Pulmonary infections span a wide spectrum, ranging from self-limited processes to life-threatening infections and from acute illnesses to chronic inflammatory diseases. This chapter details the pathophysiology, epidemiology, general features, and treatment of pulmonary infections, particularly bacterial pneumonia, and discusses the diagnosis and treatment of Legionnaires disease, chlamydial pneumonia, and aspiration pneumonia [see Table 1].

Pneumonia

Although overall hospitalization rates are declining, hospitalizations for acute lower respiratory tract infections have increased steadily since 1980. \(^1\) Taken together, pneumonia and influenza rank as the sixth leading cause of death in the United States and lead all other infectious diseases in this respect. Antibiotics have greatly modified the natural history of pneumonia and have sharply reduced the overall case-fatality rate. At the same time, the widespread use of antimicrobial agents has led to the emergence of drug-resistant strains, thereby altering and expanding the range of pathogens responsible for pneumonia, especially in hospitalized patients. The growing population of patients with chronic obstructive pulmonary disease (COPD) and other debilitating illnesses and the use of respiratory therapy and immunosuppressive drugs have contributed to the increasing incidence of nosocomial and opportunistic pneumonias, which have a very high mortality.

Pathophysiology

Host Defense Mechanisms

The lung is normally sterile. In healthy people, an intricate series of defense mechanisms maintain that sterility in the face of heavy bacterial colonization of the upper respiratory tract, inhalation of thousands of bacteria in droplet nuclei each day, and nearly universal aspiration of upper airway secretions during normal sleep each night.\(^2,3\) Defects in host defense mechanisms account for most cases of pneumonia [see Table 2].

Transmission of Organisms to Lungs

Inhalation of aerosolized droplets accounts for the transmission of respiratory viruses, such as influenza, which is highly contagious and often occurs in epidemics. Similar means of spread produce pneumonias caused by other nonbacterial agents, including mycoplasmas that are transmitted from person to person and cause primary atypical pneumonia, rickettsias that are transmitted from livestock and cause Q fever, and chlamydiae that are transmitted from birds (Chlamydia psittaci) or humans (C. pneumoniae). Mycobacterium tuberculosis is spread from person to person by aerosolized droplets. The organisms that are responsible for causing the systemic mycoses are probably inhaled from sources in nature. Among bacteria that cause pneumonia, Legionella pneumophila is the species most likely to be spread by inhalation of aerosolized organisms that originate in contaminated freshwater.

Pneumococci are spread from person to person by aerosolized droplets, but pneumococcal pneumonia is not highly contagious and is caused in many cases by aspiration of nasopharyngeal organisms, the second major mechanism of infection. Aspiration of nasopharyngeal organisms occurs in nearly all persons during sleep and is probably responsible for most bacterial pneumonias, including staphylococcal and gram-negative bacillary pneumonias; it certainly accounts for the necrotizing pneumonitis that results from the aspiration of mixed mouth flora.

Hematogenous seeding, the third and least common mechanism that causes pneumonia, accounts for occasional cases of staphylococcal pneumonia in patients with tricuspid valve endocarditis or septic thrombophlebitis. This mechanism is also responsible for various gram-negative bacillary pneumonias in patients with bacteremia.

Tissue Responses

Once organisms succeed in bypassing host defense mechanisms to arrive at the alveoli, a variety of tissue responses may ensue, depending on the nature of the pathogen and the integrity of the host inflammatory response. Although the inflammatory response is essential for the control of infection, it can produce tissue damage, impair ciliary action, and impede phagocytosis.\(^3\)

The inflammatory response to Streptococcus pneumoniae or Haemophilus influenzae often produces lobar consolidation, but tissue necrosis is rarely present. In contrast, staphylococci and many gram-negative bacilli often produce necrosis, which can lead to cavitation and even frank abscess formation; a peri-bronchial distribution is characteristic, but lobar consolidation may occur. Viruses generally produce interstitial inflammation rather than air-space exudates. The infection is usually bilateral and causes diffuse alveolar damage and interstitial edema. Similar tissue responses may be initiated by Mycoplasma, Chlamydia, and Legionella species; by gram-negative bacteremia (shock lung); and by other causes of the acute respiratory distress syndrome. Mycobacteria and fungi typically evoke a slow granulomatous response.

Table 1  Major Causes of Pulmonary Infection

<table>
<thead>
<tr>
<th>Category</th>
<th>Common Causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gram-positive coccic</td>
<td>Streptococcus pneumoniae, S. pyogenes, other streptococci, staphylococci</td>
</tr>
<tr>
<td>Gram-positive bacilli</td>
<td>Bacillus anthracis</td>
</tr>
<tr>
<td>Gram-negative coccic</td>
<td>Neisseria meningitidis, Moraxella catarrhalis</td>
</tr>
<tr>
<td>Mixed flora (aspiration</td>
<td>Pneumonia)</td>
</tr>
<tr>
<td>Mycobacteria</td>
<td>Mycobacterium tuberculosis, M. avium complex</td>
</tr>
<tr>
<td>Fungi</td>
<td>Histoplasma, Coccidioides, Blastomyces, Cryptococcus, Cândida, Aspergillus, Mucoraceae</td>
</tr>
<tr>
<td>Parasites</td>
<td>Pneumocystis carinii, Toxoplasma gondii</td>
</tr>
<tr>
<td>Mycoplasmas</td>
<td>Mycoplasma pneumoniae</td>
</tr>
<tr>
<td>Chlamydiae</td>
<td>Chlamydia psittaci, C. trachomatis, C. pneumonia</td>
</tr>
<tr>
<td>Rickettsias</td>
<td>Coxiella burnetii</td>
</tr>
<tr>
<td>Viruses</td>
<td>Influenza virus, parainfluenza virus, adenovirus, respiratory syncytial virus, rhinovirus, measles virus, varicella-zoster virus, cytomegalovirus</td>
</tr>
</tbody>
</table>
Table 2 Host Defense Mechanisms

<table>
<thead>
<tr>
<th>Mechanism</th>
<th>Modifying Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal flora of upper respiratory tract</td>
<td>Antibiotic therapy, respiratory therapy, hospitalization</td>
</tr>
<tr>
<td>Aerodynamic properties of upper respiratory tract</td>
<td>Tracheal intubation</td>
</tr>
<tr>
<td>Protective reflexes (e.g., cough, sneeze, gag, bronchoconstrictor)</td>
<td>Sedatives and hypnotics, alcohol and drug abuse, neurologic disorders, age and debility, tracheal intubation (gastrointestinal disorders)</td>
</tr>
<tr>
<td>Mucous carpet that entraps particles</td>
<td>Viral infections, smoking, chemical irritants, dehydration</td>
</tr>
<tr>
<td>Ciliary action, mucociliary transport</td>
<td>Smoking, viral infections, advanced age, aspirin (?)</td>
</tr>
<tr>
<td>Antibacterial substances in respiratory secretions (e.g., lysozyme, lactoferrin, α-antitrypsin, IgA)</td>
<td>None</td>
</tr>
<tr>
<td>Fibronectin in respiratory secretions (competitively inhibits adherence of gram-negative bacilli)</td>
<td>Decreased fibronectin levels in seriously ill patients</td>
</tr>
<tr>
<td>Free drainage of tracheobronchial tree</td>
<td>Foreign bodies, obstructing tumors, bronchostenosis</td>
</tr>
<tr>
<td>Rich blood supply</td>
<td>Vascular obstruction (e.g., emboli)</td>
</tr>
<tr>
<td>Alveolar macrophages</td>
<td>Viral infections, smoking (both increase macrophage numbers but impair function)</td>
</tr>
<tr>
<td>Lymphatic tissue</td>
<td>Cytotoxic therapy</td>
</tr>
<tr>
<td>Humoral immunity (B cells, IgG and IgA antibodies, complement, polymorphonuclear neutrophils)</td>
<td>Immunosuppressive disorders and therapy</td>
</tr>
<tr>
<td>Cellular immunity (T cells, lymphokines, mononuclear phagocytes)</td>
<td>Immunosuppressive disorders and therapy</td>
</tr>
</tbody>
</table>

