

CHAPTER 107

Croup (Laryngotracheobronchitis)

ETIOLOGY AND EPIDEMIOLOGY

Croup, or laryngotracheobronchitis, is the most common infection of the middle respiratory tract. The most common causes of croup are parainfluenza viruses (types 1, 2, and 3), respiratory syncytial virus (RSV), influenza, and adenovirus. Laryngotracheal airway inflammation disproportionately affects children because a small decrease in diameter secondary to mucosal edema and inflammation exponentially increases airway resistance and the work of breathing. During inspiration, the walls of the subglottic space are drawn together, aggravating the obstruction and producing the **stridor** characteristic of croup. Croup is most common in children 6 months to 3 years of age, with a peak in fall and early winter. It typically follows a common cold. Symptomatic re-infection is common, yet re-infections are usually mild. In adolescents, it manifests as laryngitis.

CLINICAL MANIFESTATIONS

The manifestations of croup are a harsh cough described as **barking** or **brassy**, hoarseness, inspiratory stridor, low-grade fever, and respiratory distress. **Stridor** is a harsh, high-pitched respiratory sound produced by turbulent airflow. It is usually inspiratory, but it may be biphasic and is a sign of upper airway obstruction. Signs of upper airway obstruction, such as labored breathing, cyanosis, and marked suprasternal, intercostal, and subcostal retractions, may be evident on examination (see Chapter 135). Wheezing may be present if there is associated lower airway involvement. Symptoms of croup are characteristically worse at night and are exacerbated with crying or agitation.

LABORATORY AND IMAGING STUDIES

Croup is a clinical diagnosis and does not require routine radiology or laboratory studies. If obtained, anteroposterior radiographs of the neck often show the diagnostic subglottic narrowing of croup known as the **steeple sign** (Fig. 107.1). Leukocytosis is uncommon and suggests epiglottitis or bacterial tracheitis. Many rapid tests (using polymerase chain reaction [PCR]) are available for parainfluenza viruses, RSV, and other less common viral causes of croup, such as influenza and adenoviruses.

DIFFERENTIAL DIAGNOSIS

The infectious differential diagnosis includes epiglottitis, bacterial tracheitis, and parapharyngeal abscess. Noninfectious causes of stridor include mechanical and anatomic causes (foreign body aspiration, laryngomalacia, subglottic stenosis, hemangioma, vascular ring, vocal cord paralysis). Stridor in infants younger than 4 months of age, positional stridor, or persistence of symptoms for longer than 1 week indicates an increased probability of another lesion and the need for imaging and direct laryngoscopy (see Chapter 135).

Epiglottitis is a medical emergency because of the risk of sudden airway obstruction. Following the introduction of the *Haemophilus influenzae* type b vaccine, this illness is rare and usually caused by group A streptococcus or *Staphylococcus aureus* or *H. influenzae* type b in unimmunized patients. Patients typically prefer sitting, often with the head held forward, the mouth open, and the jaw thrust forward (**sniffing position**), and they may appear distressed and toxic. Lateral radiograph reveals thickened and bulging epiglottis (**thumb sign**) and swelling of the aryepiglottic folds. The diagnosis is confirmed by direct observation of the inflamed and swollen

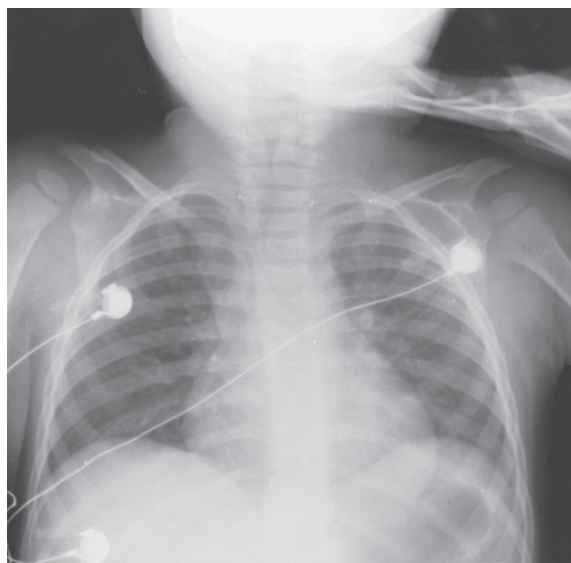


FIGURE 107.1 Croup (laryngotracheobronchitis). Radiograph of the airway and chest of a patient with croup, demonstrating the typical subglottic narrowing ("steeple sign"). (From Rodrigues KK, Roosevelt GE. Acute inflammatory upper airway obstruction [croup, epiglottitis, laryngitis, and bacterial tracheitis]. In: Kliegman RM, St. Geme III JW, eds. *Nelson Textbook of Pediatrics*. 21st ed. Philadelphia: Elsevier; 2020 [fig. 412-1].)

supraglottic structures and swollen, cherry red epiglottis. Direct observation of the larynx should only be performed in the operating room with an anesthesiologist and a competent surgeon prepared to place an endotracheal tube or perform a tracheostomy if needed. Epiglottitis requires antibiotic therapy and endotracheal intubation to maintain the airway. Both onset and clinical recovery are rapid, and most children can be extubated safely within 48–72 hours.

Bacterial tracheitis is a rare but serious superinfection of the trachea that may follow viral croup and is most commonly caused by *S. aureus*. Patients may be toxic appearing, and intubation may be required. **Spasmodic croup** describes sudden onset of croup symptoms, usually at night, but without a significant upper respiratory tract prodrome. These episodes may be recurrent and severe but usually are of short duration. Spasmodic croup has a milder course than viral croup and responds to relatively simple therapies, such as exposure to cool or humidified air. The etiology is not well understood and may be allergic.

TREATMENT

Oral or intramuscular dexamethasone for children with viral croup reduces symptoms and the need for hospitalization and shortens hospital stays. Dexamethasone (0.6 mg/kg) may be given once intramuscularly or orally. Alternatively, prednisolone (2 mg/kg/day) may be given orally for 3 days. For significant airway compromise, administration of aerosolized racemic (D- and L-) epinephrine reduces subglottic edema by adrenergic vasoconstriction, temporarily producing marked clinical improvement. The peak effect is within 10–30 minutes and fades within 60–90 minutes. A rebound effect may occur, with worsening of symptoms as the effect of the drug dissipates. Aerosol treatment may need to be repeated every 20 minutes in severe cases.

Children should be kept as calm as possible to minimize forceful inspiration. One useful calming method is for a child with croup to sit on the parent's lap. Sedatives should be used cautiously and in the intensive care unit only.

