Epidemiology of Pneumococcal Disease and Efficacy of Polysaccharide Vaccines in Adults

Pneumococcal pneumonia and invasive pneumococcal disease (IPD) remain a considerable cause of morbidity and mortality, with recent data showing a continued unacceptably high social and economic burden. *Streptococcus pneumoniae* can be isolated from 5-10% of healthy adults and 20-40% of healthy children. Infection can result in a variety of clinical syndromes with meningitis, pneumonia, and sepsis among the most critical. It is also responsible for 30-50% of all community-acquired pneumonias, with a fatality rate of 7-35% for bacteremic pneumococcal pneumonia. Vaccination with the 23-valent pneumococcal polysaccharide vaccine (PPV23) is an important preventive strategy in the United States.

**Epidemiology of Pneumococcal Disease in the United States**

Each year, pneumococcal infections are responsible for 6 million cases of otitis media, 3000 cases of meningitis, and an incident rate of pneumonia of 23-33 cases per 100,000 population. The very young and older adults are at high risk. Indeed, adults who are 65 years of age or older are extremely susceptible to IPD with an estimated 350,000 to 620,000 hospitalizations per year (Fig. 1). The fatality rate from IPD for patients in this age group is 7.2 per 100,000 population and 1 per 100,000 population for children < 1 year of age.

**Risk Factors**

In addition to age, others at high risk for infection include Blacks, Native Americans, and Alaska natives, as well as persons with certain medical and immunocompromised conditions, such as chronic heart or lung disease, HIV, or cancer. A report from the Centers for Disease Control and Prevention (CDC) compiled from data collected during 1999 and 2000 shows the dramatic effects of chronic illness and increasing age on the incidence of IPD (Figs 2A and B). Persons with chronic conditions have a 2 to 8 fold increased risk of death from IPD; this risk was higher for Blacks than for Whites. Adults in long-term care facilities are particularly at risk for IPD, as residents often suffer from a number of chronic illnesses.

**Available Vaccines for Pneumococcal Disease**

Although more than 90 serotypes of *S. pneumoniae* have been identified, the 7-valent conjugated pneumococcal vaccine (PCV7) for children covers more than 80% of isolates obtained from children less than 5 years of age. Since the introduction of this vaccine in 2000, the incidence of IPD not only decreased in children, but has apparently reduced the incidence of IPD in adults as well. In 2001, the incidence of IPD was reduced by 69%.
in children; a concurrent incident disease reduction of 32% was observed in adults 20–39 years of age, 8% in adults 40-64 years of age, and 18% for adults 65 years of age and older. In the oldest cohort, there was a 22% decrease associated with the 7-valent vaccine-related serotypes: however, this was offset slightly by a 5% increase for non-vaccine related serotypes.12

PPV23, which is available for adults, contains purified antigens from 23 different serotypes shown to account for about 85-90% of bacteremic infections in adults in the United States4,13. The serotype-specific protective effect of PPV23 and PPV14 (no longer in use) was assessed in a prospective, hospital-based, case-controlled study of 1054 adults (predominantly white; median age of 69 years of age). The aggregate protective effect for IPD was 56% for all patients, 61% for immunocompetent patients (n = 808), and 21% for immunocompromised patients (n = 175). The vaccine was not effective against serotypes not included in the vaccine. The case fatality rate, however, was similar among vaccinated and non-vaccinated patients13.

A systematic review of randomized trials (from 1976 to 1998) of various polyvalent PPV vaccines in immunocompetent adults led to a meta-analysis of 14 trials of 48,837 patients5. Overall, PPV vaccines decreased the incidence of definite pneumococcal pneumonia by 71%, presumptive pneumococcal pneumonia by 40% and mortality due to pneumonia by 32%. PPV vaccination did not prevent all-cause pneumonia or death. A subgroup analysis of patients older than 55 years of age lacked the statistical power to show differences in outcomes with vaccination; however, there was a trend toward a reduced risk of definitive pneumococcal pneumonia (odds ratio 0.58 [0.18–1.0] and mortality due to pneumonia (odds ratio 0.69 [0.28–1.27]).