Epidemiology and Etiology

**Community-Acquired Pneumonias**

Like other respiratory tract illnesses, pneumonia is most common in the winter because of the seasonal increase in viral infections and the close contact of persons confined indoors. Community-acquired pneumonias are a major problem in the United States, with at least 924,000 cases reported annually. About 485,000 cases require hospitalization, and at least 50,000 result in death. The mortality of community-acquired pneumonia ranges from less than 1% in patients who are not ill enough to require hospitalization to 13.7% for hospitalized patients, 19.6% for bacteremic patients, and 36.5% for patients admitted to intensive care units. Clinical and laboratory data can be used to determine which patients are at greatest risk for death and thus require hospitalization and aggressive therapy. Comorbidity is the strongest risk factor, with neoplastic disease, neurologic disease, and alcoholism being particularly worrisome. Advanced age is another predictor of risk, in part because older patients often underreport symptoms. Physical findings of high fever, tachypnea, confusion, hypoxia, and hypotension also portend an adverse result. The presence of extensive radiographic abnormalities, especially bilateral pleural effusions, is associated with higher risk, as are laboratory abnormalities such as hypoxia, azotemia, acidosis, hypoproteinemia, and hypophosphatemia. Patients with post-obstructive, aspiration, gram-negative, or staphylococcal pneumonias have a high mortality; patients lacking these adverse prognostic indicators have a low risk of death and can usually be treated successfully as outpatients. Patients hospitalized for pneumonia have a greater than fivefold likelihood of requiring subsequent hospitalization for pneumonia than patients with other serious illnesses. In the preantibiotic era, pneumonia was nearly synonymous with *S. pneumoniae* infection. Pneumococci still account for 30% to 60% of all community-acquired pneumonias for which an etiology can be determined. Pneumococci are particularly likely to be responsible for community-acquired pneumonias severe enough to require hospitalization and for pneumonia in persons older than 60 years.

The second most common bacterial cause of community-acquired pneumonia is *H. influenzae*, which accounts for about 10% of cases; patients with COPD are particularly vulnerable. Although infection with *Moraxella catarrhalis* is much less common than infection with *H. influenzae*, it is being recognized increasingly as a cause of community-acquired pneumonia. Like *H. influenzae*, *M. catarrhalis* has a predilection for patients with cardiopulmonary disease. In rare cases, *M. catarrhalis* causes fulminating pneumonia, bacteremia, or both.

Staphylococci and gram-negative bacilli are much less common but more serious causes of community-acquired respiratory infections. Significant predisposing conditions are required for these organisms to produce pneumonia. In the community setting, staphylococcal pneumonia usually follows influenza. Gram-negative pneumonias in the community setting are most common in patients who have recently been hospitalized and treated with antibiotics, in smokers and others with chronic lung disease, and in immunosuppressed individuals. Exposure to aerosols of contaminated water is an additional risk factor for infection with *Pseudomonas aeruginosa* and alcoholism predisposes to *Klebsiella* pneumonia. Meningococcal pneumonia is rare. A variety of other bacteria, including *L. pneumophila*, can cause pneumonia in the community setting. Aspiration of mixed mouth flora is responsible for infection in some patients.

In about half the patients with community-acquired pneumonia, the etiologic agent cannot be identified. Nonbacterial (so-called atypical) agents are responsible for many of these infections, especially in younger patients. In a study of patients with a mean age of 41 years, for example, *M. pneumoniae* accounted for 22.8% of community-acquired pneumonias, *C. pneumoniae* for 10.7%, and *influenza A* for 2.7%. *C. pneumoniae* is also increasingly being recognized as a cause of community-acquired pneumonia in adults with COPD [see 14:13 Chronic Obstructive Diseases of the Lung]. Respiratory tract viruses, including respiratory syncytial virus, adenoviruses, and those that cause influenza or parainfluenza, can also cause community-acquired pneumonias in persons of all ages.

**Hospital-Acquired Pneumonias**

Pneumonia is the second most common nosocomial infection in the United States; about 200,000 cases occur annually, accounting for 17.8% of all hospital-acquired infections and 40,000 to 70,000 deaths. Risk factors for nosocomial infections include...
Pneumonias in Immunosuppressed Patients

Immunosuppressed patients, particularly those with AIDS, are vulnerable to a broad range of pulmonary pathogens. In addition to being susceptible to the many organisms that produce community- and hospital-acquired pneumonias, these patients are susceptible to many opportunistic microbes that are unlikely to cause pneumonia in immunologically competent hosts. Such organisms include bacteria (e.g., Pseudomonas, Nocardia, and Legionella species), mycobacteria (e.g., Mycobacterium avium complex), viruses (e.g., cytomegalovirus and herpesvirus), fungi (e.g., Candida, Aspergillus, and Mucor species), and protozoa (e.g., Pneumocystis carinii and Toxoplasma gondii). As a result, immunosuppressed patients require an aggressive approach to diagnosis and therapy [see 7X Infections Due to Haemophilus, Moraxella, Legionella, Bordetella, and Pseudomonas and 7:XI Infections Due to Brucella, Francisella, Yersinia pestis, and Bartonella].

Diagnosis

Clinical Features

Classic symptoms of pneumonia include cough, sputum production, chest pain, fever, chills, hypoxia, and dyspnea. Although physical examination of patients with typical pneumonias is often nonspecific, it may reveal rales, rhonchi, or bronchial breath sounds, as well as percussion dullness over the involved segments of the lung. Pleural effusions may accompany pneumonia. The chest x-ray reveals the presence of infiltrates.

Nonbacterial and bacterial pneumonias have differing clinical presentations. Although both types of pneumonia can affect persons of all ages, nonbacterial pneumonias are most common in older children and young adults. Patients with viral, mycoplasmal, or chlamydial pneumonias will often complain of a severe hacking cough, but substantial sputum production is unusual.

Patients with bacterial pneumonias are more likely to have copious sputum production—as well as an abrupt onset of illness, high temperatures, chills, and development of significant pleural effusions—than are patients with nonbacterial pneumonias.

On physical examination, the patient with bacterial pneumonia generally looks sicker than the patient with nonbacterial pneumonia, and chest examination of patients with bacterial pneumonia usually reveals signs of consolidation or at least localized rales and rhonchi. In contrast, the chest examination of patients with nonbacterial pneumonias typically shows only fine rales, and often, the physical findings are less extensive than the radiologic abnormalities.

