

Pneumococcal Disease

Streptococcus pneumoniae causes an acute bacterial infection. The bacterium, also called pneumococcus, was first isolated by Pasteur in 1881 from the saliva of a patient with rabies. The association between the pneumococcus bacterium and lobar pneumonia was first described by Friedlander and Talamon in 1883, but pneumococcal pneumonia was confused with other types of pneumonia until the discovery of the Gram stain in 1884. From 1915 to 1945, the chemical structure and antigenicity of the pneumococcal capsular polysaccharide, its association with virulence, and the role of bacterial polysaccharides in human disease were explained. More than 80 serotypes of pneumococci had been described by 1940.

Efforts to develop effective pneumococcal vaccines began as early as 1911. However, with the advent of penicillin in the 1940s, interest in the vaccine declined, until it was observed that many patients still died despite antibiotic treatment. By the late 1960s, efforts were again being made to develop a polyvalent pneumococcal vaccine. The first pneumococcal vaccine was licensed in the United States in 1977. The first conjugate pneumococcal vaccine was licensed in 2000.

Streptococcus pneumoniae

Streptococcus pneumoniae bacteria are lancet-shaped, gram-positive, facultative anaerobic organisms. They are typically observed in pairs (diplococci) but may also occur singularly or in short chains. Some pneumococci are encapsulated, their surfaces composed of complex polysaccharides. Encapsulated organisms are pathogenic for humans and experimental animals, whereas organisms without capsular polysaccharides are not. Capsular polysaccharides are the primary basis for the pathogenicity of the organism. They are antigenic and form the basis for classifying pneumococci by serotypes. Ninety serotypes have been identified, based on their reaction with type-specific antisera. Type-specific antibody to capsular polysaccharide is protective. These antibodies and complement interact to opsonize pneumococci, which facilitates phagocytosis and clearance of the organism. Antibodies to some pneumococcal capsular polysaccharides may cross-react with related types as well as with other bacteria, providing protection against additional serotypes.

Most *S. pneumoniae* serotypes have been shown to cause serious disease, but only a few serotypes produce the majority of pneumococcal infections. The 10 most common serotypes are estimated to account for about 62% of invasive disease worldwide. The ranking and serotype prevalence differ by patient age group and geographic area. In the United States, the seven most common serotypes isolated from blood or

Pneumococcal Disease

- *S. pneumoniae* first isolated by Pasteur in 1881
- Confused with other causes of pneumonia until discovery of Gram stain in 1884
- More than 80 serotypes described by 1940
- First U.S. vaccine in 1977

Streptococcus pneumoniae

- Gram-positive bacteria
- 90 known serotypes
- Polysaccharide capsule important virulence factor
- Type-specific antibody is protective

cerebrospinal fluid (CSF) of children younger than 6 years of age account for 80% of infections. These seven serotypes account for only about 50% of isolates from older children and adults.

Pneumococci are common inhabitants of the respiratory tract and may be isolated from the nasopharynx of 5% to 70% of healthy adults. Rates of asymptomatic carriage vary with age, environment, and the presence of upper respiratory infections. Only 5%–10% of adults without children are carriers. In schools and orphanages, 27%–58% of students and residents may be carriers. On military installations, as many as 50%–60% of service personnel may be carriers. The duration of carriage varies and is generally longer in children than adults. In addition, the relationship of carriage to the development of natural immunity is poorly understood.

Clinical Features

The major clinical syndromes of pneumococcal disease are pneumonia, bacteremia, and meningitis. The immunologic mechanism that allows disease to occur in a carrier is not clearly understood. However, disease most often occurs when a predisposing condition exists, particularly pulmonary disease.

Pneumococcal pneumonia is the most common clinical presentation of pneumococcal disease among adults, although pneumonia alone is not considered to be “invasive” disease. The incubation period of pneumococcal pneumonia is short, about 1 to 3 days. Symptoms generally include an abrupt onset of fever and chills or rigors. Typically there is a single rigor, and repeated shaking chills are uncommon. Other common symptoms include pleuritic chest pain, cough productive of mucopurulent, rusty sputum, dyspnea (shortness of breath), tachypnea (rapid breathing), hypoxia (poor oxygenation), tachycardia (rapid heart rate), malaise, and weakness. Nausea, vomiting, and headaches occur less frequently.

