

Streptococcus pneumoniae causes acute bacterial infections. The bacterium, also called pneumococcus, was first isolated by Louis Pasteur in 1881 from the saliva of a patient with rabies. The association between pneumococcus and lobar pneumonia was first described in 1883, but pneumococcal pneumonia was confused with other types of pneumonia until the development of the Gram stain in 1884. Between 1915 and 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 described. 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 pneumococcal vaccination 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 for use in the United States in 1977. The first conjugate pneumococcal vaccine was licensed in the United States in 2000.

Streptococcus pneumoniae

S. 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. Most pneumococci are encapsulated, and their surfaces are composed of complex polysaccharides. Capsular polysaccharides are one determinant of the pathogenicity of the organism. They are also antigenic and form the basis for classifying pneumococci by serotypes. One hundred serotypes were documented as of 2020, based on their reaction with type-specific antisera. Type-specific antibody to capsular polysaccharide is protective against disease caused by that serotype. 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 cause most pneumococcal infections. The ranking and serotype prevalence differ by patient age group and geographic area. In the United States, prior to the widespread use of 7-valent pneumococcal conjugate vaccine (PCV7), the seven most common serotypes isolated from blood or cerebrospinal fluid (CSF) of children

Pneumococcal Disease

- *S. pneumoniae* first isolated by Pasteur in 1881
- Confused with other types of pneumonia until discovery of Gram stain in 1884
- More than 80 serotypes described by 1940
- First pneumococcal vaccine licensed in U.S. in 1977; first conjugate pneumococcal vaccine in 2000

Streptococcus pneumoniae

- Facultative anaerobic gram-positive organism
- 100 serotypes documented as of 2020
- Most serotypes cause serious disease, only a few cause most pneumococcal infections
- Serotype prevalence differ by age and geographic area

younger than age 5 years accounted for 80% of infections; these seven serotypes accounted for about 50% of isolates from older children and adults.

The clinical spectrum of pneumococcal infections ranges from invasive disease (i.e., infection of normally sterile sites including osteomyelitis, bacteremia without focus of infection, pneumonia with bacteremia, septic arthritis, and meningitis) to non-invasive infections such as pneumonia without bacteremia, otitis media, and sinusitis. Pneumococci cause more than 50% of all cases of bacterial meningitis in the United States with approximately 2,000 cases of pneumococcal meningitis occurring each year. Over 150,000 hospitalizations from pneumococcal pneumonia are estimated to occur annually in the United States and it has been demonstrated to complicate influenza infection. Pneumococci is the most common bacterial cause of childhood pneumonia, especially in children younger than age 5 years. In adults, pneumococci account for 10% to 30% of adult community-acquired pneumonia.

Pneumococcal Disease Pathogenesis

- Pneumococci commonly inhabit respiratory tract
- Asymptomatic carriage varies
 - School-age children 20% to 60%
 - Adults 5% to 10%
- Relationship of carriage to development of natural immunity is poorly understood

Pneumococcal Disease Clinical Features

- Major clinical syndromes are pneumonia, bacteremia, and meningitis

Pathogenesis

Pneumococci are common inhabitants of the respiratory tract and may be isolated from the nasopharynx of 5% to 90% of healthy persons. Rates of asymptomatic carriage vary with age, environment, and the presence of upper respiratory infections. Among school-age children, 20% to 60% may be colonized. Only 5% to 10% of adults without children are colonized, although on military installations, as many as 50% to 60% of service personnel may be colonized. The duration of carriage varies and is generally longer in children than adults. The relationship of carriage to the development of natural immunity is poorly understood.

Clinical Features

The major clinical syndromes of invasive pneumococcal disease are pneumonia, bacteremia, and meningitis.

Pneumococcal Disease in Adults

Pneumococcal pneumonia is the most common clinical presentation of pneumococcal disease among adults. The incubation period of pneumococcal pneumonia is short, about 1 to 3 days. Symptoms generally include an abrupt onset of fever and chills or a single rigor. Repeated shaking chills are uncommon. Other common symptoms include pleuritic chest pain, cough productive of mucopurulent, rusty sputum, dyspnea, tachypnea, hypoxia, tachycardia, malaise, and weakness. Nausea, vomiting, and headaches occur less frequently. Complications of pneumococcal pneumonia include bacteremia, empyema (i.e., infection of the pleural space), pericarditis (inflammation of the sac surrounding the heart), and

endobronchial obstruction, with atelectasis (partial collapse of lung tissue) and lung abscess formation.