Hospitalization is often required for children with cyanosis or stridor at rest. Children receiving aerosol treatment should be hospitalized or observed for at least 2–3 hours because of the risk of rebound airway obstruction. Decreased symptoms may indicate improvement or fatigue and impending respiratory failure.

COMPLICATIONS AND PROGNOSIS

The most common complication of croup is viral pneumonia, which occurs in 1–2% of children. Parainfluenza virus pneumonia and secondary bacterial pneumonia are more common in immunocompromised patients. Bacterial tracheitis may also be a complication of croup.

The prognosis for croup is excellent. Illness usually lasts approximately 5 days. As children grow, they become less susceptible to the airway effects of viral infections of the middle respiratory tract.

PREVENTION

There are no licensed vaccines for parainfluenza, RSV, or adenovirus. Annual influenza vaccine is recommended for children over 6 months of age.

PEARLS FOR PRACTITIONERS

See Infectious Diseases: Pearls for Practitioners at the end of this section.

CHAPTER 108

Pertussis

ETIOLOGY

Pertussis (**whooping cough**) is caused by *Bordetella pertussis*, a gram-negative pleomorphic bacillus with fastidious growth requirements. *B. pertussis* infects only humans and is transmitted person to person by coughing.

EPIDEMIOLOGY

The typical incubation period is 7–10 days but can range between 5 and 21 days. Patients are most contagious during the first 2 weeks of cough. The annual rate of pertussis was approximately 100–200 cases per 100,000 population in the pre-vaccination era; worldwide, there continue to be an estimated 20 million cases of pertussis and 200,000 childhood deaths annually. In the United States, the incidence of pertussis decreased after the introduction of vaccine, but it has increased steadily since the 1980s, with more than 15,000 cases reported in 2019. Pertussis incidence peaks among those less than 6 months of age—infants too young to be completely immunized and most likely to have severe complications—ranging from 40 to 160 cases per 100,000 population in the United States. Infection in late childhood and adolescence is likely due to a combination of waning immunity from previous vaccines, underimmunization, exposure to infected family members, and improved diagnostics. Epidemics can occur in fully immunized patients because vaccine-induced immunity wanes.

CLINICAL MANIFESTATIONS

Classic pertussis is seen in children between 1 and 10 years old. The progression of the disease is divided into catarrhal, paroxysmal, and convalescent stages. The **catarrhal stage** is marked by nonspecific signs (increased nasal secretions and low-grade fever) lasting 1–2 weeks. The **paroxysmal stage** is the most distinctive stage of pertussis and lasts 2–4 weeks. Coughing occurs in **paroxysms** during expiration, causing young children to lose their breath. This pattern of coughing is needed to dislodge plugs of necrotic bronchial epithelial tissues and thick mucus. The forceful inhalation against a narrowed glottis that follows this paroxysm of cough produces the characteristic **whoop**. Posttussive emesis is common. The **convalescent stage** is marked by gradual resolution of symptoms over 1–2 weeks. Coughing becomes less severe, and the paroxysms and whoops slowly disappear. Although the disease typically lasts 6–8 weeks, residual cough may persist for months, especially with physical stress or respiratory irritants.

Infants may not display the classic findings, and the first sign in the neonate may be apnea. Young infants are unlikely to have the classic whoop, more likely to have central nervous

system damage as a result of hypoxia, and more likely to have secondary bacterial pneumonia. Adolescents and adults with pertussis usually present with a prolonged bronchitic illness with persistent, nonproductive cough that often begins as a nonspecific upper respiratory tract infection. In general, adolescents and adults do not have a whoop with the cough, although they may have severe paroxysms.

LABORATORY AND IMAGING STUDIES

The diagnosis depends on isolation of *B. pertussis* or detection of its nucleic acids. Culture on specialized media is usually performed during the early phases of illness on specimens from nasopharyngeal swabs or aspirates, but this can be difficult to accomplish given the organism's fastidious nature. Polymerase chain reaction is available in many clinical laboratories. False-positive results can occur. Direct fluorescent antibody staining is not recommended. Serologic tests are not useful for diagnosing acute infection but can be confirmatory in the convalescent phase of illness, though there are no commercial kits approved by the U.S. Food and Drug Administration.

Lymphocytosis is present in 75–85% of infants and young children but is not diagnostic. The white blood cell count may increase from 20,000/mm³ to more than 50,000/mm³, consisting primarily of mature lymphocytes. Physical examination and radiographic signs of segmental lung atelectasis may develop during pertussis, especially during the paroxysmal stage. Perihilar infiltrates are common and are similar to those seen in viral pneumonia.

DIFFERENTIAL DIAGNOSIS

For a young child with classic pertussis, the diagnosis based on the pattern of illness is quite accurate. The paroxysmal stage is the most distinctive part of the syndrome. Other causes of pertussis-like prolonged cough illnesses include *Bordetella parapertussis* and *Bordetella holmesii*—which cause a similar but milder illness and are not prevented by *B. pertussis* vaccination—*Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, adenoviruses, and respiratory syncytial virus.

TREATMENT

Macrolide antibiotics (azithromycin, clarithromycin, or erythromycin) are recommended for treatment. Azithromycin is preferred in neonates due to the association between erythromycin treatment and the development of pyloric stenosis. Treatment during the catarrhal phase eradicates nasopharyngeal carriage of organisms within 3–4 days and may lessen symptom severity. Treatment in the paroxysmal stage does not alter the course of illness but decreases the potential for spread to others. Trimethoprim-sulfamethoxazole is an alternative therapy among children older than 2 months, although studies of its use for this indication are limited.

COMPLICATIONS AND PROGNOSIS

Major complications are most common among infants and young children and include hypoxia, apnea, pneumonia, seizures, encephalopathy, malnutrition, and death. The most frequent complication is pneumonia caused by *B. pertussis*

itself or resulting from secondary bacterial infection with *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Staphylococcus aureus*. Atelectasis may develop secondary to mucus plugs. The force of the paroxysm may produce pneumomediastinum, pneumothorax, or interstitial or subcutaneous emphysema; epistaxis; hernias; and retinal and subconjunctival hemorrhages. Otitis media and sinusitis may occur.

Most children recover normal pulmonary function with complete healing of the respiratory epithelium. Most permanent disability is a result of encephalopathy.