As many as 175,000 hospitalizations from pneumococcal pneumonia are estimated to occur annually in the United States. Pneumococci account for up to 36% of adult community-acquired pneumonia and 50% of hospital-acquired pneumonia. Pneumonia is a common bacterial complication of influenza and measles. The case-fatality rate is 5%–7% and may be much higher among elderly persons. Complications of pneumococcal pneumonia include empyema (i.e., infection of the pleural space), pericarditis (inflammation of the sac surrounding the heart), and endobronchial obstruction, with atelectasis and lung abscess formation.

More than 50,000 cases of pneumococcal bacteremia occur each year. Bacteremia occurs in about 25%–30% of patients with pneumococcal pneumonia. The overall case-fatality

Pneumococcal Pneumonia Clinical Features

- Abrupt onset
- Fever
- Shaking chills
- Pleuritic chest pain
- Productive cough
- Dyspnea, tachypnea, hypoxia

Pneumococcal Pneumonia

- Estimated 175,000 hospitalizations per year in the United States
- Up to 36% of adult community-acquired pneumonia and 50% of hospital-acquired pneumonia
- Common bacterial complication of influenza and measles
- Case-fatality rate 5%-7%, higher in elderly

Pneumococcal Bacteremia

- More than 50,000 cases per year in the United States
- Rates higher among elderly and very young infants
- Case-fatality rate ~20%; up to 60% among the elderly

rate for bacteremia is about 20% but may be as high as 60% among elderly patients. Patients with asplenia who develop bacteremia may experience a fulminant clinical course.

Pneumococci cause 13%–19% of all cases of bacterial meningitis in the United States. An estimated 3,000 to 6,000 cases of pneumococcal meningitis occur each year. One-fourth of patients with pneumococcal meningitis also have pneumonia. The clinical symptoms, CSF profile and neurologic complications are similar to other forms of purulent bacterial meningitis. Symptoms may include headache, lethargy, vomiting, irritability, fever, nuchal rigidity, cranial nerve signs, seizures and coma. The case-fatality rate of pneumococcal meningitis is about 30% but may be as high as 80% among elderly persons. Neurologic sequelae are common among survivors. Persons with a cochlear implant appear to be at increased risk of pneumococcal meningitis.

Pneumococcal Disease in Children

Bacteremia without a known site of infection is the most common invasive clinical presentation of pneumococcal infection among children 2 years of age and younger, accounting for approximately 70% of invasive disease in this age group. Bacteremic pneumonia accounts for 12%–16% of invasive pneumococcal disease among children 2 years of age and younger. With the decline of invasive Hib disease, *S. pneumoniae* has become the leading cause of bacterial meningitis among children younger than 5 years of age in the United States. Before routine use of pneumococcal conjugate vaccine, children younger than 1 year had the highest rates of pneumococcal meningitis, approximately 10 cases per 100,000 population.

Pneumococci are a common cause of acute otitis media, and are detected in 28%–55% of middle ear aspirates. By age 12 months, more than 60% of children have had at least one episode of acute otitis media. Middle ear infections are the most frequent reasons for pediatric office visits in the United States, resulting in more than 20 million visits annually. Complications of pneumococcal otitis media may include mastoiditis and meningitis.

Before routine use of pneumococcal conjugate vaccine, the burden of pneumococcal disease among children younger than 5 years of age was significant. An estimated 17,000 cases of invasive disease occurred each year, of which 13,000 were bacteremia without a known site of infection and about 700 were meningitis. An estimated 200 children died every year as a result of invasive pneumococcal disease. Although not considered invasive disease, an estimated 5 million cases of acute otitis media occurred each year among children younger than 5 years of age.

