The Shifting Dynamics of Pneumococcal Invasive Disease after the Introduction of the Pneumococcal 7-Valent Conjugated Vaccine: Toward the New Pneumococcal Conjugated Vaccines

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(See the article by Kellner et al. on pages 205–12)

Since the introduction of the first pneumococcal conjugated vaccine, the 7-valent conjugated vaccine (PCV7), a tremendous reduction in the incidence of invasive pneumococcal disease (IPD) has been observed in all countries having introduced its use [1–3]. That reduction, mainly of the serotypes included in the vaccine, has been directly observed in vaccinated children [1]. The rate of hospitalization for Streptococcus pneumoniae meningitis reported by Tsai et al. [4] decreased by 66.0% and 51.5% among children aged <2 and 2–4 years, respectively. The incidence of other S. pneumoniae–related diseases, such as community-acquired pneumonia and acute otitis media, also decreased among young children after PCV7 introduction [5, 6].

Even more dramatic was the indirect effect (herd immunity) observed in adults [7, 8]. The vaccine prevented more than twice as many IPD cases caused by the PCV7 serotypes through indirect effects on pneumococcal transmission (i.e., herd immunity) than through its direct effect on vaccinated children [9]. In addition, Tsai et al. [4] reported a 33.0% reduction in S. pneumoniae–associated meningitis among adults aged >65 years.

In this issue of Clinical Infectious Diseases, Kellner et al. [10] report on the dynamics of IPD in children and adults during a long period of time, before (1998–2001) and after (2003–2005) the introduction of PCV7 to the Calgary, Alberta, Canada, region, which has a population of ~1 million inhabitants. They used prospective population-based data from The Calgary Area Streptococcus pneumoniae Epidemiology Research (CASPER) team. Cases were identified through active laboratory based surveillance at the central microbiology laboratory. The strength of this study lies in its ability to determine the incidence of IPD in specific age groups and to determine different dynamics in serotype-specific IPD in the same age groups.

Kellner et al. [10] added another piece to the puzzle of the changing epidemiology of IPD after PCV7 introduction. Interestingly, the reduction in IPD cases caused by PCV7 serotypes was deep and abrupt in the vaccinated age groups, reaching >90% in <3 years after PCV7 introduction to the population. In contrast, the reduction of IPD disease caused by PCV7 serotypes in the older age groups was more gradual and modest, reaching 59%, 45%, 38%, 78%, and 23% among those aged 5–15, 16–64, 65–84, and ≥85 years, respectively. Thus, clearly, PCV7 succeeded to reach its primary goal—that is, the reduction in the incidence of IPD due to the serotypes included in the vaccine in the entire population, including unvaccinated persons. This decrease is in the same order of magnitude than that reported in the United States and in other countries [1, 9, 11]. Significant increases in the number of IPD cases due to non-PCV7 serotypes were observed among adults aged 16–64 years. In addition, increases in the incidence of IPD due to non-PCV7 serotypes were also observed in all age groups except among children aged 6–23 months, but these were not statistically significant.

In regions where serotypes included in the PCV7 are endemic, their reduction following PCV7 introduction is expected. However, the introduction of new serotypes can occur through 2 different mechanisms. The first mechanism is the intro-
duction of serotypes with high disease potential. These serotypes, which do not have to compete with endemic serotypes included in the vaccine in the same biological niche, such as the nasopharynx, can simply invade the mucosal area or the blood to cause disease. Serotypes 1 and 5 were reported to have high disease potential to cause both acute otitis media and IPD [12, 13]. These serotypes can cause outbreaks in closed communities [14]. An outbreak of IPD due to serotype 5, which mainly involved adults, was reported after the introduction of the PCV7 in Calgary. Of interest, in 2006, Romney et al. [15] also reported an outbreak due to a single clone of serotype 5 during the same period in the city of Vancouver, British Columbia, among residents of Downtown Eastside, a neighborhood known for its high rates of poverty and illicit drug use. Moreover, it should be emphasized that most of the increment of the non-PCV7 serotypes among adults in the Calgary region was caused by the outbreak of IPD due to serotype 5.