PREVENTION

Active immunity is induced with acellular pertussis components given as a vaccine in combination with the tetanus and diphtheria toxoids (DTaP). The acellular pertussis vaccines contain two to five antigens of *B. pertussis*, including pertussis toxin, pertactin, filamentous hemagglutinin, and fimbrial agglutinogens FIM-2 and FIM-3. DTaP vaccine is recommended at 2, 4, 6, and 15–18 months, with a booster at 4–6 years, and has an efficacy of 70–90%. A single booster dose of Tdap vaccine is recommended at 11–12 years or once for all adults. A booster dose of Tdap vaccine is recommended for pregnant women with each pregnancy, preferably in the third trimester, to provide higher levels of antibodies to the infant via transplacental transfer.

Macrolides are effective in preventing secondary cases in contacts exposed to pertussis. Underimmunized close contacts under 7 years of age should receive a booster dose of DTaP (unless a booster dose has been given within the preceding 3 years), whereas those 7–10 years of age should receive Tdap. All close contacts should receive prophylactic antibiotics for 5 days (azithromycin) or 7–14 days (clarithromycin or erythromycin, duration based on age).

PEARLS FOR PRACTITIONERS

See *Infectious Diseases: Pearls for Practitioners* at the end of this section.

CHAPTER 109

Bronchiolitis

ETIOLOGY

Bronchiolitis is a disease of small bronchioles with increased mucus production and occasional bronchospasm, sometimes leading to airway obstruction. It is commonly caused by a viral lower respiratory tract infection. Bronchiolitis is most commonly seen in infants and young children, with most severe cases occurring among infants; it is potentially life threatening.

Respiratory syncytial virus (RSV) is a primary cause of bronchiolitis, followed in frequency by human metapneumovirus, parainfluenza viruses, influenza viruses, adenoviruses, rhinoviruses, coronaviruses, and, infrequently, *Mycoplasma pneumoniae*. Viral bronchiolitis is extremely contagious and is spread by contact with infected respiratory

secretions. Although coughing produces aerosols, hand carriage of contaminated secretions is the most frequent mode of transmission.

EPIDEMIOLOGY

Bronchiolitis is a leading cause of hospitalization of infants. Bronchiolitis occurs almost exclusively during the first 2 years of life, with a peak age at 2–6 months. Many healthy children with bronchiolitis can be managed as outpatients; however, premature infants and children with chronic lung disease of prematurity, hemodynamically significant congenital heart disease, neuromuscular weakness, or immunodeficiency are at increased risk of severe, potentially fatal disease. Children acquire infection after exposure to infected family members, who typically have symptoms of an upper respiratory tract infection, or from infected children in day care. In the United States, annual peaks are usually in the late winter months from December through March.

CLINICAL MANIFESTATIONS

Bronchiolitis caused by RSV typically has an incubation period of 4–6 days. Bronchiolitis classically presents as a progressive respiratory illness similar to the common cold in its early phase, with cough and rhinorrhea. It progresses over 3–7 days to noisy, raspy breathing and audible wheezing. There is usually a low-grade fever accompanied by irritability, which may reflect the increased work of breathing. In contrast to the classic progression of disease, young infants infected with RSV may not have a prodrome and may have apnea as the first sign of infection.

Physical signs of bronchiolar obstruction include prolongation of the expiratory phase of breathing, nasal flaring, intercostal retractions, suprasternal retractions, and air trapping with hyperexpansion of the lungs. During the wheezing phase, percussion of the chest usually reveals only hyperresonance, but auscultation usually reveals diffuse wheezes and crackles throughout the breathing cycle. With more severe disease, grunting and cyanosis may be present.

LABORATORY AND IMAGING STUDIES

Routine laboratory tests are not required to confirm the diagnosis. It is important to assess oxygenation in severe cases of bronchiolitis. **Pulse oximetry** is adequate for monitoring oxygen saturation. Frequent, regular assessments and cardiorespiratory monitoring of infants are necessary because respiratory failure may develop precipitously in very tired infants even though blood gas values taken before rapid decompensation are reassuring.

Rapid viral diagnosis of nasopharyngeal secretions performed by polymerase chain reactions for RSV, human metapneumovirus, parainfluenza viruses, influenza viruses, coronaviruses, and adenoviruses are sensitive tests to confirm the infection. Identifying the viral agent is helpful for cohorting children with the same infection but is not necessary to make the diagnosis of bronchiolitis.

Chest radiographs are not always necessary but frequently show signs of lung hyperinflation, including increased lung lucency and flattened or depressed diaphragms. Areas of increased density may represent either viral pneumonia or localized atelectasis.

DIFFERENTIAL DIAGNOSIS

The major difficulty in the diagnosis of bronchiolitis is to differentiate other diseases associated with wheezing. It may be difficult to differentiate asthma from bronchiolitis by physical examination, but age of presentation, presence of fever, and absence of personal or family history of asthma are the major differential factors. Bronchiolitis occurs primarily in the first year of life and is accompanied by fever, whereas asthma usually presents in older children with previous wheezing episodes and is typically unaccompanied by fever unless a respiratory tract infection is the trigger for the asthma exacerbation.

Wheezing may also be due to an airway foreign body, congenital airway obstructive lesion, cystic fibrosis, exacerbation of chronic lung disease, viral or bacterial pneumonia, and other lower respiratory tract diseases (see [Chapter 78](#)). **Cardiogenic asthma**, which can be confused with bronchiolitis in infants, is wheezing associated with pulmonary congestion secondary to left-sided heart failure. Wheezing associated with gastroesophageal reflux is likely to be chronic or recurrent, and the patient may have a history of frequent emesis. Cystic fibrosis is associated with poor growth, chronic diarrhea, and a positive family history. A focal area on radiography that remains inflated despite changes in position suggests **foreign body aspiration**.

TREATMENT

Bronchiolitis treatment consists of supportive therapy, including respiratory monitoring, control of fever, hydration, upper airway suctioning, and, if needed, oxygen administration. Indications for hospitalization include moderate to marked respiratory distress, hypoxemia, apnea, inability to tolerate oral feeding, and lack of appropriate care available at home. Hospitalization of high-risk children with bronchiolitis should be considered. Among hospitalized infants, supplemental oxygen by nasal cannula is often necessary, but intubation and ventilatory assistance for respiratory failure or apnea are required in less than 10% of these infants. Bronchodilators, corticosteroids, chest physiotherapy, and hypertonic saline are seldom effective and are not generally recommended. Likewise, antibiotics should be avoided unless there is strong suspicion for concomitant bacterial infection.

COMPLICATIONS AND PROGNOSIS

Most hospitalized children show marked improvement in 2–5 days with supportive treatment alone. The course of the wheezing phase varies, however. Tachypnea and hypoxia may progress to respiratory failure requiring assisted ventilation. Apnea is a major concern for very young infants with bronchiolitis.