Pneumococcal bacteremia can occur with or without pneumonia and lead to arthritis, meningitis, and endocarditis. The case fatality ratio of pneumonia with bacteremia is around 10%. More than 5,000 cases of pneumococcal bacteremia without pneumonia occur each year. The overall case fatality ratio for bacteremia is about 12%. Patients with asplenia who develop bacteremia may experience a fulminant clinical course.

Some patients with pneumococcal meningitis also have pneumonia. The clinical symptoms, CSF profile, and neurologic complications of pneumococcal meningitis 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 ratio of pneumococcal meningitis is about 14% among adults. Neurologic sequelae are common among survivors.

Adults with certain medical conditions are at highest risk for invasive pneumococcal disease. For adults age 18 through 64 years with hematologic cancer, the rate of invasive pneumococcal disease in 2013–2014 was 129 per 100,000 population. Other conditions that place adults at highest risk for invasive pneumococcal disease include other immunosuppressive conditions from disease or drugs, functional or anatomic asplenia, and renal disease. Other conditions that increase the risk of invasive pneumococcal disease in adults include chronic heart disease, lung disease (including asthma), liver disease, smoking cigarettes, alcoholism, CSF leak, and having a cochlear implant.

Pneumococcal Disease in Children

Bacteremia without a known site of infection is the most common invasive clinical presentation of pneumococcal infection among children age 2 years or younger, accounting for approximately 40% of invasive disease in this age group. Bacteremic pneumonia accounts for 25% to 30% of invasive pneumococcal disease among children age 2 years or younger. With the decline of invasive *Haemophilus influenzae* type b (Hib) disease, *S. pneumoniae* has become the leading cause of bacterial meningitis among children younger than age 5 years 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 24% to 31% 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

Pneumococcal Disease in Adults

- Pneumococcal pneumonia
 - Most common clinical presentation
 - Incubation period 1 to 3 days
 - Symptoms: Fever, chills, pleuritic chest pain, cough, rusty sputum, dyspnea, tachypnea, hypoxia, tachycardia, malaise, weakness
- Pneumococcal bacteremia
 - Can lead to arthritis, meningitis, and endocarditis
 - 12% overall case fatality ratio
- Pneumococcal meningitis
 - Symptoms: Headache, lethargy, vomiting, irritability, fever, nuchal rigidity, cranial nerve signs, seizures, coma
 - 14% case fatality ratio

Pneumococcal Disease in Children

- Pneumococcal pneumonia
 - Accounts for 25% to 30% of invasive disease in children age 2 years or younger
- Pneumococcal bacteremia
 - Accounts for 40% of invasive disease in children age 2 years or younger
- Pneumococcal meningitis
 - *S. pneumoniae* leading cause of bacterial meningitis among children younger than age 5 years
- Pneumococci common cause of acute otitis media

are a leading reason for pediatric office visits in the United States, resulting in more than 10 million visits annually. Complications of pneumococcal otitis media may include mastoiditis and meningitis.

Children with functional or anatomic asplenia, particularly those with sickle cell disease, and children with immunocompromising conditions 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 to 9,000 per 100,000 population). Other conditions that increase the risk of invasive pneumococcal disease in children include chronic heart disease, lung disease (including asthma if treated with high-dose oral corticosteroid therapy), liver disease, CSF leak, and having a cochlear implant. Rates are also increased among children of certain racial and ethnic groups, including Alaska Natives, African Americans, and certain American Indian groups (Navajo and White Mountain Apache). The reason for this increased risk by race and ethnicity is not known with certainty but has also been noted for invasive *Haemophilus influenzae* infection (also an encapsulated bacterium). Attendance at a childcare center has also been shown to increase the risk of invasive pneumococcal disease and acute otitis media 2- or 3-fold among children younger than age 5 years. Children with a cochlear implant are at increased risk for pneumococcal meningitis.

Laboratory Testing

A definitive diagnosis of infection with *S. pneumoniae* generally relies on isolation of the organism from blood or other normally sterile body sites (e.g., CSF, middle ear fluid, joint fluid, and peritoneal fluid). 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 low-power field, and a predominance of gram-positive diplococci.

A urinary antigen test based on an immunochromatographic membrane technique to detect the C-polysaccharide antigen of *S. pneumoniae* as a cause of community-acquired pneumonia among adults is commercially available and has been cleared by FDA. The test is rapid and simple to use, has a reasonable specificity in adults, and has the ability to detect pneumococcal pneumonia after antibiotic therapy has been started.

