MSD MANUAL
Professional Version

Pneumococcal Infections

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Streptococcus pneumoniae **(pneumococci) are gram-positive, alpha-hemolytic, aerobic, encapsulated diplococci. In the US, pneumococcal infection is a major cause of otitis media, pneumonia, sepsis, meningitis, and death. Diagnosis is by Gram stain and culture. Treatment depends on the resistance profile and includes either a beta-lactam, a macrolide, a respiratory fluoroquinolone, a pleuromutilin, or sometimes vancomycin.**

Pneumococci are fastidious microorganisms that require catalase to grow on agar plates. In the laboratory, pneumococci are identified by

- Gram-positive lancet-shaped diplococci
- Catalase-negative
- Alpha-hemolysis on blood agar
- Sensitivity to optochin
- Lysis by bile salts

Pneumococci commonly colonize the human respiratory tract, particularly in winter and early spring. Spread is via airborne droplets.

True epidemics of pneumococcal infections are rare; however, some serotypes seem to be associated with outbreaks in certain populations (eg, military, institutional, homeless) particularly in crowded settings.

Serotypes

The pneumococcus capsule consists of a complex polysaccharide that determines serologic type and contributes to virulence and pathogenicity. Virulence varies somewhat within serologic types because of genetic diversity.

Currently, > 90 different pneumococcal serotypes have been identified based on their reaction with type-specific antisera. The pneumococcal polysaccharide capsule is critical for evading phagocytosis. Serotype 3 strains, which are more heavily encapsulated and tend to form more mucoid colonies than other serotypes, are common causes of invasive pneumococcal disease in adults. Most serious infections are caused by a small number of serotypes (3, 4, 6B, 9V, 14, 18C, 19F, and 23F) that are included in the 13-valent pneumococcal conjugate vaccine. These serotypes cause about 90% of invasive infections in children and 60% in adults. However, these patterns are slowly changing, in part because of the widespread use of polyvalent vaccine. Serotype 19A, which is highly virulent and multidrug-resistant, has emerged as an important cause of respiratory tract infection and invasive disease; it is thus now included in the 13-valent pneumococcal conjugate vaccine.

Risk factors

Patients most susceptible to serious and invasive pneumococcal infections are

- Those with chronic illness (eg, chronic cardiorespiratory disease, diabetes, liver disease, alcoholism)
- Those with immunodeficiency or immunosuppression (eg, HIV)
- Those with functional or anatomic asplenia

- Those with sickle cell disease
- Residents of long-term care facilities
- Smokers
- Aborigines, Alaskan natives, and certain American Indian populations

Older people, even those without other disease, tend to have a poor prognosis with pneumococcal infections.

Damage to the respiratory epithelium by chronic bronchitis or common respiratory viral infections, notably influenza, may predispose to pneumococcal invasion.

Diseases Caused by Pneumococci

Pneumococcal diseases include

- Otitis media
- Pneumonia
- Sinusitis
- Meningitis
- Endocarditis
- Septic arthritis
- Peritonitis (rare)
- Bacteremia

Primary pneumococcal infection usually involves the middle ear or lungs.

The diseases listed below are further discussed elsewhere in THE MANUAL.

Pneumococcal bacteremia

Pneumococcal bacteremia can occur in immunocompetent and immunosuppressed patients; patients who have had splenectomy are at particular risk.

Bacteremia may be the primary infection, or it may accompany the acute phase of any focal pneumococcal infection. Pneumococcal bacteremia can be complicated by sepsis and septic shock. When bacteremia is present, secondary seeding of distant sites may cause infections such as septic arthritis, meningitis, and endocarditis.

Despite treatment, the **overall case-fatality rate** for bacteremia is

- 15 to 20% in children (mainly in those who have meningitis, who are immunocompromised, and/or who have had splenectomy and have severe bacteremia) and in adults
- 30 to 40% in older people

Risk of death is highest during the first 3 days.

Pneumococcal pneumonia

Pneumonia is the most frequent serious infection caused by pneumococci; it may manifest as lobar

Pneumonia is the most frequent serious infection caused by pneumococci; it may manifest as lobar pneumonia or, less commonly, as bronchopneumonia. Millions of cases of community-acquired pneumonia occur each year in the US; when community-acquired pneumonia requires hospitalization, pneumococci are the most common bacterial etiologic agent in patients of all ages.

Pleural effusion occurs in up to 40% of patients, but most effusions resolve during drug treatment. Only about 2% of patients develop empyema, which may become loculated, thick, and fibrinopurulent; empyema has been most commonly associated with *S. pneumoniae* serotype 1. Lung abscess due to *S. pneumoniae* is uncommon in adults but occurs more frequently in children; serotype 3 is the usual pathogen, but other pneumococcal serotypes may be involved.

