PERSPECTIVE

Pneumonia is the seventh leading cause of death and the leading cause of death from infectious disease in the United States. The annual incidence of community-acquired pneumonia (CAP) in the United States ranges from 2 to 4 million, resulting in approximately 500,000 hospital admissions. Most cases of CAP are managed in the outpatient setting and the mortality is low (approximately 1%), but pneumonia necessitating hospitalization is associated with a higher mortality rate (approximately 15%). Pneumonia remains challenging because of an expanding spectrum of pathogens, changing antibiotic resistance patterns, the continued introduction of newer antimicrobial agents, and increasing emphasis on cost-effectiveness and outpatient management.

The epidemiology of CAP is changing. As the percentage of the population older than 65 years continues to increase, the incidence of pneumonia is expected to increase. An increasing number of patients are taking immunosuppressive drugs related to treatment of malignancy, transplantation, or autoimmune disease, resulting in more cases of pneumonia from other opportunistic pathogens. Antibiotic resistance is more common among Streptococcus pneumoniae and other pathogens. In addition, the threat exists of respiratory infections caused by biologic terrorism or resulting in more cases of pneumonia from other opportunistic pathogens. The challenge with pneumonia is identifying the causative agent rather than making the diagnosis in general. Empirical therapy should be chosen with activity against the spectrum of likely pathogens based on the overall clinical picture.

Difficulty in determining the specific cause of pneumonia exists even with advanced microbiologic and serologic testing that is not generally available during an ED evaluation. In CAP, a microbial cause cannot be determined in approximately half of cases, even after thorough investigation. Among hospitalized adults in whom a pathogen can be identified, organisms such as S. pneumoniae and Haemophilus influenzae, referred to as “typical” pathogens, account for approximately half of cases. Legionella, Mycoplasma, and Chlamydia (previously known as Chlamydia) species, referred to as “atypical” pathogens, are also common. Testing for common viral agents reveals a viral cause in approximately 18% of cases, with influenza and parainfluenza viruses being the most common.

Among adults requiring intensive care unit (ICU) admission, S. pneumoniae is the most common pathogen, with even higher prevalence among fatal cases. Legionella species, Staphylococcus aureus (including methicillin-resistant S. aureus [MRSA]), and aerobic gram-negative bacilli also appear to be relatively more common among adults with severe CAP. Atypical organisms, such as Mycoplasma species or viruses, account for a relatively higher proportion of pneumonia in patients who have milder illness that is amenable to outpatient therapy. Atypical pathogens occur with significant frequency, however, in patients with severe illness requiring hospitalization, particularly because of Legionella infection. Coinfection, such as with Chlamydia pneumoniae and S. pneumoniae, is also well recognized.

S. pneumoniae is a gram-positive coccus that is the most common cause of CAP in adults requiring hospitalization. It colonizes the nasopharynx in 40% of healthy adults. Although this organism can cause pneumonia in healthy people, patients with a history of diabetes, cardiovascular disease, alcoholism, sickle cell disease, splenectomy, and malignancy or other immunosuppressive illness are at increased risk. A vaccine containing the 23 common serotypes of S. pneumoniae is recommended for adults older than 65 years and those with underlying illness. For adults who have been reported to have had an adverse reaction to the pneumococcal vaccine or with a history of Guillain-Barré syndrome, an alternative vaccine is available.

PRINCIPLES OF DISEASE

Despite the constant presence of potential pathogens in the respiratory tract, the lungs are remarkably resistant to infection. The alveolar surface of the lungs covers an area of approximately 140 m². Approximately 10,000 L of air passes through the respiratory tract each day, and typical ambient air can contain hundreds to thousands of microorganisms per cubic meter. Although the cough and laryngeal reflexes prevent most large particulate matter from entering the lower respiratory tract, aspiration of oropharyngeal contents may be a common occurrence during normal sleep. Despite these hazards, healthy lungs are usually a virtually sterile environment.

The development of clinical pneumonia requires a defect in host defenses, the presence of a particularly virulent organism, or the introduction of a large inoculum of organisms. If the challenge of invading organisms overwhelms host defenses, then microbial proliferation leads to inflammation, an immune response, and clinical pneumonia. If host defenses are weak, then a minimal challenge may lead to the development of pneumonia.

Causative Agents

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Capsular polysaccharides of pneumococcal types most commonly associated with pneumonia reduces the likelihood of serious pneumococcal infection. It is recommended for people at increased risk because of underlying illness or age older than 65 years. Many ED patients have not received pneumococcal vaccine, and vaccinating eligible patients in this setting seems to be feasible and effective.[4] A 13-valent protein-conjugate pneumococcal vaccine effectively reduces invasive pneumococcal disease and pneumonia in infants and young children.[5]

*H. influenzae*, the second most frequently isolated organism in CAP among adults, is a pleomorphic gram-negative rod. It is a common pathogen in adults with chronic obstructive pulmonary disease (COPD), alcoholism, malnutrition, malignancy, or diabetes.

*S. aureus* may be emerging as a more common cause of CAP and has been found more frequently than *H. influenzae* in some recent series. Community-associated strains of methicillin-resistant *S. aureus* (CA-MRSA) are uncommon in CAP but are more likely to cause severe disease.[6] This is often associated with influenza. Staphylococcal pneumonias are often necrotizing, with caviation and pneumatocele formation. Intravenous drug users may develop hematogenous spread of *S. aureus* that involves both lungs with multiple small infiltrates or abscesses (e.g., tricuspid endocarditis resulting in septic pulmonary emboli).

*Klebsiella pneumoniae* is a gram-negative rod that rarely causes disease in a normal host and accounts for a small percentage of cases of CAP. It may cause severe pneumonia in debilitated patients with alcoholism, diabetes, or other chronic illness. There is a high incidence of antibiotic resistance because the organism is often hospital acquired.

