Prevention of Pneumococcal Disease: Recommendations of the Advisory Committee on Immunization Practices (ACIP)

Summary
This report updates the last recommendations by the Advisory Committee on Immunization Practices (ACIP) concerning pneumococcal polysaccharide vaccine (MMWR 1989;38:64-67) by providing new information on the epidemiology and pathogenesis of pneumococcal disease and the efficacy and safety of pneumococcal vaccines used for the prevention of invasive pneumococcal disease. The report includes recommendations for prevention of pneumococcal disease in: a) persons aged greater than or equal to 2 years who are at high risk for severe pneumococcal disease; b) persons who have underlying medical conditions that increase the risk for severe pneumococcal disease; c) persons aged greater than or equal to 65 years; d) children aged less than 2 years; e) individuals who have undergone splenectomy; f) other groups of persons at high risk for pneumococcal disease; and g) persons who need revaccination with the pneumococcal conjugate vaccine. The report also includes recommendations on the use of pneumococcal polysaccharide vaccine for preventing other pneumococcal infections, including pneumonia and meningitis. The report provides information on the prevention of pneumococcal disease through the use of pneumococcal conjugate vaccine and the use of antimicrobial agents for treatment of pneumococcal infections.

INTRODUCTION
Streptococcus pneumoniae (pneumococcus) is a bacterial pathogen that affects children and adults worldwide. It is a leading cause of illness in young children and causes illness in many older age groups. The organism colonizes the upper respiratory tract and can cause the following types of illnesses: a) disseminated invasive infections, including lower respiratory tract infections; b) meningitis; c) otitis media; d) sinusitis; e) bacteremia; f) puerperal sepsis; g) pneumonia; and h) other lower respiratory tract infections. The incidence of pneumococcal disease is influenced by the age, gender, and race of the population, as well as the prevalence of underlying medical conditions that increase the risk for severe pneumococcal disease.

BACKGROUND Incidence of Invasive Disease
Severe pneumococcal infections result from dissemination of bacteria to the bloodstream and the central nervous system. Data from community-based studies indicate that overall, the incidence of pneumococcal meningitis is 15-30 cases per 100,000 population; the rate is higher for persons aged greater than or equal to 65 years (50-83 cases per 100,000 population) and for children aged less than 2 years (5-11 cases per 100,000 population) (5-6). In adults, 60%-87% of pneumococcal meningitis is associated with pneumonia (10-12); in young children, the primary sites of infection are the nasopharynx and the respiratory tract.

In the United States, the risk for acquiring bacteremia is lower among white persons than among persons in other racial/ethnic groups (i.e., blacks, Alaskan Natives, and American Indians). The risk for invasive pneumococcal disease is highest among children aged less than 2 years, followed by persons aged greater than or equal to 65 years (6,9,24,27). Recurrent pneumococcal meningitis may occur in patients who have chronic cerebrospinal fluid (CSF) leakage resulting from congenital lesions, skull fractures, or neurosurgical procedures.

Other Pneumococcal Infections
Lower Respiratory Tract Infections
S. pneumoniae is the most common cause of community-acquired bacterial pneumonia, occurring most frequently among the elderly and young children. The incidence of pneumococcal pneumonia is highest in children aged less than 2 years and in adults aged greater than or equal to 65 years; rates for blacks are twice as high as those for whites and Hispanic populations. The incidence of pneumococcal pneumonia is highest among persons aged greater than or equal to 65 years; rates for blacks are twice as high as those for whites and Hispanic populations. The age-adjusted annual incidence of pneumococcal infections is one to two cases per 100,000 population (15). The incidence of pneumococcal meningitis is higher than that of pneumococcal pneumonia (17,20).

Acute Otitis Media and Other Upper Respiratory Tract Infections
S. pneumoniae is a substantial cause of acute otitis media (AOM) and other upper respiratory tract infections (e.g., sinusitis). Although these types of infections usually do not progress to pneumonia, they cause considerable morbidity and medical cost. In the United States, AOM results in more than 24 million visits to pediatricians per year (21); approximately 30%-50% of AOM infections are caused by S. pneumoniae (22). AOM infection most often occurs in children aged less than 4 years. In the United States, 62% of children experience an episode of AOM during their first year of life, and nearly half have had three or more episodes of pneumonia.

Mortality
Pneumococcal infection causes an estimated 40,000 deaths annually in the United States (1,2,24), accounting for more deaths than any other vaccine-preventable bacterial disease could be prevented through the use of vaccine. Case-fatality rates are highest for meningitis and bacteremia, and the highest mortality occurs among the elderly and patients who have underlying medical conditions that increase the risk for severe pneumococcal disease. Mortality is also higher among persons who have received antimicrobial therapy and intensive medical care, the overall case-fatality rate for pneumococcal meningitis is 15%-20% among adults. Among elderly patients, this rate is approximately 38%.