Most cases of bronchiolitis resolve completely, although minor abnormalities of pulmonary function and bronchial hyperactivity may persist for several years. Recurrence is common but tends to be mild and should be assessed and treated similarly to the first episode. The incidence of asthma seems to be higher in children hospitalized for bronchiolitis as infants, but it is unclear whether this is causal or whether children prone to asthma are more likely to be hospitalized with bronchiolitis. There is a 1–2% mortality rate, highest among infants with pre-existing cardiopulmonary or immunologic impairment.

PREVENTION

Monthly injections of **palivizumab**, an RSV-specific monoclonal antibody, initiated just before the onset of the RSV season confers some protection from severe RSV disease. Palivizumab is indicated for infants with prematurity (born before 29 weeks, 0 days gestation), chronic lung disease of prematurity, and those with hemodynamically significant cyanotic and acyanotic congenital heart disease in the first year of life, and, rarely, in the second year of life. Immunization with influenza vaccine is recommended for all children older than 6 months and may prevent influenza-associated disease.

PEARLS FOR PRACTITIONERS

See *Infectious Diseases: Pearls for Practitioners* at the end of this section.

CHAPTER 110

Pneumonia

ETIOLOGY

Pneumonia is an infection of the lower respiratory tract that involves the airways and parenchyma, with consolidation of the alveolar spaces. The term **lower respiratory tract infection** is often used to encompass bronchitis, bronchiolitis (see Chapter 109), pneumonia, or any combination of the three. **Pneumonitis** is a general term for lung inflammation that may or may not be associated with consolidation. **Lobar pneumonia** describes pneumonia localized to one or more lobes of the lung. **Atypical pneumonia** describes patterns typically more diffuse or interstitial than lobar pneumonia. **Bronchopneumonia** refers to inflammation of the lung that is centered in the bronchioles and leads to the production of a mucopurulent exudate that obstructs some of these small airways and causes patchy consolidation of the adjacent lobules. **Interstitial pneumonitis** refers to inflammation of the interstitium, which is composed of the walls of the alveoli, the alveolar sacs and ducts, and the bronchioles. Interstitial pneumonitis is characteristic of acute viral infections but may also be a chronic inflammatory or fibrosing process (childhood interstitial lung diseases).

Defects in host defenses increase the risk of pneumonia. Lower airways and secretions are generally considered sterile as a result of a multifactorial system. Airway contaminants are caught in the mucus secreted by the goblet cells. Cilia on epithelial surfaces, composing the ciliary elevator system, beat synchronously to move particles upward toward central airways and into the throat, where they are swallowed or expectorated. Polymorphonuclear neutrophils from the blood and tissue macrophages ingest and kill microorganisms. IgA secreted into the upper airway fluid protects against invasive infections and facilitates viral neutralization.

Infectious agents that commonly cause community-acquired pneumonia vary by age (Table 110.1). *Streptococcus pneumoniae* is the most common bacterial cause of pneumonia (particularly **lobar pneumonia**) and occurs in children of any age outside the neonatal period. Other common

causes include respiratory syncytial virus (RSV) in infants (see Chapter 109), other respiratory viruses (parainfluenza viruses, influenza viruses, human metapneumovirus, adenoviruses) in children younger than 5 years old, and *Mycoplasma pneumoniae* in children older than age 5 years. *M. pneumoniae* and *Chlamydophila pneumoniae* are principal causes of **atypical pneumonia**.

Chlamydia trachomatis and, less commonly, *Mycoplasma hominis*, *Ureaplasma urealyticum*, and cytomegalovirus (CMV) cause a similar respiratory syndrome in infants 2 weeks to 3 months of age, with subacute onset of an **afebrile pneumonia**; cough and hyperinflation are the predominant signs. These infections are difficult to diagnose and distinguish from each other. In adults these organisms are carried primarily as part of the genital mucosal flora. Women who harbor these agents may transmit them perinatally to newborns.

Additional agents occasionally cause pneumonia. **Severe acute respiratory syndrome (SARS)** is due to SARS-associated coronavirus (SARS-CoV) or SARS-CoV-2, the cause of the coronavirus infectious disease (COVID-19) pandemic. SARS-CoV-2 is an emerging pathogen but appears to cause less mortality in children than in adults; in addition to respiratory disease, it is also associated with a postinfectious multisystem inflammatory syndrome similar but not the same as Kawasaki disease (Chapter 88). SARS-CoV-2 is a highly contagious, airborne (cough, sneeze, talking, breathing) virus that presents within a broad spectrum of symptoms. Many patients are asymptomatic (but contagious) or have mild to moderate symptoms that do not require hospitalization. A minority develop a severe or critical illness.

Avian influenza (bird flu) is a highly contagious viral disease of poultry and other birds caused by **influenza A (H5N1)**. There were outbreaks among humans in Southeast Asia in 1997 and 2003–2004, with high mortality rates. A novel influenza A (H1N1) of swine origin began circulating in 2009. Other etiologic agents to consider, based on specific exposure history, include *Staphylococcus aureus* and *Streptococcus pyogenes* (especially after influenza infection), *Mycobacterium tuberculosis*, *Francisella tularensis*, *Brucella* spp., *Coxiella burnetii*, *Chlamydophila psittaci*, *Legionella pneumophila*, hantavirus, *Histoplasma capsulatum*, *Coccidioides immitis*, *Blastomyces dermatitidis*, and oral flora or gram-negative bacilli (after aspiration).

Causes of pneumonia in immunocompromised persons include gram-negative enteric bacteria, mycobacteria (*M. avium* complex), fungi (aspergillosis), viruses (CMV), and *Pneumocystis jirovecii* (formerly *carinii*). Pneumonia in patients with cystic fibrosis is usually caused by *S. aureus* in infancy and *Pseudomonas aeruginosa* or *Burkholderia cepacia* in older patients.