**Outcomes in High-risk and Older Populations**

A comprehensive 14 year surveillance study assessed the efficacy of the PPVs in high risk populations >-65 years of age) in the United States.14 Outcomes for 2837 persons showed the overall protection efficacy for serotypes included in the vaccine was 57% (95% CI: 45-66%). Efficacy for immunocompetent older adults >-65 years of age was 75% (95% CI: 57–85%). For persons with various immunocompromised clinical conditions including diabetes mellitus, and chronic heart and lung diseases, who were considered high-risk, the estimated vaccine efficacy was considerably lower, ranging from 0% to approximately 65%. Of interest, it was observed that protection did not decline over time.

The incidence of IPD in patients infected with HIV has been reported to be 46 to 100 fold higher than in the general population. The introduction of highly active antiretroviral therapy (HAART) and the more widespread use of PPV23 may impact the incidence of IPD in this population. A prospective, case-controlled study of 142 episodes of disease in 122 Spanish HIV-infected adults showed that the incidence of pneumococcal bacteremia was significantly reduced by 2.9 fold in the current era of HAART compared to that in the pre-HAART era (8.2 episodes per 1000 patient years vs 24.1 episodes per 1000 patient years, respectively, P=.010)15 in patients administered PPV23. In an earlier study that stratified HIV infected individuals by CD4 cell count, only 24% of persons with ≤ 500 CD4 cells responded to PPV compared with 75% of persons with CD4 >500 and 92% of healthy controls. Therefore, the authors suggested that pneumococcal vaccine should be administered when HIV is first diagnosed16.
Outcomes in Older Adults

The effectiveness of vaccination for pneumococcal disease in older adults remains controversial as many prospective clinical trials have not documented a significant reduction in the risk of pneumonia or mortality by PPV, although positive trends have been observed. Overall, studies of older adults have been limited by the inability to adequately power the study because of the relatively low number of vaccinated subjects. Nevertheless, several studies involving large numbers of older adults have evaluated outcomes of pneumococcal vaccination in the community setting and found that there are benefits from vaccination. For example, a large retrospective cohort study assessed 47,365 healthcare data base members 65 years of age and older over a 3-year period. Primary outcomes included hospitalization for community-acquired pneumonia, pneumonia in patients who were not hospitalized, and pneumococcal bacteremia. Prior administration of PPV was associated with a 44% decrease in pneumococcal bacteremia (hazard ratio, 0.56; P=.03), but was also associated with a small elevated risk of hospitalization for pneumonia (hazard ratio, 1.14, P=.02). Vaccination did not affect the risk of outpatient pneumonia (hazard ratio, 1.04; 95% CI [0.33–0.93]).

A large prospective cohort study in persons aged ≥65 years in Sweden assessed the effectiveness of PPV23 in reducing hospitalizations and deaths. Enrollees could also receive the influenza vaccine. Thirty-nine percent of the population was vaccinated during an 8-week campaign. The incidence of hospitalization for pneumonia was 22% lower in the group vaccinated (RR 0.78; P=.0001) compared to the unvaccinated group. The risk of IPD was also significantly reduced by 54% (RR: 0.46; P=.007). For the group that was vaccinated, the risk of dying of pneumonia while hospitalized was 45% lower (RR 0.55; P<.0001). The authors concluded that pneumococcal (and influenza) vaccination significantly decrease the number of hospitalizations and mortality in older adults.

The potential benefit of vaccination against pneumococcal disease is of particular interest in the older population with serious underlying medical conditions. In a 2-year retrospective study of 1898 persons ≥65 years of age with diagnosed chronic lung disease, vaccination with PPV23 significantly reduced hospitalization due to pneumonia and influenza by 43% (P=.005) compared with unvaccinated persons. Additionally, mortality from all causes was reduced by 29% (P=.008).
persons, provided both future cost savings and improved health benefits. In addition, Black race as a high-risk group showed a greater than average health and cost benefit of vaccination.

**Summary**

Pneumococcal pneumonia and IPD remain an important cause of morbidity and mortality in the United States. PPV23 is immunogenic and has shown efficacy in reducing IPD. Although data for reduction of pneumonia in older adults is contradictory, recent studies have suggested that vaccination may reduce hospitalization, complications, and mortality in this population. Thus, PPV23 remains a fundamental strategy for prevention of pneumococcal infection in the United States.

**REFERENCES**