Risk Factors
Children aged less than 2 years and adults aged greater than or equal to 65 years are at increased risk for pneumococcal infection. Persons who have certain underlying medical conditions are at increased risk for pneumococcal infection. Factors that increase the risk for severe pneumococcal disease include: a) the presence of underlying medical conditions that increase the risk for severe pneumococcal disease; b) the age of the population; c) the prevalence of underlying medical conditions that increase the risk for severe pneumococcal disease; d) the presence of other underlying medical conditions that increase the risk for severe pneumococcal disease; e) the presence of other underlying medical conditions that increase the risk for severe pneumococcal disease; f) the presence of other underlying medical conditions that increase the risk for severe pneumococcal disease; g) the presence of other underlying medical conditions that increase the risk for severe pneumococcal disease; h) the presence of other underlying medical conditions that increase the risk for severe pneumococcal disease; i) the presence of other underlying medical conditions that increase the risk for severe pneumococcal disease; j) the presence of other underlying medical conditions that increase the risk for severe pneumococcal disease; k) the presence of other underlying medical conditions that increase the risk for severe pneumococcal disease; l) the presence of other underlying medical conditions that increase the risk for severe pneumococcal disease; m) the presence of other underlying medical conditions that increase the risk for severe pneumococcal disease; n) the presence of other underlying medical conditions that increase the risk for severe pneumococcal disease; o) the presence of other underlying medical conditions that increase the risk for severe pneumococcal disease; p) the presence of other underlying medical conditions that increase the risk for severe pneumococcal disease; q) the presence of other underlying medical conditions that increase the risk for severe pneumococcal disease; r) the presence of other underlying medical conditions that increase the risk for severe pneumococcal disease; s) the presence of other underlying medical conditions that increase the risk for severe pneumococcal disease; t) the presence of other underlying medical conditions that increase the risk for severe pneumococcal disease; u) the presence of other underlying medical conditions that increase the risk for severe pneumococcal disease; v) the presence of other underlying medical conditions that increase the risk for severe pneumococcal disease; w) the presence of other underlying medical conditions that increase the risk for severe pneumococcal disease; x) the presence of other underlying medical conditions that increase the risk for severe pneumococcal disease; y) the presence of other underlying medical conditions that increase the risk for severe pneumococcal disease; z) the presence of other underlying medical conditions that increase the risk for severe pneumococcal disease.

Persons with functional or anatomic asplenia (e.g., sickle cell disease or splenectomy) are at highest risk for pneumococcal infection, because they lack the protective effect of the spleen. Persons with functional or anatomic asplenia are at highest risk for severe pneumococcal disease. Persons with functional or anatomic asplenia are at highest risk for severe pneumococcal disease. Persons with functional or anatomic asplenia are at highest risk for severe pneumococcal disease. Persons with functional or anatomic asplenia are at highest risk for severe pneumococcal disease. Persons with functional or anatomic asplenia are at highest risk for severe pneumococcal disease. Persons with functional or anatomic asplenia are at highest risk for severe pneumococcal disease. Persons with functional or anatomic asplenia are at highest risk for severe pneumococcal disease. Persons with functional or anatomic asplenia are at highest risk for severe pneumococcal disease. Persons with functional or anatomic asplenia are at highest risk for severe pneumococcal disease. Persons with functional or anatomic asplenia are at highest risk for severe pneumococcal disease. Persons with functional or anatomic asplenia are at highest risk for severe pneumococcal disease. Persons with functional or anatomic asplenia are at highest risk for severe pneumococcal disease. Persons with functional or anatomic asplenia are at highest risk for severe pneumococcal disease. Persons with functional or anatomic asplenia are at highest risk for severe pneumococcal disease. Persons with functional or anatomic asplenia are at highest risk for severe pneumococcal disease. Persons with functional or anatomic asplenia are at highest risk for severe pneumococcal disease. Persons with functional or anatomic asplenia are at highest risk for severe pneumococcal disease. Persons with functional or anatomic asplenia are at highest risk for severe pneumococcal disease. Persons with functional or anatomic asplenia are at highest risk for severe pneumococcal disease. Persons with functional or anatomic asplenia are at highest risk for severe pneumococcal disease. Persons with functional or anatomic asplenia are at highest risk for severe pneumococcal disease. Persons with functional or anatomic asplenia are at highest risk for severe pneumococcal disease. Persons with functional or anatomic asplenia are at highest risk for severe pneumococcal disease. Persons with functional or anatomic asplenia are at highest risk for severe pneumococcal disease. Persons with functional or anatomic asplenia are at highest risk for severe pneumococcal disease. Persons with functional or anatomic asplenia are at highest risk for severe pneumococcal disease. Persons with functional or anatomic asplenia are at highest risk for severe pneumococcal disease. Persons with functional or anatomic asplenia are at highest risk for severe pneumococcal disease. Persons with functional or anatomic asplenia are at highest risk for severe pneumococcal disease. Persons with functional or anatomic asplenia are at highest risk for severe pneumococcal disease. Persons with functional or anatomic asplenia are at highest risk for severe pneumococcal disease. Persons with functional or anatomic asplenia are at highest risk for severe pneumococcal disease. Persons with functional or anatomic asplenia are at highest risk for severe pneumococcal disease. Persons with functional or anatomic asplenia are at highest risk for severe pneumococcal disease. Persons with functional or anatomic asplenia are at highest risk for severe pneumococcal disease. Persons with functional or anatomic asplenia are at highest risk for severe pneumococcal disease. Persons with functional or anatomic asplenia are at highest risk for severe pneumococcal disease. Persons with functional or anatomic asplenia are at highest risk for severe pneumococcal disease. Persons with functional or anatomic asplenia are at highest risk for severe pneumococcal disease. Persons with functional or anatomic asplenia are at highest risk for severe pneumococcal disease.
VACCINE ADMINISTRATION

Cost-Effectiveness

Randomized controlled trials of pneumococcal vaccine concluded that pneumococcal vaccine is efficacious in reducing the frequency of bacteremic pneumococcal pneumonia among adults in low-risk groups (67). However, the included in the vaccine among persons aged greater than or equal to 6 years (44). Vaccine effectiveness of 65%-84% also was demonstrated among specific patient groups (e.g., persons who have diabetes mellitus, coronary

A serotype prevalence study based on CDC’s pneumococcal surveillance system demonstrated a 57% (95% confidence interval {CI}=45%-66%) overall protective effectiveness against invasive infections caused by serotypes

Small sample size and incomplete ascertainment of vaccination status of patients. In addition, case-patients and persons who served as controls may not have been comparable regarding the severity of their underlying medical

The prevention of common upper respiratory diseases (e.g., sinusitis or AOM) in children (82).