Pneumococcal Meningitis

- Estimated 3,000 - 6,000 cases per year in the United States
- Case-fatality rate ~30%, up to 80% in the elderly
- Neurologic sequelae common among survivors
- Increased risk after cochlear implant

Pneumococcal Disease in Children

- Bacteremia without known site of infection most common clinical presentation
- *S. pneumoniae* leading cause of bacterial meningitis among children <5 years of age
- Common cause of acute otitis media

Burden of Pneumococcal Disease in Children*

<u>Syndrome</u>	<u>Cases</u>
Bacteremia	13,000
Meningitis	700
Death	200
Otitis media	5,000,000

*Prior to routine use of pneumococcal conjugate vaccine

Children at Increased Risk of Invasive Pneumococcal Disease

- Functional or anatomic asplenia, especially sickle cell disease
- HIV infection
- Alaska Native, African American, American Indian
- Child care attendance
- Cochlear implant

Children with functional or anatomic asplenia, particularly those with sickle cell disease, and children with human immunodeficiency virus (HIV) infection are at very high risk for invasive disease, with rates in some studies more than 50 times higher than those among children of the same age without these conditions (i.e., incidence rates of 5,000–9,000 per 100,000 population). Rates are also increased among children of certain racial and ethnic groups, in particular those of Alaska Native, African American, and certain American Indian groups (Arizona, New Mexico, and Navajo populations in Colorado and Utah). The reason for this increased risk by race and ethnicity is not known with certainty but was also noted for invasive *Haemophilus influenzae* infection (also an encapsulated bacterium). Attendance at a child care center has also been shown to increase the risk of invasive pneumococcal disease and acute otitis media 2–3-fold among children younger than 59 months of age. Children with a cochlear implant are at increased risk for pneumococcal meningitis.

Laboratory Diagnosis

A definitive diagnosis of infection with *S. pneumoniae* generally relies on isolation of the organism from blood or other normally sterile body sites. Tests are also available to detect capsular polysaccharide antigen in body fluids.

The appearance of lancet-shaped diplococci on Gram stain is suggestive of pneumococcal infection, but interpretation of stained sputum specimens may be difficult because of the presence of normal nasopharyngeal bacteria. The suggested criteria for obtaining a diagnosis of pneumococcal pneumonia using Gram stained sputum includes more than 25 white blood cells and fewer than 10 epithelial cells per 100-power field, and a predominance of gram-positive diplococci.

The quellung reaction (capsular swelling; capsular precipitation reaction) is a test that provides rapid identification of pneumococci in clinical specimens, including spinal fluid, sputum, and exudates. The procedure involves mixing loopfuls of bacteria in suspension, pneumococcal antiserum, and methylene blue on the surface of a glass slide and examining under oil immersion. If the reaction is positive, the organism will be surrounded by a large capsule.

Several rapid tests for detection of pneumococcal polysaccharide antigen in CSF and other body fluids are available. These tests generally lack sufficient sensitivity or specificity to assist in the diagnosis of invasive pneumococcal disease.

Medical Management

Resistance to penicillin and other antibiotics is common. In some areas of the United States, up to 40% of invasive

pneumococcal isolates are resistant to penicillin. Treatment will usually include a broad-spectrum cephalosporin, and often vancomycin, until results of antibiotic sensitivity testing are available.

Epidemiology

Occurrence

Pneumococcal disease occurs throughout the world.

Reservoir

S. pneumoniae is a human pathogen. The reservoir for pneumococci is presumably the nasopharynx of asymptomatic human carriers. There is no animal or insect vector.

Transmission

Transmission of *S. pneumoniae* occurs as the result of direct person-to-person contact via respiratory droplets and by autoinoculation in persons carrying the bacteria in their upper respiratory tract. The pneumococcal serotypes most often responsible for causing infection are those most frequently found in carriers. The spread of the organism within a family or household is influenced by such factors as crowding, season, and the presence of upper respiratory infections or pneumococcal disease such as pneumonia or otitis media. The spread of pneumococcal disease is usually associated with increased carriage rates. However, high carriage rates do not appear to increase the risk of disease transmission in households.

Temporal Pattern

Pneumococcal infections are more common during the winter and in early spring when respiratory diseases are more prevalent.

Communicability

The period of communicability for pneumococcal disease is unknown, but presumably transmission can occur as long as the organism appears in respiratory secretions.