Antimicrobial Resistance

S. pneumoniae resistance to penicillin and other antibiotics was previously very common. Following introduction of PCV7, antibiotic resistance declined and then began to increase again. Then, in 2008, the definition of penicillin resistance was changed such that a much larger proportion of pneumococci were considered susceptible to penicillin. The revised susceptibility breakpoints for *S. pneumoniae*, published by the Clinical and Laboratory Standards Institute (CLSI) in January 2008, were the result of a reevaluation that showed clinical response to penicillin was being preserved in clinical studies of pneumococcal infection, despite reduced susceptibility response in vitro. Since introduction of 13-valent pneumococcal conjugate vaccine (PCV13) in children in 2010, antibiotic-resistant pneumococcal infections declined significantly.

Epidemiology

Occurrence

Pneumococcal disease occurs throughout the world.

Reservoir

S. pneumoniae is a human pathogen. The reservoir for pneumococci is the nasopharynx of asymptomatic humans. 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 or by autoinoculation in persons carrying the bacteria in their upper respiratory tract. Different pneumococcal serotypes have different propensities for causing asymptomatic colonization, otitis media, meningitis, and pneumonia. The spread of the organism within a family or household is influenced by such factors as household crowding and viral respiratory infections.

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.

Pneumococcal Disease Epidemiology

- Reservoir
 - Humans
- Transmission
 - Person-to-person through respiratory droplets or by autoinoculation
- Temporal pattern
 - More common during winter and early spring
- Communicability
 - Presumably transmissible as long as organism is in respiratory secretions

Pneumococcal Disease Secular Trends in the United States

- In 2017, more than 31,000 cases and 3,500 deaths from invasive pneumococcal disease; more than 50% occurred in adults
- Before routine use of pneumococcal conjugate vaccine, annual burden in children younger than age 5 years was significant:
 - 17,000 cases of invasive disease
 - 200 deaths from invasive pneumococcal disease
 - 5 million cases of acute otitis media
- Since use of pneumococcal conjugate vaccine in children, invasive disease caused by serotypes in PCV7 declined 99% in children
- Since introduction of PCV13, invasive disease caused by PCV13 serotypes declined 90% in children

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 31,000 cases and more than 3,500 deaths from invasive pneumococcal disease (bacteremia and meningitis) are estimated to have occurred in the United States in 2017. More than half of these cases occurred in adults who had an indication for pneumococcal polysaccharide vaccine.

Before routine use of pneumococcal conjugate vaccine in 2000, the burden of pneumococcal disease among children younger than age 5 years 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. The widespread use of pneumococcal conjugate vaccines in children has resulted in a decrease in transmission of vaccine-type strains, thereby preventing pneumococcal disease among unvaccinated children and adults.

Data from the Active Bacterial Core surveillance (ABCs) system indicate that in 2008, before PCV13 replaced PCV7 for routine use among children, approximately 61% of invasive pneumococcal disease cases among children younger than age 5 years were attributable to the serotypes included in PCV13, with serotype 19A accounting for 43% of cases; PCV7 serotypes caused less than 2% of cases.

ABCs data suggest that the use of pneumococcal conjugate vaccine has had a major impact on the incidence of invasive disease among young children. The reductions in overall incidence resulted from a 99% decrease in disease caused by the seven serotypes in PCV7 and serotype 6A, a serotype against which PCV7 provides some cross-protection. The decreases were offset partially by increases in invasive disease caused by serotypes not included in PCV7, in particular 19A. In 2010, PCV13 replaced PCV7 in the United States. PCV13 contains the serotypes in PCV7, plus 6 additional serotypes, including 19A. Since PCV13 introduction, invasive disease caused by PCV13 serotypes has declined 90% in children. Declines have been sustained and have not been offset by increases in non-vaccine type disease.

Among children born during 2016–2017, 91.6% had received at least 3 doses of PCV, and 81.7% had received at least 4 doses, by age 24 months. In 2017, 69.0% of persons age 65 years or older had ever received a pneumococcal vaccine. Vaccination coverage levels in 2017 were 24.5% among persons age 19 through 64 years at increased risk for pneumococcal disease.

Opportunities to vaccinate persons at increased risk of pneumococcal disease 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 persons hospitalized with severe pneumococcal disease had been admitted to a hospital in the preceding 3 to 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 increased risk of pneumococcal infection than those who require infrequent visits. Screening and subsequent immunization of hospitalized persons found to be at increased risk could have a significant impact on reducing complications and death associated with pneumococcal disease.

Pneumococcal Vaccines

The first pneumococcal polysaccharide vaccine was licensed for use in the United States in 1977. It contained purified capsular polysaccharide antigen from 14 different types of pneumococci. In 1983, a 23-valent polysaccharide vaccine (PPSV23, Pneumovax 23) was licensed and replaced the 14-valent vaccine, which is no longer produced.

