Chapter 31

Pneumococcal Conjugate Vaccines

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1. INTRODUCTION

The development of multivalent pneumococcal vaccines for the prevention of both systemic and noninvasive pneumococcal diseases in infants, older adults, and immune-compromised individuals has gained increasing importance over the last decade. The rising cost of medical care has renewed interest in prevention instead of cure for a disease and in many cases cures may not be available with the increase in antibiotic resistance in many bacteria. Capsular polysaccharide vaccines for the prevention of systemic pneumococcal disease in adults and older children have been readily available for over 17 years but use of the vaccine in these age groups has been limited. The recent licensures of Hib–protein conjugate vaccines, 1987 for toddlers, 1990 for infants, have contributed to a dramatic reduction in the incidence of invasive Haemophilus influenzae type b disease and have thus demonstrated the tremendous potential of this technology to significantly reduce the incidence of diseases caused by encapsulated bacteria.

This chapter is a review of the published literature on pneumococcal–protein conjugate vaccines. It is not meant to be a review of pneumococcal disease. For more detailed reviews of pneumococcal disease, epidemiology, or the polysaccharide vaccine, the reader is directed to the numerous review articles (MMWR, 1994; Austrian, 1981a, 1989; Becker, 1993; Bruyn et al., 1992; Dick and Beurret, 1989; Fedson, 1988; Gray and Dillon, 1989; Johnston, 1991; Robbins et al., 1983; Schneerson et al., 1982b; Shapiro, 1991; Watson et al., 1993).

1.1. Epidemiology of Pneumococcal Disease

Streptococcus pneumoniae is a capsulated, gram-positive bacterium that is present as normal flora in the human upper respiratory tract and is a major or frequent cause of three systemic diseases: pneumonia, meningitis, and bacteremia and noninvasive bacterial otitis.

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695
media. In the United States, the overall incidence of systemic pneumococcal infections is estimated at 15–19/100,000 per year with rates of 50/100,000 in the geriatric adult and 160/100,000 in children less than 2 years old (MMWR 1989; Austrian, 1981b). The disease incidence are highest at the extremes of age, the infant and geriatric adult, and it is in these two age groups that production of antibodies to capsular polysaccharides are the lowest. Case fatalities can be high (40,000/year), especially in the geriatric population, in spite of the use of antibiotics, as many serotypes of S. pneumoniae are developing resistance to the usual antibiotic treatments.

The incidence of otitis media in children approaches 90% by age 5 years and the peak incidence occurs at 6–15 months of age. It was estimated that over 1.2 million cases of otitis media occur annually (Austrian, 1981b). Recent studies in Finland (Eskola et al., 1992) and Israel (Dagan et al., 1992) have shown that the peak incidence of systemic pneumococcal disease occurs around 12 months of age for the infant and that case fatalities from bacteremia, meningitis, and pneumonia are 1.0, 3.9, 1.5% and 2.3, 5, 0.5% (respective countries). Similar studies in northern California (Black et al., 1994) have shown the same incidence of pneumococcal bacteremia and meningitis (Fig. 1) with the peak infection rates occurring around 12–18 months (232/100,000 for bacteremia and 14/100,000 for meningitis) and then dropping after 18 months.

Recent studies on the epidemiology of pneumococcal disease (Dagan et al., 1992; Eskola et al., 1992; Orange and Gray, 1993; Shapiro and Austrian, 1994) have shown that five serotypes (6B, 14, 19F, 23F, and 18C), of the 85 known serotypes, account for 70–80% of pneumococcal disease in infants and that in the United States, types 9V and 4 are ranked sixth and seventh. In Europe and developing countries, types 1 and 5 are more prevalent than types 4 and 9V. Thus, a pneumococcal conjugate vaccine targeted for infants and geriatric adults in the United States should contain at least seven serotypes (4, 6B, 9V, 14, 18C, 19F, and 23F) to achieve a 75–85% coverage. Conjugate vaccine formulations for Europe and elsewhere would include serotypes 1, 5, 6B, 14, 18C, 19F, and 23F. Other serotypes could and probably would be added as needed.

Figure 1. Incidence of systemic pneumococcal disease from 1988 to 1991 in northern California versus age in children less than 5 years of age. The graph was constructed from data provided by Dr. Stephen Black (Black et al., 1994).