Studies may have lacked sufficient statistical power to detect a difference in the incidence of laboratory-confirmed, nonbacteremic pneumococcal pneumonia between the vaccinated and nonvaccinated study groups (81). A meta-

Multivalent polysaccharide vaccine significantly reduced the occurrence of radiographically diagnosed pneumonia in this group (71,72). In non-epidemic situations in the United States, most pneumococcal disease in adults occurs in

Efficacy Against Nonbacteremic Pneumococcal Disease

Several clinical trials have been conducted evaluating the efficacy of vaccine against pneumonia and pneumococcal bacteremia. In addition, multiple case-control and serotype prevalence studies have provided evidence for

In immunocompromised patients, antibody responses to pneumococcal vaccination are often diminished or absent. In patients with leukemia, lymphoma, or multiple myeloma, antibody substantially lower than response among patients who are immunocompetent. Patients who have chronic renal failure requiring dialysis, renal transplantation, or nephrotic syndrome vaccination, resulting in lower antibody concentrations than those observed in healthy adults (24). In patients with Hodgkins disease, the antibody response to pneumococcal vaccine significantly lower than that observed in healthy subjects (12). When vaccine administration was randomized in at-risk populations, preexisting pneumococcal antibodies may decrease, and responses to pneumococcal vaccine may be diminished antibody response to pneumococcal vaccine (49,50). The reduction in titers of antibody corresponds to the degree of immunosuppression; some asymptomatic HIV-infected lymphadenopathy respond to the 23-valent polysaccharide vaccine (51). HIV-infected patients with CD4+ T-lymphocyte counts less than 500 cells/µL often have lower responses to vaccines with higher CD4+ T-lymphocyte counts or persons who are not HIV-infected (52).

Bacterial capsular polysaccharides induce antibodies primarily by T-cell- independent mechanisms. Therefore, antibody response to most pneumococcal capsular types is generally lower than immune systems are immature. Age-specific immune responses also vary by serotype, and the response to some common pediatric pneumococcal serotypes (e.g., 6A years (53-55).

Duration of Antibody Levels

Levels of antibodies to most pneumococcal vaccine antigens remain elevated for at least 5 years in healthy adults. In some persons, antibody concentrations decrease to prevaccine levels within 1-2 years (42,43) in at-risk populations in antibody concentrations may occur in certain children who have undergone splenectomy following trauma and in those who have sickle cell in children with splenectomy. Antibody concentrations also have declined after 5-10 years in elderly persons, persons who have undergone splenectomy, patients with rheumatoid arthritis, and patients who have received transfusions (24,56,57,61-63). Low or rapidly declining antibody concentrations after vaccination also have been noted among patients with Hodgkins disease (64) and may reflect decreases in antibodies do not account for the quality of the antibody being produced and the level of functional immune responses. Tests measuring opsonophagocytic activity such as pneumococcal ascites may ultimately be more relevant for evaluating response to pneumococcal vaccination (66).

Precautions and Contraindications

The safety of pneumococcal polysaccharide vaccine during the first trimester of pregnancy has not been evaluated, although no adverse consequences have been reported among women vaccinated during pregnancy. For additional information about precautions and contraindications, the vaccine manufacturer's package insert should be reviewed.

Side Effects and Adverse Reactions

Pneumococcal polysaccharide vaccine generally is considered safe based on clinical experience since 1977, when the pneumococcal polysaccharide vaccine was licensed in the United States. Some adverse local reactions (e.g., pain at the injection site, erythema, and swelling). These reactions usually persist for less than 48 hours. Modern more severe local reactions (e.g., local induration) are rare. Intradermal administration may cause severe local reactions and is inappropriate. Severe systemic adverse effects (e.g., death, after administration of pneumococcal vaccine (20,24). In a recent meta-analysis of nine randomized controlled trials of pneumococcal vaccine efficacy, local reactions were observed in 15% of recipients of the pneumococcal vaccine; however, reports of severe febrile or anaphylactic reactions (67). No other serious disorders (e.g., Guillain-Barre syndrome) have been associated with pneumococcal vaccination. Although preliminary data have suggested that the pneumococcal vaccine may cause transient increases in HIV replication (68), the importance of this occurrence is unknown. Precautions associated with death among vaccine recipients. Health-care providers should report suspected adverse events after administration of pneumococcal polysaccharide vaccine to the by calling (800) 822-7967, a 24-hour, toll-free telephone number.

Vaccine Efficacy, Effectiveness, and Cost-Effectiveness

Several clinical trials have been conducted evaluating the efficacy of vaccine against pneumonia and pneumococcal bacteremia. In addition, multiple case-control and serotype prevaccination pneumococcal vaccine effectiveness against invasive disease (Table_1) (44,89-90).

