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34 Acute Pneumonia and Its Complications

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Pneumonia is a Greek word meaning "inflammation of the lungs." It is the most common cause of morbidity and mortality in infants and children due to infection worldwide.[1]

ACUTE PNEUMONIA

Pneumonia is a lower respiratory tract disease usually caused by an infectious agent resulting in inflammation of the tissues of one or both lungs.[2] Pneumonia in developing countries occurs in >150 million new cases and results in >1.3 million preventable deaths each year.[1,3] Morbidity and mortality rates for community-acquired pneumonia (CAP) among the children in the United States is considerably less. Outpatient pediatric visit rates for CAP in the US ranges from 16.9 to 22.4 per 1000 children, with 32.3 to 49.6 cases per 1000 children 1 to 5 years of age.[4] Rate of hospitalization in the US for acute pneumonia decreased from 12–14 to 8–10 per 10,000 in children <2 years of age following universal conjugate pneumococcal vaccination.[5] In 2007, the overall mortality for acute pneumonia in US children was ≤2%, depending on factors including age, race, socioeconomic status and geographical region.[6]

Epidemiology

In the US, lower respiratory infections (LRIs) occur throughout the year but excessively during the fall and winter when children are confined indoors, resulting in more efficient spread of the infections by contact or droplet transmission.[7] Multiple factors predispose to acquisition of LRI: daycare and school attendance, indoor crowding, passive exposure to smoke, lack of or underimmunization, alcohol abuse in adolescents causing aspiration pneumonia, and underlying medical conditions such as low birth weight, bronchopulmonary dysplasia, asthma, heart disease, seizures, neuromuscular illness, gastroesophageal reflux disease, malnutrition, immunocompromised state, sickle cell disease, and cystic fibrosis.[1,8–10] Additional risk factors associated with pneumonia in children <5 years of age include frequent upper respiratory tract infections (URIs; >3 episodes in 12 months), wheezing at any age, and history of otitis media requiring tympanocentesis before 2 years of age. Risk factors for pneumonia in children >5 years of age include wheezing at any age and ≥3 episodes of URI within 12 months.[11]

Etiologic Agents

Multiple microbes, most predominantly viruses and bacteria, cause LRI in infants and children. The true prevalence of the pathogens causing LRI is uncertain because microbial etiology is ascertained infrequently, owing to difficulty in differentiating infection from colonization and lack of dependable diagnostic laboratory tests.[12] In two studies of immunocompetent children with pneumonia, specific etiologic agents were confirmed in only 43% to 66%.[13,14] Some cases have more than one pathogen identified, making assigning etiology difficult.[15] Confirming etiology of bacterial pneumonia is challenging because of coexistence of bacteria as pathogens as well as normal upper respiratory tract flora, and because of occurrence of bacteremia in only 1% to 10% of hospitalized children with presumed bacterial pneumonia.[2,16,17] Etiologic agents causing pneumonia vary by age, underlying illnesses, maturity, and condition of the immune system.[18] In most cases of acute pneumonia, extensive invasive testing is not warranted. Epidemiologic information frequently is useful in guiding differential diagnosis and management (see Chapter 21). Certain pathogens, particularly respiratory syncytial virus (RSV), rhinoviruses, influenza viruses, and *Mycoplasma,* are seasonal. In other instances, the pattern of family illness provides a clue to the causative nonbacterial agents.

For purposes of management, the relative importance of etiologic agents in a series of patients who have been extensively evaluated is extrapolated to patients with similar clinical syndromes, physical findings, and laboratory results. Table 34.1 lists the common etiologic agents of acute pneumonia in children.

Agents in Neonates and Young Infants

Pneumonia in neonates can manifest as early-onset disease (within 3 days of life) or late-onset disease (after 3 days of life). Most early-onset infections are caused by organisms acquired from the maternal genital tract through aspiration of contaminated amniotic fluid or genital tract secretions. Group B *Streptococcus* is the most frequent cause of early-onset pneumonia.[2] Early-onset infection due to group B *Streptococcus*, *Listeria monocytogenes, Escherichia coli,* and other gram-negative bacilli can cause severe respiratory distress resembling hyaline membrane disease, usually as a part of a widespread systemic infection. Prenatal and perinatal risk factors, including preterm delivery, maternal chorioamnionitis, and rupture of membranes >18 hours, increase the risk for neonatal pneumonia. Hematogenous dissemination can occur occasionally from an infected mother.

Pneumonia due to *Chlamydia trachomatis* acquired perinatally can become symptomatic 2 to 3 weeks after birth, and characteristically the infant is afebrile.[19] *Bordetella pertussis* infection in very young infants can have severe complications of apnea, bronchopneumonia, or pulmonary hypertension.[20] With wide availability of extended panels for rapid molecular diagnostic tests, viruses are increasingly confirmed as important causes of pneumonia in young infants.[21] Severe, often fatal pneumonia also can be the result of disseminated herpes simplex virus (HSV) infection in noenates.[22] Congenital cytomegalovirus (CMV) and *Treponema pallidum* are less common causes of neonatal pneumonia. Genital *Mycoplasma* and *Ureaplasma* spp. are purported causes of LRI, especially in very low birth weight infants.[23]

Agents in Infants, Children, and Adolescents

In a recent study determining the etiologic agents for CAP in children <18 years of age, viruses accounted for 66%, bacteria for 8%, and mixed infection for 7% of cases.[7] This study also noted that viral pneumonia was more common in children <2 years of age compared with older children, whereas *Mycoplasma* was more common in children >5 years of age (19%) compared with younger children (3%).

Viruses. Overall, viruses account for approximately 73% of CAP in childhood.[7] However, when categorized by age, viruses accounted for >80% of CAP in children <2 years compared with 49% in those >2 years of age.[7] RSV is the predominant viral pathogen of childhood pneumonia, accounting for 28%, with highest incidence in children <2 years of age.[7] Other viruses include human metapneumovirus (hMPV), parainfluenza viruses (types 1, 2, and 3), influenza viruses (A and B), adenoviruses, bocavirus, rhinoviruses, and enteroviruses. Rhinoviruses have been recovered from culture in 22% to 27% of cases of childhood pneumonia.[7] Although influenza, RSV, and hMPV are significantly associated with CAP in children, the roles of other viruses such as parainfluenza viruses, enteroviruses, rhinoviruses, coronaviruses and bocavirus are difficult to ascribe owing to dual virus detections in illness, detections in well children, and extended durations of shedding.[23a] In a case-control study, the latter viruses were negatively associated with CAP.[24] Varicella-zoster virus (VZV), CMV, and HSV typically cause LRI in immunocompromised or very young immune-naïve children. Cases of LRI due to human parechoviruses (HPeV types 1–4) have been reported, but a substantial role awaits description. LRI viral infections mirror general seasonality: RSV,

TABLE 34.1 Microbial Causes of Community-Acquired Pneumonia in Childhood

Age	Etiologic Agents[a]	Clinical Features
Birth–3 wk	Group B *Streptococcus*	Part of early-onset septicemia; usually severe
	Gram-negative enteric bacilli	Frequently nosocomial; occurs infrequently within 1 week of birth
	Cytomegalovirus	Part of systemic cytomegalovirus infection
	Listeria monocytogenes	Part of early-onset septicemia
	Herpes simplex virus	Part of disseminated infection
	Treponema pallidum	Part of congenital syndrome
	Genital *Mycoplasma* or *Ureaplasma*	From maternal genital infection; afebrile pneumonia
3 wk–3 mo	*Chlamydia trachomatis*	From maternal genital infection; afebrile, subacute, interstitial pneumonia
	Respiratory syncytial virus (RSV)	Peak incidence at 2–7 months of age; usually wheezing illness (bronchiolitis/ pneumonia)
	Parainfluenza viruses (PIV), especially type 3	Similar to RSV, but in slightly older infants and not epidemic in the winter
	Streptococcus pneumoniae	The most common cause of bacterial pneumonia
	Bordetella pertussis	Primarily causes bronchitis; secondary bacterial pneumonia and pulmonary hypertension can complicate severe cases
3 mo–5 yr	RSV, PIV, influenza, hMPV, adenovirus, rhinovirus	Most common causes of pneumonia
	Streptococcus pneumoniae	Most likely cause of lobar pneumonia; incidence may be decreasing after vaccine use
	Haemophilus influenzae	Type b uncommon with vaccine use; nontypable stains cause pneumonia in immunocompromised hosts and in developing countries
	Staphylococcus aureus	Uncommon, although CA-MRSA is becoming more prevalent
	Mycoplasma pneumoniae	Causes pneumonia primarily in children >4 yr
	Mycobacterium tuberculosis	Major concern in areas of high prevalence and in children with HIV
5–15 yr	*Mycoplasma pneumoniae*	Major cause of pneumonia; radiographic appearance variable
	Chlamydophila pneumoniae	Controversial, but probably an important cause in older children in this age group

[a]Ranked roughly in order of frequency. Uncommon causes with no age preference: enteroviruses (echovirus, coxsackievirus), mumps virus, Epstein-Barr virus, Hantavirus, *Neisseria meningitidis* (often group Y), anaerobic bacteria, *Klebsiella pneumoniae, Francisella tularensis, Coxiella burnetii, Chlamydia psittaci. Streptococcus pyogenes* occurs sporadically or especially associated with varicella-zoster virus infection.

CA-MRSA, community-acquired methicillin-resistant *Staphylococcus aureus;* HIV, human immunodeficiency virus; hMPV, human metapneumovirus.

hMPV, and influenza (winter), parainfluenza (spring and autumn), and rhinoviruses and adenoviruses (throughout the year).[25]

Mycoplasma pneumoniae* and *Chlamydophila pneumoniae. LRI due to *Mycoplasma pneumoniae* affects school-aged children predominantly; molecular detection in upper respiratory secretions in younger children has less clear meaning. Coinfections with either *Streptococcus pneumoniae* (30%) or *Chlamydophila pneumoniae* (15%) occurs.[26] Infections due to *M. pneumoniae* occur in 2-to 4-year cycles.[27] Unlike respiratory viruses, transmission of *M. pneumoniae* among family members is slow, with a median interval of 3 weeks between cases.[27] Pneumonia is rarely ascribed to *C. pneumoniae* in children in the US compared with European and Asian countries and is associated with reactive airway disease or asthma in children >5 years of age. Asymptomatic carriage of *C. pneumoniae* is well documented and confounds assessment of pathogenicity.