Laboratory Studies

Patients with bacterial pneumonias are more likely to have polymorphonuclear leukocytosis. If the chest x-ray reveals lobar or segmental consolidation, abscess formation, or significant pleural effusion, bacterial pneumonia is more likely. A patchy infiltrate can occur in either process, but a true interstitial infiltrate suggests a nonbacterial etiology. Computed tomography is extremely helpful in patients with complex infections.

The sputum examination is central to the etiologic diagnosis of pneumonia. The sputum of patients with bacterial pneumonia is typically thick and either green or brownish and is sometimes blood tinged. A good sputum specimen for microscopic examination and culture is crucial. If the patient cannot expectorate spontaneously, pulmonary physiotherapy, intermittent positive pressure ventilation with humidified air, or nasotracheal suction may be used to obtain the specimen. The Gram stain of sputum from patients with bacterial pneumonia usually reveals abundant polymorphonuclear leukocytes and will often disclose the primary pathogens. Patients with nonbacterial pneumonias or Legionnaires disease generally produce only scant quantities of thin sputum. In influenza pneumonia, the sputum may be bloody. The Gram stain of sputum from patients with bacterial pneumonia reveals an absence of bacteria and a scant cellular response; in patients with mycoplasmal pneumonia, mononuclear cells may predominate. It can be difficult to determine the etiology in patients with nosocomial pneumonias; prolonged hospitalization, antibiotic administration, and ventilatory therapy predispose to colonization with organisms that contaminate sputum specimens but can also cause pneumonia. Bronchoalveolar lavage is effective in identifying the responsible pathogen.

Kits for the detection of nucleic acids from Legionella, Mycoplasma, and mycobacterial species in sputum are currently available, and similar tests may soon be available for the detection of other pathogens.

Invasive Studies

In immunocompromised patients, numerous opportunistic agents can cause pneumonia, and aggressive techniques may be
required to obtain a satisfactory specimen. Although invasive procedures rarely are necessary in immunocompetent patients, they may be required in patients who present with unusual features, are critically ill, or fail to respond to conventional therapy. Procedures such as transtracheal aspiration, bronchoscopy (sometimes including transbronchial biopsies), bronchial brushing, or percutaneous lung taps may be necessary [see 7:X Infec-
tions Due to Haemophilus, Moraxella, Legionella, Bordetella, and Pseudomonas]; bronchoalveolar lavage is a particularly useful technique and is generally well tolerated. If these less invasive techniques fail to produce a diagnosis, open lung biopsy should be considered.

Differential Diagnosis

Noninfectious diseases can be mistaken for infections of the respiratory tract. Asthmatic bronchitis and hypersensitivity pneumonitis are common examples. COPD, including emphysema and bronchiectasis, may be misleading if previous x-rays are not available. Atelectasis, pulmonary infarction, pulmonary edema, and lung tumors may also be confused with pneumonia. Hypersensitivity reactions and toxins—in the form of aerosols, systemic drugs, or chemicals—produce clinical illnesses and pulmonary infiltrates simulating those of infectious pneumonia. Radiation pneumonitis, sarcoidosis, vasculitis, uremic pneumonitis, pulmonary hemorrhage, eosinophilic pneumonia, organizing pneumonia, and lipoid pneumonitis are included in the differential diagnosis.

One of the primary considerations in patients with a lower respiratory tract infection is to distinguish between acute bronchitis and pneumonia. The distinction is anatomic rather than etiologic because the same basic range of organisms can cause the two syndromes. As a result, these conditions often overlap clinically, but bronchitis requires less intensive therapy [see Acute Bronchitis, below].

Treatment

Certain general principles are useful in the care of all patients with pneumonia. Adequate hydration is important to help clear secretions; hydration can be achieved by systemic administration of fluids and local airway humidification. Expectorants such as guaifenesin may be helpful in loosening the sputum. Although clinical trials have demonstrated that chest physiotherapy does not hasten the resolution of pneumonia, this traditional therapeutic modality may provide symptomatic benefit to patients with copious airway secretions. In general, the cough reflex should not be suppressed in patients with bacterial infections, because coughing is an important mechanism for clearing secretions. If severe paroxysms of coughing produce respiratory fatigue or harsh pain, however, temporary relief may be obtained with small doses of codeine. Chest pain should be treated with analgesics that do not suppress cough. If hypoxia is present, oxygen should be administered. Persons who have COPD and retain carbon dioxide must be monitored very closely because oxygen therapy can lead to respiratory depression.

Specific antimicrobial therapy depends on the etiologic agent. Whereas culture and sensitivity testing require at least 24 to 48 hours to provide definitive information, the clinical setting, chest x-ray, and sputum Gram stain usually enable the physician to make a reasonable presumptive diagnosis and to initiate therapy at once. Treatment can then be modified as necessary on the basis of culture results. Because antibiotics penetrate sputum by passive diffusion, it is important to maintain adequate blood levels of these drugs. The administration of antibiotics by aerosol is not indicated for most cases of pneumonia but may help patients with cystic fibrosis and endobronchial Pseudomonas infections.

It is best to choose an antibiotic regimen directed specifically at organisms seen on Gram stain and, after 24 to 48 hours, identified from sputum or blood cultures. Even if these data are lacking, however, a reasonable choice of initial antimicrobial therapy can be made on the basis of the patient’s epidemiologic setting and clinical features.

Community-Acquired Pneumonia

Several factors are responsible for rapid changes in the empirical treatment of community-acquired pneumonias: the emergence of drug-resistant pneumococci; the increasing population of elderly or chronically ill patients who are vulnerable to infections caused by H. influenzae and M. catarrhalis; the increased importance of atypical pathogens such as M. pneumoniae, C. pneumoniae, and L. pneumophila; and the availability of new fluoroquinolones with enhanced activity against gram-positive cocci (including penicillin-nonsensitive pneumococci) and anaerobes

<table>
<thead>
<tr>
<th>Table 3</th>
<th>Initial Antibiotic Therapy for Community-Acquired Pneumonia in Outpatients*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Drug</strong></td>
<td><strong>Typical Dose</strong></td>
</tr>
<tr>
<td>Fluroquinolones</td>
<td></td>
</tr>
<tr>
<td>Levofoxacin</td>
<td>500 mg p.o., q. 24 hr</td>
</tr>
<tr>
<td>Sparfloxacin</td>
<td>400 mg p.o. day 1, then 200 mg p.o., q. 24 hr</td>
</tr>
<tr>
<td>Gatifloxacin</td>
<td>400 mg p.o., q. 24 hr</td>
</tr>
<tr>
<td>Moxifloxacin</td>
<td>400 mg p.o., q. 24 hr</td>
</tr>
<tr>
<td>Macrolides</td>
<td></td>
</tr>
<tr>
<td>Erythromycin</td>
<td>250–500 mg p.o., q. 6 hr</td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>250–500 mg p.o., q. 12 hr</td>
</tr>
<tr>
<td>Azithromycin</td>
<td>500 mg p.o. day 1, then 250 mg p.o. days 2–5</td>
</tr>
<tr>
<td>Doxycycline</td>
<td>100 mg p.o., q. 12 hr</td>
</tr>
</tbody>
</table>

*See text for details.