The first pneumococcal conjugate vaccine (Pneumovax 7, PCV7) was licensed for use in the United States in 2000. It included purified capsular polysaccharide of seven serotypes of *S. pneumoniae*. In 2010, a 13-valent pneumococcal conjugate vaccine (PCV13, Prevnar 13) was licensed in the United States. It contains the same 7 serotypes of *S. pneumoniae* as PCV7 plus serotypes 1, 3, 5, 6A, 7F, and 19A.

In 2008, the serotypes covered in PCV13 caused 53%, 49%, and 44% of invasive pneumococcal disease cases among persons age 18 through 49 years, 50 through 64 years, and 65 years or older, respectively; serotypes covered in PPSV23 caused 78%, 76%, and 66% of IPD cases among persons in these age groups.

Characteristics

Pneumococcal Polysaccharide Vaccine

PPSV23 is composed of purified preparations of pneumococcal capsular polysaccharide from 23 types of pneumococci. The serotypes are: 1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19A, 19F, 20, 22F, 23F, and 33F. PPSV23 is administered by either intramuscular or subcutaneous injection. Each dose of PPSV23 contains phenol as a preservative. It contains no adjuvant or antibiotic.

Pneumococcal Vaccines

- PPSV23 (Pneumovax 23)
- PCV13 (Prevnar 13)

Pneumococcal Vaccine Characteristics

- PPSV23
 - Administered by intramuscular or subcutaneous injection
 - Contains phenol as a preservative
- PCV13
 - Administered by intramuscular injection
 - Contains aluminum phosphate as an adjuvant

Pneumococcal Conjugate Vaccine

PCV13 contains 13 serotypes of *S. pneumoniae* (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F) conjugated to a nontoxic variant of diphtheria toxin known as CRM197. PCV13 is administered by intramuscular injection. Each dose of PCV13 contains aluminum phosphate as an adjuvant. It contains no antibiotic or preservative.

Vaccination Schedule and Use

All children age 2 through 59 months should routinely receive PCV13, and all adults age 65 years or older should receive PPSV23. In addition, persons age 2 years or older with certain conditions (see table “Conditions with Pneumococcal Vaccination Indications” below) should receive both PCV13 and PPSV23, or PPSV23 alone. PPSV23 is not recommended for children younger than age 2 years. Children and adults who have a condition for which PCV13 is indicated should receive PCV13 first, followed by PPSV23 at least 8 weeks later. Adults age 65 years or older, who do not have any conditions for PCV13 indication (see table “Conditions with Pneumococcal Vaccination Indications” below), can discuss with their clinician and decide whether to receive PCV13 (shared clinical decision making). If the decision is made to receive PCV13 based on shared clinical decision making, it should be given at least 1 year before PPSV23.

Pneumococcal Vaccination Schedule

- PCV13
 - 3-dose primary series at age 2, 4, and 6 months
 - Booster at age 12 through 15 months
 - Minimum age for dose 1 is 6 weeks
 - Minimum interval for doses before age 1 year is 4 weeks and age 1 year or older is 8 weeks
 - Unvaccinated children age 7 months or older require fewer doses
 - Shared clinical decision making for age 65 years or older
- PPSV23
 - 1 dose for all adults age 65 years or older
- Schedule for PCV13 and PPSV23 varies by medical condition

Conditions with Pneumococcal Vaccination Indications

Conditions	PCV13 indicated for 2 through 71 Months*	PCV13 indicated for 6 through 18 Years*	PCV13 indicated for 19 Years or Older	PPSV23 indicated for 2 through 64 Years
Chronic heart or lung disease [†]	Yes	No	No	Yes
Diabetes	Yes	No	No	Yes
Chronic liver disease, including cirrhosis	Yes	No	No	Yes
Cigarette smoking (in adults)	Yes	No	No	Yes
Alcoholism (in adults)	Yes	No	No	Yes
Cerebrospinal Fluid (CSF) leak	Yes	Yes	Yes	Yes
Cochlear implant	Yes	Yes	Yes	Yes
Functional or anatomic asplenia, including sickle cell disease	Yes	Yes	Yes	Yes
Immunocompromising conditions [§]	Yes	Yes	Yes	Yes
Persons living in special environments or social settings [¶]	No	No	No	Consider

*PCV13 only recommended if child is unvaccinated or received incomplete vaccine schedule.

[†]Includes congestive heart failure, cardiomyopathies, chronic obstructive pulmonary disease, emphysema, and asthma. Asthma only included for children (through age 18 years) if treated with high-dose oral corticosteroid therapy.

[§]Includes congenital or acquired immunodeficiencies, Hodgkin's Disease, lymphoma, leukemia, multiple myeloma, generalized malignancy, and other cancers if on immunosuppressive therapy; HIV infection; chronic renal failure; nephrotic syndrome; organ transplant; and immunosuppressive medications, including chemotherapy and high-dose corticosteroid treatment.

