Chapter 11

Streptococcus pneumoniae (Pneumococcal) Disease

*Streptococcus* is a genus of nonmotile (with few exceptions), nonspore-forming, aerobic to facultatively anaerobic bacteria (family Lactobacillaceae) that occur in pairs (diplococci) or short or long chains and that contain Gram-positive, spherical or ovoid cells. The type species is *Streptococcus pyogenes*. The *Streptococcus* bacteria are divided into two major groups, A and B. Group A *streptococci* (GAS) causes a broad spectrum of diseases that range from uncomplicated pharyngitis (“strep throat”) to life-threatening illnesses, including pneumonia, bacteremia, necrotizing fasciitis (soft tissue disease), and streptococcal toxic shock syndrome (multiorgan failures). In addition, acute rheumatic fever and rheumatic heart disease can be potential complications after untreated strep throat infections. Group B *streptococci* (GBS) causes serious illness in newborns, pregnant women, postpartum women, and adults with chronic medical conditions (http://www3.niaid.nih.gov/research/topics/bacterial/AboutPneumococcalDisease.htm).

*Streptococcus pneumoniae* (also known as pneumococcus) is a group A, lancet-shaped bacterium (cocci) usually seen in pairs (diplococci), but it also may be observed as a single organism and in short chains. It is often found in the noses and throats of healthy persons and is spread person-to-person through close contact. Pneumococcus is a common cause of mild illness, such as sinus and ear infections (otitis media), but can also cause life-threatening infections, such as pneumonia, meningitis, and infections of the bloodstream. Many strains are resistant to antibiotics.

Severe, sometimes life-threatening GAS disease may occur when bacteria get into parts of the body where bacteria usually are not found, such as blood, muscle, or the lungs. These infections are termed invasive GAS disease. Two of the most severe, but least common, forms of invasive GAS disease are necrotizing fasciitis and streptococcal toxic shock syndrome (STSS). Necrotizing fasciitis (occasionally described by the media as “the flesh-eating bacteria”) destroys muscles, fat, and skin tissue. STSS causes blood pressure to drop rapidly and organs (e.g., kidney, liver, lungs) to fail. It should be noted that STSS is not the same as the “toxic shock syndrome” frequently associated with tampon usage. About 20% of patients with necrotizing fasciitis and more than half with STSS die. About 10% to 15% of patients with other forms of invasive GAS disease die. Severe invasive GAS disease is believed to have re-emerged during the past 10 to 20 years. It is estimated that 9,600 to 9,700 cases of invasive GAS disease occur in the United States each year, resulting in 1,100 to 1,300 deaths (http://www.cdc.gov/ncidod/dbmd/abcs/survreports/gbs05.pdf) (1).

Pneumonia is a disease of the lung that is caused by a variety of bacteria, including *Streptococcus*, *Staphylococcus*, *Pseudomonas*, *Haemophilus*, *Chlamydia*, and *Mycoplasma*, several viruses, and a certain fungi and protozoans. The disease may be divided into two forms: bronchial pneumonia and lobar pneumonia. Bronchial pneumonia is most prevalent in infants, young children, and aged adults. It is caused by various bacteria, including *Streptococcus pneumoniae*, and involves the alveoli contiguous to the larger bronchioles of the bronchial tree. Lobar pneumonia is more prone to occur in younger adults. More than 80% of all cases of lobar pneumonia are caused by *Streptococcus pneumoniae*. Lobar pneumonia involves all of a single lobe of the lungs (although more than one lobe may be affected), wherein the entire area of involvement tends to become a consolidated mass (http://www3.niaid.nih.gov/research/topics/bacterial/AboutPneumococcalDisease.htm).

According to estimates by WHO, *S. pneumoniae* kills worldwide close to 1 million children under 5 years of age annually, especially in developing countries where pneumococcus is one of the most important bacterial pathogens in early infancy. In developed countries, virtually every child becomes a nasopharyngeal carrier of *S. pneumoniae* during the first year of life. Many go on to develop one or more episodes of otitis media, and a smaller number develop more serious invasive pneumococcal infections.

Data from the CDC have shown a 70% decrease in the incidence of GBS infections among newborn infants when antibiotics have been administered to pregnant
women at the time of labor (http://www.cdc.gov/ncidod/dbmrd/abcs/survreports/gbs05.pdf) (2, 3).

**Acute rheumatic fever (ARF)** is the major cause of heart disease in children worldwide. Whereas the incidence of ARF has declined in industrialized countries since the 1950s, in developing countries ARF remains an endemic disease with estimated annual median incidences ranging from 20 to 374 per 100,000 school-aged children. Global estimates for rheumatic heart disease include 16 million existing cases, 282,000 new cases each year, and 233,000 deaths each year (4).