EPIDEMIOLOGY

Immunizations have markedly reduced the incidence of pneumonia caused by pertussis, diphtheria, measles, *Haemophilus influenzae* type b, and *S. pneumoniae*. Where used, bacille Calmette-Guérin (BCG) immunization for tuberculosis has also had some impact. Pneumonia is the single largest contributor of childhood mortality worldwide, killing an estimated 1 million children under 5 years of age annually. Risk factors for lower respiratory tract infections include exposure to infected persons, gastroesophageal reflux, neurologic

TABLE 110.1 Etiologic Agents and Empirical Antimicrobial Therapy for Pneumonia in Patients Without History of Recent Antibiotic Therapy

AGE GROUP	COMMON PATHOGENS* (IN APPROXIMATE ORDER OF FREQUENCY)*	LESS COMMON PATHOGENS	OUTPATIENTS (7–10 DAYS TOTAL DURATION OF TREATMENT) [†]	PATIENTS REQUIRING HOSPITALIZATION (10–14 DAYS TOTAL DURATION OF TREATMENT) [‡]	PATIENTS REQUIRING INTENSIVE CARE (10–14 DAYS TOTAL DURATION OF TREATMENT) ^{*,‡}
Neonates (up to 1 mo of age)	Group B streptococcus, <i>Escherichia coli</i> , other gram- negative bacilli, <i>Streptococcus</i> <i>pneumoniae</i>	Cytomegalovirus, herpes simplex virus, <i>Listeria monocytogenes</i> , <i>Treponema pallidum</i> , <i>Haemophilus influenzae</i> (type b, [§] nontypable)	Outpatient management not recommended	Ampicillin plus ceftazidime or an aminoglycoside plus an antistaphylococcal agent if <i>Staphylococcus aureus</i> is suspected	Ampicillin plus ceftazidime or an aminoglycoside plus an antistaphylococcal agent if <i>S. aureus</i> is suspected
1–3 mo					
Febrile pneumonia	Respiratory syncytial virus, other respiratory viruses (parainfluenza viruses, influenza viruses, adenoviruses), <i>S. pneumoniae</i> , <i>H.</i> <i>influenzae</i> (type b, [§] nontypable)		Initial outpatient management not recommended	Amoxicillin or ampicillin if fully immunized for age for <i>S.</i> <i>pneumoniae</i> and <i>H. influenzae</i> type b. Alternatives: ceftriaxone if not fully immunized or local <i>S. pneumoniae</i> penicillin resistance is significant, with clindamycin if MRSA suspected	Ceftriaxone plus nafcillin, oxacillin, clindamycin, or vancomycin
Afebrile pneumonia	<i>Chlamydia trachomatis</i> , <i>Mycoplasma hominis</i> , <i>Ureaplasma</i> <i>urealyticum</i> , cytomegalovirus <i>Bordetella pertussis</i>		Erythromycin, azithromycin, or clarithromycin with close follow-up	Erythromycin, azithromycin, or clarithromycin	Erythromycin, azithromycin, or clarithromycin plus ceftriaxone plus nafcillin, oxacillin, clindamycin, or vancomycin
3 mo to 5 yr	Respiratory syncytial virus, other respiratory viruses (parainfluenza viruses, influenza viruses, human metapneumovirus adenoviruses), <i>S. pneumoniae</i> , <i>H. influenzae</i> (type b, [§] nontypable)	<i>C. trachomatis</i> , <i>Mycoplasma pneumoniae</i> , <i>Chlamydia</i> <i>Chlamydophila</i> <i>pneumoniae</i> , group <i>A streptococcus</i> , <i>S.</i> <i>aureus</i> , <i>Mycobacterium</i> <i>tuberculosis</i>	Amoxicillin plus erythromycin, azithromycin, or clarithromycin if atypical pneumonia suspected	Ampicillin Alternatives: ceftriaxone if not fully immunized or local <i>S. pneumoniae</i> penicillin resistance is significant, with clindamycin if MRSA suspected; add erythromycin, azithromycin, or clarithromycin if atypical pneumonia suspected	Cefuroxime or ceftriaxone plus azithromycin, erythromycin, or clarithromycin with or without clindamycin or vancomycin
5–18 yr	<i>M. pneumoniae</i> , <i>S. pneumoniae</i> , <i>C. pneumonia</i>	<i>H. influenzae</i> (type b, [§] nontypable), influenza viruses, adenoviruses, coronaviruses, other respiratory viruses	Amoxicillin plus erythromycin, azithromycin, or clarithromycin if atypical pneumonia suspected	Ampicillin plus erythromycin, azithromycin, or clarithromycin if atypical pneumonia suspected	Cefuroxime or ceftriaxone plus azithromycin, erythromycin, or clarithromycin with or without clindamycin or vancomycin
≥18 y [§]	<i>M. pneumoniae</i> , <i>S. pneumoniae</i> , <i>C. pneumoniae</i> , <i>H. influenzae</i> (type b, [§] nontypable), influenza and coronaviruses, adenoviruses	<i>Legionella pneumophila</i> , <i>M. tuberculosis</i>	Amoxicillin, or erythromycin, azithromycin, clarithromycin, doxycycline, moxifloxacin, gatifloxacin, levofloxacin, or gemifloxacin if atypical pneumonia suspected	Ampicillin plus erythromycin, azithromycin, or clarithromycin if atypical pneumonia suspected or moxifloxacin, gatifloxacin, levofloxacin, or gemifloxacin	Ceftriaxone, plus either azithromycin or clarithromycin with or without clindamycin or vancomycin, or moxifloxacin, gatifloxacin, levofloxacin, or gemifloxacin with or without clindamycin or vancomycin

*Severe pneumonia, from *Streptococcus pneumoniae*, *Staphylococcus aureus*, group A streptococcus, *Haemophilus influenzae*, or *Mycoplasma pneumoniae* requiring admission to an intensive care unit. Antipseudomonal agents should be added if *Pseudomonas* is suspected.

[†]Oral administration.

[‡]Intravenous administration for inpatients except for the macrolides (erythromycin, azithromycin, and clarithromycin), which are given orally.

[§]*Haemophilus influenzae* type b infection is uncommon with universal H. influenzae type b immunization. Pandemic viruses vary from influenza to coronaviruses (location and year dependent).

^{||}Fluoroquinolones are contraindicated for children younger than 18 years of age and pregnant or lactating women. Tetracyclines are not recommended for children younger than 9 years.

MRSA, Methicillin-resistant *Staphylococcus aureus*.

impairment (aspiration), immunocompromised states, anatomic abnormalities of the respiratory tract, residence in residential care facilities, and hospitalization, especially in an intensive care unit.

CLINICAL MANIFESTATIONS

Age is a determinant in the clinical manifestations of pneumonia. Neonates may have fever or hypoxia only, with subtle or absent physical examination findings (see Chapter 65). With a young infant, apnea may be the first sign of pneumonia. Fever, chills, tachypnea, cough, malaise, pleuritic chest pain, retractions, and apprehension—because of difficulty breathing or shortness of breath—are common in older infants and children. Dominant features of the pulmonary symptoms of **COVID-19** include cough, fever, dyspnea, and myalgias. Other common features include abdominal pain and diarrhea, headache, sore throat, as well as loss of taste or smell sensations. Severe involvement includes worsening dyspnea, hypoxia, and greater than 50% lung infiltrates on imaging. Critical illness includes respiratory failure requiring mechanical ventilation or extracorporeal membrane oxygenation (ECMO) and multiorgan system dysfunction (myocarditis, hypercoagulability, acute kidney injury).