Bacterial Pathogens. Bacterial pneumonia is more common in children living in developing countries, related to several factors, including chronic malnutrition, crowding, inadequate vaccinations, and constant exposure to biomass fuels without adequate ventilation.[28] Various tests that determine bacterial products in blood, respiratory tract secretions, and urine have been used in an attempt to assign a causative LRI role of bacteria but are positive in <10% of cases.[7,15,29] Evidence from multiple sources indicates that *S. pneumoniae* is the single most common cause of bacterial pneumonia beyond the first few weeks of life, causing >76% of bacterial pneumonia cases.[15,16,29] Pneumococcal serotypes causing uncomplicated pneumonia in the US generally are similar to those that cause bacteremia and other invasive pneumococcal disease (IPD) or acute otitis media (see Chapter 123). In the PCV13 era, IPD, including pneumonia, occurs increasingly in older children with underlying medical condtions.[29a] Pneumococcal pneumonia occurs in all age groups, but especially in those <2 years of age.[15]

In countries with widespread immunization with the Hib conjugate vaccine, the frequency of *Haemophilus influenzae* type b (Hib) infection, including pneumonia, has plummeted.[30] Pneumonia due to non–type B and nontypable *H. influenzae* is uncommon in otherwise healthy children in the US, except in premature infants and in children with underlying chronic conditions or diseases or with hospital-associated pneumonia.[31] Acute pneumonia and necrotizing pneumonia can be caused by methicillin-susceptible *Staphylococcus aureus* (MSSA), methicillin-resistant *S. aureus* (MRSA) or community-associated MRSA (CA-MRSA), especially carrying virulence factors like Panton-Valentine leukocidin.[32] *Streptococcus pyogenes* (group A *Streptococcus*) is not a frequent cause of acute pneumonia but can cause rapidly progressive and severe pneumonia, frequently leading to hypoxemia and pleural effusion within hours. Other bacteria, especially gram-negative organisms, are rare causes of pneumonia in previously healthy children but can cause LRI in premature babies, neonates, and patients with cystic fibrosis, sickle cell disease, primary or acquired immune deficiency, or immune suppression.

Other Pathogens. A variety of epidemiologic and host factors prompt consideration of specific organisms (Table 34.2). The most important of these is tuberculosis, which should always be suspected if there is a history of exposure, in the presence of hilar adenopathy, or when pneumonia does not respond to usual therapy. In North America and Europe, primary tuberculosis pneumonia occurs predominantly in children born to or in contact with recent immigrants from countries where tuberculosis is endemic, after contact with infected adults, or in HIV-infected children.

Residing in or traveling to certain geographic areas raises concern for special pathogens. *Coccidioides immitis* is endemic in the southwestern US, northern Mexico, and parts of Central and South America. *Histoplasma capsulatum* is endemic in the eastern and central US and Canada.

TABLE 34.2 Occasional Causes of Pneumonia in Special Circumstances

Organism	Risk Factors	Diagnostic Methods
Histoplasma capsulatum	Exposure in certain geographic areas (Ohio and Mississippi river valleys, Caribbean)	Culture of respiratory tract secretions; urine antigen; serum immunodiffusion antibody test; and serum *Histoplasma* complement fixation antibody test
Coccidioides immitis	Exposure in certain geographic areas (southwestern United States, Mexico, and Central America)	Culture of respiratory tract secretions; serum immunodiffusion antibody test
Blastomyces dermatitidis	Exposure in certain geographic areas (Ohio, Mississippi, St. Lawrence river valleys)	Culture of respiratory tract secretions; serum immunodiffusion antibody test
Legionella pneumophila	Exposure to contaminated water supply	Culture or direct fluorescent assay of respiratory tract secretions; antigen test on urine
Francisella tularensis	Exposure to infected animals, usually rabbits	Acute and convalescent serology
Pseudomonas pseudomallei (melioidosis)	Travel to rural areas of Southeast Asia	Culture of respiratory tract secretions; acute and convalescent serology
Brucella abortus	Exposure to infected goats, cattle, or their products of conception; ingestion of unpasteurized milk	Acute and convalescent serology
Leptospira spp.	Exposure to urine of infected dogs, rats, or swine, or to water contaminated by their urine	Culture of urine; acute and convalescent serology
Chlamydia psittaci	Exposure to certain infected birds (often parakeets)	Acute and convalescent serology
Coxiella burnetii	Exposure to infected sheep	Acute and convalescent serology
Hantavirus	Exposure to dried mouse dung in a closed structure (opening cabins after winter closure)	Acute and convalescent serology; PCR test on the respiratory tract secretions

PCR, polymerase chain reaction.

Chlamydia psittaci and *Coxiella burnetii* are transmitted from infected birds, animals, or humans. *Pneumocystis jirovecii* causes pneumonia in unrecognized HIV-infected infants at 3 to 6 months of age, in severely malnourished children, and in other immunocompromised or immunosuppressed hosts not receiving prophylaxis. *Legionella pneumophila* is a rare cause of pneumonia in children, affecting older or immunocompromised children after certain water-associated environmental exposures.

Pathogenesis and Pathology

Pneumonia occurs when a host susceptible to a virulent pathogen is exposed to a high-density aerosol inoculum, has a compromised systemic or secretory immunity, or has an impaired clearance mechanism.[33,34] Most patients with pneumonia have initial colonization or infection of the upper respiratory tract. Invasion of the lower respiratory tract usually occurs when normal defense mechanisms are impaired, such as associated with a viral infection, chronic malnutrition, chronic aspiration, impaired cough reflex (e.g., after sedation, neurologic damage, intubation) or after exposure to environmental pollutants. Bacterial pneumonia can occasionally occur by the hematogenous route. In the early stages of lobar or bacterial pneumonia, protein-rich edema fluid containing numerous organisms fill the alveoli, leading to marked capillary congestion and causing neutrophil exudation and intra-alveolar hemorrhage. There is decrease in lung compliance, increase in pulmonary resistance, small airway obstruction, air trapping, and change in ventilation-perfusion ratio, all leading to the clinical signs of respiratory distress.

Defense mechanisms against LRI consist of (1) anatomic and physiologic barriers; (2) humoral and cell-mediated protection; and (3) phagocytic activity. The presence of hairs in the anterior nares (that trap particles >10 μm in size), configuration of the nasal turbinates, and acute branching of airways form protective anatomic barriers. Filtration and humidification capacities of the upper airways, mucus production, and middle airway protection by the epiglottis and cough reflex (eliminating particles 2–10 μm) form physiologic barriers. The mucociliary blanket transports microscopic amounts of normally aspirated oropharyngeal flora and particulate matter up the tracheobronchial tree, minimizing the presence of bacteria below the carina. Particles <1 μm can escape into the lower airways. Immunoglobulin A (IgA) antibody is secreted into the upper airways, and IgG and IgM leach from the local capillaries into the lower airways. Alveolar fluid surfactant, fibronectin, complement, lysozyme, and iron-binding proteins also have antimicrobial activity. The lower respiratory tract has three distinct populations of macrophages: alveolar, interstitial, and intravascular macrophages. Alveolar macrophages are the preeminent phagocytic cells that ingest and kill bacteria. In addition to phagocytic function, interstitial macrophages are antigen-processing cells, whereas the intravascular macrophages clear inflammatory debris through the bloodstream. Viral infection (especially due to influenza virus), high oxygen concentration, uremia, and use of alcohol or drugs can impair function of alveolar macrophages, predisposing to pneumonia. Cell-mediated immunity plays an important role in pulmonary infections caused by viruses and intracellular organisms such as *Mycobacterium tuberculosis* and *Legionella* that survive within pulmonary macrophages.

Viral Pneumonia

Viral pulmonary infections follow three pathologic patterns: bronchiolitis, interstitial pneumonia, and parenchymal infection. The first two patterns often overlap.[35,36] Viral pneumonia is characterized by neutrophilic infiltration of the lumen of the airway with lymphocytic infiltration of the interstitium and parenchyma of the lungs.[37] Giant cell formation and viral inclusions within the nucleus of the respiratory cells are histologically evident in many viral infections, including those caused by adenovirus, measles, varicella, CMV, and Epstein-Barr virus, especially in children with immune deficiency. Air trapping with disturbances in ventilation-perfusion ratio occur when obstructed or obliterated small airways and thickened septa impede oxygen diffusion. Necrosis of bronchial or bronchiolar epithelium occurs in severe, sometimes fatal, viral infections (e.g., adenovirus infection).

Bacterial Pneumonia

Bacterial pneumonia can follow five pathologic patterns: (1) parenchymal infection, inflammation, and consolidation of a lobe or a segment of a lobe (lobar pneumonia, the classical pattern of *S. pneumoniae*; (2) primary infection of the airways and surrounding interstitium (bronchopneumonia, often due to *S. pyogenes* and *S. aureus*); (3) necrotizing

parenchymal pneumonia that occurs after aspiration of anaerobes or with certain *S. aureus* or *S. pneumoniae*; (4) caseating granulomatous disease, as due to *M. tuberculosis*; and (5) peribronchial and interstitial disease with secondary parenchymal infiltration, as can occur when viral pneumonia is complicated by bacterial infection. In bacterial pneumonia, airspaces become filled with transudates and neutrophilic exudates, impairing oxygen diffusion. The proximity of the infected alveoli to the rich pulmonary vascular bed increases the risk for bacteremia, septicemia, or shock.

Clinical Manifestations

The symptoms of pneumonia are varied and nonspecific and may be subtle depending on several factors, including the etiologic agents, age of the host, inoculum size, and individual's immune response (see Chapter 21). Acute onset of fever, rapid breathing (tachypnea), and cough are classical.[38] Fever can be absent in very young infants with *C. trachomatis*, *B. pertussis,* or *Ureaplasma* infection.[39] Infants can manifest only poor feeding and increased fussiness.[40] Children <5 years of age often have a prodrome of low-grade fever and rhinorrhea due to a viral URI before developing lower respiratory tract symptoms. Fever and rapid breathing can precede onset of cough in some children. Older children can complain of pleuritic chest pain or nuchal rigidity (each referable to lobe involvement). Signs of respiratory distress include tachypnea, hypoxemia (oxygen saturation <92%), apnea, increased work of breathing (subcostal, intercostal or suprasternal retractions; nasal flaring; or grunting) or altered mental status.[41] Guidelines developed by the World Health Organization (WHO) for the clinical diagnosis of pneumonia in developing countries highlight tachypnea and retractions as the two best indicators of LRI.[42] Tachypnea is defined as >50 breaths/min in infants <12 months, >40 for those 1 to 5 years, and >30 for children >5 years of age. Among children <5 years of age, tachypnea (as defined by WHO) had the highest sensitivity (74%) and specificity (67%) for radiologically confirmed pneumonia, but was less sensitive and specific in early disease.[38,43] Tachypnea can occur with other conditions, such as fever, asthma, cardiac disease, and metabolic acidosis. The predictive values of clinical findings for pneumonia have been studied repeatedly.[44–47] In one study, the combination of a respiratory rate >50 breaths/min, oxygen saturation <96%, and the presence of nasal flaring in children <12 months of age was highly associated with radiographically confirmed pneumonia.[40] Oxygen saturation is frequently decreased with moderate to severe pneumonia and is an indication for hospital admission.[41,48] A hypoxemic infant or child may not appear cyanotic.[49] Although hypoxemia, use of accessory muscles of respiration, head bobbing, nasal flaring, and grunting are predictive of pneumonia, their absence does not exclude pneumonia.[46,50] Decreased and bronchial breath sounds, egophony ("E" to "A" change), bronchophony, tactile fremitus, and dullness to percussion are specific signs of lung consolidation. Crackles can be absent in a dehydrated patient.[51] Isolated wheezing or prolonged expiration is associated with bronchiolitis and is uncommon in bacterial pneumonia.[44] Almost three fourths of children with radiographically confirmed pneumonia appear ill. Severity of illness correlates with the likelihood of a bacterial cause. Approximately 6% to 25% of children <5 years of age with body temperature >39°C and a white blood cell (WBC) count >20,000/mm^3 without an alternative source of major infection and with no symptoms or signs of lower respiratory tract disease have radiographically confirmed pneumonia.[47]