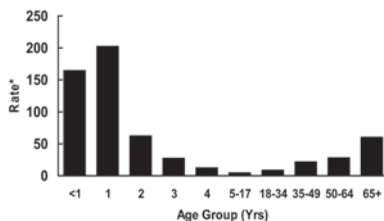
Secular Trends in the United States

Estimates of the incidence of pneumococcal disease have been made from a variety of population-based studies. More than 40,000 cases and more than 4,400 deaths from invasive pneumococcal disease (bacteremia and meningitis) are estimated to have occurred in the United States in 2005.

Pneumococcal Disease Epidemiology

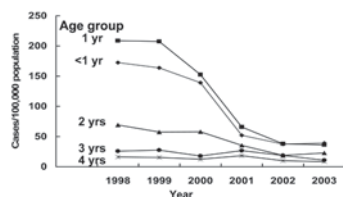
- Reservoir Human carriers
- Transmission Respiratory Autoinoculation
- Temporal pattern Winter and early spring
- Communicability Unknown
Probably as long as organism in respiratory secretions

Invasive Pneumococcal Disease Incidence by Age Group—1998



*Rate per 100,000 population
Source: Active Bacterial Core surveillance/EIP Network

Invasive Pneumococcal Disease by Age and Year—Children <5 Years, 1998-2003*



*2003 data are preliminary.
Source: Active Bacterial Core Surveillance/EIP Network

Pneumococcal Disease Outbreaks

- Outbreaks not common
- Generally occur in crowded environments (jails, nursing homes)
- Persons with invasive disease often have underlying illness
- May have high fatality rate

Pneumococcal Vaccines

- | | |
|-------------|---|
| 1977 | 14-valent polysaccharide vaccine licensed |
| 1983 | 23-valent polysaccharide vaccine licensed (PPV23) |
| 2000 | 7-valent polysaccharide conjugate vaccine licensed (PCV7) |

More than half of these cases occurred in adults who had an indication for pneumococcal polysaccharide vaccine. In addition, there are thousands of cases of nonbacteremic pneumonia, and millions of cases of otitis media, which are considered noninvasive infections.

The overall incidence of invasive pneumococcal disease (bacteremia, meningitis, or other infection of a normally sterile site) in the United States in 1998–1999 was estimated to be approximately 24 cases per 100,000 population. However, incidence rates vary greatly by age group. The highest rates of invasive pneumococcal disease occur among young children, especially those younger than 2 years of age. In 1998, the rate of invasive disease in this age group was estimated to be 188 per 100,000 population; this age group accounted for 20% of all cases of invasive pneumococcal disease. Incidence was lowest among persons 5–17 years of age, and increased to 61 per 100,000 population among persons 65 years of age and older.

Data from the Active Bacterial Core surveillance (ABCs) system suggest that the use of pneumococcal conjugate vaccine is having an impact on the incidence of invasive disease among young children. Data from 2003 indicate that rates of invasive pneumococcal disease have declined 70%–80% among children younger than 2 years of age, compared with 1998–1999 (prior to licensure of the vaccine). Rates of invasive disease have also declined among older age groups, although the decline is less than among young children. The decline among older age groups may indicate a reduction in transmission from vaccinated children to their household and other close contacts.

Community-acquired pneumococcal pneumonia is usually a sporadic disease in carriers who have a breakdown in their pulmonary defense mechanisms. Outbreaks of pneumococcal pneumonia are not common. When outbreaks occur, they are usually in crowded environments, such as correctional facilities and nursing homes. During outbreaks, persons with invasive disease often have underlying illness and may have a high fatality rate.

Pneumococcal Vaccines

Characteristics

Pneumococcal Polysaccharide Vaccine

Pneumococcal polysaccharide vaccine is composed of purified preparations of pneumococcal capsular polysaccharide. The first polysaccharide pneumococcal vaccine was licensed in the United States in 1977. It contained purified capsular polysaccharide antigen from 14 different types of pneumococcal

bacteria. In 1983, a 23-valent polysaccharide vaccine (PPV23) was licensed and replaced the 14-valent vaccine, which is no longer produced. PPV23 contains polysaccharide antigen from 23 types of pneumococcal bacteria that cause 88% of bacteremic pneumococcal disease. In addition, cross-reactivity occurs for several capsular types that account for an additional 8% of bacteremic disease.