†For details, see 7:XIV Chemotherapy of Infection (especially Tables 3 and 4).
GI—gastrointestinal
(including mouth flora). For patients who do not require hospitalization, several options are available [see Table 3]. Erythromycin is cost-effective, but the macrolides clarithromycin and azithromycin may be preferable because of their better gastrointestinal tolerance and their activity against *Haemophilus* and *Moraxella* species. Doxycycline is an effective and inexpensive alternative. However, because of the increasing prevalence of drug-resistant pneumococci, use of one of the newer fluoroquinolones (e.g., levofloxacin, sparfloxicin, gatifloxicin, or moxifloxicin) is recommended. These agents have excellent activity against the major causes of community-acquired pneumonia; prospective trials have been favorable. The newer fluoroquinolones may also emerge as drugs of choice for patients with community-acquired pneumonia who require hospitalization; levofloxicin and gatifloxicin are available in preparations for I.V. administration [see Table 4]. Although it is still uncommon, the emergence of levofloxicin-resistant pneumococci is a concern. In addition, dual therapy may be preferable for patients with severe pneumococcal pneumonia. As a result, patients with moderate to severe community-acquired pneumonia may benefit from cefotaxime or ceftriaxone in combination with a macrolide or a fluoroquinolone. Because vancomycin is active against virtually all pneumoocci, it can be substituted for the third-generation cephalosporin in patients allergic to β-lactams; linezolid is another alternative. When aspiration is suspected, penicillin, clindamycin, or metronidazole is useful; amoxicillin-clavulanate, imipenem, meropenem, and newer fluoroquinolones, such as gatifloxicin, moxifloxicin, and levofloxicin, are also active against oral anaerobes [see Table 5].

In all cases, antibiotic therapy should be tailored according to the results of culture and sensitivity, the clinical response, and the occurrence of side effects. Many patients who require intravenous antibiotics initially can be switched to oral therapy within 3 days, facilitating early hospital discharge. In most patients with uncomplicated pneumococcal pneumonia, antibiotics can be discontinued after 3 afebrile days; most patients with other

### Table 4 Initial Antibiotic Therapy for Community-Acquired Pneumonia in Patients Who Require Hospitalization*

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Typical Dose</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cephalosporins</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cefotaxime or ceftriaxone + a macrolide or a fluoroquinolone</td>
<td></td>
<td>First-line treatment of choice for severely ill patients</td>
</tr>
<tr>
<td></td>
<td>Cefotaxime, 1–2 g I.V. q. 4 hr; ceftriaxone, 1–2 g I.V. q. 12–24 hr</td>
<td></td>
</tr>
<tr>
<td>Fluoroquinolones</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Levofloxicin</td>
<td>500 mg p.o. or I.V. q. 24 hr</td>
<td>First-line treatment, either alone or with a third-generation cephalosporin</td>
</tr>
<tr>
<td>Gatifloxicin</td>
<td>400 mg p.o. or I.V. q. 24 hr</td>
<td></td>
</tr>
<tr>
<td>Vancomycin + a macrolide or a fluoroquinolone</td>
<td>Vancomycin, 1 g I.V. q. 12 hr</td>
<td>Alternative for severely ill patients who are allergic to β-lactams</td>
</tr>
<tr>
<td>Linezolid + a macrolide or a fluoroquinolone</td>
<td>Linezolid, 600 mg p.o. or I.V. q. 12 hr</td>
<td>For severely ill patients who cannot tolerate β-lactams or vancomycin</td>
</tr>
</tbody>
</table>

*See text for details.†For details, see 7:XIV Chemotherapy of Infection (especially Tables 3 and 4).‡For macrolide doses, see Table 3; azithromycin may be administered intravenously.

### Table 5 Antibiotic Choices for Aspiration Pneumonia*

<table>
<thead>
<tr>
<th>Drug</th>
<th>Typical Dose</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penicillin</td>
<td></td>
<td>Traditional drug of choice</td>
</tr>
<tr>
<td></td>
<td>500 mg p.o., q. 6 hr to 1–2 million units I.V. q. 4 hr, depending on severity of infection</td>
<td></td>
</tr>
<tr>
<td>Clindamycin</td>
<td></td>
<td>May be superior to penicillin</td>
</tr>
<tr>
<td></td>
<td>150–300 mg p.o., q. 6 hr to 600 mg I.V. q. 8 hr, depending on severity of infection</td>
<td></td>
</tr>
<tr>
<td>Metronidazole</td>
<td></td>
<td>Excellent alternative</td>
</tr>
<tr>
<td></td>
<td>500 mg p.o., q. 8 hr to 500 mg I.V. q. 6 hr, depending on severity of infection</td>
<td></td>
</tr>
<tr>
<td>Ampicillin-sulbactam</td>
<td></td>
<td>Alternative useful in hospitalized patients</td>
</tr>
<tr>
<td></td>
<td>1–2 g ampicillin + 0.5–1 g sulbactam I.V. q. 6 hr</td>
<td></td>
</tr>
<tr>
<td>Imipenem</td>
<td></td>
<td>Alternative useful in hospitalized patients</td>
</tr>
<tr>
<td></td>
<td>0.5–1 g I.V. q. 6–8 hr</td>
<td></td>
</tr>
<tr>
<td>Meropenem</td>
<td></td>
<td>Alternative useful in hospitalized patients</td>
</tr>
<tr>
<td></td>
<td>1 g I.V. q. 8 hr</td>
<td></td>
</tr>
<tr>
<td>Fluoroquinolones</td>
<td></td>
<td>Excellent for community-acquired pneumonias but less active against oral anaerobes than penicillin, clindamycin, and metronidazole</td>
</tr>
<tr>
<td>Gatifloxicin</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>400 mg p.o. or I.V. q. 24 hr</td>
<td></td>
</tr>
<tr>
<td>Moxifloxicin</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>400 mg p.o., q. 24 hr</td>
<td></td>
</tr>
<tr>
<td>Levofoxacin</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>500 mg p.o. or I.V. q. 24 hr</td>
<td></td>
</tr>
</tbody>
</table>

*See text for details.†For details, see 7:XIV Chemotherapy of Infection (especially Tables 3 and 4).
bacterial pneumonias are treated for 7 to 14 days, and most with atypical pneumonias are treated for 10 to 21 days.

Hospital-Acquired Pneumonia

Because nosocomial pneumonias are often caused by gram-negative bacilli and *S. aureus*, patients with hospital-acquired pneumonias require broad antimicrobial coverage until the results of Gram stains, cultures, and sensitivity tests permit focused therapy. Options for the initial treatment of hospital-acquired pneumonia include ticarcillin–clavulanic acid or piperacillin–tazobactam, meropenem or imipenem-cilastatin, a third-generation cephalosporin with nafcillin or vancomycin, a first-generation cephalosporin with an aminoglycoside, or vancomycin with an aminoglycoside. The prevalence of resistant bacteria in a particular hospital or patient care unit should help guide the initial therapy; for example, if methicillin-resistant staphylococci are common, vancomycin is a desirable component of the initial therapy, and when multidrug-resistant *Klebsiella* organisms are common, meropenem or imipenem-cilastatin should be considered. Linezolid is an effective alternative to vancomycin for the treatment of nosocomial pneumonia caused by methicillin-resistant gram-positive cocci.

Infections Caused by Legionella Species

**Epidemiology and Etiology**

Since it was first recognized in 1976, Legionnaires disease has become recognized as a common cause of both community-acquired and hospital-acquired pneumonias. Worldwide, it accounts for between 2% and 15% of all community-acquired pneumonias severe enough to require hospitalization. It is estimated that 10,000 to 25,000 cases occur in the United States each year, but only 1,200 to 1,500 are reported annually. Legionnaires disease is caused by *L. pneumophila*, a fastidious, filamentous, flagellated, aerobic gram-negative bacillus. The organism can be grown on charcoal–yeast extract agar; optimal growth occurs at 35°C in 5% carbon dioxide, but growth is slow, and a period of 3 to 6 days is required for colonies to form.