In one study determining the interobserver agreement of signs of pneumonia, there was more observer agreement with clinical signs (respiratory rate and cyanosis) compared with auscultatory signs (crackles, retractions, and wheezing) of pneumonia.[40] Unfortunately, neither respiratory rate nor cyanosis is a sensitive or specific indicator of hypoxia. Oxygen saturation should be measured in any child with respiratory distress.[52]

Neonates and Young Infants

The neonate with bacterial infection due to group B *Streptococcus*, *L. monocytogenes,* or gram-negative bacilli usually manifests with respiratory distress in the first few hours of life. Septicemia and infection at other sites can dominate the clinical presentation. Pneumonia in children <2 months of age usually is characterized by tachypnea (respiratory rate >60 breaths/min), intercostal retractions, or both.[52] In very young infants, particularly those who are born prematurely, fever can be absent and apneic spells can be the prominent initial finding.[53] *C. trachomatis* pneumonia in infants is insidious, with infants coming to attention at 3 to 12 weeks with staccato cough, tachypnea, and crackles in absence of fever. Wheezing is uncommon.[54] Eosinophilia and elevated total serum IgM concentration can be present.[55,56]

Infants, Children, and Adolescents

Viruses. Viral pneumonia usually occurs in the context of a preceding upper respiratory tract illness with gradual increase in irritability, respiratory congestion, cough, posttussive emesis, and fever. The patient may not appear toxic, although hypoxia can be marked, particularly in a young infant whose initial presentation can also be apnea. The auscultatory findings are not anatomically confined, but rather there are diffuse, bilateral wheezes and crackles. Although adenovirus usually follows the pattern of other viral infections, adenovirus can cause severe pneumonia with lobar consolidation similar to a bacterial infection and is especially severe in immunocompromised hosts.[58]

Bacterial Pneumonia. Bacterial pneumonia may follow several days of mild URI, but onset then usually is abrupt. The patient usually is ill and toxic appearing with high fever, rigors, and tachypnea. Respiratory distress and hypoxemia can be absent or mild unless there is widespread disease or a large pleural effusion. Cough occurs later in the course of the illness when alveolar debris is swept into the upper airway. Unilateral pleuritic chest pain, abdominal pain, neck pain, or sepsis in the presence of radiographically demonstrable infiltrate are specific signs of bacterial pneumonia. Unless there is a parapneumonic effusion, auscultatory findings usually are few and are limited to an anatomic lung segment.

Other Pathogens. The major symptoms of LRI due to *M. pneumoniae, C. pneumoniae,* and *C. burnetii* (Q fever) are fever and cough that persist for more than 7 to 10 days. The onset of pneumonia caused by *M. pneumoniae* usually is not well demarcated; malaise, headache, photophobia, sore throat, fever, and chills occur early and sometimes subside when the gradually worsening, nonproductive cough ensues. Although coryza is unusual, otitis media can occur.[59] Findings on physical examination and auscultation can be minimal with confined rales, wheezing, or both.[60] The presence of Stevens-Johnson syndrome or hemolytic anemia in a patient with pneumonia suggests *M. pneumoniae* infection.[61] *M. pneumoniae* can cause severe disease in persons with sickle cell disease in whom acute chest syndrome is common.[62] Pneumonia due to *C. pneumoniae* usually has an insidious onset with sore throat, hoarseness, and associated sinusitis.[63] Pneumonia due to *C. burnetii* is rare and usually is mild in children. Symptomatic patients can have intractable headache, myalgia, arthralgia, and nonproductive cough. Chest radiograph findings include segmental or lobar consolidation; "round pneumonia" has been described with Q fever.[64]

Differential Diagnosis

Pneumonia is highly probable in children with fever, cough, tachypnea, and shortness of breath in whom chest radiograph demonstrates pulmonary infiltrates. There are many alternative diagnoses, particularly in the absence of fever, or with chronic, relapsing symptoms and signs. These include foreign-body aspiration, asthma, gastroesophageal reflux, cystic fibrosis, congestive cardiac failure, systemic vasculitis, and bronchiolitis obliterans. Children who develop chemical pneumonia after ingestion of volatile hydrocarbons can have severe necrotizing pneumonia with high fever and peripheral neutrophil counts exceeding 15,000/mm^3.[65]

Imaging and Laboratory Findings

Chest radiography often is obtained to determine whether a patient with respiratory symptoms and signs has pneumonia. However, accurate interpretation of a chest radiograph for pneumonia has multiple challenges: insensitivity in differentiating bacterial from nonbacterial cause, falsely negative in children examined early in the course of pneumonia or in dehydrated patients, lag in abnormal findings, substantial inconsistency in reading by radiologists, and influence of radiologist's knowledge

of clinical information on accuracy of interpretation.[44,48,66–70] Prescription of an antibiotic has been linked to radiography,[67] but because routine chest radiography does not appear to alter the clinical outcome of acute LRI,[71,72] radiography should be restricted to special circumstances.

Chest radiography is indicated to confirm the presence and determine the location of pneumonia in children who are hospitalized or are severely ill; have recurrent disease or chronic medical conditions, poor response to initial antibiotic therapy, or complicated pneumonia; and in whom the diagnosis is uncertain or alternative causes of respiratory distress must be excluded.

Bilateral diffuse infiltrates are seen with pneumonia caused by viruses, *P. jirovecii*, *L. pneumophila,* and occasionally with *M. pneumoniae.* Both *C. pneumoniae* and *M. pneumoniae* (Fig. 34.1) cause focal radiographic abnormalities, which are out of proportion to clinical findings. Distinctly confined lobar or segmental abnormality or a large pleural effusion suggests bacterial infection (Fig. 34.2), but rarely, *M. pneumoniae* or adenovirus can manifest with these findings.[73–75] "Round" pneumonia is the circular appearance of a lung infiltrate. It is common in children <8 years of age with bacterial pneumonia and most often is due to *S. pneumoniae,* although in rare cases, *H. influenzae*, *S. aureus,* or atypical organisms (*C. burnetii*) can be responsible.

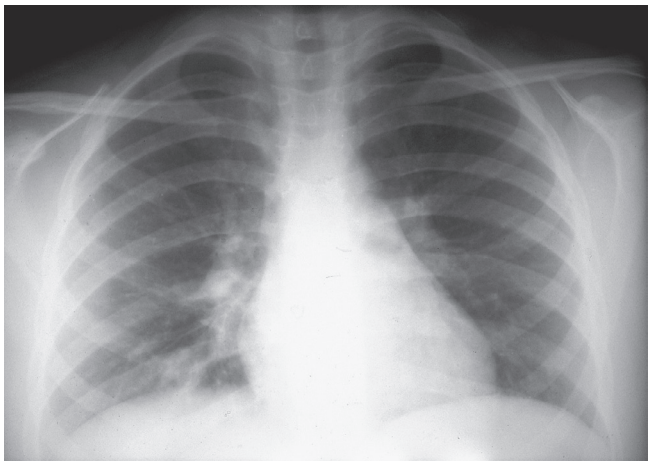

FIGURE 34.1 Plain radiograph showing patchy infiltrates in the right lower lobe, typical of *Mycoplasma* or other "atypical" pneumonias. (Courtesy of S. S. Long, St. Christopher's Hospital for Children, Philadelphia, PA.)

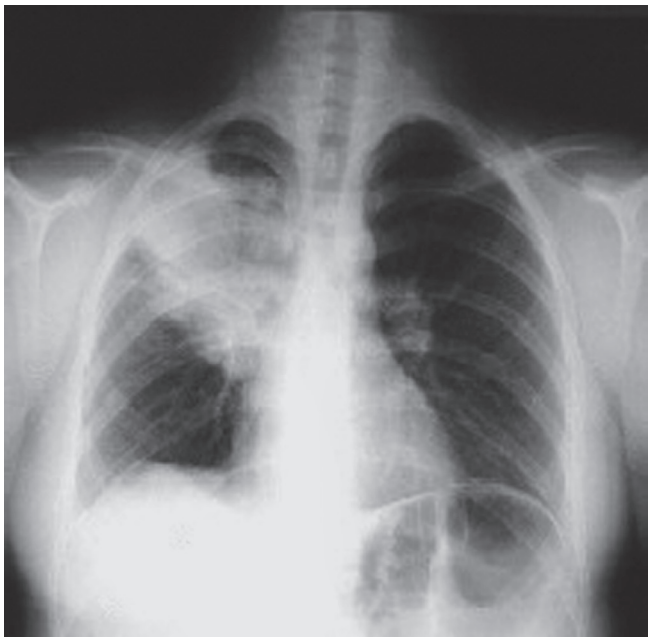

FIGURE 34.2 Plain radiograph showing consolidative pneumonia in the right upper lobe, typical of acute bacterial pneumonia.

Enlarged or calcified hilar lymph nodes suggest tuberculosis or a fungal infection such as *Histoplasma* or *Coccidioides. Mycoplasma* and chronic infection in cystic fibrosis can cause hilar lymphadenopathy. Pneumatoceles (thin-walled, air- or fluid-filled cavities) resulting from alveolar rupture usually are associated with infection due to *S. aureus* but can be a necrotizing component of *S. pneumoniae*, *S. pyogenes*, *H. influenzae*, gram-negative bacteria, or anaerobe infection. See Chapter 35 for other considerations.

Radiographic improvement of pneumonia lags clinical improvement, and complete resolution of radiologic abnormalities in children may take 4 to 6 weeks. Follow-up radiography is indicated only for persistent atelectasis, complicated pneumonia, recurrent pneumonia, or round pneumonia (to exclude tumor as the cause).[76,77]

A prospective study examining the utility of routine acute-phase reactants in children (WBC count and differential, C-reactive protein, erythrocyte sedimentation rate) with pneumonia concluded that these tests do not differentiate bacterial and viral pneumonia accurately.[78,79] A Cochrane meta-analysis found that patients with bacterial pneumonia usually have C-reactive protein level ≥4 mg/dL.[80]

Diagnosis of Specific Agents

Detecting the causative agent of pneumonia is very important for optimal management but is challenging without use of invasive techniques. Mild to moderately ill ambulatory patients usually can be managed empirically without specific diagnostic tests. Identifying the specific etiologic agent is important for all patients admitted to the hospital, those with underlying conditions, and when there is a community outbreak caused by an apparent emerging agent. A number of investigations may be necessary to confirm an etiologic diagnosis.