*Mycoplasma pneumoniae* is one of the most common causes of CAP in previously healthy patients younger than age 40 years. Another important organism in CAP is *C. pneumoniae*, an intracellular parasite that is transmitted between humans by respiratory secretions or aerosols. Seroprevalence studies indicate that virtually everyone is infected with *C. pneumoniae* at some time and that reinfection is common, particularly in older adults. It accounts for at least 8% of cases, although this is an underestimate owing to difficulty in diagnosing infection with this organism.

At least 30 species of *Legionella* have been isolated since the 1976 convention-related outbreak in Philadelphia, from which the organism derives its name. At least 19 are known human pathogens. *Legionella* is an intracellular organism that lives in aquatic environments. There is no person-to-person transmission. Although it is implicated in point outbreaks related to cooling towers and similar aquatic sources, the organism also lives in ordinary tap water and is underdiagnosed as a cause of CAP. *Legionella* prevalence seems to vary greatly by region.

Lower respiratory infections caused by anaerobic organisms generally result from the aspiration of oropharyngeal contents with large amounts of bacteria. These infections are typically polymicrobial, including *Peptostreptococcus*, *Bacteroides*, *Fusobacterium*, and *Prevotella* species. Presentation is often subacute or chronic and may be difficult to distinguish clinically from other causes of pneumonia. Clinical factors that suggest an anaerobic infection include risk factors for aspiration, such as central nervous system depression or swallowing dysfunction, severe periodontal disease, fetid sputum, and the presence of a pulmonary abscess or empyema.

Viral pneumonias are common in infants and young children and are recognized as an important cause of pneumonia in adults. Respiratory syncytial virus and parainfluenza viruses are the most common causes of pneumonia in infants and small children, occurring mostly during autumn and winter. Influenza viruses are the most common cause of viral pneumonia in adults. Winter influenza outbreaks, usually of influenza type A, may cause 40,000 deaths annually in the United States. More than 90% occur in people age 65 years or older.[7] Metapneumovirus is a parainfluenza virus that seems to be an important cause of viral pneumonia in children and adults.

Fungal infections caused by organisms such as *Histoplasma capsulatum*, *Blastomyces dermatitidis*, and *Coccidioides immitis* commonly manifest as pulmonary disease. These organisms are present in the soil in various geographic areas of the United States: *H. capsulatum* in the Mississippi and Ohio River valleys, *C. immitis* in desert areas of the Southwest, and *B. dermatitidis* in a poorly defined area extending beyond that of *H. capsulatum*. These infections should be considered in people in appropriate geographic areas, especially in those who are near activities that disturb the soil, such as construction or dirt bike riding, and in patients who do not respond to antibacterial antibiotics. Clinical presentation varies from an acute or chronic pneumonia to asymptomatic granulomas and hilar adenopathy.

*Pneumocystis pneumonia* (PCP) occurs in immunocompromised hosts, principally people with acquired immunodeficiency syndrome (AIDS) or malignancy. *Pneumocystis jiroveci* (previously known as *Pneumocystis carinii*) is one of the most common infections leading to a diagnosis of HIV infection and AIDS. Patients with pulmonary complaints should be questioned about HIV risk factors, and clinicians should search for signs of HIV-related immunosuppression, such as weight loss, lymphadenopathy, and oral thrush. PCP typically manifests subacutely with fatigue, exertional dyspnea, nonproductive cough, pleuritic chest pain, and fever.

*Mycobacterium tuberculosis* is a slow-growing bacterium transmitted between people by droplet nuclei produced from coughing and sneezing. *M. tuberculosis* survives within macrophages as a facultative intracellular parasite and may remain dormant in the body for many years. Active tuberculosis (TB) develops within 2 years of infection in approximately 5% of patients, and another 5% develop reactivation disease at some later time. Reactivation is more likely to occur in people with impaired cell-mediated immunity, such as patients with diabetes, renal failure, immunosuppressive therapy, malnutrition, or AIDS. Approximately one third of the world’s population is infected with *M. tuberculosis*. Approximately 8 million new cases of active disease develop annually, resulting in 3 million deaths worldwide. An estimated 10 to 15 million people in the United States (3-5% of the population) are infected with TB. Multidrug-resistant strains of *M. tuberculosis* are found in increasing numbers, especially among immigrants from Southeast Asia and AIDS patients.

**CLINICAL FEATURES**

ED evaluation should focus on establishing the diagnosis of pneumonia and determining the presence of epidemiologic and clinical features that would influence decisions regarding hospitalization and antibiotics. Key history includes character of symptoms, setting in which the pneumonia is acquired, geographic or animal exposures, and host factors that predispose to certain types of infections and are associated with outcome.

Pneumonia generally manifests as a cough productive of purulent sputum, shortness of breath, and fever. In most healthy older children and adults, the diagnosis can be reasonably excluded on the basis of history and physical examination, with suspected cases confirmed by chest radiography. The absence of any abnormalities in vital signs or chest auscultation substantially reduces the likelihood of pneumonia as demonstrated by radiography. No single isolated clinical finding, however, is highly reliable in establishing or excluding a diagnosis of pneumonia.[8]

Elder or debilitated patients with pneumonia often have nonspecific complaints, such as acute confusion or a deterioration of baseline function, without classic symptoms. Elder patients
are more likely to have advanced illness at the time of presentation and may have sepsis in the absence of a previous syndrome suggestive of pneumonia. Rarely, patients with lower lobe pneumonia have abdominal or back pain as a presenting symptom. The diagnosis may be more difficult in infants and small children who are unable to give an adequate history. Pneumonia may manifest in infants as a fever associated with irritability, tachypnea, tachycardia, intercostal retractions, nasal flaring, or grunting. Cough may be minimal or absent.