At least nine serogroups of *L. pneumophila* exist; most clinical isolates belong to serogroup 1. By special staining techniques, large numbers of the organism can be identified in tissue sections of alveoli, both within macrophages and extracellularly. Virulence factors of *L. pneumophila* and various extracellular enzymes that the organism secretes have been identified. *L. pneumophila* is able to survive intracellularly in host leukocytes. Antibody is not protective, but cell-mediated immunity does promote recovery and prevent reinfection.

In nature, *L. pneumophila* survives principally in water and, to a lesser extent, in soil. Human disease is acquired primarily by inhalation of aerosols contaminated with organisms; person-to-person transmission has not been documented. Contaminated water systems have been responsible for both community-acquired and hospital-acquired outbreaks.

The attack rate for Legionnaires disease appears to be higher in elderly persons and persons with underlying conditions such as COPD, neoplastic disease, organ transplants, and renal failure. Although *L. pneumophila* is a relatively uncommon pathogen in persons infected with HIV, it can cause severe disease in these patients.

**Diagnosis**

**Clinical features** Legionnaires disease is characterized by a 1-day prodrome of myalgias, malaise, and slight headache after an incubation period of 2 to 10 days. Acute onset of high fever, shaking chills, nonproductive cough, tachypnea, and, often, pleuritic pain ensues. The cough may subsequently become slightly productive, but the sputum is not purulent. Obnubilation or toxic encephalopathy is common, but frank meningitis is not a feature. Abdominal pain, vomiting, and, especially, diarrhea may be present. Signs of consolidation on physical examination are present infrequently, but rales are commonly heard. Chest radiographs show patchy or interstitial infiltrates, which often progress to areas of nodular consolidation in a single lobe or multiple lobes; minimal effusions are present in up to one third of cases. Abscess formation is uncommon but has been observed. Pulmonary fibrosis may occur in some survivors.

Although pneumonia is present in nearly all patients with Legionnaires disease, extrathoracic symptoms can be the presenting or predominant features. Central nervous system, GI, and renal manifestations are especially common. *L. pneumophila* has been isolated from blood cultures, and the organism can be found in many organs both in immunosuppressed patients and in previously normal patients who are afflicted with severe disease. Extrapulmonary manifestations include ocular and pericardial involvement, perirectal abscess, wound infection, peritonitis, cellulitis, rhabdomyolysis and acute renal failure, neutropenia, hemolytic anemia, and thrombotic thrombocytopenic purpura. Implanted devices such as heart valves and hemodialysis fistulas can become infected.

A nonpneumonic form of legionellosis called Pontiac fever has a short incubation period and a low mortality. It has been responsible for at least four outbreaks of illness, including several related to whirlpools and hot tubs.

**Laboratory studies** The peripheral white blood cell count is mildly elevated to between 8,000 and 16,000/mm³. Cold agglutinins are negative. Other laboratory findings may include an elevated erythrocyte sedimentation rate, hypoxia, abnormal liver function test results, and elevated creatine phosphokinase levels. Proteinuria and microscopic hematuria have been observed, and acute renal failure may complicate the course on occasion.

Gram stains of the sputum or tracheal secretions fail to reveal *L. pneumophila*. The organism can be isolated from sputum and other specimens by using charcoal–yeast extract extract agar. The diagnosis can be established rapidly in about 20% of cases by demonstrating the organism with direct immunofluorescent staining of sputum specimens; bronchoalveolar lavage may be helpful in immunosuppressed patients. A kit that uses radiolabeled complementary DNA is commercially available, but clinical experience is still limited. A very promising polymerase chain reaction assay has been developed.

Another method of rapid diagnosis involves detection of *L. pneumophila* antigen in the urine; the radioimmunoassay test is highly specific and has a sensitivity of about 80% to 90%. However, this test is available only for *L. pneumophila* serogroup 1, which is the most common cause of Legionnaires disease. Most often, however, the diagnosis is established by an indirect fluorescent antibody technique involving staining of the causative bacterium. With this technique, a fourfold or greater rise in titer during the illness or a stable titer of 1:256 or greater is considered diagnostic.

The clinical picture and radiologic findings in Legionnaires disease are not specific. The diagnosis should be considered in...
patients with segmental, lobar, or interstitial pneumonia in which the etiologic agent is not evident on Gram stains of sputum or tracheal secretions. A mild case may resemble *Mycoplasma* pneumonia or other types of atypical pneumonia.

**Treatment**

On in vitro susceptibility testing, *L. pneumophila* has been shown to be susceptible to a variety of antimicrobial agents, including erythromycin, clarithromycin, azithromycin, tetracycline, rifampin, and the fluoroquinolones. Current evidence indicates that azithromycin or levofloxacin is the treatment of choice. Occasionally, patients may experience a relapse if antibiotics are discontinued prematurely; recovery occurs during a second, more prolonged course of treatment. A combination of rifampin and either azithromycin or levofloxacin may be considered in patients who fail to respond to monotherapy alone and in immunologically impaired patients with overwhelming disease. Improvements in diagnosis and therapy have produced a dramatic decline in the case-fatality rate of *L. pneumophila* infection, from 34% in 1980 to 12% in 1998.

**Infections Caused by Other Legionella Species**

Since 1943, unusual, fastidious *Rickettsia*-like organisms have been identified as causes of isolated cases of pneumonia. Long considered medical curiosities, these organisms were named after their discoverers or the patients from whom they were isolated. Such obscure nomenclature (e.g., TATLOCK, OLDA, HEBA, and WIGA) reflected the absence of knowledge concerning these agents. Subsequent studies of these organisms led to their reclassification as *Legionella* species. Of the more than 30 *Legionella* species that have been identified, at least 19 have been recognized as causes of pneumonia, particularly in immunosuppressed hosts.

The clinical picture is not distinctive. Fever is the most common feature, cough is variable in severity, and sputum production is absent or scant. Pleurisy or dyspnea may develop, and chest x-rays show a patchy or nodular, progressive bronchopneumonia. *L. micdadei* is the most important of these organisms. Previously known as TATLOCK and HEBA, this organism was rediscovered as the Pittsburgh pneumonia agent that caused acute suppurative pneumonia in 13 immunosuppressed patients from two centers. *L. micdadei* can also cause pneumonia in immunologically intact hosts and extrathoracic infections in immunologically impaired hosts. It has been isolated from hospital water supplies and can cause nosocomial infections in immunosuppressed patients.

In the first 13 patients with Pittsburgh pneumonia, the diagnosis was established through a lung biopsy or autopsy that revealed acute alveolar inflammation and short, weakly acid-fast gram-negative bacilli. More recent cases have been diagnosed by cultivating the agent on charcoal–yeast extract agar or by serologic means. Erythromycin has been used with success. Unlike *L. pneumophila*, *L. micdadei* is susceptible to penicillins and cephalosporins in vitro; however, there are no data on the use of these drugs in clinical *L. micdadei* infection.