Viruses

A viral pathogen is best identified by recovering or detecting the organism in tissue culture or by detecting viral antigens or nucleic acid in respiratory tract secretions using immunofluorescence or polymerase chain reaction (PCR) techniques. Although viral culture is still considered the gold standard to confirm a diagnosis, clinical utility is low because of difficulty and duration of in vitro growth. Real-time PCR test panels rapidly detect common viral and atypical bacterial agents of CAP.[81] Added advantages include the facilitation of appropriate treatment decisions and cohorting of contagious patients. A nasopharyngeal wash or aspirate is the most sensitive specimen because it contains infected epithelial cells. Clinical interpretation of PCR detections is essential. Detection may be related to prolonged shedding.[23a] The presence of a viral agent in the upper respiratory tract does not exclude the presence of secondary bacterial pneumonia. Obtaining acute and convalescent sera to assess rising specific antibodies is usually confined to research settings.

Bacteria

The specific diagnosis of bacterial pneumonia is problematic in infants and children. You do not effectively cough up sputum. In older children, a sputum sample is considered appropriate for microbiologic evaluation when Gram stain reveals <10 squamous epithelial cells and >25 neutrophils per low-power field with a predominant organism. Cultures of nasopharyngeal specimens are not reliable. Tracheal aspiration is useful for culture if performed with direct laryngoscopy. Culture samples obtained through a catheter directly passed through a tracheostomy or an endotracheal or nasotracheal tube have limitations because of frequent contamination with upper respiratory tract organisms; these, however, could be evaluated as for a sputum sample. Quantitative culture performed on a bronchoalveolar lavage (BAL) specimen is useful when the isolate colony count is $>10^4$/mL. BAL is recommended in severely ill, intubated, or immunocompromised individuals not responding to initial antibiotic therapy.[82] The prevalence of bacteremia with pneumonia is reported to be 2.6% to 7%, depending on whether illness is mild or

required hospitalization, but increases to 13% to 26% in cases of complicated pneumonia and parapneumonic effusion or empyema.[83–85] *S. pneumoniae* is the most frequent cause of bacteremic pneumonia with or without empyema.[85] Blood culture can confirm etiologic diagnosis, provide susceptibility test results, and alter antibiotic management.[82] Blood cultures are recommended in children who are hospitalized, especially with parapneumonic effusion or empyema.[41] Urine antigen test to detect pneumococcal infection in children in the US is no longer recommended because of low specificity for disease and low sensitivity. *Legionella* urine antigen testing has high sensitivity and specificity and should be performed selectively.[86] Research is ongoing to develop tests to identify pneumonia and characterize etiology (e.g., urine metabolic and exhaled breath condensate tests) that could aid clinical diagnosis in the future.[87–89]

Other Pathogens

M. pneumoniae is detectable by expanded respiratory panels for PCR testing used broadly. *Mycoplasma* culture also is available in some commercial and hospital laboratories but can take 3 weeks to complete. Cold agglutinins (*Mycoplasma*-specific IgM antibodies that agglutinate human red cells) are found in only 30% to 50% of individuals with *M. pneumoniae* pneumonia during the acute phase of the disease.[90] Low titers of cold agglutinins occur in other respiratory viral infections, some collagen vascular diseases, malignancies, and some tropical diseases, making this a less specific diagnostic test as well.[91] Complement fixation (CF) continues to be a widely used serodiagnosis test for *Mycoplasma* pneumonia with sensitivity and specificity of ≥90%.[92] A positive titer is defined as fourfold or higher increase in titer in paired sera or a single titer >1:32. The CF test can be negative in young children and in those with mild disease and can be falsely positive in certain inflammatory and autoimmune conditions (including neurologic diseases and bacterial meningitis) or acute pancreatitis because of cross-reactivity between host autoantibodies and the CF antigen.[93,94] Commercially available enzyme immunoassays for anti–*M. pneumoniae* IgM and IgA have unacceptably high false-positive rates.

Comparison of real-time PCR testing with microimmunofluorescence serology shows superiority of PCR for early detection of *C. pneumoniae* infection.[95] Interpretation of detection is required because asymptomatic infection occurs. Specific serology is effective in detecting infections with other agents that cause atypical pneumonia, namely *C. psittaci* and *C. burnetii.*

Screening tests for *M. tuberculosis* includes placing a skin test or obtaining a whole blood specimen for interferon γ release assay (IGRA). Patients and all immediate family members and other significant contacts also should be tested. In children with primary infection and acutely ill patients, IGRA and the skin test can be nonreactive because of general or specific anergy. Additionally, there are data on the utility of IGRA in diagnosis of tuberculosis in children <5 years of age. With suspicion of tuberculosis, multiple specimens should be obtained for smear and culture, including 3 daily samples of sputum (spontaneous or induced) or gastric aspirate, with or without BAL specimen.[96] PCR testing of specimens for *M. tuberculosis* compared with microscopy and culture has higher sensitivity in children with clinical disease.[97]

See also the pathogen-specific chapters in this text.

Treatment

All neonates with pneumonia are best managed, at least initially, in the hospital because of risk for rapid decompensation. Empiric antimicrobial therapy is similar to treatment for neonatal sepsis (see Chapter 92). Therapy is modified based on culture results, clinical response, and severity at presentation.

Outpatient Treatment

Infants 1 to 6 months of age with mild pneumonia can be managed as outpatients with close medical supervision, provided that they do not appear ill or have respiratory distress, hypoxemia (oxygen saturation <92%), feeding intolerance, signs of dehydration, or an underlying chronic medical condition.[98] It is preferable to hospitalize during the peak stage of illness in young infants <4 months of age suspected of having pertussis or viral bronchiolitis because of risk for apnea or hypoxia and, for pertussis, pulmonary hypertension. Infants 1 to 6 months of age should be hospitalized if they have uncertain follow-up, have failed initial oral antibiotic therapy, or have pneumonia that is necrotizing or associated with parapneumonic effusion, empyema, or lung abscess. Most children >6 months of age with mild to moderately severe pneumonia can be managed effectively without hospitalization provided they have reliable follow-up and absence of complication. Diagnostic tests to determine the etiology of pneumonia or radiography are seldom required or useful in most infants and children who are managed as outpatients. In influenza season, suspected influenza should be treated with oseltamivir. Antibiotic therapy is prescribed only when findings suggest bacterial infection. Treatment is empiric, based on likely etiologic agent by age, considering underlying medical conditions, and likely antimicrobial susceptibility, tolerability, and cost. Azithromycin is appropriate for the treatment of infants for infections with pertussis, *C. trachomatis* and *Ureaplasma.* Vigilence for drug-associated infantile hypertrophic pyloric stenosis is prudent, especially in infants <2 weeks of age.[99] Azithromycin dose for pertussis is 10 mg/kg per day once daily for 5 days.

High-dose amoxicillin therapy at 90 mg/kg/day is the preferred outpatient therapy for CAP in infants and children.[41,48,100,101] A pharmacokinetic simulation study predicted excessive failure of treatment of pneumonia due to *S. pneumoniae* with minimal inhibitory concentration (MIC) ≥2 μg/mL using high-dose amoxicillin in 2 divided doses.[102] Dosing in 3 divided doses is preferable in areas where *S. pneumoniae* with MICs ≥2 μg/mL occur. In antibiotic-experienced children, high-dose amoxicillin-clavulanate (14:1 formulation) and ceftriaxone given intravenously are the most active agents for likely gram-positive or gram-negative respiratory pathogens, whereas trimethoprim-sulfamethoxazole, azithromycin, cefaclor, and cefprozil are the least active.[103] Cefuroxime axetil could be used in patients with pneumonia and non–type 1 hypersensitivity reaction to penicillin. Clindamycin could be used in patients with type 1 hypersensitivity reaction to penicillin and in those suspected to have staphylococcal pneumonia or aspiration pneumonia. In one study from the central US, however, 40% of *S. pneumoniae* cases were resistant to clindamycin.[103] Empiric use of cefdinir or azithromycin is an option for mild pneumonia in patients who are allergic or unresponsive to initial therapy with amoxicillin, but these drugs have limited activity against *S. pneumoniae* and nontypable *H. influenzae*.[103]

In children >5 years of age in whom *Mycoplasma* or *C. pneumoniae* are suspected, empiric treatment with a macrolide or doxycycline may be appropriate as single therapy or in combination with amoxicillin if pyogenic bacteria also are suspected. High-dose amoxicillin-clavulanate or clindamycin is effective for children with aspiration pneumonia. Fluoroquinolone therapy or treatment using agents with enhanced gram-positive activity (e.g., levofloxacin, moxifloxacin) can be considered in adolescents with frequent aspiration, as well as in those infected with atypical organisms, because their activity includes *M. pneumoniae* and *C. pneumoniae*.[104]

Duration of antibiotic therapy for pneumonia also is empiric and depends on several factors including patients' age, severity of illness, underlying illnesses, and response to therapy. In most cases the duration of therapy is 7 to 10 days. Oseltamivir therapy for influenza is initiated as soon as possible (i.e., before test results) for children at high risk for complications (e.g., underlying medical conditions including asthma) and for all children hospitalized with influenza. Oral oseltamivir phosphate is approved by the US Food and Drug Administration for children >2 weeks of age. Inhaled zanamavir also is approved as an alternative anti-influenza therapy in children >5 years of age with influenza and no underlying pulmonary disease.

Inpatient Treatment

Hypoxemia (oxygen saturation <92%) is the single most important indication for hospitalization because a hypoxemic child has greater risk for death than an adequately oxygenated child.[51] Other indications include cyanosis, rapid respiratory rate (>70 breaths/min in an infant or >50 breaths/min in a child), apnea, dyspnea, expiratory grunting, dehydration, toxic appearance, poor oral intake, recurrent pneumonia, underlying medical condition, or uncertain observation at home.

Supportive Therapy

Oxygenation is assessed continuously by measuring oxygen saturation or arterial Po_2. Hypoxic infants and children may not appear cyanotic until terminal. Mental agitation, clinically evident as increased irritability, can be an indication of hypoxemia. Supplemental oxygen therapy is indicated in any patient whose oxygen saturation is persistently ≤92%. Sole reliance on pulse oximetry values, without blood gas determination, is hazardous in ill patients because hypercarbia is an important sign of impending respiratory failure.