Pneumonia can be divided based on clinical patterns into typical pneumonia caused by pyogenic bacteria, such as *S. pneumoniae* or *H. influenzae*, and atypical pneumonia caused by organisms such as *Mycoplasma* and *Chlamydia* species. This division is artificial, and a clear differentiation between these two types of pneumonia on clinical grounds alone is impossible. Certain clinical factors are often said to be suggestive of atypical organisms. Factors studied prospectively and found not to help differentiate atypical pneumonias from those with pyogenic bacterial causes include gradual onset, viral prodrome, absence of rigor, nonproductive cough, lower degree of fever, absence of pleurisy or consolidation, normal leukocyte count, and an ill-defined infiltrate on a chest radiograph. Although it is impossible to determine with a high degree of certainty the specific cause of pneumonia without results of microbiologic or serologic tests, certain clinical factors suggest that a specific pathogen should be considered.

Patients with pneumococcal pneumonia usually appear acutely ill, and the classic presentation is the abrupt onset of a single shaking chill, followed by fever, cough productive of rust-colored sputum, and pleuritic chest pain. Patients with a history of asplenia, sickle cell disease, AIDS, multiple myeloma, or agammaglobulinemia are at increased risk of pneumococcal bacteremia and sepsis with high mortality rates. Adults with chronic lung disease who develop pneumonia caused by *H. influenzae* typically demonstrate an insidious worsening of baseline cough and sputum production, and bacteremia is rare. *K. pneumoniae* may cause severe pneumonia in elderly or debilitated patients. Sputum is often described as “currant jelly” because of the necrotizing, hemorrhagic nature of the infection. Abscess formation, empyema, and bacteremia are common with this organism, and mortality is high.

Atypical pneumonia is caused by organisms such as *M. pneumoniae*, *C. pneumoniae*, viruses, *Legionella* species, or rickettsiae such as *Coxiella burnetii*. Mycoplasmal infection usually begins as a flu-like illness with headache, malaise, fever, and nonproductive cough. Skin lesions, including maculopapular, vesicular, urticarial, or erythema multiforme-type rashes, are common, especially in younger patients. Although bullous myringitis is described as a classic finding, it is not specific for mycoplasmal infection and is present in only a few cases. Patients generally do not have a toxic appearance, and most can be treated as outpatients. Although mucopurulent sputum generally indicates the presence of pyogenic bacterial pneumonia or bronchitis, it may also be present with mycoplasmal or viral pneumonia. Viral pneumonia in adults is often preceded by symptoms of upper respiratory infection, such as rhinitis or sore throat. Most *C. pneumoniae* infections in young adults cause a minor, self-limited upper respiratory illness that is subacute in onset. This organism is also associated with bronchitis, wheezing, sinusitis, and pharyngitis. Development of radiographically evident pneumonia is more common in the elderly. Some patients with *Legionella* infection have a mild, self-limited atypical pneumonia presentation. Older patients, smokers, and those with chronic disease or immunosuppression are more prone to develop the more acute and severe systemic illness of legionnaires’ disease. Gastrointestinal symptoms, such as diarrhea and abdominal cramping, confusion, and muscle aches are sometimes prominent.

In addition to age, the presence of underlying illness, and presenting symptoms, the setting of acquisition of pneumonia may provide clues to likely causes. CAP that occurs in otherwise healthy individuals is likely to be caused by viruses, *Mycoplasma* species, or *S. pneumoniae*. *S. aureus*, including MRSA, can cause severe pneumonia associated with influenza. Recently hospitalized and long-term care patients may develop pneumonia from agents that are uncommon in CAP, such as *Enterobacteriaceae*, *Pseudomonas aeruginosa*, and *S. aureus*. Healthy patients in an institutional setting, such as a dormitory or military barracks, are likely to have pneumonia caused by *Mycoplasma* species or viruses.

Patients with underlying lung disease, especially COPD, constitute an important group likely to develop pneumonia. The lower respiratory tract of these patients is commonly colonized with organisms such as *S. pneumoniae*, *H. influenzae*, and *Moraxella catarrhalis*. Cystic fibrosis patients are prone to pneumonia caused by *P. aeruginosa* or *S. aureus*. Defective mucociliary clearance in both of these groups makes them highly susceptible to repeated episodes of pneumonia.

Patients with immunosuppression as a result of hematologic malignancy, patients receiving chemotherapy for malignancy, and transplant recipients are prone to pulmonary infections with a wide variety of organisms. In addition to the usual pathogens, these patients may develop pneumonia secondary to viruses such as cytomegalovirus (CMV), varicella, or herpes simplex virus. They are also more likely to develop pneumonia caused by aerobic gram-negative bacilli, *Aspergillus* and geographic fungi, and *P. jiroveci*.

Although the use of highly active antiretroviral therapy (HAART) has decreased the incidence of opportunistic infections among HIV-infected patients, individuals who are not under regular care often come to the ED. In addition to *P. jiroveci*, there is also an increased incidence of *M. tuberculosis* and common bacterial pathogens such as *S. pneumoniae*. Other less common causes of pneumonia in HIV-infected patients include *Mycobacterium avium* complex, CMV, aerobic gram-negative bacilli, *Cryptococcus neoformans*, and *Rhodococcus equi*. PCP usually has a subacute presentation characterized by nonproductive cough, exertional dyspnea, and weight loss. Tachypnea and tachycardia are usually present. Hypoxemia, hypocapnia, and an increased arterial-alveolar oxygenation gradient are usually present.

The potential for opportunistic pulmonary infection can be predicted by a recent absolute CD4 lymphocyte count less than 200/mm^3^. This count is often known by patients with recognized HIV infection or may be surmised by a peripheral total lymphocyte count less than 1000/mm^3^ in patients who do not know their HIV status, the presence of findings such as weight loss, hairy leukoplakia, and oral candidiasis strongly suggests immunosuppression.