Many other *Legionella* species have been identified as causes of pneumonia. These organisms grow on charcoal–yeast extract agar. Some cases in which *Legionella* species have been implicated share common features: patients have been exposed to infected water and have COPD or are immunosuppressed.

Therapy with erythromycin, alone or with rifampin, has been suggested.

**CHLAMYDIA PNEUMONIAE**

*C. pneumoniae*, initially known as the Taiwan acute respiratory disease (TWAR) agent, is an important pathogen, accounting for up to 10% of all pneumonias in the United States. Serologic surveys suggest that a majority of adults have been infected at some point, indicating that most cases are mild or subclinical.

Unlike psittacosis, which is a true zoonosis that spreads only from animals to humans, *C. pneumoniae* spreads from person to person via respiratory droplets. The incubation period of *C. pneumoniae* is long. Unlike *Chlamydia trachomatis*, which causes neonatal pneumonia, *C. pneumoniae* affects mainly older children and young adults; however, older patients (especially those with COPD) also may be affected. The clinical features of *C. pneumoniae* pneumonia in young patients resemble those of *M. pneumoniae* pneumonia; after a prodrome of pharyngitis that lasts no more than 2 weeks, nonproductive cough and fever occur. Pulmonary infiltrates are mild. The infection is usually self-limited. In older patients with underlying COPD, *C. pneumoniae* can cause bronchitis that may be mild or very persistent. Bronchospasm may be prominent. These organisms can sometimes cause severe pneumonia in patients with COPD, and fatalities have been reported in debilitated patients. A macrolide, a tetracycline, or a fluoroquinolone is recommended for therapy.

**Recurrent Pneumonia**

Patients with recurrent pneumonia present a diagnostic and therapeutic challenge. Anatomic abnormalities should be carefully sought in all such patients and should be suspected particularly when the infections recur in one bronchopulmonary segment. Examples of anatomic abnormalities include cysts, blebs, abscess cavities, bronchiectasis, and bronchial obstruction by tumors, foreign bodies, or bronchiostenosis. If shifting locations are involved, systemic abnormalities may be present. Examples include defects of leukocyte function, immunoglobulin deficiencies, α1-antitrypsin globulin deficiency, and cystic fibrosis. Recurrent aspiration may be responsible, in which case a carefully performed neurologic examination and a barium swallow may reveal the proper diagnosis. It is important to remember that noninfectious processes may produce recurrent pulmonary infiltrates that may be accompanied by cough and fever. Examples of such processes include organizing pneumonia, eosinophilic pneumonia, hypersensitivity pneumonitis, vasculitis, pulmonary hemosiderosis, and pulmonary emboli.

**Chronic Pneumonia**

Often, bacterial pneumonias exhibit delayed resolution, in which radiographic abnormalities persist for weeks or even months after clinical recovery. Infrequently, pyogenic infection pursues a slow but progressively destructive course despite antibiotic therapy; *K. pneumoniae* and other gram-negative bacilli have been implicated in some patients with such chronic bacterial pneumonias. *Mycobacteria* and *Actinomyces* are common causes of chronic pulmonary infection; fungi are particularly common in patients treated with corticosteroids. Persistent infiltration caused by neoplasia, sarcoidosis, pulmonary hemorrhage, vasculitis, fibrosing alveolitis, alveolar proteinosis, lipid pneumonia, toxins, and other processes may mimic chronic pulmonary infection. Fiberoptic bronchoscopy is very useful for diagnosis, but lung biopsy may be needed.
Aspiration Pneumonia

EPIDEMIOLOGY AND ETIOLOGY

Seventy percent of patients with depressed consciousness have demonstrable pharyngeal aspiration, often involving much larger volumes of material than that aspirated by healthy persons. Because of the larger volumes of aspirated material, underlying diseases impairing host defenses, and alterations in oropharyngeal flora, patients with altered consciousness are most prone to aspiration pneumonia. In clinical practice, alcoholism, drug abuse, administration of sedatives or anesthesia, head trauma, and seizures or other neurologic disorders are most often responsible for the development of aspiration pneumonia. In addition, patients with abnormalities of deglutition or esophageal motility resulting from placement of nasogastric tubes, esophageal carcinoma, bowel obstruction, or repeated vomiting from any cause are prone to aspiration of GI contents. Poor oral hygiene and periodontal disease predispose to aspiration pneumonia because of the increased bacterial flora in these patients.

The clinical results of pulmonary aspiration depend in large part on the nature and volume of material aspirated. Aspiration of gastric contents is a common problem that may produce Mendelson syndrome, a fulminating illness, if a large volume of acid gastric juice is aspirated. Aspiration of particulate material can produce acute airway obstruction and death by asphyxiation; aspiration of smaller particles may produce atelectasis of a pulmonary segment or even an entire lung with dyspnea, wheezing, and cyanosis. Characteristic pulmonary injuries and distinctive clinical syndromes are produced by aspiration of smoke, freshwater or saltwater, and fats or oils (lipoid pneumonitis). Whereas aspiration is probably the mechanism responsible for most bacterial pneumonias, the term aspiration pneumonia is best reserved for infection caused by mixed mouth flora.

DIAGNOSIS

Clinical Features

Patients with mixed aspiration pneumonia may present with an acute febrile illness, or the illness may follow a more indolent course, extending over many days or even weeks. Fever, cough, and sputum production are the dominant symptoms; the sputum may be copious, foul smelling, or both. Physical examination typically discloses rales and signs of pulmonary consolidation. An evaluation of dental hygiene and of the gag reflex is helpful; disordered pharyngeal sensation is a better predictor of vulnerability than is an absent gag reflex.

Laboratory Studies

Radiographically, infiltrates are most common in dependent areas of the lung, especially the apical segments of the lower lobes and the posterior segments of the upper lobes. Tissue necrosis can occur. Without treatment, aspiration pneumonia may produce multiple small cavities, which reflect a necrotizing pneumonitis. Lung abscesses or empyemas may ensue.

The sputum of patients with classic aspiration pneumonia contains abundant polymorphonuclear leukocytes and a mixed mouth flora. If specimens are obtained by transtracheal aspiration or other procedures that avoid contamination of sputum by organisms from the oral cavity, aerobic and anaerobic bacteriologic techniques can reveal the specific causative bacteria. Because anaerobes are the dominant flora of the upper respiratory tract (outnumbering aerobic or facultative bacteria by 10 to 1), it is not surprising that anaerobes are the dominant organisms in aspiration pneumonia. Of particular importance are Prevotella melaninogenica and other Prevotella (formerly oral strains of Bacteroides) species (slender, pleomorphic, pale gram-negative rods), Fusobacterium nucleatum (slender gram-negative rods with pointed ends), and anaerobic or microaerophilic streptococci and Peptostreptococcus (small gram-positive cocci in chains or clumps). As expected, multiple organisms are recovered from most patients.

TREATMENT

With the exception of B. fragilis, which can be identified along with other anaerobic species in 17% of patients with classic aspiration pneumonia, all the anaerobes found are penicillin sensitive. Penicillin is effective when B. fragilis is present in combination with penicillin-sensitive organisms, suggesting that aspiration pneumonias are synergistic infections that can be treated successfully by elimination of most but not necessarily all of the organisms involved. Penicillin dosages of 2.4 to 6.0 million units daily are generally effective. Parenteral therapy is advisable initially, but a 10- to 14-day course of treatment can be concluded with orally administered antibiotics if the patient responds well. Clindamycin represents an excellent alternative agent and may even be superior to penicillin for treatment of necrotizing aspiration pneumonias and lung abscesses.