Rapid breathing, fever, decreased oral intake, and fatigue increase the fluid requirements. Most patients can be hydrated orally if given small volumes of fluids frequently, but intravenous fluids usually are necessary for seriously ill children with rapid breathing because of increased likelihood for pulmonary aspiration. The syndrome of inappropriate secretion of antidiuretic hormone (SIADH) can occur in up to one third of patients hospitalized with pneumonia and is associated with more severe disease and with poor outcome.[105] Fluid restriction is required in these cases to improve outcome.

Malnutrition has been associated with a worse prognosis of pneumonia. Infants and small children fare better if fed in small quantities and more frequently to prevent aspiration.[106] Placement of an enteral feeding tube or parenteral nutrition may be necessary in a seriously ill or intubated child to maintain nutritional balance.

Persistent and high fever increases the basal metabolic rate and oxygen consumption. Similarly, pain interferes with the depth of breathing and with the ability to cough effectively. Age-appropriate antipyretic or analgesic agents may be necessary.

Oral antibiotics can be effective in certain hospitalized older infants and children with uncomplicated pneumonia who have good oral intake. Otherwise, initial intravenous therapy with ampicillin is appropriate. Ampicillin-sulbactam or a third-generation cephalosporin should be considered for those who previously received antibiotics or have severe pneumonia. A third-generation cephalosporin should be considered in areas where *S. pneumoniae* with MICs ≥2 μg/mL are prevalent. Intravenous clindamycin may be considered in patients with type-1 hypersensitivity to penicillin, suspected staphylococcal infection or aspiration pneumonia. Intravenous cefepeme, ceftazidime, or piperacillin-tazobactam is used for empiric therapy in immunocompromised patients with pneumonia, especially in those with neutropenia. Empiric antifungal therapy is considered initially or if there is inadequate response to antibiotic therapy. Vancomycin or linezolid usually is given for MRSA-confirmed infection or empirically in children with severe, life-threatening pneumonia. Patients with cystic fibrosis will need adequate antibiotic coverage for *S. aureus* and *Pseudomonas* spp. until sputum cultures guide further choices. Broad antibiotic therapy is reconsidered pending identification of an organism by susceptibility test results or pending the clinical course. Generally, appropriate oral antibiotic is selected to complete therapy for uncomplicated pneumonia when the patient responds to therapy and begins to tolerate oral fluids.

Viral pneumonia is complicated by bacterial superinfection with variable frequency.[107,108] Evidence suggests that withholding antibiotics from hospitalized children with pneumonia clinically compatible or proved to be of viral origin is safe and is preferable to broad use of empiric antibiotic treatment.[109] Use of specific antiviral therapy other than for influenza depends on the pathogen, the severity of the clinical course, and benefit-versus-risk considerations. Use of aerosolized ribavirin for the treatment of RSV and acute LRI is guided by recommendations from the American Academy of Pediatrics,[110] although the value of treatment has been questioned.[111]

Prognosis and Sequelae

Mortality due to CAP is uncommon beyond infancy in Europe and North America because of improved and enhanced immunization rates, early access to medical care, and availability of appropriate antimicrobial therapy. Most healthy children with acute LRIs recover without complications or sequelae. In some patients, especially premature infants, immunocompromised hosts, or children with chronic lung, neuromuscular, or sickle cell disease or cardiovascular disease, acute complications are more common.

Several epidemiologic studies have questioned a linkage of asthma and other respiratory morbidity occurring later in childhood to viral bronchiolitis or atypical pneumonia in infancy, but not to bacterial pneumonia.[112–114] RSV and *C. trachomatis*, in particular, have been implicated,[112–115] and one study linked asthma with *C. pneumoniae* infection.[116] Abnormal pulmonary function in adults has been reported after pneumonia or pertussis in early childhood.[117,118] Other longitudinal studies of pulmonary function in children with bronchiolitis, however, have suggested that abnormalities may have preceded the acute infectious illness.[119,120] Thus it remains unclear whether childhood pneumonia causes chronic pulmonary disease.

Prevention

Most respiratory viral infections are transmitted by direct inoculation from hands contaminated with respiratory secretions on to conjunctival and nasal mucosa. Spread by airborne droplets also occurs occasionally. Adequate hand hygiene by caregivers and medical personnel is the single most important method of preventing hospital-associated infections. Hospitalized patients with respiratory tract infection who are <5 years of age, and older children who are unable to follow proper respiratory etiquette, are cared for under isolation precautions (droplet and contact) to prevent transmissions by large droplets. Spread of infection by small droplets (pertussis) is reduced by use of airborne precautions in a negative-pressure room.

Universal immunization with pneumococcal conjugate vaccines, PCV7 and then PCV13, has reduced dramatically the incidence of invasive pneumococcal disease and pneumonia in children as well as in young adults and elderly people through community (herd) protection.[121–123] Children ≥2 years of age and adolescents at heightened risk for invasive pneumococcal disease should receive PCV13 followed by pneumococcal polysaccharide vaccine 23 (PPV23).

RSV bronchiolitis and pneumonia can be reduced in high-risk infants by avoidance of multiple environmental risk factors (see Chapter 225). Monthly administration of RSV monoclonal antibody can reduce by 50% hospitalization due to RSV and is recommended for certain high-risk infections.[124] Annual vaccination against influenza is recommended for all individuals ≥6 months of age, with emphasis on strict implementation for those with underlying medical conditions such as chronic lung diseases (including mild asthma), neuromuscular disorders, congenital cardiac conditions, and diabetes who have high risk for severe and complicated lower respiratory tract influenza infection.[125,126] It is anticipated that prevention of influenza (and varicella) by immunization reduces the incidence of bacterial pneumonia in children due to *S. pneumoniae*, *S. aureus,* and *S. pyogenes.*

ACUTE COMPLICATED PNEUMONIA

The acute complications of bacterial pneumonia include parapneumonic effusion, empyema, necrotizing pneumonia, pneumatocele formation, and lung abscess.

In the late 1990s, there was a significant increase in the relative incidence of complications from bacterial pneumonia in infants and children living in North America, the exact reason for which is still obscure.[16]

Pleural Effusion, Parapneumonic Effusion, and Empyema

Pleural effusion is the presence of abnormal fluid collection between the visceral and parietal pleurae. Pleural effusions are classified as a *transudate* or an *exudate* based on Light criteria for the biochemical characteristics of the fluid.[127] The relative concentration of pleural fluid protein to serum protein is <0.5 in a transudate versus >0.5 in an exudate (Table 34.3). Transudates are infrequently caused by infection, whereas exudates can have an infectious or noninfectious cause. Noninfectious causes of pleural effusions are listed in Table 34.4. Several drugs, including hydralazine, nitrofurantoin, dantrolene, amiodarone, methysergide, procarbazine, bromocriptine, methotrexate, and agents associated with a lupus-like reaction, are associated with pleural effusion.[128]

Parapneumonic effusion is an inflammatory fluid collection adjacent to a pneumonic process, seen overall in 2% to 12% of children with

TABLE 34.3 Biochemical Characteristics of Parapneumonic Pleural Effusions

Laboratory Value	Uncomplicated Effusion Transudate	Complicated Effusion Exudate
pH	>7.2	<7.1
Glucose level	>40 mg/dL	<40 mg/dL
Lactate dehydrogenase concentration	<1000 IU/mL	>1000 IU/mL
Pleural protein–to–serum protein ratio	<0.5	>0.5

pneumonia and in up to 28% of hospitalized children.[129] Parapneumonic effusion can be classified as uncomplicated or complicated based on fluid pH, glucose, and lactate dehydrogenase (LDH) concentrations (see Table 34.3).[130] *Empyema* refers to purulent collection (exudate) in the pleural sac[131] and represents a spectrum from uncomplicated to complicated parapneumonic effusion.

Parapneumonic effusion usually occurs as a complication of pyogenic bacterial pneumonia but can occur occasionally, secondary to other etiologic agents (e.g., *Mycoplasma*, adenovirus)[132] or as a consequence of an infection from another contiguous site.[133] The estimated incidence of empyema in hospitalized children in the US was reported to be approximately 3.7 per 100,000 (range, 3.3–4.2) from 1997–2006, which was a 70% increase that occurred while the incidence of bacterial pneumonia, especially that due to *S. pneumoniae,* decreased.[134] The increase in empyema is thought to be related to increase in *S. pneumoniae* serotypes 1, 3, and 19A; *S. pyogenes*; and CA-MRSA.[135,136] Most cases of complicated pneumonia requiring surgical drainage occur in children <5 years of age.[137] Necrotizing pneumonia with pneumatoceles frequently coexists with empyema, predominantly in children <3 years of age.[138] The risk for developing empyema also is increased in children with certain underlying infectious (influenza) and medical conditions, including congenital heart disease, chronic pulmonary conditions, immune deficiencies, and neuromuscular disorders.[139,140] Complicated effusion or empyema is a serious illness often associated with significant morbidity (such as that needed for care in an intensive care unit), surgical drainage, longer hospital stay, and longer antibiotic course, resulting in high healthcare costs; mortality rates, however, have been low except in children <2 years of age.[85,141,142]

Etiologic Agents

S. pneumoniae is the most common cause of culture-confirmed and culture-negative parapneumonic effusions.[132] Although penicillin-nonsusceptible *S. pneumoniae* strains were recognized in the late 1980s to early 1990s, serotype 1, a highly invasive but penicillin-susceptible pneumococcal strain developed. During the late 1990s in Utah, *S. pneumoniae* serotype 1 emerged as a virulent agent of complicated pneumonia.[85] In the mid-2000s, before the introduction of PCV13, serotypes 1, 3, 7F, and 19A were detected in other areas of the US in more than half of cases of empyema in children.[132,143,144] In many cases, *S. pneumoniae* was detected by PCR in fluid or blood and not by culture, especially in patients pretreated with antibiotics. In a recent study from Greece, one third of 15 children with *S. pneumoniae* serotype 3 pneumonia and pleural effusion had been immunized with PCV13 after 12 months of age (with the then recommended 2 doses); no case occurred in children whose immunizations began in infancy and included all 4 recommended PCV13 doses.[145] Universal childhood immunization against Hib has made Hib a rare cause of parapneumonic effusion. CA-MRSA is an important cause of complicated pneumonia[146,147]; in southeast Asia, *S. aureus* is the most common cause.[148] Less frequently, group A *Streptococcus*, *Pseudomonas aeruginosa,* mixed anaerobic pathogens, *Mycobacterium* spp. and, rarely, fungi and parasites can be the etiologic agents.[149] Although effusion can accompany pneumonia due to *M. pneumoniae* and common viruses, they seldom are large enough to require intervention.[149,150] Parapneumonic fluid, other than in *S. aureus* infection, frequently is sterile, especially if the patient has received antibiotics or when the infection is caused by fastidious organisms.[132,143,146] In such situations, PCR testing often can confirm the etiology.