The polysaccharide vaccine currently available in the United States (Pneumovax 23, Merck) contains 25 mcg of each antigen per dose and contains 0.25% phenol as a preservative. The vaccine is available in a single-dose vial or syringe, and in a 5-dose vial. Pneumococcal vaccine is given by injection and may be administered either intramuscularly or subcutaneously.

Pneumococcal Conjugate Vaccine

The first pneumococcal conjugate vaccine (PCV7) was licensed in the United States in 2000. It includes purified capsular polysaccharide of seven serotypes of *S. pneumoniae* (4, 9V, 14, 19F, 23F, 18C, and 6B) conjugated to a nontoxic variant of diphtheria toxin known as CRM197. The serotypes included in PCV7 accounted for 86% of bacteremia, 83% of meningitis, and 65% of acute otitis media among children younger than 6 years of age in the United States during 1978–1994. Additional pneumococcal polysaccharide conjugate vaccines containing 9 and 11 serotypes of *S. pneumoniae* are being developed. The vaccine is administered intramuscularly. It does not contain thimerosal as a preservative, and is available only in single-dose vials.

Immunogenicity and Vaccine Efficacy

Pneumococcal Polysaccharide Vaccine

More than 80% of healthy adults who receive PPV23 develop antibodies against the serotypes contained in the vaccine, usually within 2 to 3 weeks after vaccination. Older adults, and persons with some chronic illnesses or immunodeficiency may not respond as well, if at all. In children younger than 2 years of age, antibody response to most serotypes is generally poor. Elevated antibody levels persist for at least 5 years in healthy adults but decline more quickly in persons with certain underlying illnesses.

PPV23 vaccine efficacy studies have resulted in various estimates of clinical effectiveness. Overall, the vaccine is 60%–70% effective in preventing invasive disease. The vaccine may be less effective in preventing pneumococcal infection in some groups, particularly those with significant underlying illness. Although the vaccine may not be as effective in some persons, especially those who do not have

Pneumococcal Polysaccharide Vaccine

- Purified capsular polysaccharide antigen from 23 types of pneumococcus
- Account for 88% of bacteremic pneumococcal disease
- Cross-react with types causing additional 8% of disease

Pneumococcal Conjugate Vaccine

- Pneumococcal polysaccharide conjugated to nontoxic diphtheria toxin (7 serotypes)
- Vaccine serotypes account for 86% of bacteremia and 83% of meningitis among children <6 years of age

Pneumococcal Polysaccharide Vaccine

- Purified pneumococcal polysaccharide (23 types)
- Not effective in children <2 years
- 60%-70% against invasive disease
- Less effective in preventing pneumococcal pneumonia

Pneumococcal Conjugate Vaccine

- Highly immunogenic in infants and young children, including those with high-risk medical conditions
- >90% effective against invasive disease
- Less effective against pneumonia and acute otitis media

Pneumococcal Polysaccharide Vaccine Recommendations

- Adults 65 years of age or older
- Persons 2 years of age or older with
 - chronic illness
 - anatomic or functional asplenia
 - immunocompromised (disease, chemotherapy, steroids)
 - HIV infection
 - environments or settings with increased risk
 - cochlear implant

normal resistance to infection, it is still recommended for such persons because they are at high risk of developing severe disease. PPV23 has not been demonstrated to provide protection against pneumococcal pneumonia. For this reason, providers should avoid referring to PPV23 as “pneumonia vaccine.”

Studies comparing patterns of pneumococcal carriage before and after PPV23 vaccination have not shown clinically significant decreases in carrier rates among vaccinees. In addition, no change in the distribution of vaccine-type and non-vaccine-type organisms has been observed as the result of vaccination.

Pneumococcal Conjugate Vaccine

After four doses of PCV7 vaccine, more than 90% of healthy infants develop antibody to all seven serotypes contained in the vaccine. PCV7 has been shown to be immunogenic in infants and children, including those with sickle cell disease and HIV infection. In a large clinical trial, PCV7 was shown to reduce invasive disease caused by vaccine serotypes by 97%, and reduce invasive disease caused by all serotypes, including serotypes not in the vaccine, by 89%. Efficacy against pneumonia varied depending on the specificity of the diagnosis. The vaccine reduced clinically diagnosed pneumonia by 11%, but reduced pneumonia confirmed by x-ray with consolidation of 2.5 or more centimeters by 73%. Children who received PCV7 had 7% fewer episodes of acute otitis media and underwent 20% fewer tympanostomy tube placements than did unvaccinated children. The duration of protection following PCV7 is currently not known. There is evidence that PCV7 reduces nasopharyngeal carriage of pneumococcal serotypes included in the vaccine.