Hospitalization or antibiotic therapy alters the usual oropharyngeal bacterial flora, so that staphylococci, facultative gram-negative bacilli, or both may be identified in patients. As a result, aspiration pneumonia in hospitalized patients often involves pathogens that are uncommon in community-acquired pneumonias. Gram stains and cultures of sputum are especially important for identifying gram-negative bacilli and staphylococci in the hospital setting. Broad antimicrobial coverage is required until specific pathogens have been identified by culture and sensitivity testing. Although tube feedings are often recommended to prevent aspiration pneumonia, there is no evidence that they are effective.

Other Pulmonary Infections

ACUTE BRONCHITIS

Cough was the chief complaint responsible for an estimated 30 million physician office visits in the United States in 1997. For about 12 million of these patients, the clinical diagnosis was acute bronchitis.

Acute bronchitis is commonly defined as an acute respiratory tract infection in which cough, with or without sputum production, is a prominent feature. In most cases, an etiologic diagnosis is not established. When sputum is absent or scant, the illness is often attributed to a respiratory tract virus; when purulent sputum is present, the bacteria that cause community-acquired pneumonias are considered likely causes.

Most otherwise healthy individuals recover from acute bronchitis in 1 to 3 weeks, but the cough can linger for more than a month in up to 20% of patients. Although 70% to 90% of patients are treated with antibiotics, published trials demonstrate little clinical benefit, even if purulent sputum is present. Guidelines of the Infectious Disease Society of America, the American College of Physicians–American Society of Internal Medicine, and the American Academy of Family Physicians state, “Routine antibiotic treatment of uncomplicated acute bron-
Chronic Bronchitis

Patients with chronic bronchitis characteristically produce sputum on most days for at least 3 months each year for more than 2 years. The sputum is frequently colonized by H. influenzae (nontypable), S. pneumoniae, or M. catarrhalis, singly or in combination. Although it is not certain whether the bacteria themselves produce additional airway damage, heavy bacterial loads correlate with increased inflammation. Patients who acquire a new strain of bacteria are at increased risk of symptomatic exacerbations of their chronic bronchitis. The role of long-term prophylactic antibiotic therapy in chronic bronchitis is controversial. Long-term antibiotic therapy may provide symptomatic relief in certain patients who experience multiple exacerbations of bronchitis during the winter, but it is not useful in improving or preserving pulmonary function. However, short-term antibiotic therapy is effective in treating acute exacerbations of chronic bronchitis.

Bronchiectasis

True saccular, or cystic, bronchiectasis involves both dilata
tion of the bronchi and destruction of the bronchial walls. Bronchiectasis results most often from neglected or recurrent infection, especially in childhood; therefore, bronchiectasis has become much less common since the introduction of antibiotics. Aggressive medical therapy has greatly improved the prognosis.

Symptoms include cough that may be dry or productive of copious foul sputum, recurrent lower respiratory tract infection, and hemoptysis. In rare instances, bronchiectasis can present as pleuritic chest pain. In advanced cases, fibrosis can lead to cor pulmonale and respiratory failure. The chest x-ray may show increased lung markings, honeycombing, atelectasis, or pleural changes, but high-resolution or helical chest computed tomography is required for definitive diagnosis [see 14:III Chronic Obstructive Diseases of the Lung].

Lung Abscess

Epidemiology and etiology

In the antibiotic era, lung abscesses have become less common and less serious. The most common variety has been termed the primary, simple, nontuberculous, or putrid abscess. Primary lung abscess accounts for about 60% of all lung abscesses and originates from a necrotizing suppurative bronchopneumonia caused by the aspiration of mixed oropharyngeal bacteria. Thus, both the predisposing factors and the causative organisms are similar to those identified in aspiration pneumonia. Patients with primary lung abscesses typically have alterations of consciousness because of underlying problems such as alcoholism and neurologic disorders; periodontal disease is often present. The organisms causing the abscess are much more reliably identified by transtracheal aspirates than by sputum cultures, which are invariably contaminated with anaerobes and other mouth flora. Percutaneous lung aspiration and bronchoalveolar lavage may also be useful for bacteriologic diagnosis. Mixed anaerobic bacteria are seen in most cases; Fusobacterium nucleatum, P. melaninogenica, Peptostreptococcus, and anaerobic or microaerophilic streptococci predominate. B. fragilis is recovered with other organisms in 15% of cases.

Many other conditions can lead to lung abscess. Necrotizing bacterial pneumonias caused by S. aureus, K. pneumoniae, or other gram-negative bacilli can lead to abscess formation. In other patients, abscess develops as a result of bronchial obstruction caused by tumors, foreign bodies, or bronchial stenosis. Septic pulmonary embolization is a cause of abscess formation. Pulmonary tuberculosis, fungal infection, or actinomycosis often leads to cavity formation. In the immunosuppressed host, Nocardia and other opportunistic organisms may also produce cavitary lung abscesses. Lung abscesses in patients with AIDS occur in the setting of advanced HIV infection; they are caused by a wide array of organisms and respond poorly to therapy.

Noninfectious processes can produce cavitary lung lesions. Primary and metastatic tumors, bullae, cysts, intralobar pulmonary sequestration, pulmonary infarcts, vasculitis (including Wegener granulomatosis), and rheumatoid lung disease must be considered in the differential diagnosis of lung abscess.

Diagnosis

Clinical Features

The clinical presentation of the patient with a lung abscess depends on the type of abscess. Patients with abscesses resulting from necrotizing staphylococcal or gram-negative bacillary pneumonias are usually acutely ill and exhibit clinical features of the underlying pneumonia. Although patients with primary lung abscess may also present acutely with aspiration pneumonia, they more often experience insidiously progressive symptoms for weeks or even months before diagnosis. Cough is present in almost all patients; when the abscess drains into the bronchial tree, production of copious foul-smelling sputum is characteristic. Hemoptysis is present in approximately one third of cases and may occasionally reach life-threatening proportions. Chest pain consisting of either a dull ache or a true pleurisy is common. Most patients have fever, but frank rigors are unusual. Often, patients with a chronic course of lung abscess lasting many weeks have anorexia, weight loss, and debility.

Physical Examination and Imaging

Physical examination of a patient with a lung abscess may disclose pulmonary rales, signs of consolidation, or, rarely, clubbing of the nails. These findings are not diagnostic, however, and chest x-rays or CT scans are required to establish the presence of an abscess. Although any lung segment may be involved, abscesses are most common in the posterior segments of the upper lobes and the apical segments of the lower lobes, because these areas are dependent when the patient is recumbent. Abscesses may be single or, less often, multiple. The finding of air-fluid levels signifies rupture into the bronchial tree.