Pneumococcal acute otitis media

Acute otitis media in infants (after the neonatal period) and children is caused by pneumococci in about 30 to 40% of cases. More than one third of children in most populations develop acute pneumococcal otitis media during the first 2 years of life, and pneumococcal otitis media commonly recurs. Relatively few serotypes of *S. pneumoniae* are responsible for most cases. After universal immunization of infants in the US beginning in 2000, nonvaccine serotypes of *S. pneumoniae* (particularly serotype 19A—not in the original protein-conjugated pneumococcal vaccine) have become the most common pneumococcal cause of acute otitis media.

Complications include

- Mild conductive hearing loss
- Vestibular balance dysfunction
- Tympanic membrane perforation
- Mastoiditis
- Petrositis
- Labyrinthitis

Intracranial complications are rare in developed countries but may include meningitis, epidural abscess, brain abscess, lateral venous sinus thrombosis, cavernous sinus thrombosis, subdural empyema, and carotid artery thrombosis.

Pneumococcal paranasal sinusitis

Paranasal sinusitis may be caused by pneumococci and may become chronic and polymicrobic.

Most commonly, the maxillary and ethmoid sinuses are affected. Infection of the sinuses causes pain and purulent discharge and may extend into the cranium, causing the following complications:

- Cavernous sinus thrombosis
- Brain, epidural, or subdural abscesses
- Septic cortical thrombophlebitis
- Meningitis

Pneumococcal meningitis

Acute purulent meningitis is frequently caused by pneumococci and may be secondary to bacteremia from other foci (notably pneumonia); direct extension from infection of the ear, mastoid process, or

paranasal sinuses; or basilar fracture of the skull involving one of these sites or the cribriform plate (usually with cerebrospinal fluid leakage), thus giving bacteria in the paranasal sinuses, nasopharynx, or middle ear access to the central nervous system.

Typical meningitis symptoms (eg, headache, stiff neck, fever) occur.

Complications after pneumococcal meningitis include

- Hearing loss (in up to 50% of patients)
- Seizures
- Learning disabilities
- Mental dysfunction
- Palsies

Pneumococcal endocarditis

Acute bacterial endocarditis may result from pneumococcal bacteremia, even in patients without valvular heart disease, but pneumococcal endocarditis is rare.

Pneumococcal endocarditis may produce a corrosive valvular lesion, with sudden rupture or fenestration, leading to rapidly progressive heart failure requiring valve replacement. Austrian syndrome is a rare condition characterized by the triad of pneumococcal meningitis, pneumonia, and endocarditis due to *S. pneumoniae* and has a high fatality rate. Native aortic valve insufficiency is the most common cause of heart failure in affected patients.

Pneumococcal septic arthritis

Septic arthritis, similar to septic arthritis caused by other gram-positive cocci, is usually a complication of pneumococcal bacteremia from another site.

Spontaneous pneumococcal peritonitis

Spontaneous pneumococcal peritonitis occurs most often in patients with cirrhosis and ascites, with no features to distinguish it from spontaneous bacterial peritonitis of other causes.

Diagnosis of Pneumococcal Infections

- Gram stain and culture

Pneumococci are readily identified by their typical appearance on Gram stain as lancet-shaped diplococci.

The characteristic capsule can be best detected using the Quellung test. In this test, application of antiserum followed by staining with India ink causes the capsule to appear like a halo around the organism. The capsule is also visible in smears stained with methylene blue.

Culture confirms identification; antimicrobial susceptibility testing should be done. Serotyping and genotyping of isolates can be helpful for epidemiologic reasons (eg, to follow the spread of specific clones and antimicrobial resistance patterns). Differences in virulence within a serotype may be distinguished by techniques such as pulsed-field gel electrophoresis and multilocus sequence typing.

The urine antigen detection test has high specificity (> 90%) but poor sensitivity (50 to 80%) and is greatly influenced by concurrent bacteremia. The positive predictive value (the proportion of patients with a positive test that actually have the disease) is high (> 95%). However, the negative predictive value (the proportion of patients with a negative test that are actually disease free) is low, so a negative urine antigen test should not be used to rule out pneumococcal disease.

Treatment of Pneumococcal Infections

- A beta-lactam, macrolide, respiratory fluoroquinolone (eg, levofloxacin, moxifloxacin, gemifloxacin), tetracycline (eg, omadacycline), or pleuromutilin (eg, lefamulin)

If pneumococcal infection is suspected, initial therapy pending susceptibility studies should be determined by local resistance patterns.