[¶]Includes Alaska Native, Navajo, and White Mountain Apache populations.

Children Age 2 Through 23 Months

Children should routinely receive a 3-dose primary series of PCV13 at age 2, 4, and 6 months, and dose 4 (booster) at age 12 through 15 months. Dose 1 can be administered as early as 6 weeks. For doses given before the 1st birthday, the minimum interval between doses is 4 weeks; doses given at age 12 months or older should be separated by at least 8 weeks. PCV13 can be administered at the same time as other routine immunizations.

Unvaccinated children age 7 months or older do not require a full series of four doses. The number of doses depends on the child's current age and the age at which the first dose of PCV13 was administered. If the child's current age is 7 through 11 months, the recommended series is 2 doses at least 4 weeks apart, and a booster dose at age 12 through 15 months. If the vaccination series is initiated at age 7 through 11 months, and the next dose is administered after the 1st birthday, another dose should be administered 8 weeks later. If the child's current age is 12 through 23 months, the recommended series is 2 doses at least 8 weeks apart.

Healthy Children Age 24 through 59 Months

Healthy children age 24 through 59 months should receive 1 dose of PCV13 if child is unvaccinated or received any incomplete schedule. Routine use of PCV13 is not recommended for healthy children age 5 years or older.

Children Age 24 through 71 Months, with Certain Medical Conditions

Children age 24 through 71 months with certain conditions (see table “Conditions with Pneumococcal Vaccination Indications” above) should receive 2 doses of PCV13 separated by 8 weeks if they are unvaccinated or received any incomplete schedule of less than 3 doses. Children with any incomplete schedule of 3 doses should receive 1 dose of PCV13 at least 8 weeks after the most recent dose.

These children should receive a dose of PPSV23 at least 8 weeks after the final dose of PCV13. Additionally, if they are immunocompromised (see table “Conditions with Pneumococcal Vaccination Indications” above for list of conditions) or have functional or anatomic asplenia, they should receive a second dose of PPSV23 five years after the first.

Children and Adolescents Age 6 through 18 Years, with Certain Medical Conditions

Unvaccinated children and adolescents age 6 through 18 years with certain medical conditions (see table “Conditions with Pneumococcal Vaccination Indications” above) should receive both PCV13 and PPSV23. A single dose of PCV13 should be given followed by a dose of PPSV23 at least 8 weeks later. A second dose of PPSV23 is recommended 5 years after the first PPSV23 dose for children with anatomic or functional asplenia, or other immunocompromising conditions (see footnote in table “Conditions with Pneumococcal Vaccination Indications” above for complete list of conditions).

If a complete schedule of PCV13 has been given, no additional PCV13 doses are required. If PCV13 has not been given, and two doses of PPSV23 have already been given, a dose of PCV13 should be given at least 8 weeks after the most recent dose of PPSV23. PCV13 may also be given between two doses of PPSV23.

Some children and adolescents in this age group with certain conditions should only receive one dose of PPSV23, if they have not already.

Pneumococcal Vaccination Schedule for Children and Adolescents Age 6 through 18 years with Certain Chronic or Immunocompromising Conditions

Condition(s)	Prior Pneumococcal Doses	Recommendation
Chronic heart disease, chronic lung disease, diabetes, chronic liver disease (including cirrhosis)	PPSV23 (or PPSV23 & PCV13)	No pneumococcal vaccine needed
	None, or if PCV13 only	<ul style="list-style-type: none"> • PPSV23 at least 8 weeks after previous PCV13
Cerebrospinal fluid leak, cochlear implant	None	<ul style="list-style-type: none"> • PCV13 • PPSV23 at least 8 weeks after PCV13
	PCV13 (No PPSV23)	<ul style="list-style-type: none"> • PPSV23 at least 8 weeks after previous PCV13
	PPSV23 (No PCV13)	<ul style="list-style-type: none"> • PCV13 at least 8 weeks after previous PPSV23
Functional and/or anatomic asplenia (including sickle cell disease), immunocompromising conditions*	None	<ul style="list-style-type: none"> • PCV13 • PPSV23 at least 8 weeks after PCV13 • PPSV23 at least 5 years after previous PPSV23
	PCV13 (No PPSV23)	<ul style="list-style-type: none"> • PPSV23 at least 8 weeks after previous PCV13 • PPSV23 at least 5 years after 1st PPSV23
	PPSV23 (No PCV13)	<ul style="list-style-type: none"> • PCV13 at least 8 weeks after previous PPSV23 • PPSV23 at least 8 weeks after PCV13 and at least 5 years after previous PPSV23

*Includes congenital or acquired immunodeficiencies, Hodgkin's Disease, lymphoma, leukemia, multiple myeloma, generalized malignancy, and other cancers if on immunosuppressive therapy; HIV Infection; chronic renal failure; nephrotic syndrome; organ transplant; and immunosuppressive medications, including chemotherapy and high-dose corticosteroid treatment.