Physical examination findings cannot reliably distinguish viral and bacterial pneumonias, but complete physical examination may help identify other foci of disease or associated findings to suggest an etiology.

Viral pneumonias are generally associated more often with cough, wheezing, or stridor; fever is less prominent than with bacterial pneumonia. Mucosal congestion and upper airway inflammation suggest a viral infection. Bacterial pneumonias are typically associated with higher fever, chills, cough, dyspnea, and auscultatory findings of lung consolidation. Atypical pneumonia in young infants is characterized by tachypnea, cough, and crackles on auscultation. Concomitant conjunctivitis may be present in infants with chlamydial pneumonia. Other signs of respiratory distress include nasal flaring, intercostal and subcostal retractions, and grunting.

Asymmetry or shallow breathing may be due to splinting from pain. Hyperexpansion, common in asthma but also frequently accompanying viral lower respiratory infections, may cause a low diaphragm seen on a chest x-ray. Poor diaphragmatic excursion may indicate hyperexpanded lungs or an inability for expansion due to a large consolidation or effusion. Dullness to percussion may be due to lobar or segmental infiltrates or pleural fluid. Auscultation may be normal in early or very focal pneumonia, but the presence of localized crackles, rhonchi, and wheezes may help one detect and locate pneumonia. Distant breath sounds may indicate a large, poorly ventilated area of consolidation or pleural fluid.

LABORATORY AND IMAGING STUDIES

Bacterial flora of the upper respiratory tract does not accurately reflect flora present in lower respiratory tract infections, and high-quality sputum is rarely obtainable from children. In otherwise healthy children without life-threatening disease, invasive procedures to obtain lower respiratory tissue or secretions are seldom indicated. Serologic

tests are not useful for the most common causes of bacterial pneumonia.

The white blood cell (WBC) count with viral pneumonias is often normal or mildly elevated, with a predominance of lymphocytes, whereas with bacterial pneumonias, the WBC count can be elevated ($>15,000$ – $20,000/\text{mm}^3$) and with a predominance of neutrophils. Mild eosinophilia is characteristic of infant *C. trachomatis* pneumonia. Blood cultures should be performed on moderately to severely ill, hospitalized children to attempt to diagnose a bacterial cause of pneumonia. Blood cultures identify a bacterial respiratory pathogen in approximately 5–10% of children hospitalized for pneumonia (and 10–20% of those with pneumonia with empyema or large effusion). Urinary antigen tests are especially useful for *L. pneumophila* (Legionnaires disease).

Viral respiratory pathogens can be diagnosed using polymerase chain reaction (PCR) or rapid viral antigen detection. *M. pneumoniae* can be confirmed by *Mycoplasma* PCR. CMV pneumonitis can be diagnosed with PCR from bronchoalveolar lavage fluid. The diagnosis of *M. tuberculosis* is established by the tuberculin skin test, serum interferon- γ release assay, or analysis of sputum or gastric aspirates by culture, antigen detection, or PCR.

The need to establish an etiologic diagnosis of pneumonia is greater in immunocompromised patients, patients with recurrent pneumonia, or those with pneumonia unresponsive to empirical therapy. For these patients, bronchoscopy with bronchoalveolar lavage and brush mucosal biopsy, needle aspiration of the lung, and open lung biopsy are methods of obtaining material for microbiologic diagnosis.

When there is a pleural **effusion or empyema**, a thoracentesis to obtain pleural fluid can be diagnostic and therapeutic. Evaluation differentiates between empyema and a sterile parapneumonic effusion caused by irritation of the pleura contiguous with the pneumonia. Gram stain, bacterial culture, or broad-range bacterial PCR may lead to microbiologic diagnosis. The pleural fluid can also be cultured for mycobacteria and fungi. Removal of grossly purulent pleural fluid reduces the patient's toxicity and associated discomfort and may facilitate more rapid recovery. Drainage of large pleural accumulations also improves pulmonary mechanics and gas exchange by increasing the ability of the lung to expand.

Frontal and lateral radiographs are required to localize disease and adequately visualize retrocardiac infiltrates; they are recommended for diagnosis among hospitalized children but are not necessary to confirm the diagnosis in well-appearing outpatients. Although there are characteristic radiographic findings of pneumonia, radiography alone cannot provide a definitive microbiologic diagnosis. Bacterial pneumonia characteristically shows lobar consolidation or a round pneumonia, with pleural effusion in 10–30% of cases (Fig. 110.1). Viral pneumonia characteristically shows diffuse, streaky infiltrates of bronchopneumonia (Fig. 110.2) and hyperinflation. Atypical pneumonia, as with *M. pneumoniae* and *C. pneumoniae*, shows increased interstitial markings or bronchopneumonia. Chest radiographs may be normal in early pneumonia, with infiltrates appearing during treatment as hydration is restored. Hilar lymphadenopathy is uncommon with bacterial pneumonia but may be a sign of tuberculosis, endemic mycoses, autoimmune conditions, or an underlying malignant neoplasm. Decubitus views or

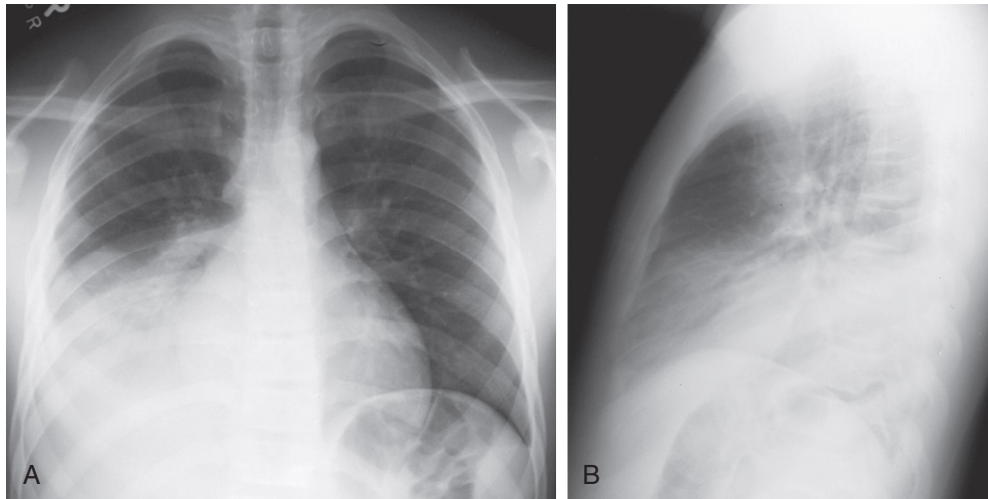


FIGURE 110.1 Acute lobar pneumonia of the right lower lobe in a 14-year-old boy with fever and cough. (A) Posteroanterior and (B) lateral chest radiographs demonstrate right-lower-lobe airspace consolidation, which obliterates the silhouette of the right heart border. (From Kelly MS, Sandora TJ. Community-acquired pneumonia. In: Kliegman RM, St. Geme III JW, eds. *Nelson Textbook of Pediatrics*. 21st ed. Philadelphia: Elsevier; 2020 [fig. 428.3].)