Patients in nursing homes or other extended-care facilities are at increased risk for infection with resistant organisms such as *P. aeruginosa*, *K. pneumoniae* (including strains producing extended-spectrum β-lactamases), *Acinetobacter* species, and hospital-associated strains of MRSA. Other risk factors for infection with multidrug-resistant pathogens include (1) hospitalization for 2 or more days in an acute care facility within 90 days of infection; (2) attendance at a hemodialysis clinic; and (3) intravenous antibiotic therapy, chemotherapy, or wound care within 30 days of infection. Any patient with pneumonia in whom any one of these historical features is present, including patients from a nursing home or long-term care facility, is designated as having health care–associated pneumonia (HCAP). HCAP is associated with a greater likelihood of resistant pathogens such as *Pseudomonas* and MRSA, and mortality is higher than that for CAP.\(^\text{12}\)
An interstitial pattern on a chest radiograph (Fig. 76-2) typically is caused by *Mycoplasma* species, viruses, or *P. jiroveci*. The classic radiographic findings in PCP are bilateral interstitial infiltrates that begin in the perihilar region (Fig. 76-3). Radiographic manifestations of PCP can vary considerably, including normal appearance and lobar infiltrates, pleural effusions, hilar

**Figure 76-1.** Posteroanterior chest radiograph reveals a left upper lobe pneumonia. A variety of organisms can produce this pattern, most commonly *Streptococcus pneumoniae*, *Haemophilus influenzae*, or gram-negative bacilli, but also *Chlamydophila pneumoniae*, *Mycoplasma*, or *Legionella* species.

**Figure 76-2.** Posteroanterior chest radiograph reveals patchy interstitial infiltrates. Viruses and *Mycoplasma* are the most likely causes in an otherwise healthy patient, but many bacterial organisms may also produce this pattern.
Cavitation also may be present in fungal disease or TB and with noninfectious processes (e.g., malignancy and pulmonary vascular disease). Pneumatoceles or spontaneous pneumothorax may be seen in AIDS patients with PCP. Pleural effusions occur with a wide variety of organisms, including many types of pyogenic bacterial pneumonias, Chlamydophila species, Legionella species, and TB. Anaerobic infections associated with an effusion are especially prone to development of empyema. The diagnosis and aspiration of pleural effusions can be aided by use of ED bedside ultrasonography.

Radiographic findings are nonspecific for predicting a particular infectious cause. Mycoplasma pneumonia may manifest as a dense infiltrate, or pneumococcal pneumonia may manifest as a diffuse interstitial infiltrate. Immunocompromised patients are particularly prone to having atypical radiographic appearances.
Rarely, patients with a clinical picture strongly suggestive of pneumonia have a normal chest radiograph, and some are found to have an infiltrate within the next 24 to 48 hours. The absence of findings on a chest radiograph should not preclude the use of antimicrobial therapy in appropriate patients with a clinical diagnosis of pneumonia. Laboratory studies also are nonspecific for identifying the cause of pneumonia. Although the finding of a white blood cell (WBC) count greater than 15,000/mm³ increases the probability of the patient having a pyogenic bacterial cause rather than a viral or atypical cause, the predictive value of this finding depends on the stage of the illness and likely prevalences of various causes. This is neither sensitive nor specific enough to aid decisions regarding therapy in an individual patient. A WBC count may be helpful if it yields evidence of immunosuppression, such as neutropenia, or if it reveals lymphopenia that may indicate immunosuppression from AIDS. Basic metabolic panels may help identify patients with renal or hepatic dysfunction or metabolic acidosis associated with sepsis. These findings predict a complicated course and influence decisions regarding disposition, choice of antimicrobial agents, and dosages. Serum lactate dehydrogenase is significantly elevated in AIDS patients with PCP compared with patients with non-PCP pneumonia. Inflammatory markers such as erythrocyte sedimentation rate and C-reactive protein are not helpful in clinical decision-making regarding pneumonia. Procalcitonin level has been suggested as a means to assess likelihood of bacterial cause, response to antimicrobial therapy, and prognosis in pneumonia. Its utility in the ED to assess need for hospitalization or ICU admission compared with other risk-stratification systems (see later) has not been validated.

Assessment of respiratory function with pulse oximetry is important in evaluation of patients with pneumonia because clinical assessment of oxygenation can be inaccurate. Pulse oximetry should be performed in any patient suspected to have pneumonia, and pneumonia should be considered in patients with a low oxygen saturation.

Sputum Gram’s stain rarely results in a change in therapy or outcome. Correlation between identification of pneumococcus on Gram’s stain and sputum culture results is poor, even when commonly used criteria for an adequate sputum specimen (fewer than five squamous epithelial cells and more than 25 WBCs per high-power field) are applied. Gram’s stains are even less likely to show gram-negative pathogens, such as H. influenzae, and should not be relied on to rule out a gram-negative cause. Empirical antimicrobial agents are usually highly clinically effective if chosen based on clinical information without sputum analysis. Guidelines for management of CAP from the Infectious Diseases Society of America (IDSA) and American Thoracic Society (ATS) support limiting sputum Gram’s stain and culture to those patients with more severe disease or risk factors for unusual pathogens. Confirmation of the diagnosis of PCP requires sputum induction and staining and, in some cases, further invasive procedures, such as bronchoscopy with bronchoalveolar lavage or biopsy.

Routine blood cultures are of essentially no value in nonimmunocompromised adults with pneumonia, in whom there is a very low prevalence of bacteremia, and management is rarely changed based on the results. Follow-up of false-positive blood cultures is costly and labor-intensive and may lead to unnecessary use of antibiotics such as vancomycin or linezolid when contaminant growth is initially reported as gram-positive cocci. Blood cultures should be obtained from immunocompromised patients, those with severe sepsis or shock, or those with risk factors for endovascular infection (e.g., prosthetic valves, intravenous drug use, or cavitary infiltrates). When culture specimens are drawn, they should be obtained before the initiation of antibiotics (although antibiotics should not be delayed for this reason).