In supporting research for streptococcal diseases, the major thrust of the NIAID Streptococcal Program is toward developing and testing new streptococcal vaccines that are safe, immunogenic, and provide prolonged protective immunity. An important emphasis will be placed on the immunologic response of infants, the elderly, and other high-risk populations. Examples of current vaccine development and testing relate to prevention of pharyngitis, sinusitis, bronchitis, chronic obstructive pulmonary disease, pneumonia, meningitis, bacteremia, neonatal sepsis, arthritis, epiglottitis, and rheumatic fever. Although the most mature area is the development and clinical evaluation of protein-polysaccharide conjugate vaccines, NIAID will actively support research to develop alternative vaccines that might provide immunity at an earlier age or that are more broadly protective than the conjugate vaccines. Toward this goal, NIAID is also supporting research on the pathogenesis, immunity, genomics, and structural biology of streptococcal bacteria (http://www3.niaid.nih.gov/research/topics/bacterial/AboutPneumococcalDisease.htm).

### 11.1 Streptococcal Vaccines

Currently, two vaccines are available to prevent pneumococcal disease: the pneumococcal conjugate vaccine (PCV) (Prevnar; Wyeth Vaccines) and the pneumococcal polysaccharide vaccine (PPV) (Pneumovax; Merck & Co.). Both vaccines provide protection by inducing antibodies to specific types of the pneumococcal capsule (90 different serotypes of pneumococcal capsule have been identified). The conjugate vaccine protects against the 7 serotypes most common in young children in the United States; the 23-valent polysaccharide vaccine includes 23 serotypes. Both vaccines are effective in preventing invasive disease (the severe form of pneumococcal disease in which the pathogen is found in the blood, spinal fluid, or other typically sterile bodily fluids). The conjugate vaccine, licensed for use in young children, also prevents some pneumonia and ear infections (http://www2.ncid.cdc.gov/travel/yb/utils/ybGet.asp?section=dis&obj=strep.htm).

#### 11.1.1 Pneumococcal Conjugate Vaccine

The pneumococcal conjugate vaccine is part of the routine infant immunization schedule (all children younger than 2 years old). It is also administered to children 2 to 4 years of age who have (i) sickle cell hemoglobinopathies; (ii) functional or anatomic asplenia; (iii) received or will receive a cochlear implant; (iv) HIV infection; (v) chronic disease, including chronic cardiac and pulmonary disease excluding asthma, diabetes mellitus, or cerebrospinal fluid leak; and (vi) immunocompromising conditions, including hematologic or other disseminated malignancies, chronic renal failure or nephritic syndrome, ongoing immunosuppressive therapy, and solid organ transplant (http://www2.ncid.cdc.gov/travel/yb/utils/ybGet.asp?section=dis&obj=strep.htm).

Pneumococcal conjugate vaccine should also be considered for healthy children 2 to 4 years of age, especially those 24 to 35 months old, those attending group child care, and those in the United States who are of African American, Alaskan Native, or Native American descent.

#### 11.1.2 Pneumococcal Polysaccharide Vaccine

The pneumococcal polysaccharide vaccine is part of the routine adult immunization schedule, but many adults who should have received the vaccine have not. In 2003, only 62% of adults 62 years of age or older had received the vaccine.

The pneumococcal polysaccharide vaccine is recommended for all adults age 65 or older and for persons 2 to 64 years of age with certain chronic illnesses or immunocompromised conditions, including (i) chronic cardiovascular disease (e.g., congestive heart failure or cardiomyopathies); (ii) chronic pulmonary disease (e.g., chronic obstructive pulmonary disease or emphysema, but not asthma); (iii) diabetes mellitus; (iv) alcoholism; (v) chronic liver disease (cirrhosis); (vi) cerebrospinal fluid leaks; (vii) functional or anatomic asplenia; (viii) cochlear implant (or those planning to receive a cochlear implant); (ix) HIV infection; (x) multiple myeloma; or (xi) immunocompromising conditions, including hematologic or other generalized malignancies, chronic renal failure or nephritic syndrome, ongoing immunosuppressive therapy, and bone marrow or solid organ transplantation.

The polysaccharide vaccine should also be given to those 2 to 64 years of age who are living in settings in which the risk for invasive pneumococcal disease is increased, such as certain Native American communities (e.g., Alaskan Natives and certain American Indian populations) and residents of nursing homes and other long-term care facilities.