt carriage includes the administration of pneumococcal conjugate vaccine to young infants [13]. The use of this vaccine has been shown to reduce the use of antibiotics in the treatment of upper respiratory tract infections [14, 15], but the long-term impact that the use of the vaccine has on otitis media and on the patterns of antibiotic use remains unclear, because replacement of serotypes occurs in the nasopharynx [13] and because resistance has emerged in non-vaccine serotypes [16, 17].

The study by Libson et al. [6] also raises the broader issue of the importance of the reservoir of carriage of pneumococci in children as a risk for pneumococcal disease in the community. The serotypes implicated in both carriage and recurrent otitis media are the so-called pediatric serotypes (serotypes belonging to serogroups 6, 9, 19, 23, and serotype 14), which were found in 20 of 24 of the paired middle ear fluid and nasopharyngeal culture specimens from patients with recurrent disease in this study [6].

The carried pediatric serotypes are not only a major cause of acute and recurrent otitis media in children but are also an emerging cause of invasive pneumococcal disease in adults. Respiratory infections are the leading infectious cause of death in children and adults [18]. When pneumococci isolated from the blood of infected adults were serotyped in the pre-antibiotic era, they were numbered according to their prevalence. Thus, studies completed through 1937 refer to the dominant pneumococcal types as groups I, II, and III. These 3 serogroups caused >60% of the invasive disease in adults, and all other pneumococci were initially classed...
as group IV [19]. Today, there are 90 recognized serotypes of pneumococci, as determined by differences in their capsular polysaccharide. Only a small fraction of these serotypes, however, regularly cause invasive disease [20].

The epidemiological characterization of invasive pneumococcal disease in adults has changed dramatically in the United States since 1937, with the progressive disappearance of the originally dominant endemic and epidemic serotypes 1–5 and the emergence of these pediatric serotypes (all part of the original group IV) as a major cause of disease in adults [21]. Pediatric serotypes have likely increased in prevalence because the population of patients at risk for invasive pneumococcal disease has aged and includes many immunocompromised persons [21]. The increased prevalence of pediatric serotypes in adults was first found in HIV-infected patients in Africa [22] and was subsequently confirmed in the United States, where the dominance of these serotypes was noted not only in HIV-infected persons but also in those with other immunocompromising conditions [23]. In Africa, pediatric serotypes are more common not only in HIV-infected adults but also in women, who are at particular risk for disease caused by these antibiotic-resistant pediatric serotypes [24], suggesting the possibility of child-to-mother transmission. Analyses of risk factors for pneumococcal bacteraemia in the United States have identified exposure to children as a risk, both for all adults at risk for invasive pneumococcal disease [25] and for HIV-infected adults [26].

Direct studies of the transmission of Streptococcus pneumoniae between parents and children living in the same household have provided apparently conflicting results. A study from the Gambia showed that, in the absence of prevalent HIV infection in the parents, the same serotype of pneumococci isolated from an ill child was more likely to be isolated from a sibling than from an adult living in the same household [27]. More recent studies that used molecular tools to identify pneumococcal clones within serotypes found that antimicrobial-resistant pediatric strains obtained from attendees of day care centers were not isolated from the children’s healthy parents, which is in keeping with the presence of an “immunologic barrier” in the adults [28, 29]. When the index case in a family transmission study was defined as an adult with invasive pneumococcal disease [30], however, 62% of the paired isolates from parents and their children had identical serotypes. Thus, children were shown to be an important reservoir of pneumococcal strains that infected a susceptible adult in the family, and the immunological barrier was broken. Compelling data supporting the importance of family transmission of pneumococci as a risk for invasive disease in adults in the United States have come from studies of the introduction of conjugate pneumococcal vaccination of US children. These vaccines interrupt transmission of vaccine serotypes [13], and, as is shown in a number of recent studies from the United States [31–33], a dramatic decrease in vaccine serotypes causing invasive pneumococcal disease in adults occurred after the introduction of conjugate pneumococcal vaccination of children.

In a randomized trial in which children were given a pneumococcal or a control vaccine, depending on their community of residence [34], adults residing in the community where children were vaccinated had lower rates of carriage of vaccine strains, compared with adults in the control community. Similar data have recently emerged from postvaccination carriage studies in Alaska [35].

Vaccines and antibiotics are designed to respectively prevent and cure pneumococcal infections. The study by Libson et al. [6], as well as numerous studies on the epidemiological characterization of pneumococcal disease, suggest that knowledge of the impact that vaccines and antibiotics have on the nasopharyngeal carriage of pneumococci is essential to our understanding of the future evolution of pneumococcal disease.

References

13. Klugman KP. Efficacy of pneumococcal conjugate vaccines and their effect on carriage and