Effectivity Against Nonbacteremic Pneumococcal Disease

Precisely controlled randomized controlled trials (RCTs) of pneumococcal vaccine efficacy were conducted in the 1970s among young, healthy gold miners in South Africa who had high rates of multivalent polysaccharide vaccine significantly reduced the occurrence of radiographically diagnosed pneumonia in this group (71,72). In non-epidemic situations in the United States the elderly or in persons with chronic medical conditions. Vaccine efficacy for nonbacteremic pneumonia was not demonstrated for these populations in two postlicensure RCTs concordantly, have lacked sufficient statistical power to detect a difference in the incidence of laboratory-confirmed, nonbacteremic pneumococcal pneumonia between the vaccinated and unvaccinated groups. The pneumococcal analysis evaluating pneumococcal vaccine efficacy by combining the results of nine randomized, controlled trials also did not demonstrate a protective effect for nonbacteremic pneumococcal ability to evaluate vaccine efficacy in these studies is limited because of the lack of specific and sensitive diagnostic tests for nonbacteremic pneumococcal pneumonia. The pneumococcal prevalence of common upper respiratory diseases (e.g., sinusitis or AOM) in children (82).

Effectivity Against Invasive Disease

Effectivity in case-control studies generally has ranged from 56% to 81% (75,78-80). Only one case-control study did not document effectivity against bacteremic disease (77 studies and are large in size and not all are based on sequential cases).

In addition, case-patients and persons who served as controls may not have been comparable reg conditions, potentially creating a biased underestimate of vaccine effectiveness (81).

A serotype prevalence study based on CDC’s pneumococcal surveillance system demonstrated a 57% (95% confidence interval {CI}=45%-66%) overall protective effectiveness against included in the vaccine among persons aged greater than or equal to 6 years (44). Vaccine effectiveness of 65%-84% also was demonstrated among specific patient groups (e.g., patients with chronic heart failure, chronic pulmonary disease, and anatomic aplasia). Effectiveness in immunocompetent persons aged greater than or equal to 65 years could not be confirmed for certain groups of immunocompromised patients (e.g., those with sickle cell disease, chronic renal failure, immunoglobulin deficiency, Hodgkin’s disease, and myeloma). However, this study could not accurately measure effectivity in each of these groups because of the minimal numbers of unvaccinated patients with these illnesses. In adults aged 2-29 years who have sickle cell disease, bacterial skin infections are significantly less bacteremic pneumococcal disease than patients who were not randomized controlled trials of pneumococcal vaccine concluded that pneumococcal vaccine is efficacious in reducing the frequency of bacteremic pneumococcal pneumonia among vaccine ineffective in preventing disease caused by non-vaccine serotype organisms (79).

Cost-Effectivity

Preliminary results of a cost-effectiveness analysis indicate that pneumococcal polysaccharide vaccine is cost-effective and potentially cost-saving among persons aged greater than (83). The vaccine compares favorably with other standard preventive practices.
Pneumococcal vaccine is administered intramuscularly or subcutaneously as one 0.5-ml dose. Pneumococcal vaccine may be administered at the same time as influenza vaccine (increase in side effects or decreased antibody response to either vaccine (62,84). Pneumococcal vaccine also may be administered concurrently with other vaccines. The administration of diphtheria, tetanus, and pertussis (DTP); poliomyelitis; or other vaccines does not increase the severity of reactions or diminish antibody responses (85).

RECOMMENDATIONS FOR VACCINE USE

The vaccine is both cost effective and protective against invasive pneumococcal infection when administered to immunocompetent persons aged greater than or equal to 2 years. It should receive the 23-valent pneumococcal polysaccharide vaccine (Table_2). If earlier vaccination status is unknown, persons in these categories should be administered pneumococcal vaccine.

Persons Aged Greater than or equal to 65 Years

All persons in this category should receive the pneumococcal vaccine, including previously unvaccinated persons and persons who have not received vaccine within 5 years (and are vaccinated). All persons who have unknown vaccination status should receive one dose of vaccine (Figure_1).

Persons Aged 2-64 Years Who Have Chronic Illness

Persons aged 2-64 years who are at increased risk for pneumococcal disease or its complications if they become infected should be vaccinated. Persons at increased risk for severe chronic cardiovascular disease (e.g., congestive heart failure (CHF) or cardiomyopathies), chronic pulmonary disease (e.g., COPD or emphysema, but not asthma), diabetes mellitus CSF leaks.

Persons aged 50-64 years commonly have chronic illness, and 12% have pulmonary risk factors for invasive pneumococcal disease. Therefore, persons in this age group who have carried 4 years 0 years should have their overall vaccination status reviewed to determine whether they have risk factors that indicate a need for pneumococcal vaccination (87). Vaccination of elderly immunization visit at 11-12 years of age (88).

Persons Aged 2-64 Years Who Have Functional or Anatomic Asplenia

Persons aged 2-64 years who have functional or anatomic asplenia (e.g., sickle cell disease or splenectomy) also should be vaccinated. Persons with such a condition should be given protection against fulminating pneumococcal disease, for which the case-fatality rate is 50%-80%. Asplenic patients with unexplained fever or manifestations of sepsis should receive treatment for suspected bacteremia. Chemoprophylaxis also should be considered in these patients (see Other Methods of Prevention). When elective splenectomy is being planned, at least 2 weeks before surgery.

Persons Aged 2-64 Years Who Are Living in Special Environments or Social Settings

Persons aged 2-64 years who are living in environments or social settings in which the risk for invasive pneumococcal disease or its complications is increased (e.g., Alaskan Native should be vaccinated. Addition of recently reported outbreaks of pneumococcal disease (89), vaccination status should be assessed for residents of nursing homes and other health care facilities. Recurrent upper respiratory tract diseases, including otitis media and pneumococcal vaccine.