Patients with a pleural effusion greater than 5 cm on lateral upright posterior-anterior chest radiograph should undergo diagnostic thoracentesis, with fluid sent for cell count, differential, pH (pH below 7.2 predicts the need for a thoracostomy tube), Gram’s stain, and culture. For most patients, thoracentesis can be safely deferred until after hospital admission. Patients in significant respiratory distress, however, or with evidence of tension and mediastinal shift require emergent diagnostic and therapeutic thoracentesis.

Serologic tests are available for the diagnosis of many organisms, including C. pneumoniae, Legionella species, and fungi. The use of serologic tests to determine the cause of pneumonia may be helpful retrospectively, but they usually require acute and convalescent serum titers and are of little use in the ED. Urine antigen tests for S. pneumoniae and Legionella are available, and in some facilities results can be obtained within the time frame of an ED evaluation. It is not clear, however, that a positive result should prompt a change in empirical treatment. Rapid diagnostic tests for viral antigens are available for several viruses, including respiratory syncytial virus (RSV) and influenza. These tests may be useful for infection control decisions in hospitalized patients, and they may provide an indication for influenza therapy and family prophylaxis. Some commercially available rapid influenza tests are insensitive for certain strains, notably the 2009 pandemic H1N1 strain. Rapid testing for respiratory viruses (i.e., RSV, influenza A including the H1 subtype, influenza B, metapneumovirus, adenovirus, and entero-rhinovirus) with use of technology such as the polymerase chain reaction may become increasingly available to emergency physicians to determine the specific cause of pneumonia.

**Differential Diagnosis Considerations**

Differentiation between upper and lower respiratory tract infections may be difficult. A chest radiograph helps differentiate between upper respiratory tract infection or bronchitis and pneumonia, but it is probably unnecessary for all patients with cough and sputum production unless other factors are present that suggest the possibility of pneumonia or obscure its clinical diagnosis (e.g., toxic appearance, extremes of age, underlying illness, and abnormal chest examination).

Many noninfectious conditions may result in inflammatory lung processes, including exposure to mineral dusts (e.g., silicosis), chemical fumes (e.g., chlorine and ammonia), toxic drugs (e.g., bleomycin), radiation, thermal injury, or oxygen toxicity. Immunologic diseases (e.g., sarcoidosis, Goodpasture’s syndrome, and collagen vascular disease) or hypersensitivity to environmental agents (e.g., farmer’s lung disease) may also result in pneumonia. Tumors may be confused with pneumonia radiographically or may appear initially as a postobstructive infection or adenopathy with peripheral infiltrates. Lymphangitic spread of lung malignancy may resemble interstitial pneumonia.

**Aspiration**

It is important to distinguish between the acute aspiration of gastric contents or other liquids and bacterial pneumonia that may develop later as a complication of aspiration. Aspiration of liquids into the lung disrupts surfactant and causes an inflammatory response that may lead to hypoxia and respiratory failure. Aspiration of acidic gastric contents is particularly damaging to lungs and is common in patients who are unconscious from intoxication or anesthesia or who have neurologic deficits. Patients may initially have coughing or shortness of breath or may appear well initially and then develop respiratory dysfunction during the next several hours.

Acute aspiration of acidic fluid into the lungs may produce fever, leukocytosis, purulent sputum, and radiographic infiltrates.
that mimic bacterial pneumonia. Although many such patients go on to develop bacterial pneumonia, prophylactic administration of antibiotics is controversial.\textsuperscript{19} Antibiotics should be initiated if the patient develops signs of bacterial pneumonia, including new fever, expanding infiltrate appearing more than 36 hours after aspiration, or unexplained deterioration. Systemic corticosteroids for acute aspiration are of no benefit.

**MANAGEMENT**

The possibility of communicable disease should suggest early isolation.\textsuperscript{20} Patients with a history of TB exposure or suggestive symptoms (e.g., persistent cough, weight loss, night sweats, and hemoptysis) or who belong to a group at high risk for TB (e.g., homeless, intravenous drug user, alcoholic, HIV risk, and immigrant from high-risk area) should be given a mask and placed in respiratory isolation before evaluation, including chest radiography.\textsuperscript{21} Because AIDS patients with pulmonary TB cannot be distinguished reliably from AIDS patients with other pulmonary infections at presentation, TB should be considered in all HIV-infected patients with respiratory complaints, and respiratory isolation should be initiated. EDs that frequently care for patients at risk for TB should consider triage protocols to identify these individuals rapidly before patients, visitors, or staff are unnecessarily exposed. Suspected infection with organisms transmitted by respiratory droplet (e.g., influenza) should prompt infection control precautions such as a mask being placed on the patient.

Antimicrobials should be administered in the ED for patients who are being admitted to the hospital. Timely administration of antimicrobials is associated with improved outcomes for hospitalized pneumonia patients,\textsuperscript{22} although confounding factors limit a full understanding of this relationship. A rush to treatment without a diagnosis of pneumonia, however, can result in inappropriate antibiotic use. Although the Centers for Medicare and Medicaid Services have used specific time cutoffs for blood culture and antibiotic administration as a quality measure, the evidence that antibiotic delay on the order of hours is significantly deleterious is weak, and the IDSA/ATS guidelines for management of pneumonia do not recommend use of a specific time threshold. Any presumed benefit of early antibiotic administration should be weighed against the risk of inappropriate use for cases in which the diagnosis is unclear. The antibiotics selected should cover the likely causes based on clinical, laboratory, radiologic, and epidemiologic information. The regimen should also be as selective as possible to avoid drug toxicity, emergence of resistance to broad-spectrum agents, and excessive cost.