Adults Age 19 through 64 Years, with Certain Chronic or Immunocompromising Conditions

Routine use of PCV13 or PPSV23 is not recommended for healthy adults age 19 through 64 years. Unvaccinated persons age 19 through 64 years with certain chronic conditions (see table "Conditions with Pneumococcal Vaccination Indications" above) should receive one dose of PPSV23 if they have not already.

Unvaccinated persons age 19 years or older with certain immunocompromising conditions, cerebrospinal fluid leak, or cochlear implant (see table "Conditions with Pneumococcal Vaccination Indications", above) should receive a single dose of PCV13 followed by a dose of PPSV23 at least 8 weeks later. If a dose of PPSV23 was given first, PCV13 should be administered at least 1 year later. A second dose of PPSV23 is recommended 5 years after the first PPSV23 dose for adults with anatomic or functional asplenia, or other immunocompromising conditions.

Pneumococcal Disease

Conditions for Administration of PCV13 and PPSV23 in Adults

Medical Condition(s)	PCV 13 indicated for age 19 years or older	PSV23 indicated for age 19 through 64 years	PPSV23 revaccination indicated for age 19 through 64 years	PCV13 indicated for age 65 years or older	PPSV23 indicated for age 65 years or older
None	No	No	No	Based on shared clinical decision-making	Yes If PCV13 has been given, then give PPSV23 at least 1 year after PCV13
Chronic heart disease, chronic lung disease, diabetes, alcoholism, chronic liver disease (including cirrhosis), current cigarette smoking, asthma	No	Yes	No	Based on shared clinical decision-making	Yes If PCV13 has been given, then give PPSV23 at least 1 year after PCV13 and at least 5 years after any PPSV23 given at less than age 65 years
Cerebrospinal fluid leak, cochlear implant	Yes	Yes At least 8 weeks after PCV 13	No	Yes If no previous PCV13 vaccination	Yes At least 8 weeks after PCV13 and at least 5 years after any PPSV23 given at less than age 65 years
Functional or anatomic asplenia (including sickle cell disease/other hemoglobinopathies)	Yes	Yes At least 8 weeks after PCV13	Yes At least 5 years after first dose of PPSV23	Yes If no previous PCV13 vaccination	Yes At least 8 weeks after PCV13 and at least 5 years after any PPSV23 given at less than age 65 years
Immunocompromising conditions*	Yes	Yes At least 8 weeks after PCV13	Yes At least 5 years after first dose of PPSV23	Yes If no previous PCV13 vaccination	Yes At least 8 weeks after PCV13 and at least 5 years after any PPSV23 given at less than age 65 years

*Includes congenital or acquired immunodeficiencies, Hodgkin's Disease, lymphoma, leukemia, multiple myeloma, generalized malignancy, and other cancers if on immunosuppressive therapy; HIV infection; chronic renal failure; nephrotic syndrome; organ transplant; and immunosuppressive medications, including chemotherapy and high-dose corticosteroid treatment.

Adults Age 65 Years or Older, without Immunocompromising Conditions, Cerebrospinal fluid leak, or Cochlear Implant

A single dose of PPSV23 is recommended for all adults age 65 years or older, regardless of previous pneumococcal vaccination history. If any PPSV23 dose(s) were given before age 65 years, a single, final dose of PPSV23 should be given at age 65 or at least 5 years after the last PPSV23 dose. If PPSV23 was administered at age 65 years or later, no additional doses are needed.

Adults age 65 years or older without immunocompromising conditions (see table "Conditions with Pneumococcal Vaccination Indications" above) may discuss with their clinician and decide whether to receive PCV13 if a dose was not received

before (i.e., shared clinical decision making). If a decision is made to receive PCV13, a dose of PCV13 should be given first, followed by a dose of PPSV23 at least one year later.

Additional Scheduling and Timing Considerations

Additional information on the timing of pneumococcal vaccination for adults and children can be found at <https://www.cdc.gov/vaccines/vpd/pneumo/hcp/recommendations.html>. PCV13 and PPSV23 should not be administered simultaneously (i.e., on the same clinic day). Studies evaluating immune responses to PCV13 and PPSV23 administered in series showed the immune response was better when PCV13 was given first. The minimum interval between PCV13 and PPSV23 is 8 weeks for adults with immunocompromising conditions and 1 year for immunocompetent adults. However, in adults, if they are administered simultaneously or at an interval less than 8 weeks, neither dose needs to be repeated. In children, if they are administered simultaneously, PCV13 should be repeated at least 8 weeks later.