Immunocompromised Persons

Persons who have conditions associated with decreased immunologic function that increase the risk for severe pneumococcal disease or its complications should be vaccinated. All immunocompromised patients as it is for immunocompetent persons, the potential benefits and safety of the vaccine justify its use.

The vaccine is recommended for persons in the following groups: immunocompromised persons aged greater than or equal to 2 years, including persons with HIV infection, leukemi generalization of malignancy, chronic renal failure, nephrotic syndrome, or other conditions (e.g., nephritic syndrome) associated with immunosuppression (e.g., organ or bone marrow transplantation); and persons including long-term systemic corticosteroids. If earlier vaccination status is unknown, immunocompromised persons should be administered pneumococcal vaccine.

Persons with asymptomatic or symptomatic HIV infection should be vaccinated as soon as possible after their diagnosis is confirmed. Plasma HIV levels have been found to be trans studies (88); other studies have not demonstrated such an elevation (90). However, no adverse effects 6 immunosuppressive therapy is being considered (e.g., for patients with Hodgkins disease or those who undergo organ or bone marrow transplantation), the interval between vaccination should be at least 2 weeks. Vaccination during chemotherapy or radiation therapy should be avoided.

REVACCINATION Duration of Immunity

Following pneumococcal vaccination, serotype-specific antibody levels decline after 5-10 years and decrease more rapidly in some groups than others (56,57,61-63), which suggest continued protection. However, data concerning serologic correlates of protection are not conclusive, which limits the ability to precisely define indications for revaccination based on including the currently available pneumococcal vaccine, do not induce T-cell-dependent responses associated with immunologic memory. Antibody levels increase after revaccination The overall increase in antibody levels among elderly persons has been determined to be lower after revaccination than following primary vaccination (92). Long-term follow-up data have been reactivated are not yet available.

Data from one epidemiologic study have suggested that vaccination may provide protection for at least 9 years after receipt of the initial dose (44). Decreasing estimates of effectiveness particularly among the very elderly (i.e., persons aged greater than or equal to 85 years), have been reported (79).

Adverse Reactions Following Revaccination

Early studies have indicated that local reactions (i.e., arthus-type reactions) among infants receiving the second dose of 14-valent vaccine within 2 years after the first dose are more (2093). However, subsequent studies have suggested that revaccination after intervals of greater than or equal to 4 years is not associated with an increased incidence of adverse reactions may occur following a second dose of pneumococcal vaccine, the rate of adverse reactions is no greater than the rate after the first dose. An evaluation of 1,000 elderly Mr pneumococcal vaccine indicated that they were not significantly more likely to be hospitalized in the 30 days after vaccination than were the approximately 66,000 persons who receive available to allow estimates of adverse reaction rates among persons who received more than two doses of pneumococcal vaccine.

Indications for Revaccination

Routine revaccination of immunocompetent persons previously vaccinated with 23-valent polysaccharide vaccine is not recommended. However, revaccination once is recommende who are at highest risk for serious pneumococcal infection and those who are likely to have a rapid decline in pneumococcal antibody levels, provided that 5 years have elapsed since vaccination. Revaccination 3 years after the previous dose may be considered for children at highest risk for severe pneumococcal infection who would be aged less than or equal to 10 years at those with functional or anatomic asplenia (e.g., sickle cell disease or splenectomy) and those with conditions associated with rapid antibody decline after initial vaccination (e.g., ne transplantation). Revaccination is contraindicated for persons who have a severe reaction (e.g., anaphylactic reaction or localized arthus-type reaction) to the initial dose they receive.

Persons at highest risk and those most likely to have rapid declines in antibody levels include persons with functional or anatomic asplenia (e.g., sickle cell disease or splenectomy), disseminated intravascular coagulation syndrome, chronic renal failure, nephrotic syndrome, or other conditions associated with immunosuppression (e.g., organ or bone marrow transplant immunosuppressive chemotherapy (including long-term systemic corticosteroids). If vaccination status is unknown, patients in these categories should be administered pneumococcal vaccine.

Persons aged greater than or equal to 65 years should be administered a second dose of vaccine if they received the vaccine greater than or equal to 5 years previously and were a vaccination. Elderly persons with unknown vaccination status should be administered one dose of vaccine (Figure_1).

The need for subsequent doses of pneumococcal vaccine is unclear and will be assessed when additional data become available. Because data are insufficient concerning the safer three or more times, revaccination following a second dose is not routinely recommended.

Persons with Uncertain Vaccination Status

To help avoid the administration of unnecessary doses, every patient should be given a record of the vaccination. However, providers should not withhold vaccination in the absence record. The patient's verbal history should be used to determine prior vaccination status. When indicated, vaccine should be administered to patients who are uncertain about their vaccination status.

OTHER METHODS OF PREVENTION

Chemoprophylaxis

Oral penicillin V (125 mg, twice daily), when administered to infants and young children with sickle cell disease, has reduced the incidence of pneumococcal bacteremia by 84% over daily prophylaxis for children with sickle cell hemoglobinopathy is recommended beginning before 4 months of age. Consensus on the age at which prophylaxis should be a children with sickle cell anemia who had received prophylactic penicillin for prolonged intervals (but who had not had a prior severe pneumococcal infection or a splenectomy) have 4 times without increased incidence of pneumococcal bacteremia or meningitis (98).