The prevalence of drug-resistant \textit{S. pneumoniae} (DRSP) is increasing. In most areas of the United States, high-level penicillin resistance occurs in approximately 15 to 20% of outpatient pneumococcal sputum isolates. DRSP that is resistant to penicillin is usually resistant to other \(\beta\)-lactams, macrolides, tetracyclines, and trimethoprim-sulfamethoxazole (TMP-SMX). Extended-spectrum or “respiratory” fluoroquinolones, such as levofloxacin and moxifloxacin, are active against DRSP and other typical and atypical bacterial pathogens. Because oral bioavailability of fluoroquinolones is high, oral therapy provides serum and tissue levels essentially equivalent to parenteral therapy. It is not clear, however, the extent to which in vitro resistance is related to adverse clinical outcome. Most cephalosporins and macrolides achieve adequate levels in serum and tissues to successfully treat \textit{S. pneumoniae} respiratory tract infections, even if the laboratory reports that the organism is resistant.

CA-MRSA is the most common pathogen isolated in community-acquired skin and soft tissue infections. It causes severe, rapidly progressing pneumonia with sepsis, often in children or healthy young adults with influenza.\textsuperscript{23} CA-MRSA remains an uncommon cause of CAP in the United States,\textsuperscript{3} but empirical coverage of MRSA should be strongly considered for patients with severe pneumonia associated with sepsis,\textsuperscript{24} especially those with a presumed influenza infection, contact with someone infected with MRSA, or radiographic evidence of necrotizing pneumonia. Antimicrobials with consistent in vitro activity against CA-MRSA isolates include vancomycin, TMP-SMX, daptomycin, tigecycline, linezolid, and ceftaroline. Although vancomycin is used most often for documented MRSA infections, vancomycin may be losing efficacy in light of increasing minimum inhibitory concentrations. Daptomycin is inactivated by pulmonary surfactant and consequently is not indicated for pneumonia.

**Table 76-1**

<table>
<thead>
<tr>
<th>CLINICAL SETTING</th>
<th>ANTIBIOTIC REGIMEN*</th>
<th>COMMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Previously healthy, no antimicrobials in last 3 mo</td>
<td>Doxycycline 100 mg PO bid</td>
<td>Preferred for adolescent or young adult when likelihood of \textit{Mycoplasma} is high; variable activity vs. \textit{Streptococcus pneumoniae}.</td>
</tr>
<tr>
<td>Azithromycin 500 mg once, followed by 250 mg daily for 4 days</td>
<td>Treats common typical bacterial and atypical pathogens. Clarithromycin can be substituted.</td>
<td></td>
</tr>
<tr>
<td>Comorbidities, or antimicrobials in last 3 mo</td>
<td>Levofloxacin 750 mg PO daily for 5 days</td>
<td>Can substitute moxifloxacin 400 mg daily for 7-14 days.</td>
</tr>
<tr>
<td>Cefpodoxime 200 mg PO bid + azithromycin 500 mg PO daily</td>
<td>Treats common typical and atypical bacterial pathogens; active vs. DRSP. Use fluoroquinolone if recently received (\beta)-lactam or macrolide. Use if fluoroquinolones recently received. Can substitute cefdinir, cefprozil, or amoxicillin-clavulanate for cefpodoxime. Variable activity against DRSP.</td>
<td></td>
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</tbody>
</table>

DRSP, drug-resistant \textit{S. pneumoniae}; PO, orally.

* Doses are for 70-kg adult with normal renal and hepatic function.
β-lactam agent, such as ceftriaxone 1 g intravenously (IV) q24h (or cefotaxime, ceftepime, ampicillin-sulbactam, or ertapenem), plus a macrolide (e.g., intravenous or oral azithromycin 500 mg daily) is the preferred regimen. Alternatively, an extended-spectrum fluoroquinolone (levofloxacin or moxifloxacin) can be given as monotherapy, but this regimen may be more likely to promote antimicrobial resistance. Fluoroquinolones have some activity against TB and should be avoided in patients for whom TB is a possible cause, owing to risk of obscuring the correct diagnosis and selection of resistant TB. These regimens treat the most common bacterial pathogens, such as S. pneumoniae, and H. influenzae, and atypical pathogens, such as Mycoplasma, Chlamydophila, and Legionella species A regimen with activity against atypical pathogens is recommended by IDSA/ATS guidelines, but studies do not clearly demonstrate better outcomes in hospitalized patients compared with regimens without atypical activity.26 Intravenous azithromycin alone may be an option for patients with milder illness who are unlikely to be bacteremic; it does not achieve significant serum levels and lacks significant activity against many aerobic gram-negative bacilli and DRSP. If anaerobic organisms are suspected (e.g., aspiration), clindamycin or metronidazole could be added to the regimen, or the regimen could include an antibiotic with anaerobic activity, such as ertapenem, ampicillin-sulbactam, piperacillin-tazobactam, tigecycline, or moxifloxacin (Table 76-2).

