Chapter 5
Aging, Inflammation, and Pneumococcal Disease

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5.1 Introduction

Streptococcus pneumoniae (the pneumococcus) is the leading cause of community-acquired pneumonia (CAP) and otitis media, and a primary cause of bacteremia and meningitis (Pneumococcal vaccines 1999). As with most infectious diseases, the poorest nations experience the greatest burden of disease. This can be attributed to reduced vaccine use, decreased standards of living, and limited access to supportive critical care (Dopazo et al. 2001; Robinson et al. 2001). Worldwide, the incidence of invasive pneumococcal disease (IPD) is greatest in children. However, death, as a result of infection, primarily occurs in the elderly (>65 years of age) (Atkinson et al. 2007; Lexau et al. 2005). The World Health Organization (WHO) estimates that pneumococcal disease is responsible for 1.6 million deaths annually (Pneumococcal vaccines 1999).

Pneumococcal disease in the elderly is characterized by its rapid onset, severity, and high case-fatality rate; in the United States, the mortality rate for the elderly with pneumococcal pneumonia is 13–23%, compared to 5–7% in the general population. Likewise, case-fatality rates for the elderly with pneumococcal bacteremia and meningitis are 60% and 80%, respectively; in contrast, they are 20% and 30% for the general population (Atkinson et al. 2007). Risk factors for IPD include advanced age, alcoholism, bronchial asthma, immunosuppression, lung disease, heart disease, asplenia, diabetes, and institutionalization (Loeb 2004; Mufson 1999). It is of note that the majority of the elderly have one or more underlying medical conditions that puts them at increased risk for IPD (Robinson et al. 2001). Moreover, the elderly experience age-related changes in immune function that increase their susceptibility to infection.

5.1.1 Clinical Presentation

Clinical presentation of pneumonia in healthy adults includes fatigue, fever, chills, anorexia, sweats, myalgia, pleuritic chest pain, and cough with purulent sputum production (Johnson 2000; Koivula 1994). In the elderly, there are often fewer
symptoms including a lack of fever or cough (Granton and Grossman 1993). Notably, absence of fever has been associated with a poor prognosis. Elderly patients with pneumonia often present with neurological symptoms, in particular an altered mental state. By and large it is dependent on the physician to recognize that the lack of overt clinical signs does not rule out the possibility of pneumonia in the elderly and that diagnosis of pneumonia is dependent on a thorough pulmonary lung exam and most importantly, visualization by chest X-ray of lobar involvement.

It is beyond the scope of this review to detail clinical management of pneumococcal pneumonia, bacteremia, or sepsis. However, several studies have documented that antibiotic therapy within the first 8 h of hospitalization was associated with decreased 30-day mortality rates (Loeb 2004; Niederman et al. 2001). Currently, the American Thoracic Society guidelines for treatment of pneumonia include administration of a second-generation cephalosporin with a macrolide, sulfamethoxazole-trimethoprim, or β-lactam with a macrolide if a susceptible strain is found (Niederman et al. 2001).

5.1.2 Vaccines

Immunity against pneumococcal disease is mediated by antibodies against the capsular serotype involved. At this time, only one vaccine, Pneumovax® 23 (Merck & Co. Inc.), is licensed by the United States Food and Drug Administration for use in adults against S. pneumoniae. Pneumovax® 23 is composed of capsular polysaccharide (CPS) from the 23 most common serotypes and has an overall protective efficacy of 55–70% against bacteremia and meningitis (Pneumococcal vaccines 1999; Shapiro et al. 1991). Unfortunately, Pneumovax® 23 does not protect against nonbacteremic disease (i.e., pneumonia without bloodstream infection) (French et al. 2000; Whitney et al. 2003). This is a major concern, as S. pneumoniae is the most frequent cause of CAP, and CAP is most severe in the elderly (Lexau et al. 2005; Gutierrez et al. 2006; Janssens 2005). In addition, the elderly do not produce a robust response to the vaccine as evidenced by a lack of protective antibody to the polysaccharide capsule (Bruyn and Van Furth 1991; Regev-Yochay et al. 2004). Currently, the United States Centers for Disease Control and Prevention recommends vaccination of all high-risk groups, and revaccination of the elderly every 5 years.

Children in the United States are vaccinated with a conjugate vaccine composed of CPS linked to the diphtheria toxoid (Prevnar®; Wyeth Inc.). Use of Prevnar® has not only led to a decrease in the incidence of IPD among children, but also to decreased nasopharyngeal colonization of the serotypes included in the vaccine (Whitney et al. 2003; McBean et al. 2006). Decreased carriage rates have in turn led to improved “herd immunity” and a reduction in incidence of IPD in the elderly. From 1998 to 2003, the incidence of invasive disease among the elderly has decreased by 18% (McBean et al. 2006).

Vaccination is the only proven method shown to reduce IPD. Unfortunately, protein conjugation is costly and imposes steric hindrances that limit the numbers