Oral penicillin G or V is recommended for prevention of pneumococcal disease in children with functional or anatomic asplenia (85). Antimicrobial prophylaxis against pneumococcal infection not likely to respond to the polysaccharide vaccine (e.g., those aged less than 2 years or those receiving intensive chemotherapy or cytoreduction therapy). However, the im
pneumococcal pneumonia is the effectiveness of antimicrobial prophylaxis is not known.

Passive Immunization

Intramuscular or intravenous immunoglobulin administration may be useful for preventing pneumococcal infection in children with congenital or acquired immunodeficiency diseases or recurrent, serious bacterial infections (i.e., two or more serious bacterial infections (e.g., bacteremia, meningitis, or pneumonia) in a 1-year period (65-99). Data are inadequate to recommend it in the prevention of pneumococcal disease among HIV-infected adults.

STRATEGIES FOR IMPLEMENTING RECOMMENDATIONS FOR THE USE OF VACCINE

The use of pneumococcal polysaccharide vaccine consistently has been recommended by ACIP (20, 100), the American Academy of Pediatrics (85), the American College of Physicians (86), and the Medicare program (87). In addition, the Medicare has provided a payment for pneumococcal vaccine since 1981 and a specific billing code (i.e., G0009) for its administration since 1994. Roster bill S2969 August 1996. Hospitals may receive a separate payment for pneumococcal vaccination of Medicare beneficiaries independent of reimbursement based on prospective payment system. Despite these factors, the vaccine remains underutilized.

Pneumococcal vaccine is recommended for approximately 31 million persons aged greater than or equal to 65 years and approximately 23 million persons aged less than 65 years (immunization Survey, 1985). The year 2000 objectives of the Public Health Service call for vaccinating at least 60% of persons at risk for influenza and pneumococcal disease (and 101). Most persons considered at risk for pneumococcal infection also should receive annual influenza vaccinations. However, as of 1993, only 28% of persons aged greater than or equal to 65 years had received pneumococcal vaccine. This percentage is considerably lower than the reported annual influenza vaccination rates (52%) for the same population (102).

Barriers to achieving high pneumococcal vaccination levels among adults include a) missed opportunities to vaccinate adults during contacts with health-care providers in offices, out-patient settings and private and public settings that can reach adults in different settings (e.g., health-care, workplace, and college or university settings); b) patients and provider factors; and c) lack of awareness among both patients and providers of the seriousness of pneumococcal disease and benefits of pneumococcal vaccination (2,103). Because the incidence of bacteremia, the use of vaccine must be increased in accordance with recommendations.

Age-Based Strategies

Persons aged 50-64 years commonly have chronic illness, and 12% have pulmonary conditions that place them at increased risk for pneumococcal disease (86). However, less than half have received pneumococcal vaccine. A specific age-based standard should improve vaccination rates among persons with high-risk conditions. Therefore, age 50 years has been established as the immunization status of patients; risk factors that indicate the need to administer pneumococcal vaccine should be evaluated at this visit (86,87). Vaccination status also should be age 11-12 years (88). This visit provides an opportunity to review the need for pneumococcal vaccine; adolescents with high-risk conditions should be vaccinated.

Organizational Strategies

Organizational strategies (e.g., standing orders (rather than requiring a physician's order) for pneumococcal vaccination of high-risk patients who are eligible to receive vaccine) are the most effective methods for increasing pneumococcal vaccination rates among persons at high risk (104). In one New York hospital, instituting standing orders for pneumococcal vaccination of the elderly and at-risk patients zero to 78% (105). Similar increases were achieved for influenza vaccination in community hospitals in Minnesota (106). The health care system recently has had orders to administer pneumococcal vaccine to Medicare patients (103). Pneumococcal vaccination also should be routinely provided for residents of nursing homes and other long-term care facilities. High vaccination coverage rates can be achieved when pneumococcal vaccination programs are targeted to hospitalized patients at high risk (104). A hospital-based immunization s system was implemented in a large community hospital to improve pneumococcal vaccination rates (105-109). Two thirds of persons with serious pneumococcal disease had been hospitalized within the previous 4 years before pneumococcal infection (109). Among these patients, 87% had one or more high-risk conditions. Administration of pneumococcal vaccine should be included in routine clinical practice before discharge to hospitalized patients to prevent subsequent admissions for pneumococcal disease. Eligible patients in high-risk groups can be identified by physician and clinical pharmacists.

Community-Based Vaccination Programs

Vaccination coverage rates increase when public health departments promote and offer the vaccine. A community-based immunization program implemented in public health jurisdiction Services resulted in a 33% higher rate of pneumococcal vaccination than jurisdictions without such immunization programs (110). This program included interventions such as a public health department-sponsored outreach clinics, health-center clinics, and nursing and convalescent homes and b) promoting pneumococcal vaccination through leaflets, posters, and c) offering vaccination. Because rates of pneumococcal disease are high among blacks, particularly those of lower socioeconomic status, community outreach programs that are focused or effective in preventing life-threatening pneumococcal disease among persons in these groups.

A community-based pneumococcal vaccine campaign was conducted as part of the Hawaii Pneumococcal Disease Initiative, which employed public and private sector partnerships to substantially increase vaccine delivery and improve vaccination rates. Vaccination coverage rates increase when public health departments promote and offer the vaccine. A community-based immunization program implemented in public health jurisdiction Services resulted in a 33% higher rate of pneumococcal vaccination than jurisdictions without such immunization programs (110). This program included interventions such as a public health department-sponsored outreach clinics, health-center clinics, and nursing and convalescent homes and b) promoting pneumococcal vaccination through leaflets, posters, and c) offering vaccination. Because rates of pneumococcal disease are high among blacks, particularly those of lower socioeconomic status, community outreach programs that are focused or effective in preventing life-threatening pneumococcal disease among persons in these groups.