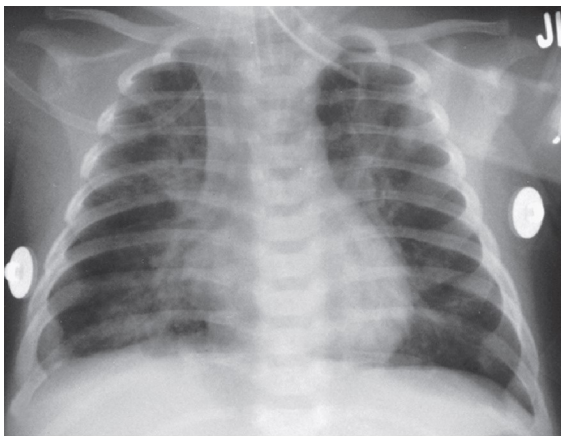


FIGURE 110.2 Diffuse respiratory syncytial virus pneumonia in a 6-month-old infant with tachypnea and fever. Anteroposterior chest radiograph shows bilateral, perihilar, peribronchovascular thickening and fine airspace disease with hyperinflation. (From Kelly MS, Sandora TJ. Community-acquired pneumonia. In: Kliegman RM, St. Geme III JW, eds. *Nelson Textbook of Pediatrics*. 21st ed. Philadelphia: Elsevier; 2020 [fig. 428.2A].)

ultrasound should be used to assess the size of pleural effusions and whether they are freely mobile. Computed tomography (CT) is used to evaluate serious disease, lung abscesses, bronchiectasis, and effusion characteristics. Unusual etiologies or recurrent pneumonias require special considerations (Table 110.2). Lung abscesses, pneumatoceles, and empyema may require surgical management.

DIFFERENTIAL DIAGNOSIS

Pneumonia must be differentiated from other acute pulmonary diseases, including allergic hypersensitivity pneumonitis, e-cigarette or vaping product use–associated lung injury

(EVALI), asthma, and cystic fibrosis; cardiac diseases, such as pulmonary edema caused by heart failure; and autoimmune diseases, such as certain vasculitides and systemic lupus erythematosus. Radiographically, pneumonia must be differentiated from lung trauma and contusion, hemorrhage, foreign body aspiration, and sympathetic effusion due to subdiaphragmatic inflammation.

TREATMENT

Therapy for pneumonia includes supportive and specific treatment and depends on the degree of illness, complications, and knowledge of the infectious agent likely causing the pneumonia. Most cases of pneumonia in healthy children can be managed on an outpatient basis. However, children with hypoxemia, inability to maintain adequate hydration, or moderate to severe respiratory distress should be hospitalized. Hospitalization should be considered in infants under 6 months with suspected bacterial pneumonia, those in whom there is a concern for a pathogen with increased virulence (e.g., methicillin-resistant *S. aureus* [MRSA]), or when concern exists about a family's ability to care for the child and to assess symptom progression.

Because viruses cause many community-acquired pneumonias in young children, not all children require empiric antibiotic treatment for pneumonia. Recommended therapies in those without recent antibiotic exposure are listed in Table 110.1. Exceptional situations include lack of response to empirical therapy, unusually severe presentations, nosocomial pneumonia, and immunocompromised children susceptible to infections with opportunistic pathogens (Table 110.3). Presumed pneumococcal pneumonia can be treated with high-dose ampicillin therapy. Ceftriaxone and/or vancomycin can be used if the isolate shows high-level resistance and the patient is severely ill. For infants 2–18 weeks old with afebrile pneumonia most likely caused by *C. trachomatis*, a macrolide is the recommended treatment. Oseltamivir or zanamivir

TABLE 110.2 Differential Diagnosis of Recurrent Pneumonia

HEREDITARY DISORDERS
Cystic fibrosis
Sickle cell disease
DISORDERS OF IMMUNITY
AIDS
Bruton agammaglobulinemia
Complement deficiency
Selective IgG subclass deficiencies
Common variable immunodeficiency syndrome
Severe combined immunodeficiency syndrome
DISORDERS OF LEUKOCYTES
Chronic granulomatous disease
Hyperimmunoglobulin E syndrome (Job syndrome)
Leukocyte adhesion defect
DISORDERS OF CILIA
Primary ciliary dyskinesia
Kartagener syndrome
ANATOMIC DISORDERS
Sequestration
Lobar emphysema
Foreign body
Tracheoesophageal fistula (H type)
Congenital pulmonary airway malformation (cystic adenomatoid malformation)
Gastroesophageal reflux
Bronchiectasis
Aspiration (oropharyngeal incoordination)
NONINFECTIOUS MIMICS OF PNEUMONIA
Autoimmune diseases (e.g., granulomatosis with polyangiitis)
Hypersensitivity pneumonitis

should be used if influenza is identified or suspected, ideally within 48 hours of symptom onset.

Severe or critical COVID-19 is treated with oxygen, dexamethasone, remdesivir, mechanical ventilation, and ECMO.

COMPLICATIONS AND PROGNOSIS

Bacterial pneumonias frequently cause inflammatory fluid to collect in the adjacent pleural space, causing a **parapneumonic effusion** or, if grossly purulent, an **empyema**. Small effusions may not require any special therapy. Large effusions may restrict breathing and require drainage. Air dissection within lung tissue results in a **pneumatocele**. Scarring of the airways and lung tissue may leave dilated bronchi, resulting in **bronchiectasis** and increased risk for recurrent infection.