Pathogenesis and Pathologic Findings

Under normal circumstances, the pleural space contains a small amount (0.1–0.2 mL/ kg) of low protein fluid that forms a lubricant film between the two layers of the pleura.[151] The pleural circulation is maintained by a delicate balance between secretion and absorption of pleural fluid by lymphatic vessels. When this balance is disturbed, fluid accumulates. Transudate occurs when there are changes in the hydrostatic forces with normal capillary permeability, whereas exudate results when there is increased capillary permeability and lymphatic obstruction.[152,153] Pleural mesothelial macrophages contribute to the innate local defense against infection.[154] Pathogens can gain entry into the pleural space by direct extension from the alveoli, by hematogenous spread from the skin surface through a penetrating injury, from rupture of the esophagus, or from an intra-abdominal site through the diaphragm.[155] Direct extension from the alveoli is by far the most common. Certain pathogens such as *S. aureus, S. pneumoniae,* and *S. pyogenes* demonstrate tropism for the pleural surface for reasons that are not well understood but that likely include virulent factors such as exotoxins, endotoxins, or attachment molecules. Exposure of the pleural mesothelial cells to lipopolysaccharide, thrombin, or bacteria can incite an innate and adaptive inflammatory response causing pleural mesothelial macrophage dysfunction.[156,157] Vascular endothelial growth factor is released, which potentiates endothelial injury, increased capillary permeability, and extravasation of pulmonary interstitial fluid into the pleural space.[158] Mesothelial cells recruit neutrophils and monocytes and secrete large amounts of chemokines, including interleukin-8 (IL-8), into the pleural fluid that, when inhibited by bacterial proteins, results in an acidic, purulent fluid (i.e., empyema).[159] Acidic environment of the pleural fluid both suppresses bacterial growth and interferes with antibiotic activity. With disease progression, more inflammatory cytokines are released, and there is activation of coagulation leading to deposition of fibrin.

Three stages in the natural course of empyema are recognized. First, in the *exudative phase*, the fluid has low cellular content, normal glucose, and normal pH. Second, in the *fibrinopurulent phase*, frank pus containing neutrophils and fibrin is formed, and glucose and pH of fluid are low. This fibrinous pus coats the inner surfaces of the pleura, interfering with lung expansion, and leads to loculations. Third, in the *organizational phase* (late stage), fibroblasts migrate into the exudate from visceral and

TABLE 34.4 Noninfectious Causes of Pleural Effusion in Children

Transudate	Exudate	
Hypoalbuminemia	Spontaneous chylothorax	Malignancy
Congestive heart failure	Posttrauma or postsurgical	Collagen vascular disease
Cirrhosis with ascites	Postoperative chylothorax	Pancreatitis
Myxedema	Pulmonary lymphangiectasia	Subphrenic or other intra-abdominal abscess
Peritoneal dialysis	Uremic pleuritis	Drug reaction
Central venous catheter leak	Sarcoidosis	Meig syndrome (pelvic tumor)
Fluid mismanagement	Dressler syndrome (postmyocardial infarction)	
Adult respiratory distress syndrome		

parietal pleurae, producing a nonelastic membrane called the *pleural peel*. Before the availability of antibiotics, spontaneous drainage through the chest wall (empyema necessitans) or into the bronchus (bronchopleural fistula) sometimes followed. Such events now are rare and usually are due to healthcare-associated antibiotic-resistant bacteria or insidiously progressive actinomycosis.

Clinical and Radiographic Manifestations[85,138,141,149]

Effusion should be suspected when the response of a lobar, lobular, or alveolar pneumonia to appropriate antibiotic therapy is slow, or if there is clinical deterioration during treatment. Symptoms of pleural effusion can begin nonspecifically with malaise, lethargy, and fever, followed by cough and rapid breathing, the latter which are expected in >90% of children with complex parapneumonic effusion.[141] Dyspnea, difficulty breathing, and grunting become apparent as the effusion progresses. Pain in the chest or abdomen develops on the involved side and is associated with high fever, chills, and rigors. The child may splint or lie on the involved side to minimize pain. The patient usually is ill, toxic appearing, and febrile, with significant tachypnea and shallow respirations, or can have severe respiratory distress, hypotension, and septic shock. Scoliosis may be noted on the involved side, and the affected side may be tender to palpation. On auscultation of the involved side, breath sounds usually are frankly diminished, crackles from the associated pneumonia may be audible, pleural rub may be audible when the effusion is small, and the percussion note is dull when the effusion is free flowing. By contrast, dullness can decrease as the effusion organizes.

Plain chest radiography is more sensitive than physical examination but less sensitive than ultrasonagraphy in detecting small effusions.[160] A chest radiograph can indicate size and loculation of effusion and whether drainage likely is indicated and can define parenchymal lung consolidation as well as an unexpected underlying cause of the effusion, such as a mass, hilar adenopathy, or cardiomegaly. Blunting of the costophrenic angle, thickening of the normally paper-thin, pleural-shadow, and a subpulmonic density all suggest pleural effusion (Fig. 34.3). Compression of the lung, with shift of the trachea away from the effusion, may be seen when the effusion is large, usually ≥1000 mL.[161] Lateral decubitus films can differentiate free effusion from loculated collections, pulmonary consolidation, and pleural thickening. Chest radiographs, however, cannot differentiate between a parapneumonic effusion and an empyema.[149] Ultrasonography is the imaging modality of choice because it is portable, inexpensive, and involves no radiation exposure; differentiates parenchymal from pleural space disease; helps localize and estimate the size of an effusion precisely; identifies the best site for thoracentesis and chest tube placement; and is superior to computed tomography (CT) in detecting early loculation and septation.[162] Quality of ultrasonography is dependent on level of experience of the operator. Although CT is not necessary routinely to differentiate simple parapneumonic effusion from empyema, CT may be indicated to evaluate parenchymal disease (necrotizing pneumonia or lung abscess), to determine noninfectious causes, or to aid the surgeon before thoracotomy or thoracoscopy.[16]

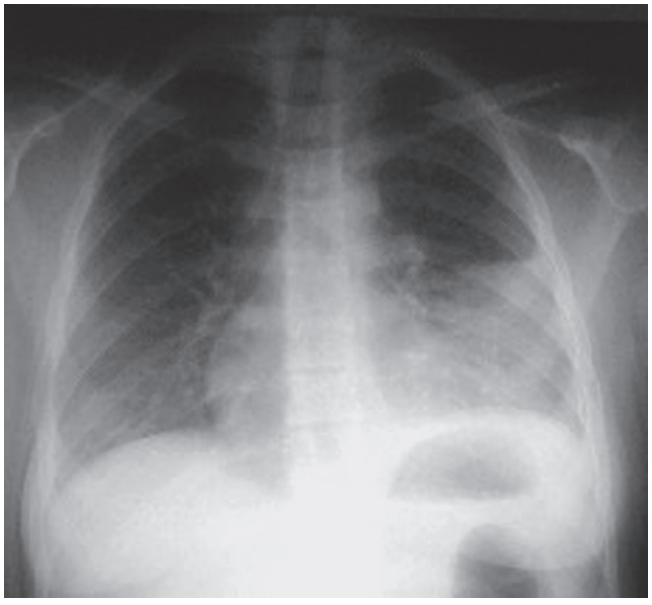

FIGURE 34.3 Plain radiograph showing left lower lobe pneumonia and a parapneumonic effusion, typical of acute bacterial pneumonia.

Laboratory Findings and Diagnosis

Children with parapneumonic effusion or empyema often have an elevated peripheral WBC count, left shift of neutrophils, elevated C-reactive protein, and thrombocytosis (>500,000 platelets/mm^3). Hypoalbuminemia can occur if the effusion is large and proteinaceous and hyponatremia raises consideration of SIADH. Blood cultures are obtained before therapy because a positive result (10%–22%) is useful for management when pleural fluid is sterile.[85,145] Culture of sputum or tracheal aspirate, if possible, may be useful. Gram staining determines whether the quality of the sample is good (>25 neutrophils/low-power field and absent squamous epithelial cells) and if a single organism type is predominant.

Pleural fluid specimen is inspected to determine color, odor (putrid odor being pathognomonic of anaerobic infection), and character (bloody, purulent, seropurulent, or serosanguineous); centrifuged if cloudy (persistent cloudiness is suggestive of a chylothorax); and analyzed for total WBC count with differential and by special stains and culture. Cellular histology and flow cytometry are performed if infectious etiology is uncertain. Empyema is likely when biochemical analysis reveals pleural fluid-to-serum ratio for LDH >0.6, pH <7, glucose <40 mg/dL, and LDH >1000 U/L.[163] Because biochemical analysis rarely influences management, Pediatric Infectious Diseases Society and Infectious Diseases Society of America guidelines do not recommend evaluation unless the patient has an underlying condition (e.g., collagen vascular disease).[41] Cytokine levels in pleural fluid, especially IL-8, are expected to be high in empyema.[156] IL-8 level may be useful to differentiate a complex from simple parapneumonic effusion.

Total and differential WBC count of pleural fluid is helpful in differentiating bacteria, mycobacteria, or fungi infection and malignancy.[149] Presence of >50,000 neutrophils/mm^3 is usual in empyema. Lymphocytic predominance suggests tuberculosis and some fungal or *Mycoplasma* infections but also can indicate a chylothorax. Mixed mononuclear cell types suggest a more chronic process, such as tuberculosis, malignancy, uremia, or collagen vascular disease. Eosinophilic effusion in adults, especially with air or blood in the pleural space, suggests tuberculosis, asbestosis, malignancy, paragonimiasis, drug-related hypersensitivity, pleurisy, collagen vascular disease, other parasitic infections, or an idiopathic case (14%–20%).[164–167]

Bacteriologic examination always includes Gram stain and culture for aerobic and anaerobic bacteria. Acid-fast stain and culture for *M. tuberculosis*, as well as fungal stain and culture, should be obtained from both fluid and sputum when clinically indicated. Rapid non–culture-based diagnostic tests such as PCR, immunoassay, and rapid antigen testing increasingly are performed because their rate of culture positivity is low and the knowledge of etiology aids management.[168]

Tuberculous pleural effusion usually is caused by a delayed hypersensitivity reaction to mycobacterial antigens in the pleural space.[169] Diagnosis often is delayed because of paucity of organisms in pleural fluid, anergy to tuberculin skin test, and IGRA in blood.[170,171] High levels of adenosine deaminase (>40 IU/L) and interferon γ (>75 pg/mL) in pleural fluid are very suggestive of tuberculous effusion.[172] Rapid and accurate diagnosis, as well as prediction of rifampin resistance, is possible using the Xpert MTB/RIF (Cepheid, Sunnyvale, CA) assay on pleural biopsy and pleural fluid specimens in patients with suspected tuberculous pleural effusion who have a negative sputum smear for acid-fast bacilli.[173] Pleural biopsy is considered to diagnose other granulomatous infections (histoplasmosis, other fungal infections, and *Francisella tularensis)* and malignancies.