Vaccination Schedule and Use

Pneumococcal Polysaccharide Vaccine

Pneumococcal polysaccharide vaccine should be administered routinely to all adults 65 years of age and older. The vaccine is also indicated for persons 2 years of age and older with a normal immune system who have a chronic illness, including cardiovascular disease, pulmonary disease, diabetes, alcoholism, cirrhosis, cerebrospinal fluid leak, or a cochlear implant.

Immunocompromised persons 2 years of age and older who are at increased risk of pneumococcal disease or its complications should also be vaccinated. This group includes persons with splenic dysfunction or absence (either from disease or surgical removal), Hodgkin disease, lymphoma, multiple myeloma, chronic renal failure, nephrotic syndrome (a type of

kidney disease), or conditions such as organ transplantation associated with immunosuppression. Persons immunosuppressed from chemotherapy or high-dose corticosteroid therapy (14 days or longer) should be vaccinated. Persons 2 years of age and older with asymptomatic or symptomatic HIV infection should be vaccinated. Pneumococcal vaccine should be considered for persons living in special environments or social settings with an identified increased risk of pneumococcal disease or its complications, such as certain Native American (i.e., Alaska Native, Navajo, and Apache) populations.

If elective splenectomy or cochlear implant is being considered, the vaccine should be given at least 2 weeks before the procedure. If vaccination prior to the procedure is not feasible, the vaccine should be given as soon as possible after surgery. Similarly, there should also be a 2-week interval between vaccination and initiation of cancer chemotherapy or other immunosuppressive therapy, if possible.

Providers should not withhold vaccination in the absence of an immunization record or complete record. The patient's verbal history may be used to determine vaccination status. Persons with uncertain or unknown vaccination status should be vaccinated.

The target groups for pneumococcal polysaccharide vaccine and influenza vaccine overlap. These vaccines should be given at the same time at different sites if indicated, although most recipients need only a single lifetime dose of PPV23 (see Revaccination).

Pneumococcal Conjugate Vaccine

All children younger than 24 months of age and children age 24–59 months with a high-risk medical condition should be routinely vaccinated with PCV7. The primary series beginning in infancy consists of three doses routinely given at 2, 4, and 6 months of age. A fourth (booster) dose is recommended at 12–15 months of age. PCV7 should be administered at the same time as other routine childhood immunizations, using a separate syringe and injection site. For children vaccinated at younger than 12 months of age, the minimum interval between doses is 4 weeks. Doses given at 12 months of age and older should be separated by at least 8 weeks.

Unvaccinated children 7 months of age and older do not require a full series of four doses. The number of doses a child needs to complete the series depends on the child's current age. Unvaccinated children aged 7–11 months should receive two doses of vaccine at least 4 weeks apart, followed by a booster dose at age 12–15 months.

Pneumococcal Conjugate Vaccine

- Routine vaccination of children age <24 months and children 24–59 months with a high-risk medical condition
- Doses at 2, 4, 6, months of age, booster dose at 12–15 months of age
- Unvaccinated children ≥7 months of age require fewer doses

Pneumococcal Conjugate Vaccine

- Children aged 24–59 months at high risk and previously vaccinated with PPV23 should receive 2 doses of PCV7
- Children at high risk who previously received PCV7 should receive PPV23 at age ≥2 years

Unvaccinated children aged 12–23 months should receive two doses of vaccine, at least 8 weeks apart. Previously unvaccinated healthy children 24–59 months of age should receive a single dose of PCV7. Unvaccinated children 24–59 months of age with sickle cell disease, asplenia, HIV infection, chronic illness, cochlear implant, or immunocompromising conditions should receive two doses of PCV7 separated by at least 8 weeks.