Pneumonia that causes necrosis of lung tissue may evolve into a **lung abscess**. Lung abscess is an uncommon problem in children and is usually caused by aspiration, infection behind an obstructed bronchus, or certain virulent organisms. Anaerobic bacteria usually predominate, along with various streptococci, *Escherichia coli*, *Klebsiella pneumoniae*, *P. aeruginosa*, and *S. aureus*. Chest radiograph or CT scan reveals a cavitary lesion, often with an air-fluid level, surrounded by parenchymal inflammation. If the cavity communicates with the bronchi, organisms may be isolated from sputum. Diagnostic bronchoscopy may be indicated to exclude a foreign body and obtain microbiologic specimens. Lung abscesses usually respond to appropriate antimicrobial therapy with clindamycin or ampicillin-sulbactam.

Most children recover from pneumonia rapidly and completely, although radiographic abnormalities may persist for 6–8 weeks. In a few children, symptoms may last longer than 1 month or may be recurrent. In such cases, the possibility of underlying disease must be investigated further, such as with the tuberculin skin test, sweat chloride determination for cystic fibrosis, serum immunoglobulin (Ig) and IgG subclass determinations, bronchoscopy to identify anatomic abnormalities or foreign body, and barium swallow for gastroesophageal reflux.

Severe adenovirus pneumonia may result in **bronchiolitis obliterans**, a subacute inflammatory process in which the small airways are replaced by scar tissue, resulting in a reduction in lung volume and lung compliance. **Unilateral hyperlucent lung**, or **Swyer-James syndrome**, is a focal sequela of severe necrotizing pneumonia in which all or part of a lung has increased translucency radiographically; it has been linked to adenovirus type 21.

PREVENTION

Annual influenza vaccine is recommended for all children over 6 months of age (see Chapter 94). Trivalent or quadrivalent, inactivated influenza vaccines are licensed for use beginning at 6 months of age; live-attenuated vaccine can be used for persons 2–49 years of age. Universal childhood vaccination with conjugate vaccines for *H. influenzae* type b and *S. pneumoniae* has greatly diminished the incidence of these pneumonias. RSV infections can be prevented by use of palivizumab in some high-risk patients (see Chapter 109). Prevention of COVID-19 includes the use of face masks, physical distancing, avoiding contact with infected patients, and contact isolation. As of mid-2021, three SARS-CoV-2 vaccines are available under emergency use authorization in the United States and are recommended for all children age 12 and older, with studies under way to evaluate safety and efficacy in younger children. Visit the CDC website for updated information (<https://www.cdc.gov/vaccines/covid-19/index.html>).

Reducing the duration of mechanical ventilation and administering antibiotics judiciously reduces the incidence of ventilator-associated pneumonias. The head of the bed should be raised to 30–45 degrees for intubated patients to minimize risk of aspiration, and all suctioning equipment and saline should be sterile. Handwashing before and after every patient contact and use of gloves for invasive procedures are important measures to prevent nosocomial transmission of infections. Hospital staff with respiratory illnesses or who are carriers of certain organisms, such as MRSA, should comply with infection control policies to prevent transfer of organisms to patients. Treating sources of aerosols, such as air coolers, can prevent *L. pneumoniae*.

TABLE 110.3 Antimicrobial Therapy for Pneumonia Caused by Specific Pathogens*

PATHOGEN	RECOMMENDED TREATMENT	ALTERNATIVE TREATMENT
<i>Streptococcus pneumoniae</i> with MIC for penicillin $\leq 2.0 \mu\text{g/mL}$	Ampicillin or penicillin IV; amoxicillin PO	Ceftriaxone, clindamycin, or vancomycin IV; cefuroxime, cefpodoxime, levofloxacin, [†] or linezolid PO
<i>S. pneumoniae</i> with MIC for penicillin $\geq 4.0 \mu\text{g/mL}$	Ceftriaxone IV; levofloxacin [†] or linezolid PO	Ampicillin, levofloxacin, [†] clindamycin, or vancomycin IV; clindamycin PO
Group A streptococcus	Penicillin or ampicillin IV; amoxicillin or penicillin PO	Ceftriaxone, clindamycin, or vancomycin IV; clindamycin PO
Group B streptococcus	Penicillin or ampicillin IV; amoxicillin or penicillin PO	Ceftriaxone, clindamycin, or vancomycin IV; clindamycin PO
<i>Haemophilus influenzae</i>	Ampicillin IV or amoxicillin PO if β -lactamase negative; ceftriaxone IV or amoxicillin-clavulanate PO if β -lactamase positive	Ciprofloxacin [†] or levofloxacin [†] IV; cefdinir, cefixime, or cefpodoxime PO
<i>Mycoplasma pneumoniae</i> , <i>Chlamydia pneumoniae</i> , or <i>Chlamydia trachomatis</i>	Azithromycin IV or PO	Erythromycin or levofloxacin IV; clarithromycin, erythromycin, doxycycline, [†] or a fluoroquinolone [†] PO
<i>Staphylococcus aureus</i> , methicillin susceptible (MSSA)	Cefazolin, oxacillin, or nafcillin IV; cephalexin PO	Clindamycin or vancomycin IV; clindamycin PO
<i>S. aureus</i> , methicillin resistant (MRSA)	Clindamycin or vancomycin IV; clindamycin PO	TMP-SMX or linezolid IV or PO
Gram-negative aerobic bacilli (except <i>P. aeruginosa</i>)	Ceftriaxone with or without an aminoglycoside IV; amoxicillin-clavulanate, cefdinir, or cefixime PO	Piperacillin-tazobactam plus an aminoglycoside [‡] ; fluoroquinolone [†] PO
<i>P. aeruginosa</i>	Ceftazidime IV with or without an aminoglycoside [‡] ; ciprofloxacin [†] if susceptible PO	Piperacillin-tazobactam IV with or without an aminoglycoside [‡]
Herpes simplex virus	Acyclovir IV	

*Oral outpatient therapy may be used for mild illness. Intravenous inpatient therapy should be used for moderate to severe illness.

[†]Appropriate respiratory fluoroquinolones include moxifloxacin, gatifloxacin, levofloxacin, and gemifloxacin. Fluoroquinolones are contraindicated for children younger than 18 years of age and pregnant or lactating women. Tetracyclines are not recommended for children younger than 9 years.

[‡]Aminoglycoside dosing should be guided by serum antibiotic concentrations after a steady state has been reached.

IV, Intravenous; MIC, minimum inhibitory concentration; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-susceptible *Staphylococcus aureus*; PO, per os (orally); TMP-SMX, trimethoprim-sulfamethoxazole.

PEARLS FOR PRACTITIONERS

See Infectious Diseases: *Pearls for Practitioners* at the end of this section.