(500–750 mg/d as a single dose) and moxifloxacin (400 mg/d as a single dose) also are highly likely to be effective in the United States except in patients who come from closed populations where these drugs are used widely or who have themselves been treated recently with a quinolone. Clindamycin (600–1200 mg/d every 6 h) is effective in 90% of cases and azithromycin (500 mg on day 1 followed by 250–500 mg/d) or clarithromycin (500–750 mg/d as a single dose) in 80% of cases. Treatment failure resulting in bacteremic disease due to macrolide-resistant isolates has been amply documented in patients given azithromycin empirically. As noted above, rates of resistance to all these antibiotics are relatively low in some countries and much higher in others; high-dose amoxicillin remains the best option worldwide.

The optimal duration of treatment for pneumococcal pneumonia is uncertain, but its continuation for at least 5 days once the patient becomes afebrile appears to be a prudent approach. Cases with a second focus of infection (e.g., empyema or septic arthritis) require longer therapy.

ACUTE OTITIS MEDIA

Amoxicillin (80–90 mg/kg per day) is recommended for children with acute otitis media except in situations where observation and symptom-based treatment without antibiotics are advocated. These situations include nonsevere illness and an uncertain diagnosis in children 6 months to 2 years of age and nonsevere illness (even if the diagnosis seems certain) in children >2 years of age. Although the optimal duration of therapy has not been conclusively established, a 10-day course is recommended for younger children and for children with severe disease at any age. For children >6 years old who have mild or moderate disease, a course of 5–7 days is considered adequate. Patients whose illness fails to respond should be reassessed at 48–72 h. If acute otitis media is confirmed and antibiotic treatment has not been started, administration of amoxicillin should be commenced. If antibiotic therapy fails, a change is indicated. Failure to respond to second-line antibiotics as well indicates that myringotomy or tympanocentesis may need to be undertaken in order to obtain samples for culture.

The above recommendations can also be followed for the treatment of sinusitis. Detailed information on the further management of these conditions in children has been published by the American Academy of Pediatrics and the American Academy of Family Physicians.

PREVENTION

Measures to prevent pneumococcal disease include vaccination against *S. pneumoniae* and influenza viruses, reduction of comorbidities that increase the risk of pneumococcal disease, and prevention of antibiotic overuse, which fuels pneumococcal resistance.

Capsular Polysaccharide Vaccines The 23-valent pneumococcal polysaccharide vaccine (PPSV23), containing 25 μg of each capsular polysaccharide, has been licensed for use since 1983. Recommendations for its use vary by country. The U.S. Advisory Committee on Immunization Practices recommends PPSV23 for all persons ≥65 years of age and for those 2–64 years of age who have underlying medical conditions that put them at increased risk for pneumococcal disease or, if infected, disease of increased severity (Table 171-1; see also *www.cdc.gov/vaccines/schedules/*). The committee recently updated their recommendations to include the combined use of PPSV23 and a conjugate vaccine in at-risk individuals (see "Polysaccharide–Protein Conjugate Vaccines," below). Revaccination 5 years after the first dose is recommended for persons >2 years of age who have underlying medical conditions but not routinely for those whose only indication is an age of ≥65 years. PPSV23 does not induce an anamnestic response, and antibody concentrations wane over time; thus revaccination is particularly important for individuals with conditions resulting in loss of antibody. Concerns about repeated revaccination have focused on safety (i.e., local reactions) and the induction of immune hyporesponsiveness. Neither the clinical relevance nor the biologic basis of hyporesponsiveness is clear, but, given the possibility of its occurrence, more than one revaccination has not been recommended.

The effectiveness of PPSV23 against IPD, pneumococcal pneumonia, all-cause pneumonia, and death is controversial, with wide variation in observations. The many published meta-analyses of PPSV efficacy have often reached opposing conclusions with regard to a given clinical entity. Generally, observational studies cite greater effectiveness than do controlled clinical trials. The consensus is that PPSV is effective against IPD but is less effective or ineffective against nonbacteremic pneumococcal pneumonia. However, published trials, observational studies, and meta-analyses contradict this view. Efficacy is often lower in the elderly and in immunodeficient patients whose condition is associated with reduced antibody responses to vaccines than in younger, healthier populations. When PPSV is effective, the duration of protection following a single dose of vaccine is estimated to be ~5 years.

What is not disputed is that improved pneumococcal vaccines are needed for adults. Even in the setting of routine pneumococcal conjugate vaccination of infants (which indirectly protects adults from vaccine-serotype strains), disease caused by serotypes not represented in the conjugate vaccine continues to be a significant burden among adults.

Polysaccharide–Protein Conjugate Vaccines Infants and young children respond poorly to PPSV, which contains T cell–independent antigens. Consequently, another class of pneumococcal vaccines, the PCVs, were developed specifically for infants and young children. The first product, a 7-valent PCV, was licensed in 2000 in the United States. Three PCV products—containing 7, 10, and 13 serotypes, respectively—are currently (2014) commercially available. The serotypes included in these PCV formulations are important causes of IPD and antibiotic resistance among young children. Randomized controlled trials have demonstrated a high degree of efficacy of PCVs against vaccine-serotype IPD as well as efficacy against pneumonia, otitis media, nasopharyngeal colonization, and all-cause mortality. PCVs are recommended by the World Health Organization for inclusion in routine childhood immunization schedules worldwide, especially in countries with high infant mortality rates.

The United States was the first country to introduce PCV and therefore has the longest experience with its community-wide effects. The introduction of PCV in the United States has resulted in a >90% reduction in vaccine-serotype IPD among the whole population (Fig. 171-7). This decline has been noted not only in those age groups immunized but also in adults and is attributable to the near elimination of vaccine-serotype nasopharyngeal colonization in immunized infants, which reduces spread to adults. This protection of unimmunized community members through vaccination of a subset of the community is termed *the indirect effect*. Increases in colonization with—and concomitantly in disease due to—non-vaccine-serotype strains (i.e., replacement colonization and disease) have been seen; however, the absolute rate increases in IPD caused by non-vaccine serotypes are generally small, especially relative to decreases in vaccine-serotype IPD (see "Epidemiology," above). Since vaccine-serotype strains are more commonly resistant to antibiotics than are non-vaccine serotypes, use of PCV has also resulted in dramatic declines in the proportion and absolute rates of drug-resistant pneumococcal disease. The recommendations of the Advisory Committee on Immunization Practices for the use of conjugate vaccines can be found at *www.cdc.gov/MMWR/pdf/wk/mm5909.pdf*. Recently, PCV has been shown to prevent pneumococcal infection in HIV-infected adults. In the United States, PCV13 followed by a dose of PPSV23 is now recommended for all immunocompromised children and adults.

Other Prevention Strategies Pneumococcal disease can also be averted through the prevention of illnesses that predispose individuals to pneumococcal infections. Relevant measures include influenza vaccination and improved management and control of diabetes, HIV infection, heart disease, and lung disease. Finally, the reduction of antibiotic misuse is a strategy for the prevention of pneumococcal disease in that