PCV7 is not routinely recommended for persons older than 59 months of age.

Few data are available on the use of PCV7 among children previously vaccinated with PPV23. Children 24–59 months of age who have already received PPV23 and who are at high risk of invasive pneumococcal disease (sickle cell disease, asplenia, cochlear implant, HIV infection or other immunocompromising conditions or chronic diseases) could benefit from the immunologic priming induced by PPV23. ACIP recommends that these children receive two doses of PCV7 separated by at least 8 weeks. The first dose of PCV7 should be given no sooner than 2 months after PPV23. Similarly, children 24–59 months of age who have already received one or more doses of PCV7 and who are at high risk of invasive pneumococcal disease will benefit from the additional serotypes included in PPV23. Vaccination with PPV23 should be considered for these high-risk children. PPV23 should be given no sooner than 2 months after the last dose of PCV7. Routine administration of PPV23 to healthy children 24–59 months of age is not recommended.

Revaccination

Pneumococcal Polysaccharide Vaccine

Following vaccination with PPV23, antibody levels decline after 5–10 years and decrease more rapidly in some groups than others. However, the relationship between antibody titer and protection from invasive disease is not certain (i.e., higher antibody level does not necessarily mean better protection), so the ability to define the need for revaccination based only on serology is limited. In addition, currently available pneumococcal polysaccharide vaccines elicit a T-cell-independent response, and do not produce a sustained increase (“boost”) in antibody titers. Available data do not indicate a substantial increase in protection in the majority of revaccinated persons.

Because of the lack of evidence of improved protection with multiple doses of pneumococcal vaccine, routine revaccination of immunocompetent persons previously vaccinated with 23-valent polysaccharide vaccine is not recommended. However, revaccination is recommended for persons 2 years of age and older who are at highest risk for serious pneumococcal infection

Pneumococcal Polysaccharide Vaccine Revaccination

- Routine revaccination of immunocompetent persons is not recommended
- Revaccination recommended for persons age ≥ 2 years at highest risk of serious pneumococcal infection
- Single revaccination dose ≥ 5 years after first dose

and for those who are likely to have a rapid decline in pneumococcal antibody levels. Only one PPV23 revaccination dose is recommended for high-risk persons. The second dose should be administered 5 or more years after the first dose. Revaccination 3 years after the previous dose may be considered for children at highest risk for severe pneumococcal infection who would be 10 years of age or less at the time of revaccination, including children who received PCV7.

Persons at highest risk include all persons 2 years of age and older with functional or anatomic asplenia (e.g., from sickle cell disease or splenectomy), HIV infection, leukemia, lymphoma, Hodgkin disease, multiple myeloma, generalized malignancy, chronic renal failure, nephrotic syndrome, or other conditions associated with immunosuppression (e.g., organ or bone marrow transplantation) and those receiving immunosuppressive chemotherapy, including long-term corticosteroids. Persons aged 65 years and older should be administered a second dose of pneumococcal vaccine if they received the vaccine more than 5 years previously, and were younger than 65 years of age at the time of the first dose.

Pneumococcal Conjugate Vaccine

Revaccination after an age-appropriate primary series with PCV7 is not currently recommended.

Adverse Reactions Following Vaccination

Pneumococcal Polysaccharide Vaccine

The most common adverse reactions following either pneumococcal polysaccharide or conjugate vaccine are local reactions. For PPV23, 30%–50% of vaccinees report pain, swelling, or erythema at the site of injection. These reactions usually persist for less than 48 hours.

Local reactions are reported more frequently following a second dose of PPV23 vaccine than following the first dose. Moderate systemic reactions (such as fever and myalgia) are not common (fewer than 1% of vaccinees), and more severe systemic adverse reactions are rare.

A transient increase in HIV replication has been reported following PPV23 vaccine. No clinical or immunologic deterioration has been reported in these persons.

Pneumococcal Conjugate Vaccine

Local reactions following PCV7 occur in 10%–20% of recipients. Fewer than 3% of local reactions are considered to be severe (e.g., tenderness that interferes with limb movement).