Management

The main objectives of therapy are eradication of infection and reestablishment of pleural fluid circulation, thereby reinstating normal lung

function.[174] These can be achieved by either medical or surgical interventions depending on the age of the patient, size of the effusion, severity of respiratory distress, loculation, and failure of initial medical therapy. Supportive care using appropriate antipyretics, analgesics, oxygen supplementation, and fluid therapy must be instituted early and patients must be monitored closely to recognize respiratory deterioration, central respiratory depression from excessive analgesics, or fluid overload related to SIADH. Chest physiotherapy is avoided because this causes discomfort and can further compromise the respiratory effort.[149]

Antimicrobial Therapy. In choosing therapy, consideration is given to probable pathogens (predicted by age), pathogen and geographic resistance patterns, clinical circumstances (community or healthcare onset), host factors (immunocompetent or compromised), radiographic findings, and Gram stain and culture of the pleural fluid. Children with small, uncomplicated effusion can be managed as outpatients with an empiric antibiotic regimen as for CAP. In most hospitalized patients, ceftriaxone or cefotaxime given intravenously is recommended as empiric therapy to adequately treat *S. pneumoniae* and *S. pyogenes*. Vancomycin is added if the patient is very ill appearing or CA-MRSA or hospital-acquired MRSA is considered a potential pathogen. In areas where CA-MRSA is highly clindamycin susceptible, clindamycin could be an adequate addition. Vancomycin has poor pharmacokinetics for infections in the lung. Other agents with good MRSA activity include linezolid, telavancin, ceftaroline, and quinupristin-dalfopristin; these agents are considered second-line treatment for patients who do not respond to vancomycin therapy. Daptomycin should not be used because it is inactivated by surfactant. In patients with suspected pneumonia aspiration, clindamycin can be used instead of vancomycin to cover anaerobic bacteria. In cases in which atypical pathogens are suspected, a macrolide (for children <7 years) or doxycycline (for children >7 years) may be added. When a specific pathogen is detected, or when the clinical course and microbiologic screening cultures make Staphylococcal infection highly unlikely, the antibiotic spectrum should be narrowed. Duration of parenteral therapy and total treatment is individualized on the basis of clinical response and adequacy of drainage. It is common practice to replace parenteral therapy with oral therapy when substantial improvement occurs and the patient has good oral intake, with continuation of antibiotics for a total course of 2 to 4 weeks for empyema.[41] The treatment may be prolonged when drainage is delayed and systemic manifestations are protracted. In circumstances in which the effusion persists and the microbial etiology is unknown, it is important to remember that even with optimal antibiotic therapy, fever, anorexia, and toxicity can be due to a prolonged inflammatory response. Additions or changes in appropriately selected antibiotic therapy should be avoided.

Surgical Intervention. Thoracentesis is recommended to relieve moderate to large effusions, defined as fluid layering >1 cm on lateral decubitus radiograph or opacifying more than one fourth of the hemithroax.[41,149,162] A therapeutic approach to moderate-sized, nonloculated parapneumonic effusion not associated with respiratory compromise is to slowly drain 10 to 20 mL/kg, send the fluid for microbiologic studies, and begin empiric antibiotic therapy intravenously. It is important not to drain fluid too rapidly because reexpansion pulmonary edema can occur, causing increased morbidity and even mortality.[175] The course is observed over 48 to 72 hours. Many patients improve. If the patient does not improve or worsens, ultrasonography is performed to determine the extent of reaccumulation. If fluid has reaccumulated, continuous drainage is required; if not, an antibiotic regimen is reconsidered. For patients with a large effusion or patients with respiratory compromise, a chest tube is placed as soon as possible for continuous drainage. A small bore chest tube is preferable for patient comfort and was associated with shorter hospital stay and found to be superior to surgical stiff drains in two studies.[176,177] Chest radiography is repeated to verify chest tube placement and to exclude the development of pneumothorax during placement. Complications of chest tube placement include bleeding or infection at the exit site, persistent atelectasis, development of bronchopleural fistula, or (very rarely) laceration of the lung.[178]

Loculated complex parapneumonic effusion or empyema usually requires more aggressive management, but optimal management remains controversial. According to the British Thoracic Society and American Pediatric Surgical Association guidelines,[149,162] medical therapy (chemical debridement with fibrinolysis) should be considered as initial therapy of choice followed by video-assisted thoracic surgery (VATS) in patients who fail medical therapy. Recommendations are based on several studies showing comparable outcomes and complications for procedures, with safety and cost favoring chemical debridement with fibrinolysis.[179,180] However, a 2005 meta-analysis showed that primary operative therapy compared with nonoperative therapy was associated with a lower cumulative in-hospital mortality rate (0% vs. 3.3%) and rate of reintervention (2.5% vs. 23.5%). In addition, primary operative therapy was associated with shorter duration of hospitalization (10.8 vs. 20 days), chest tube days (4.4 vs. 10.6 days), and antibiotic therapy (12.8 vs. 21.3 days), respectively.[181] Most experts agree that either approach is reasonable and that choice of procedure will depend on local expertise, cost considerations, and patient preference.

Available fibrinolytic agents include urokinase, streptokinase, and alteplase. Alteplase is the most commonly used fibrinolytic agent in the US because urokinase is not available and streptokinase has limited efficacy and possible allergic reactions.[182] Common adverse effects of fibrinolytic therapy include fever, discomfort, intrapleural bleeding, and anaphylaxis.[177] Fibrinolysis is contraindicated in patients with bronchopleural fistula or when there is an air leak because this could cause tension pneumothorax.

In VATS surgery, fibrinous material is debrided, loculations are broken, and drainage of purulent material from the pleural space is established. VATS is most effective when performed early in the course of complex effusions or empyema, has good outcomes, and is relatively safe. Compared with open thoracotomy, VATs is less invasive and has a comparable success rate, earlier resolution of the disease, shorter hospital stay, and better cosmetic appeal.[183,184] Partial decortication frequently can be accomplished when necessary. The few contraindications to performing VATS include inability to access the pleural cavity because of thick, purulent fluid and severe fibrosis.

Bronchoscopy may be indicated in anaerobic infections to hasten drainage or the removal of a foreign body. Open pleural decortication is reserved for patients who have come to optimal management late and have entrapment of lung with persistent and severe restrictive lung disease.

Most children improve after surgical drainage, as evidenced by improved activity, appetite, vital signs, and chest physical findings and resolving acute phase reactants. After radiographic examinations related to chest tube removal, follow-up chest radiograph usually is not necessary unless the child has persistent symptoms or has had a previous episode. Follow-up chest radiograph for the latter indication should be delayed 4 to 6 weeks because radiographic resolution lags clinical resolution.[174]

Prognosis

Most children with complex parapneumonic effusion or empyema recover completely despite the severity of their initial presentation. The mortality rate was about 3% in previously healthy children medically managed with antibiotics and chest tube drainage, but no deaths were reported in children who underwent a fibrinolytic procedure, VATS, or open thoracotomy.[181] Historically, mortality was highest in small infants.[185] Increased morbidity can be expected in children with underlying medical conditions (e.g., malnutrition, neuromuscular disorders, or chronic pulmonary disease) or with infection due to MRSA or multidrug-resistant organisms. A long-term prospective follow-up study of children treated for complex effusions or empyema showed no sequelae despite substantial complications within 1 month of illness.[186] A recent study evaluating the long-term effect of parapneumonic effusion, especially in children with prior history of asthma, concluded that there were no long-term important effects despite small changes in lung function and exercise capacity.[187]

Necrotizing Pneumonia and Lung Abscess

Necrotizing pneumonia and lung abscess represent the spectrum of disease. The etiology and course in children differ compared with adults. Lung abscess usually occurs as a consequence of a localized lung infection by particularly virulent, pyogenic bacteria. Necrotizing pneumonia in an otherwise healthy child usually resolves with antimicrobial treatment, but occasionally can progress to formation of pneumatoceles (blebs in the lung parenchyma created by coalescence of alveolar spaces after rupture

of septa), lung abscess, or bronchopleural fistula. Lung abscess is usually the outcome of widely variable pathogenic processes; it can be the consequence of (1) necrotizing pneumonia; (2) localized infection after aspiration of heavily infected mouth secretions (sometimes along with a foreign body); (3) focal infection of the lung that occurs during high-grade bacteremia or as a result of infarcting septic emboli from distant sites; or (4) complication of a subacute or chronic airway infection seen as a late result of cystic fibrosis, after prolonged intubation, or after nosocomial pneumonia. In immunocompromised hosts, bacteria or fungi can invade the vessel walls, leading to subsequent lung infarction and necrotizing pneumonia (see Chapter 36).

Etiologic Agents

Community-acquired bacterial pneumonia can result in necrosis of parenchyma, which often is discovered on chest radiography or increasingly because CT is performed in a child with prolonged fever and ill appearance.[188] The causative pathogen is not identified in many cases, but when detected, *S. pneumonia* is most common.[189] Less commonly, *S. aureus* (especially CA-MRSA), *S. pyogenes* (especially after influenza illness), β-hemolytic streptococci (Lancefield groups C and G), and other streptococcal species are causative.[190–192] Pneumatoceles can complicate *S. pneumoniae* or *S. aureus* pneumonia, and the latter can lead to abscess formation.[190,193,194] Rarely, severe *M. pneumoniae* pneumonia is accompanied by abscess formation.[195,196]

When pneumonia follows aspiration of oropharyngeal flora, or regurgitated stomach contents and obstruction, the volatile fatty acids produced by anaerobic bacteria are particularly prone to cause necrosis and abscess. Most aspiration pneumonias, lung abscesses, and empyema are mixed infections.[197,198] The predominant anaerobic bacteria isolated are *Peptostreptococcus*, *Fusobacterium*, *Prevotella melaninogenica,* and *Porphyromonas* spp.[197] *Veillonella* may be more likely isolated in children with prior surgery, malignancy, corticosteroid therapy, aspirated foreign body, or immunodeficiency.

Single or multiple lung abscesses (usually due to *S. aureus* infections) can result from right-sided endocarditis, severe septicemia, or distant osteoarticular or deep muscle infection with thrombosis. Necrotizing pneumonia and lung abscess also can follow endovascular infection or phlebothrombosis of the large veins in the neck (Lemierre syndrome).[199] *Fusobacterium necrophorum* is the most common pathogen, but *S. aureus,* α-hemolytic streptococci, *Streptococcus anginosus* group, *Actinomyces* spp., or molds can be causative.[200]

Lung abscesses in intubated infants and children usually are due to hospital-associated pathogens.[201] Abscesses can develop in the later stages of cystic fibrosis secondary to chronic bronchiectasis. In such cases, *S. aureus, P. aeruginosa,* and atypical mycobacteria should be considered.[202,203]

Pathogenesis

Necrotizing pneumonia is a consequence of severe inflammation confined to a cluster of alveoli or a lobe resulting in significant parenchymal damage and tissue necrosis. Abscess formation can follow even when treatment is adequate but more frequently when treatment is delayed or inadequate.