<table>
<thead>
<tr>
<th>CLINICAL SETTING</th>
<th>ANTIBIOTIC REGIMEN*</th>
<th>COMMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Community-acquired, nonimmunocompromised</td>
<td>Ceftriaxone 1 g q24h + azithromycin 500 mg q24h IV or PO</td>
<td>Can substitute cefotaxime, ceftriazone, ampicillin-sulbactam, or ertapenem for ceftriaxone. Treats most common bacterial and atypical pathogens. Active vs. DRSP.</td>
</tr>
<tr>
<td>Respiratory fluoroquinolone (levofloxacin 750 mg IV q24h or moxifloxacin 400 mg IV q24h)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe pneumonia (ICU)</td>
<td>Ceftriaxone 1 g IV q24h + levofloxacin 750 mg IV q24h + vancomycin 1 g IV q12h</td>
<td>Can substitute cefotaxime, cefepime, ceftriazone, ertapenem, or β-lactam or β-lactamase inhibitor for ceftriaxone. Can substitute moxifloxacin for levofloxacin. Can substitute linezolid for vancomycin.</td>
</tr>
<tr>
<td>Health care–associated pneumonia or severe pneumonia with neutropenia, bronchiectasis (risk for Pseudomonas)</td>
<td>Cefepime 2g IV q12h + ciprofloxacin 500 mg IV q12h + vancomycin 1 g IV q12h</td>
<td>Can substitute other antipseudomonal β-lactam, such as piperacillin-tazobactam, imipenem, meropenem, or doripenem, for cefepime. Can substitute aminoglycoside plus macrolide for ciprofloxacin.</td>
</tr>
<tr>
<td>Presumed PCP</td>
<td>TMP-SMX 240/1200 mg IV q6h</td>
<td>Add ceftriaxone to TMP-SMX if severe, until PCP confirmed. Alternatives for sulfa allergy include clindamycin + primaquine.</td>
</tr>
</tbody>
</table>

DRSP: drug-resistant S. pneumoniae; ICU, intensive care unit; IV, intravenously; PCP, Pneumocystis pneumonia; PO, orally; TMP-SMX, trimethoprim-sulfamethoxazole.

*Doses are for a 70-kg adult with normal renal and hepatic function.

Because HCAP is associated with higher mortality and a greater likelihood of unusual pathogens, the use of broader-spectrum empirical therapy is appropriate, usually with a combination of antimicrobials to increase the chance that at least one antibiotic will be active against the causative pathogen. Appropriate combinations include an antipseudomonal β-lactam agent, such as piperacillin-tazobactam, cefepime, imipenem, or meropenem, with either an aminoglycoside or a fluoroquinolone and vancomycin or linezolid may be considered. The regimen should also cover atypical pathogens and gram-negative bacilli.

For patients with AIDS, it is important to treat P. jiroveci and bacterial pathogens such as S. pneumoniae. TMP-SMX is the treatment of choice; the usual regimen is 15 mg/kg of TMP and 75 mg/kg of SMX daily in four divided doses, to be continued for 21 days, in addition to a regimen to cover CAP organisms.20 For most adult patients a regimen of three amuples (80 mg of TMP and 400 mg of SMX per amuple) every 6 hours is appropriate. For patients allergic to sulfa, options include clindamycin 600 mg IV every 8 hours plus primaquine 30 mg PO daily. The addition of corticosteroids (prednisone 40 mg PO twice daily) reduces mortality and clinical deterioration in patients with partial arterial oxygen tension (Pao₂) less than 70 mm Hg or alveolar-arterial gradient greater than 35 mm Hg. Mycoplasma, Legionella, and Chlamydophila species are uncommon causes of severe pneumonia in AIDS patients, so empirical therapy with erythromycin or doxycycline is not routinely recommended.

Moderately ill patients for whom hospitalization might be considered can be treated with an initial parenteral dose of a long-acting antibiotic, such as ceftriaxone, and observed (e.g., 12-24 hours) while supportive care, such as hydration, antipyretics, and bronchodilators, is administered, before discharge on an oral regimen. Patients at higher risk for deterioration (e.g., comorbidities, borderline hypoxia) may be brought back to the ED for follow-up in 24 hours and receive a second parenteral or observed oral dose of antibiotics. An extended-spectrum fluoroquinolone (oral or parenteral) is another option that may be
advantageous because of additional activity against atypical pathogens and DRSP.

CAP guidelines recommend a 7- to 10-day duration of antimicrobial treatment and further indicate that antibiotic discontinuation can be considered in a patient who is afebrile for 48 to 72 hours. Levofoxacin 750 mg daily and azithromycin are approved as a 5-day course for CAP.

Patients with influenza may benefit from antiviral treatment as described in Chapter 130.

**DISPOSITION**

There is tremendous variability in physician admission decisions for pneumonia. The more common tendency is overestimation of disease severity, leading to hospitalization of patients at low risk for death or serious complications. The decision to hospitalize a patient with pneumonia does not necessarily mean that a prolonged inpatient stay is required. Observation for 12 to 24 hours in the ED observation unit or hospital may allow the early discharge of certain moderate-risk patients. Inpatient treatment of pneumonia is 15 to 20 times more expensive per patient than outpatient treatment, and most patients are more comfortable in a home environment.

Although no firm guidelines exist regarding hospital admission, scoring systems may assist with hospitalization decisions. One commonly used system is based on the Pneumonia Outcomes Research Team study, a prospectively validated predictive rule for mortality among immunocompetent adults with CAP. This model (also known as the Pneumonia Severity Index [PSI]) suggests a two-step approach to assess risk. Patients in the lowest risk class who are recommended for outpatient management are those younger than 50 years, without significant comorbid conditions (neoplasm, congestive heart failure, cerebrovascular disease, renal disease, liver disease, or HIV), and without the following findings on physical examination: altered mental status, pulse 125 beats/min or greater, respiratory rate 30 breaths/min or greater, systolic blood pressure less than 90 mm Hg, or temperature less than 35°C or greater patients who do not fit the lowest risk category are classified into categories based on a scoring system that accounts for age, comorbid illness, physical examination findings, and laboratory abnormalities (Table 76-3). Hospitalization is recommended for patients with a score greater than 91, and brief admission or observation may be considered for patients with a score of 71 to 90. Although this method of assessing the likelihood of successful outpatient management is helpful, it can be cumbersome, is not modeled to predict acute life-threatening events, does not take into account dynamic evaluation over time, and has many important exceptions (e.g., an otherwise low-risk patient with severe hypoxia would be discharged by strict interpretation of this rule). Clinical judgment should supersede a strict interpretation of this scoring system. A study in which physicians were educated, however, and provided the patient’s risk score revealed a significantly lower overall admission rate, cost savings, and similar quality-of-life scores compared with those for patients conventionally managed by their physicians. Additional discharge criteria include improving and stable vital signs over a several-hour observation period, ability to take oral medications, an ambulatory pulse oximetry greater than 90%, home support, and access to follow-up.