The target groups for pneumococcal vaccines and influenza vaccines overlap. Either pneumococcal vaccine may be given at the same time as influenza vaccine, if indicated, but at different anatomical sites. Most healthy adults age 65 years or older need only a single lifetime dose of PPSV23 and may be administered PCV13 on or after the 65th birthday based on shared clinical decision making.

While for most other vaccines health care providers should only accept written, dated records as evidence of vaccination, self-reported doses of adult PPSV23 (but not PCV13) are acceptable. Persons with uncertain or unknown vaccination status should be vaccinated.

When elective splenectomy, immunocompromising therapy, or cochlear implant placement is being planned, providers should choose the vaccines appropriate to the level of risk for invasive pneumococcal disease which would exist after the surgery or treatment. For example, a person who will undergo splenectomy should be considered asplenic when applying these vaccine recommendations. The choice of vaccine also depends on past history of pneumococcal vaccination. If PCV13 and PPSV23 are both recommended, they both need to be administered, preferably before treatment or surgery. PCV13 should be administered first, and PPSV23 at least 8 weeks later. PPSV23 should be given at least 2 weeks before the treatment or surgery. If treatment or surgery cannot be delayed, providers can consider administering pneumococcal vaccines afterward.

Following vaccination with PPSV23, antibody levels decline after 5 to 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 for adults, so the ability to define the need for revaccination based only on serology is limited. In addition, currently available pneumococcal polysaccharide vaccine elicits a T-cell-independent response, and does not produce a sustained increase (“boost”) in antibody titers. Available data do not indicate a substantial increase in antibody level in the majority of revaccinated persons.

Immunogenicity and Vaccine Efficacy

Pneumococcal Polysaccharide Vaccine

More than 80% of healthy adults who receive PPSV23 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. Elevated antibody levels following vaccination persist for at least 5 years in healthy adults but decline more quickly in persons with certain underlying illnesses. In children younger than age 2 years, antibody response to PPSV23 is generally poor.

PPSV23 vaccine efficacy studies have resulted in various estimates of clinical effectiveness. Overall, the vaccine is 60% to 70% effective in preventing invasive disease caused by serotypes included in the vaccine. Despite the vaccine’s reduced effectiveness among immunocompromised persons,

Pneumococcal Vaccine Efficacy

- PPSV23
 - 60-70% effective in preventing invasive disease caused by serotypes in vaccine
- PCV13
 - Induces levels of antibodies comparable to those induced by PCV7, which was shown to reduce invasive disease caused by vaccine serotypes by 97% in children
 - 45.6% efficacy against vaccine-type pneumococcal pneumonia, 45.0% efficacy against vaccine-type nonbacteremic pneumococcal pneumonia, 75.0% efficacy against vaccine-type IPD in adults

PPSV23 is still recommended for such persons because they are at increased risk of developing severe disease. There is no consensus regarding the ability of PPSV23 to prevent non-bacteremic pneumococcal pneumonia. For this reason, providers should avoid referring to PPSV23 as a “pneumonia vaccine.”

Studies comparing patterns of pneumococcal carriage before and after PPSV23 vaccination have not shown clinically significant decreases in carriage rates among vaccine recipients.

Pneumococcal Conjugate Vaccine

In a large clinical trial, PCV7 was shown to reduce invasive disease caused by vaccine serotypes by 97%. Children who received PCV7 had 20% fewer episodes of chest X-ray confirmed pneumonia, 7% fewer episodes of acute otitis media, and underwent 20% fewer tympanostomy tube placements than did unvaccinated children. There is evidence that PCV7 reduced nasopharyngeal carriage among children of pneumococcal serotypes included in the vaccine.

PCV13 was licensed in the United States based upon studies that compared the serologic response of children who received PCV13 to those who received PCV7. These studies showed that PCV13 induced levels of antibodies that were comparable to those induced by PCV7 and shown to be protective against invasive disease.

In another study of PCV13, children age 7 through 11 months, 12 through 23 months, and 24 through 71 months who had not received pneumococcal conjugate vaccine doses previously were administered 1, 2, or 3 doses of PCV13 according to age-appropriate immunization schedules. These schedules resulted in antibody responses to each of the 13 serotypes that were comparable to those achieved after the 3-dose infant PCV13 series in the U.S. immunogenicity trial, except for serotype 1, for which IgG geometric mean concentration (GMC) was lower among children age 24 through 71 months.