The second mechanism is the increase of endemic serotypes not included in PCV7, called “the replacement phenomenon.” This replacement of non-PCV7 serotypes, especially of serotype 19A, was reported in IPD in Alaska native children [16]. However, increased rates of serotype 19A have not been observed since the introduction of PCV7 among non-Alaska Native and Navajo [16, 17]. In some regions, such as Israel, Spain, and Korea, the occurrence of serotype 19A IPD had increased significantly before the introduction of the PCV7, probably in association with increased antibiotic use, which promoted this antibiotic-resistant serotype to replace antibiotic-susceptible ones [18, 19].

In this issue, Kellner et al. [10] reported a significant increase in the incidence of IPD cases of serotype 19A after the introduction of PCV7. However, all cases were reported in adults and none in children. Thus, no true replacement was observed among vaccine-eligible children. Children are generally considered to be the natural reservoir for S. pneumoniae, mainly during the first years of life, because of the high carriage rate of the bacteria in the nasopharynx, compared with adults [20]. Thus, it is reasonable to assume that this serotype is commonly carried in children and is also an increasing cause of acute otitis media, as has been reported in other studies [21, 22].

In addition, the incidence of IPD due to serotypes 8 and 12F increased after the introduction of PCV7 in adults but not in children. This increase can also be related to the introduction of new serotypes with high disease potential, because these serotypes were also reported in outbreaks [23]. These serotypes are included in the 23-valent polysaccharide vaccine, and effort should probably be made toward increased use of this vaccine among adults in the Calgary area.

After the introduction of PCV7 in Calgary, both a reduction in the incidence of IPD due to PCV7 serotypes and an increase in the incidence of IPD due to non-PCV7 serotypes in adults were observed. However, although the incidence of PCV7 serotype–associated IPD decreased in children, the incidence of non-PCV7 serotype–associated IPD did not increase in that age group. One cannot rule out the spread of non-PCV7 serotypes, such as 8, 19A, and 12F, from children to adults. It is possible that carriage of these serotypes increased among children but did not cause more cases of disease in this age group. However, the reduction in PCV7 serotypes together with the increase in non-PCV7 serotypes—which point to replacement—do not prove that the vaccine was the sole culprit for serotype-related disease replacement. In the report by Kellner and colleagues, the most prevalent non-PCV7 serotype was serotype 5, which was known to be an epidemic serotype. These dynamics are also true for serotypes 12F and 8 and even for serotype 19A [21]. Thus, secular trends of specific serotypes, such as serotype 5 during the last 2 years of the study, cannot be excluded, although the incidence of IPD due to these serotypes can change over time. Additional studies from the Calgary region that directly address the issues of IPD both in adults and in children, to monitor these dynamics in IPD, should be conducted. Moreover, studies of carriage—both in children and in adults—could answer the question of whether specific serotypes spread from children to adults. This information should include other potential factors that can influence the spread of specific serotypes, such as antibiotic use in the community that can select toward more-resistant serotypes (e.g., serotype 19A), as has been reported in Calgary and elsewhere [21, 24, 25]. New serotypes, such as 6C, should also be monitored in future studies conducted in the Calgary region.

The increase in the non-PCV7 serotypes is important and should be taken into consideration in the future use of the new generation of conjugated vaccines, to prevent outbreaks of IPD due to invasive serotypes (e.g., serotype 5) and to avoid replacement by serotypes such as 19A. The new generation of pneumococcal conjugated vaccines may potentially be more efficient at preventing IPD among children, and the effect of this vaccination will probably extend to other age groups. These vaccines have the potential to prevent additional cases of IPD if vaccination is introduced to the elderly population. Future development of expanded vaccines containing serotypes such as 8, 12F, and 22F may also be considered because of their prevalence and invasiveness potential for both adults and children.

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References

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