A simpler tool is the CURB-65 rule. This rule uses only five simple criteria to determine patients at lower risk for adverse events: confusion, uremia (blood urea nitrogen >20 mg/dL), respiratory rate greater than 30, blood pressure less than 90 systolic or less than 60 diastolic, and age 65 years or greater. The risk of 30-day mortality increases with a greater number of these factors present: 0.7% with zero factors, 9.2% with two factors, and 57% with five factors. Patients with zero or one feature can receive outpatient care, those with two should be admitted, and ICU care should be considered for those with three or more. No randomized trials of hospital admission strategies directly compare the PSI with the CURB-65 score. In a comparison of scores in the same population of CAP patients, the PSI yields a slightly higher percentage of patients in the low-risk category, with a similar low mortality rate.

The decision to admit a patient to the ICU is straightforward when patients are intubated or require vasopressors. It is more difficult to identify patients who do not require these interventions initially but may be at greater risk for deterioration and require a level of monitoring that may be beyond that available on the typical hospital ward. Objective criteria using the PSI (class V) and CURB-65 have been proposed but are not prospectively validated for the ICU admission decision. When similar criteria were retrospectively studied in a cohort of CAP patients, they did not perform better than actual physician decisions. IDSA/ATS guidelines include criteria for defining severe CAP (Box 76-1), but these have not been validated. An ICU risk-stratification score is abbreviated SMART COP; intensive respiratory or vasopressor support is predicted by low systolic blood pressure (2 points), multilobar chest radiography involvement (1 point), low albumin level (1 point), high respiratory rate (1 point), tachycardia (1 point), confusion (1 point), poor oxygenation (2 points), and low arterial pH (2 points). A SMART-COP score above 3 points identified 92% of patients who received intensive respiratory or vasopressor support, including 84% of patients who did not need immediate admission to the ICU. The decision to admit a patient to the hospital largely reflects the potential for acute deterioration, and some rate of floor to ICU transfer is inevitable.

Most patients with CAP do not need respiratory isolation. Patients who could pose a threat of transmission to other patients (e.g., influenza, varicella, TB, and plague) should be isolated. Neutropenic patients generally are placed in reverse isolation.

### Table 76-3 Scoring System for Pneumonia Mortality Prediction

<table>
<thead>
<tr>
<th>PATIENT CHARACTERISTICS</th>
<th>POINTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographic factor</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>No. years of age</td>
</tr>
<tr>
<td>Female</td>
<td>No. years of age – 10</td>
</tr>
<tr>
<td>Nursing home resident</td>
<td>10</td>
</tr>
<tr>
<td>Comorbid illness</td>
<td></td>
</tr>
<tr>
<td>Neoplastic disease</td>
<td>30</td>
</tr>
<tr>
<td>Liver disease</td>
<td>20</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>10</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>10</td>
</tr>
<tr>
<td>Renal disease</td>
<td>10</td>
</tr>
<tr>
<td>Physical examination finding</td>
<td></td>
</tr>
<tr>
<td>Altered mental status</td>
<td>20</td>
</tr>
<tr>
<td>Respiratory rate &gt;30</td>
<td>20</td>
</tr>
<tr>
<td>Systolic blood pressure &lt;90 mm Hg</td>
<td>20</td>
</tr>
<tr>
<td>Temperature &lt;35°C or &gt;40°C</td>
<td>15</td>
</tr>
<tr>
<td>Pulse &gt;125 beats/min</td>
<td>10</td>
</tr>
<tr>
<td>Laboratory or radiographic finding</td>
<td></td>
</tr>
<tr>
<td>Arterial pH &lt;7.35</td>
<td>30</td>
</tr>
<tr>
<td>Blood urea nitrogen &gt;30mg/dL</td>
<td>20</td>
</tr>
<tr>
<td>Sodium &lt;130 mEq/L</td>
<td>20</td>
</tr>
<tr>
<td>Glucose &gt;250 mg/dL</td>
<td>10</td>
</tr>
<tr>
<td>Hematocrit &lt;30%</td>
<td>10</td>
</tr>
<tr>
<td>Arterial Po2 &lt;60 mm Hg</td>
<td>10</td>
</tr>
<tr>
<td>Pleural effusion</td>
<td>10</td>
</tr>
</tbody>
</table>

Empirical antimicrobial therapy should be started in the ED for patients admitted with pneumonia. Empirical therapy should treat the most likely pathogens, including *S. pneumoniae*, *H. influenzae*, *M. pneumoniae*, and *C. pneumoniae*, and should be consistent with current national treatment guidelines, such as those from the IDSA. HIV or other immunosuppressive conditions should be considered in all patients in whom pneumonia is suspected. The disposition of patients with pneumonia is dictated by the patient’s underlying medical conditions, the severity of illness and likelihood of clinical deterioration, and the feasibility of home care and outpatient follow-up. *Mycoplasma pneumoniae* may manifest as a dense infiltrate, and pneumococcal pneumonia may manifest as a diffuse interstitial infiltrate.

HIV-infected patients with pneumonia should be isolated until TB status can be evaluated via sputum acid-fast bacilli smears; this is particularly true for patients with other risk factors for TB. The chest radiograph cannot exclude TB in AIDS patients because it often does not have the typical appearance of TB. Isolation should be strongly considered for others at high risk for TB, such as inner-city homeless people and intravenous drug users.
References