Provider-Based Strategies

Provider-based strategies that have proved effective in increasing adult vaccination rates include practice-based tracking systems and physician reminder systems. In practice-based tracking systems, providers identify the total number of their patients who are at risk and maintain rosters showing the proportion of patients who receive vaccination. Physicians using such a tracking system have administered 30% more influenza vaccine than those not using such a system (110).

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Physician reminder systems consisting of charts, computers, or preventive-health checklists remind physicians to review the need for pneumococcal vaccine for each patient and to pneumococcal disease. Staff in physicians' offices, clinics, health maintenance organizations, and employee health clinics can be instructed to identify and label the medical records of preventive-health checklists has increased pneumococcal vaccination rates fourfold (113) and from 5% to 42% (114). In one hospital, implementation of a computer reminder system increased pneumococcal vaccination status before discharge increased pneumococcal vaccination rates from less than 4% to 45% (115).

Health-care providers in facilities providing episodic or acute care (e.g., emergency rooms and walk-in clinics) should be familiar with pneumococcal vaccine recommendations. They or provide written information concerning why, where, and how to obtain the vaccine.

Simultaneous Administration of Pneumococcal and Influenza Vaccines

Because the indications for pneumococcal and influenza vaccines are similar, the time of administration of influenza vaccine -- including mass vaccination at outpatient clinics -- should be coordinated to occur within 28 days or pneumococcal vaccine.

CONJUGATE VACCINE DEVELOPMENT

Additional immunogenic pneumococcal vaccines that provide long-term immunity are needed -- especially for children aged less than 2 years, because incidence of disease high in this age group. The most promising approach is the development of a protein-polysaccharide conjugate vaccine for selected serotypes, which improves the efficacy of pneumococcal vaccination -- especially in young children. Immune response to many capsular polysaccharides can be improved by coating of the polysaccharide conjugate vaccines. A different approach that has focused on the serotypes most commonly causing infections in childhood. Candidate vaccine formulations in development and evaluation phase conjugate vaccines conjugated to one or several protein carriers. An effective conjugate vaccine protecting against the most severe common serotypes (4, 6B, 9V, 14, 18C, 19F, and 23F) could potentially prevent 86% of bacteremia, 65% of meningitis, and 65% of otitis media cases among children aged less than 6 years in the United States (45). In persons age have accounted for 50% of the cerebrospinal fluid and blood isolates (44). Preliminary results obtained in phase I and phase II studies suggest that these vaccines generally are safe responses in children aged 2-5 years and infants aged 2 months (118-121). Multicenter trials to evaluate conjugate vaccine efficacy against acute pneumococcal otitis media and intranasal administration of the polysaccharide vaccine has not reduced nasopharyngeal carriage of S. pneumoniae among children (122). However, preliminary data suggest that conjugate vaccines may reduce carriage rates included in the vaccine (123). Reduction in carriage rates of S. pneumoniae would potentially increase the overall impact of the vaccine by reducing transmission and, in randomized trials are required to demonstrate the protective efficacy of conjugate vaccines against invasive pneumococcal infections. These vaccines also should be evaluated for u immunocompromised adults who respond poorly to the current 23-valent pneumococcal vaccine.

References


60. Mushar DM, Luchi M, Watson DA, Hamilton R, Baughn RE. Pneumococcal polysaccharide vaccine in young adults and older bronchitics: determination of IgG responses by ELI.


Table 1. Studies of pneumococcal vaccine efficacy and effectiveness

<table>
<thead>
<tr>
<th>Study, publication</th>
<th>Population studied</th>
<th>Study design</th>
<th>Type of pneumococcal infection studied</th>
</tr>
</thead>
<tbody>
<tr>
<td>MacLeod, 1945 (69)</td>
<td>Young U. S. military recruits</td>
<td>Clinical trial: 4-valent vaccine</td>
<td>Pneumonia</td>
</tr>
<tr>
<td>(79-100)</td>
<td></td>
<td></td>
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<tr>
<td>Kaufman, 1947 (70)</td>
<td>Long-term-care facility residents (98% were aged &gt;60 years) in New York City</td>
<td>Clinical trial: 3-valent vaccine</td>
<td>Pneumonia</td>
</tr>
<tr>
<td>(45-100)</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Austrian, 1976 (71)</td>
<td>Young adult gold miners in South Africa</td>
<td>Clinical trial: 13-valent vaccine</td>
<td>Pneumonia</td>
</tr>
<tr>
<td>(65-88)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(66-92)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Smit, 1977 (72)</td>
<td>Young adult gold miners in South Africa</td>
<td>Clinical trial: 6-valent vaccine</td>
<td>Pneumonia</td>
</tr>
<tr>
<td>(52-89)</td>
<td></td>
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</tr>
<tr>
<td>(49-100)</td>
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<td></td>
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<tr>
<td>Riley, 1977 (73)</td>
<td>Persons aged &gt;10 years in Southern Highlands Province, Papua, New Guinea</td>
<td>Clinical trial: 14-valent vaccine</td>
<td>Bacteremic pneumonia</td>
</tr>
<tr>
<td>(99)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Austrian, unpublished &amp; (74)</td>
<td>Outpatients aged &gt;45 years in San Francisco</td>
<td>Clinical trial: 12-valent vaccine</td>
<td>Pneumonia</td>
</tr>
<tr>
<td>(52)</td>
<td></td>
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<tr>
<td>(40-100)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Shapiro, 1984 (75)</td>
<td>Patients admitted to Yale-New Haven Hospital</td>
<td>Case-control</td>
<td>Invasive infection</td>
</tr>
<tr>
<td>(87)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Simberkoff, 1986</td>
<td>Veterans at risk for pneumococcal infection because of chronic, underlying medical conditions</td>
<td>Clinical trial: 14-valent vaccine</td>
<td>Pneumonia/bronchitis</td>
</tr>
<tr>
<td>(76)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(45)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Forrester, 1987 (77)</td>
<td>Patients admitted to Denver Veterans Administration Medical Center</td>
<td>Case-control</td>
<td>Bacteremia</td>
</tr>
<tr>
<td>(35)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(55)</td>
<td>Patients with pneumococcal bacteremia at Denver Veterans Administration Medical Center</td>
<td>Indirect cohort</td>
<td>Bacteremia</td>
</tr>
<tr>
<td>Sima, 1988 (78)</td>
<td>Patients admitted to one of five participating hospitals in Oregon</td>
<td>Case-control</td>
<td>Invasive infection</td>
</tr>
<tr>
<td>(86)</td>
<td></td>
<td></td>
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</tbody>
</table>
### Groups for which vaccination is recommended