Pneumococcal Polysaccharide Vaccine Candidates for Revaccination

- Persons ≥ 2 years of age with:
 - functional or anatomic asplenia
 - immunosuppression
 - transplant
 - chronic renal failure
 - nephrotic syndrome
- Persons vaccinated at <65 years of age

Pneumococcal Vaccines Adverse Reactions

- Local reactions
 - polysaccharide 30%-50%
 - conjugate 10%-20%
- Fever, myalgia
 - polysaccharide $<1\%$
 - conjugate 15%-24%
- Severe adverse reactions rare

Pneumococcal Vaccines Contraindications and Precautions

- Severe allergic reaction to vaccine component or following prior dose of vaccine
- Moderate or severe acute illness

Local reactions are more common with the fourth dose than with the first three doses. In clinical trials of pneumococcal conjugate vaccine, fever (higher than 100.4°F [38°C]) within 48 hours of any dose of the primary series was reported for 15%–24% of children. However, in these studies, whole-cell pertussis vaccine was administered simultaneously with each dose, and some or most of the reported febrile episodes may be attributable to the DTP. In one study, acellular pertussis vaccine (DTaP) was given at the same visit as the booster dose of PCV7. In this study, 11% of recipients had a temperature higher than 102.2°F (39°C). No severe adverse events attributable to PCV7 have been reported.

Contraindications and Precautions to Vaccination

For both pneumococcal polysaccharide and conjugate vaccines, a severe allergic reaction to a vaccine component or following a prior dose is a contraindication to further doses of vaccine. Such allergic reactions are rare. Persons with moderate or severe acute illness should not be vaccinated until their condition improves. However, minor illnesses, such as upper respiratory infections, are not a contraindication to vaccination.

The safety of PPV23 vaccine for pregnant women has not been studied, although no adverse consequences have been reported among newborns whose mothers were inadvertently vaccinated during pregnancy. Women who are at high risk of pneumococcal disease and who are candidates for pneumococcal vaccine should be vaccinated before pregnancy, if possible.

Vaccine Storage and Handling

Pneumococcal polysaccharide vaccine should be shipped in an insulated container with coolant packs. Although pneumococcal polysaccharide vaccine can tolerate room temperature for a few days, CDC recommends that the vaccine be stored at refrigerator temperature (35°–46°F [2°–8°C]).

Pneumococcal conjugate vaccine should be stored at refrigerator temperature. Pneumococcal vaccines must not be frozen.

Opened multidose vials may be used until the expiration date printed on the package if they are not visibly contaminated.

Goals and Coverage Levels

The *Healthy People 2010* goal is to achieve at least 90% coverage for pneumococcal polysaccharide vaccine among persons 65 years of age and older. Data from the 2003 Behavioral Risk Factor Surveillance System (BRFSS, a population-based, random-digit-dialed telephone survey of the noninstitutionalized U.S. population 18 years of age and older) estimate that 64% of persons 65 years of age or older had ever received pneumococcal polysaccharide. Vaccination coverage levels were lower among persons 18–64 years of age with a chronic illness.

Opportunities to vaccinate high-risk persons are missed both at the time of hospital discharge and during visits to clinicians' offices. Effective programs for vaccine delivery are needed, including offering the vaccine in hospitals at discharge and in clinicians' offices, nursing homes, and other long-term care facilities.

More than 65% of the persons who have been hospitalized with severe pneumococcal disease had been admitted to a hospital in the preceding 3–5 years, yet few had received pneumococcal vaccine. In addition, persons who frequently visit physicians and who have chronic conditions are more likely to be at high risk of pneumococcal infection than those who require infrequent visits. Screening and subsequent immunization of hospitalized persons found to be at high risk could have a significant impact on reducing complications and death associated with pneumococcal disease.

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Pneumococcal Polysaccharide Vaccine Coverage

- Healthy People 2010 goal: 90% coverage for persons ≥ 65 years
- 2003 BRFSS: 64% of persons ≥ 65 years of age ever vaccinated
- Vaccination coverage levels were lower among persons 18-64 years of age with a chronic illness

Pneumococcal Polysaccharide Vaccine Missed Opportunities

- >65% of patients with severe pneumococcal disease had been hospitalized within preceding 3-5 years yet few had received vaccine
- May be administered simultaneously with influenza vaccine

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