Aspiration and obstruction of the airways predispose to polymicrobial and anaerobic lung abscess. Risk factors include decreased level of consciousness due to neurologic disease, anesthesia, alcohol, or drugs or during surgical instrumentation; neuromuscular disorders depressing the gag reflex; esophageal abnormalities; gastroesophageal reflux; and prolonged endotracheal intubation. Poor dental hygiene and periodontal infection increase the density of anaerobes and predispose to lung abscess in adolescents. Impaired phagocytic responses as seen in neutropenic patients or after viral infections with influenza, measles, and VZV also can predispose to complicated pneumonia. Aspirated acid contents of the stomach cause chemical injury to lung tissue.[204] Location of abscess favors the middle or right lower lobe in patients who aspirate while erect, and favors the posterior upper or lower lobes in the supine patient. Abnormal drainage as occurs in congenital pulmonary sequestration, lobar emphysema, and pneumatocele formation can predispose to abscess formation. Experimental studies in animals show a timeline from aspiration to pneumonia to lung abscess of at least 1 to 2 weeks.[205]

Heavy seeding of the pulmonary circulation during high-grade bacteremia can lead to lung abscess, as can pulmonary infarction associated with septic embolization. These circumstances usually lead to multiple abscesses, unilaterally or bilaterally. Chronic airway disease, cystic fibrosis, congenital ciliary dysfunction, and bronchiectasis predispose to lung abscess. The inherited abnormalities of humoral or cellular immune responses, such as chronic granulomatous disease or hyper-IgM syndrome, permit persistence of certain pathogens, which can result in abscess formation.

Clinical Manifestations

Clinical manifestations of necrotizing pneumonia are similar to but usually more severe than those of nonnecrotizing pneumonia due to the same bacteria. The evolution from necrotizing pneumonia to abscess frequently is insidious.[206] Lung abscess after aspiration usually manifests 1 to 2 weeks after the event. Prolonged fever and a toxic appearance or persistent hypoxia despite appropriate antimicrobial therapy is characteristic. Fever is the most common sign in patients with lung abscess.[188] Cough, dyspnea, and sputum production are present in approximately one half of patients.[188,206] Cough usually is nonproductive, but with spontaneous rupture of the abscess into the bronchus, it can be massively productive. Hemoptysis can be seen in necrotizing pneumonia. Older children may report chest pain with or without radiation. Other symptoms are nonspecific and include rhinorrhea, sore throat, lymphadenopathy, decreased appetite, irritability, and malaise or lethargy.[188] Physical findings also are nonspecific unless there is accompanying pleural fluid.

The differential diagnosis of lung abscess includes common necrotizing bacterial infections as well as tuberculosis, nocardiosis, fungal infections, melioidosis, paragonimiasis, and amebic abscess. Certain noninfectious diseases, such as malignancy, sarcoidosis, and pulmonary infarction, can produce lesions that mimic abscess on chest radiograph.

Diagnosis

A chest radiograph should be obtained in a child whose symptoms do not respond to appropriate antibiotic treatment (Fig. 34.4). The initial finding usually is an irregular cavitary lesion (with or without a thick wall) with air-fluid level adjacent to a segmental or lobar lung infiltrate, without prominent hilar adenopathy. Multilobar involvement can be seen

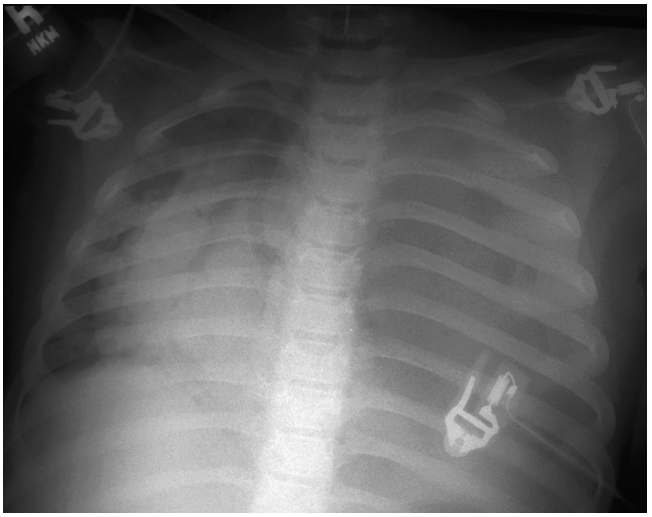

FIGURE 34.4 Anaerobic pleural empyema in a 5-year-old girl who came to medical attention because of a 1-month history of abdominal pain, tiredness, and constipation, but no history of an aspiration event, fever, respiratory distress, or cough. This radiograph was obtained after an acute respiratory event during evaluation for constipation. Note complete opacification of the left hemithorax with severe shift of the heart and trachea to the right. Three liters of putrid pus was drained, revealing a left lower lobe abscess. Gram stain and culture revealed polymicrobial anaerobic and facultative oropharyngeal flora. (Courtesy of E. N. Faerber and S. S. Long, St. Christopher's Hospital for Children, Philadelphia, PA.)

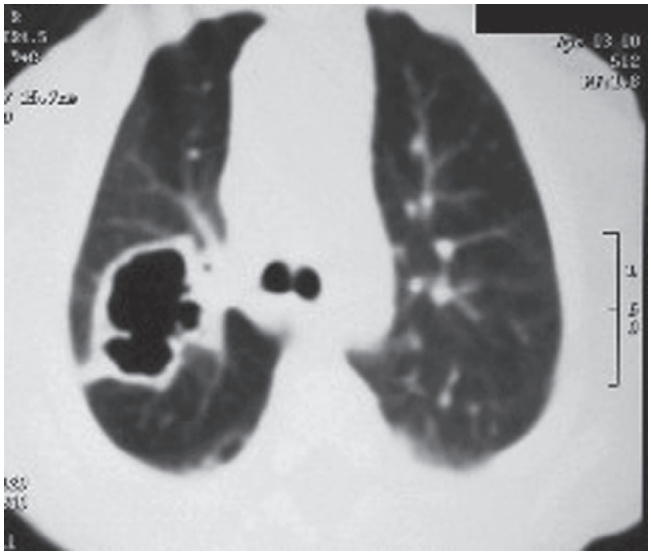

FIGURE 34.5 Lung windows of computed tomography study showing right lower lobe abscess.

in patients with underlying immune dysfunction or after septic embolization.[207] Chest radiography may not be diagnostic initially in approximately 20% of cases. In one study of 18 cases, abscess location was the right lower lobe (8), left lower lobe (6), right upper lobe (3), and left upper lobe (1).[206] CT is more sensitive than plain radiography and often is useful to define the extent of disease, underlying anomalies, presence or absence of a foreign body (Fig. 34.5), and endobronchial obstruction and to distinguish parenchymal abscess from air-fluid levels in the pleural space.[208]

Ultrasonography using color Doppler is a powerful diagnostic tool to differentiate fluid-filled lung abscess from empyema and has the advantages of greater convenience, lower cost, and avoidance of radiation.[209]

Bronchoscopy may be a therapeutic means to facilitate the removal of a foreign body or to promote the drainage of purulent fluid, or both.[206] Only 3% of bronchoscopic specimen cultures grew an organism that later was recovered from a lung abscess.[210] Cultures of sputum, BAL, or blood are of limited diagnostic value compared with culture of direct lung aspirate. In one study, 94% of the specimens obtained by transthoracic aspiration yielded a pathogen despite prior receipt of an antibiotic compared with only 11% of sputum cultures and 3% each of blood and BAL cultures.[210] Ultrasound-guided transthoracic aspiration technique was used successfully to obtain specimens for diagnosis to drain lung abscesses in 3 premature infants.[211] There is a potential risk for spillage of contaminated fluid into the pleural space during ultrasound- or CT-guided transthoracic aspiration; procedures are reserved for patients not improving clinically on antibiotic therapy and for those who have a large abscess that must be drained.

Management

Prolonged antibiotic administration is the mainstay of therapy for necrotizing pneumonia and lung abscess. Duration of therapy is based on clinical response and usually is 4 weeks, or at least 2 weeks after the patient becomes afebrile and has clinical improvement. In most cases, parenteral therapy is initiated. Two randomized clinical trials in adults found clindamycin to be superior to penicillin for the treatment of anaerobic lung abscess.[123,212,213] A randomized clinical trial for treatment of children with aspiration pneumonia found no difference between these two drugs. Ampicillin-sulbactam has an excellent spectrum of activity against organisms in aspiration lung abscesses.[214] Parenteral clindamycin is appropriate empiric therapy in children with complicated lung infection possibly due to *S. aureus* or CA-MRSA. Vancomycin is an alternative in patients with allergy or where clindamycin resistance of *S. aureus* is prevalent. Other antistaphylococcal medications, such as linezolid, could be used in case of allergy or poor response to vancomycin or clindamycin.[215] Combination therapy with ticarcillin or piperacillin and a β-lactamase inhibitor (e.g., tazobactam) with or without an aminoglycoside may be considered when necrotizing pneumonia follows aspiration in a hospitalized child or in a child for whom an Enterobacteriaceae (e.g., *E. coli, Klebsiella* spp.) or *P. aeruginosa* infection is suspected or has been identified from a percutaneous lung aspirate. Metronidazole would be effective treatment for β-lactamase–producing anaerobes in lung abscess after aspiration but cannot be used alone without an agent active against aerobic and microaerophilic streptococci.[216]

Necrotizing pneumonia or abscess frequently is complicated by parapneumonic effusion, which benefits from percutaneous drainage or other invasive procedures depending on size and other clinical factors. Previously, percutaneous drainage of the abscess often was complicated with the development of bronchopleural fistula.[217,218] Because of expected good outcome with medical therapy, percutaneous drainage should be considered only in patients with poor response 5 to 7 days after initiating therapy, for an abscess >4 cm in diameter, for presence of mediastinal shift, or for an abscess resulting in ventilator dependency. Surgical wedge resection or lobectomy is rarely required and is reserved for cases in which medical management and drainage fail, or bronchiectasis has occurred.

Prognosis and Complications

Most cases of necrotizing pneumonia in otherwise healthy children resolve with antibiotic treatment alone.[188] Similarly, 80% to 90% of lung abscesses resolve with antibiotic therapy alone provided there is no associated bronchial obstruction or underlying lung disease such as cystic fibrosis. Fever can persist for an average of 4 to 8 days despite appropriate therapy. Complications due to lung abscess are rare in developed countries and in otherwise healthy hosts. These could include intracavitary hemorrhage with hemoptysis, spillage of abscess with spread of infection to other parts of the lung, empyema, bronchopleural fistula, septicemia, cerebral abscess, and SIADH.

ACKNOWLEDGMENT

The author acknowledges previous contributions of Dennis Murray to this chapter.

All references are available online at www.expertconsult.com.

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