<table>
<thead>
<tr>
<th>Groups for which vaccination is recommended</th>
<th>Strength of recommendation</th>
<th>Revaccination +</th>
</tr>
</thead>
</table>

### Immunocompetent persons &

<table>
<thead>
<tr>
<th>Persons aged &gt;=65 years</th>
<th>A</th>
<th>Second dose of vaccine if patient received vaccine &gt;=5 years previously and were aged &lt;65 years at the time of vaccination.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Persons aged 2-64 years with chronic cardiovascular disease, chronic pulmonary disease, &amp; diabetes mellitus</td>
<td>A</td>
<td>Not recommended.</td>
</tr>
<tr>
<td>Persons aged 2-64 years with alcoholism, chronic liver disease, &amp; cerebral spinal fluid leaks</td>
<td>B</td>
<td>Not recommended.</td>
</tr>
<tr>
<td>Persons aged 2-64 years with functional or anatomic asplenia &amp;</td>
<td>A</td>
<td>If patient is aged &gt;10 years: single revaccination &gt;=5 years after previous dose. If patient is aged &lt;=10 years: consider revaccination 3 years after previous dose.</td>
</tr>
<tr>
<td>Persons aged 2-64 years living in special environments or social settings &amp;</td>
<td>C</td>
<td>Not recommended.</td>
</tr>
</tbody>
</table>

### Immunocompromised persons &

| Immunocompromised persons aged >=2 years, including those with HIV infection, leukemia, lymphoma, Hodgkins disease, multiple myeloma, generalized malignancy, chronic renal failure, or nephrotic syndrome; those receiving immunosuppressive chemotherapy (including corticosteroids); and | C | Single revaccination if >=5 years have elapsed since receipt of first dose. If patient is aged <=10 years: consider revaccination 3 years after previous dose. |

---

* For prevention of infection caused by pneumococcal serotypes included in the vaccine.
+ If not provided in the published report, 95% confidence intervals were calculated by using Epi-Info version 5.01a (CDC/World Health Atlanta, GA).
\* Unpublished study summarized in reference 74.
\# S. pneumoniae recovered from a normally sterile body site.
\& Included persons with anatomic or functional asplenia, dysgammaglobulinemia, hematologic malignancy, metastatic cancer, or systemic lupus erythematosus.
\&\& Efficacy during first 3 years after vaccination.
\&\&\& Efficacy during first 3 years after vaccination.
\&\&\&\& Efficacy during first 3 years after vaccination.
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\&\&\&\&\&\&\& Efficacy during first 3 years after vaccination.

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**Note:** To print large tables and graphs users may have to change their printer settings to landscape and use a small font size.
those who have received an organ
or bone marrow transplant.

* The following categories reflect the strength of evidence supporting the recommendations
for vaccination:
A=Strong epidemiologic evidence and substantial clinical benefit support the
recommendation for vaccine use.
B=Moderate evidence supports the recommendation for vaccine use.
C=Effectiveness of vaccination is not proven, but the high risk for disease and the potential
benefits and safety of the vaccine justify vaccination.
+ Strength of evidence for all revaccination recommendations is "C."
† If earlier vaccination status is unknown, patients in this group should be administered
pneumococcal vaccine.
§ Including congestive heart failure and cardiomyopathies.
** Including chronic obstructive pulmonary disease and emphysema.
++ Including cirrhosis.
&& Including sickle cell disease and splenectomy.
@@ Including Alaskan Natives and certain American Indian populations.

---

**FIGURE 1. Algorithm for vaccinating persons aged ≥65 years**

```
Has the person been vaccinated previously?
   Yes                  No or unsure
   /-------------------/-------------------/
   |                  |                  |
   |  Yes              |  No               |
   |                  |                  |
   |  Was the person aged ≥65 years at the time of last vaccination? |
   |                  |                  |
   |  Yes*            |  No               |
   |                  |                  |
   |  Have ≥5 years elapsed since the first dose? |
   |                  |                  |
   |  Yes            |  No               |
   |                  |                  |
   |  Vaccination indicated |
   |                  |                  |
   |  Vaccination not indicated |
```

*Note: For any person who has received a dose of pneumococcal vaccine of age ≥65 years, revaccination is not indicated.*

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