Laboratory Studies

As is the case with other pulmonary infections, examination of the sputum is crucial to the diagnosis of lung abscess. In patients with primary lung abscesses, the sputum is often putrid and contains numerous polymorphonuclear leukocytes and an abundant mixed microbial flora. Sputum cultures reveal only normal mouth flora. Meaningful anaerobic bacteriology de-
bacteremia with metastatic infection such as brain abscess. Penicillin has been the drug of choice. Prospective studies comparing penicillin therapy with clindamycin therapy in 66 patients with lung abscess found clindamycin to be the superior agent; however, the long clinical experience with penicillin warrants retaining penicillin as the drug of choice, with clindamycin an excellent alternative for patients who are allergic to penicillin or who respond poorly to that drug. Despite its excellent bactericidal activity against anaerobic bacteria, metronidazole appears less effective in treating lung abscess. Most centers initiate treatment with I.V. penicillin in a dosage range of 6 to 12 million units a day or with I.V. clindamycin in a dosage of 600 mg every 8 hours. After a clear-cut clinical response is observed, oral penicillin V in a dosage of 750 mg four times a day or oral clindamycin in a dosage of 300 mg every 6 hours can be substituted. Parenteral therapy is often required for 2 to 4 weeks before the occurrence of defervescence, diminished sputum production, and reduction in cavity size. The duration of therapy depends on the clinical course, but prolonged treatment for 4 to 8 weeks is usually required.

In addition to administration of antibiotics, adequate drainage is essential and can usually be achieved with intensive pulmonary physiotherapy and postural drainage. Bronchoscopy can be very useful in promoting drainage and for excluding the diagnosis of cancer. Although surgery was once the mainstay of treatment for lung abscess, antibiotics are now almost always able to control infection, and surgery is needed only when complications occur. Massive hemothorax is an indication for lung resection. Uncontrolled sepsis may occasionally necessitate lobectomy. CT-guided percutaneous tube drainage may be very helpful in patients who are too ill to tolerate thoracotomy and may be the treatment of choice for lung abscesses that are refractory to medical management. Empyema, another complication of lung abscess, requires external drainage by thoracentesis, chest tube, or rib resection. The persistence of a thin-walled cavity after other medical treatments is not an indication for surgery. Recurrent or persistent infection, recurrent hemothorax, or the suspicion of tumor may mandate operative intervention. Shaggy, thick-walled cavities may be suggestive of tumor. Complications of lung abscess that have become uncommon because of antibiotic therapy include bronchogenic spread of infection to other pulmonary segments, bronchiectasis, and bacteremia with metastatic infection such as brain abscess.

Empyema

ETIOLOGY

Bacteria can reach the pleural space by many routes. Most often, empyema results from the direct spread of bronchopulmonary infections, including pneumonias, lung abscesses, and bronchiectasis. Less often, empyema develops as a complication of thoracotomy or, rarely, thoracentesis. Open chest trauma provides another means for the direct introduction of microorganisms. Intra-abdominal infections, especially subphrenic abscesses, can penetrate the diaphragm to cause empyemas. Uncommonly, esophageal rupture can cause spread of infection from the mediastinum to the pleural space. Finally, hematogenous seeding is an infrequent mechanism of empyema formation. S. aureus, various species of Streptococcus, and gram-negative bacilli are the most common causes of empyema; among the gram-negative bacilli, K. pneumoniae has been linked with diabetes. Many infections are mixed. Anaerobes have been recognized in 25% to 76% of empyemas and may occur in pure culture or in combination with aerobic or facultative organisms. Fusobacterium, Prevotella, and anaerobic gram-positive cocci are the anaerobes most often seen. M. tuberculosis has become a relatively rare cause of pleural space infections, and fungi are implicated uncommonly. Transdiaphragmatic rupture of a liver abscess occasionally produces aseptic empyema.

DIAGNOSIS

In most patients, the clinical presentation of empyemas includes fever, dyspnea, chest pain, and cough. Hemothorax is less common than these other symptoms. If diagnosis and treatment are delayed, weight loss and debility may be prominent. The physical findings in patients with empyemas are no different from those in other patients with pleural effusions. In addition, chest wall tenderness may be present, and there may be signs of an underlying pneumonia or intra-abdominal infection. Tachypnea and respiratory distress may occur, and septic shock may complicate advanced cases. Polymorphonuclear leukocytosis is common; other laboratory findings may include anemia and hypoxia. Chest x-rays reveal pleural effusions that are free flowing in early disease but frequently loculated in late cases. Ultrasonography may be necessary to distinguish fluid from pleural fibrosis. Unless surgery or thoracentesis has been performed, air-fluid levels in the pleural space suggest a bronchopleural fistula.

DIFFERENTIAL DIAGNOSIS

In the differential diagnosis of empyema, it is important to consider the many causes of noninfected pleural effusions. Most important is the distinction between sterile parapneumonic effusions and true empyemas. Thoracentesis is mandatory for the diagnosis of empyema. Several thoracenteses may be needed if the fluid is loculated; CT or ultrasound guidance is very helpful in these circumstances. Gross purulence is diagnostic for empyema, but the absence of frank pus does not rule out infection. Like other inflammatory effusions, empyema fluids have the characteris-
tics of exudates: protein levels greater than 3 g/dl and lactic dehydrogenase values in excess of 550 units. Pleural fluid acidosis is characteristic of empyemas, but alkalosis can occur if the infection is caused by a urea-splitting organism such as Proteus. Pleural fluid glucose levels are depressed in empyemas, and although white cell counts are variable, counts above 5,000/mm³ are common, with polymorphonuclear leukocytes predominating. Gram stains of the pleural fluid will often reveal the causative organisms. Both aerobic and anaerobic cultures are mandatory; a foul odor suggests anaerobic infection. Stains and cultures for mycobacteria and fungi are important in selected cases.

**TREATMENT**

Treatment of empyemas involves two elements. Antibiotics should be selected on the basis of the causative pathogens. High-dose parenteral therapy is required, and prolonged antibiotic courses of 3 weeks or more are often needed. Adequate drainage is of paramount importance. In acute empyemas, the pleural cavity is lined by acute fibrinous inflammation, and percutaneous drainage of free-flowing fluid may be possible by repeated thoracentesis or tube thoracostomy. Closed chest tube drainage is the traditional method for draining empyemas, but image-guided catheter drainage is also effective, particularly when the fluid is loculated. Resolution of fever generally signifies satisfactory drainage. If complete drainage cannot be achieved with chest tubes, video-assisted thoracoscopic surgery (VATS) can often disrupt intrapleural adhesions and achieve excellent drainage of loculated effusions; although VATS requires endotracheal intubation and general anesthesia, it is less invasive than the next alternative, rib resection with thoracotomy for decortication. Enzymatic debridement with streptokinase may enable some patients to avoid surgery.

**Septic Pulmonary Embolism**

Although once uncommon, septic pulmonary embolism is now encountered because of narcotic addiction, which accounts for more than 75% of cases; tricuspid valve endocarditis and direct injection of infected material cause most of these cases. S. aureus and gram-negative bacilli are the predominant etiologic agents in addiction-related septic pulmonary embolism. Septic pulmonary embolism may also develop in patients with septic phlebitis of peripheral veins (especially phlebitis related to I.V. lines or pelvic infections), abscesses, or other bacteremic infections.

Unlike bland emboli, septic pulmonary emboli produce pulmonary infarction in most instances. Small emboli produce flame-shaped or patchy infiltrates that may shift in location; these manifestations generally resolve with antibiotic therapy. Larger emboli often cavitate and may lead to lung abscess, empyema, or bronchopleural fistula formation. In addition to antibiotics, surgical drainage may be required for such complications. Operative intervention may be needed to control the source of emboli in some patients. Heparin can be useful in patients with septic phlebitis.

References


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38. Gatifloxacin and moxifloxacin: two new fluoroquinolones. Med Lett Drugs Ther 41:15, 2000