Licensure of PCV13 for adults age 50 years or older was based on serologic studies comparing immune response of PCV13 recipients to immune response following a dose of PPSV23. In two randomized, multicenter immunogenicity studies conducted in the United States and Europe, immunocompetent adults age 50 years or older received a single dose of PCV13 or PPSV23. In adults age 60 through 64 years and age 70 years or older, PCV13 elicited opsonophagocytic activity geometric mean antibody titers that were comparable with, or higher than, responses elicited by PPSV23. Persons who received PPSV23 as the initial study dose had lower opsonophagocytic antibody

responses after subsequent administration of a PCV13 dose 1 year later than those who had received PCV13 as the initial dose. Since introduction of PCV13 in children in 2010, invasive disease caused by PCV13 serotypes has declined over 60% among adults age 65 years or older through PCV13 indirect effects.

A randomized placebo-controlled trial was conducted in the Netherlands among approximately 85,000 adults age 65 years or older during 2008–2013 to evaluate the clinical benefit of PCV13 in the prevention of pneumococcal pneumonia. The results of this trial demonstrated 45.6% efficacy of PCV13 against vaccine-type pneumococcal pneumonia, 45.0% efficacy against vaccine-type nonbacteremic pneumococcal pneumonia, and 75.0% efficacy of PCV13 against vaccine-type IPD.

Pneumococcal Vaccine Contraindications and Precautions

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

Contraindications and Precautions to Vaccination

As with other vaccines, a history of a severe allergic reaction (anaphylaxis) to a vaccine component or following a prior dose is a contraindication to further doses. Moderate or severe acute illness (with or without fever) in a patient is considered a precaution to vaccination, although persons with minor illness may be vaccinated.

Vaccine Safety

Studies support the safety of PCV13 and PPSV23 in children and adults.

Pneumococcal Polysaccharide Vaccine

In pre-licensure PPSV23 studies, the most common adverse reactions reported were local reactions (pain, soreness, tenderness, injection-site swelling, and induration), headache, fatigue, and muscle pain. These reactions usually resolved within 48 hours. In study participants age 65 years or older, systemic adverse reactions that were related to the vaccine were more frequent following the second dose than the first dose.

Results from studies done after PPSV23 was licensed have been consistent with the safety findings in the pre-licensure studies. A transient increase in viral replication among HIV-positive persons has been reported following PPSV23 vaccine. No clinical or immunologic deterioration has been reported in these persons.

Pneumococcal Conjugate Vaccine

In the pre-licensure studies, the common adverse reactions reported were local reactions (pain, tenderness, swelling and erythema), decreased appetite, fatigue, headache, muscle pain, irritability, and fever. Increased and decreased sleep was also commonly reported in infants and toddlers.

Pneumococcal Vaccine Safety

- PPSV23
 - Pain, soreness, tenderness, injection site swelling, induration, headache, fatigue, muscle pain
- PSV13
 - Pain, tenderness, swelling, erythema, decreased appetite, fatigue, headache, muscle pain, irritability, fever
 - Simultaneous administration of PCV13 and inactivated influenza vaccine associated with an increased risk of febrile seizures

In young children, studies done after PCV13 was licensed showed simultaneous PCV13 and inactivated influenza vaccine was associated with an increased risk of febrile seizures during some influenza seasons. Febrile seizures can be concerning to caregivers, but they are brief and are not associated with any long-term complications. A review of adverse events reported to the Vaccine Adverse Event Reporting System after PCV13 vaccination in children age 6 weeks through 59 months was consistent with the pre-licensure studies.

Vaccination in Pregnancy

ACIP recommendations for use of PCV13 during pregnancy do not exist.

The safety of PPSV23 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 increased risk of pneumococcal disease and who are candidates for pneumococcal vaccine should be vaccinated before pregnancy, if possible.

Vaccine Storage and Handling

PCV13 and PPSV23 should be maintained at refrigerator temperature between 2°C and 8°C (36°F and 46°F). Manufacturer package inserts contain additional information. For complete information on best practices and recommendations for vaccine storage and handling, please refer to CDC's Vaccine Storage and Handling Toolkit, www.cdc.gov/vaccines/hcp/admin/storage/toolkit/storage-handling-toolkit.pdf.

Surveillance and Reporting of Pneumococcal Disease

Invasive pneumococcal disease is a notifiable condition in most states. For information on guidance for state and local health department staff who are involved in surveillance activities for vaccine-preventable diseases, please consult the Manual for the Surveillance of Vaccine-Preventable Diseases, www.cdc.gov/vaccines/pubs/surv-manual/chapters.html.