Although preferred treatment for pneumococcal infections is a beta-lactam or macrolide antibiotic, treatment has become more challenging because resistant strains have emerged. Strains highly resistant to penicillin, ampicillin, and other beta-lactams are common worldwide. The most common predisposing factor to beta-lactam resistance is use of these drugs within the past several months. Resistance to macrolide antibiotics has also increased significantly; these drugs are no longer recommended as monotherapy for hospitalized patients with community-acquired pneumonia.

Intermediately resistant organisms may be treated with usual or high doses of penicillin G or another beta-lactam.

Seriously ill patients with nonmeningeal infections caused by organisms that are resistant to penicillin can often be treated with ceftriaxone, cefotaxime, or ceftaroline. Very high doses of parenteral penicillin G (20 to 40 million units/day IV for adults) also work, unless the minimum inhibitory concentration of the isolate is very high, indicating resistance. Fluoroquinolones (eg, moxifloxacin, levofloxacin, gemifloxacin), omadacycline, and lefamulin are effective for respiratory infections with highly penicillin-resistant pneumococci in adults. Evidence suggests that the mortality rate for bacteremic pneumococcal pneumonia is lower when combination therapy (eg, macrolide plus beta-lactam) is used.

All penicillin-resistant isolates have been susceptible to vancomycin so far, but parenteral vancomycin does not always produce concentrations in cerebrospinal fluid adequate for treatment of meningitis (especially if corticosteroids are also being used). Therefore, in patients with meningitis, ceftriaxone or cefotaxime, rifampin, or both are commonly used with vancomycin.

Prevention of Pneumococcal Infections

Infection produces type-specific immunity that does not generalize to other serotypes. Prevention involves

- Vaccination
- Prophylactic antibiotics

Pneumococcal vaccines

See Pneumococcal Vaccine for more information, including indications, contraindications and precautions, dosing and administration, and adverse effects. See also the vaccine schedules for children and adults from the Centers for Disease Control and Prevention (CDC) and pneumococcal vaccine recommendations from the Advisory Committee on Immunization Practices (ACIP).

Two pneumococcal vaccines are available:

- Pneumococcal conjugated vaccine (PCV13): A conjugated vaccine against 13 serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F)
- Pneumococcal polysaccharide vaccine (PPSV23): A polyvalent polysaccharide vaccine directed against the 23 serotypes (1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19F, 19A, 20, 22F, 23F, 33F) that account for > 90% of serious pneumococcal infections in adults and children

The vaccine schedules vary depending on age and medical conditions present in the patient. All children 2 months through 6 years of age should receive PCV13 as part of the routine childhood vaccination schedule as should all people 65 years of age or older and people of other ages who have certain high-risk conditions.

Prophylactic antibiotics

For functional or anatomic asplenic children < 5 years of age, prophylactic penicillin V 125 mg orally 2 times a day is recommended. The duration for chemoprophylaxis is empiric, but some experts continue prophylaxis throughout childhood and into adulthood for high-risk patients with asplenia. Penicillin 250 mg orally 2 times a day is recommended for older children or adolescents for at least 1 year after splenectomy.

Key Points

- **Pneumococci cause many cases of otitis media and pneumonia and can also cause meningitis, sinusitis, endocarditis, and septic arthritis.**
- **Patients with chronic respiratory tract disease or asplenia are at high risk of serious and invasive pneumococcal infections, as are immunocompromised patients.**
- **Treat uncomplicated or mild infection with a beta-lactam or macrolide antibiotic.**
- **Because resistance to beta-lactam and macrolide antibiotics is increasing, seriously ill patients may be treated with an advanced-generation cephalosporin (eg, ceftriaxone, cefotaxime, ceftaroline), a respiratory fluoroquinolone (eg, moxifloxacin, levofloxacin, gemifloxacin), tetracycline (eg, omadacycline), or pleuromutilin (eg, lefamulin).**
- **Severe or bacteremic pneumococcal pneumonia is treated with combination therapy (eg, macrolide plus beta-lactam).**
- **Routine vaccination with PCV13 is recommended for all children aged 2 months through 6 years, people of other ages with certain risk factors, and for adults ≥ 65 years based on shared clinical decision making.**
- **Routine vaccination with PPSV23 is recommended for all adults ≥ 65 years and under certain clinical circumstances for people age 19 to 64 years.**

More Information

The following are some English-language resources that may be useful. Please note that THE MANUAL

is not responsible for the content of these resources.

Centers for Disease Control and Prevention (CDC): Recommended Child and Adolescent Immunization Schedule for ages 18 years or younger, United States, 2020

CDC: Recommended Adult Immunization Schedule for ages 19 years or older, United States, 2020

Advisory Committee on Immunization Practices (ACIP): Pneumococcal vaccine recommendations