TODAY'S PRACTICE OF CARDIOPULMONARY MEDICINE

Bacterial Infections of the Lung*

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It has been estimated that greater than 1,200,000 cases of bacterial pneumonia (with 55,000 deaths) occur annually in the United States. The purpose of this article is to review bacterial pneumonia in adults.

FACTORS THAT PREDISPOSE TO DEVELOPMENT OF PNEUMONIA

Pulmonary defense mechanisms are normally effective in preventing pneumonia.1 These defenses include humidification of inspired air, mucus secretion and ciliary action of airway epithelium, cough, lymphoid tissue, immunoglobulins and complement, pulmonary macrophages and leukocytes, and leukocyte chemotactic factors.

Community-acquired pneumonia typically involves organisms such as *Streptococcus pneumoniae*, *Haemophilus influenzae* and, in the case of gross aspiration of oropharyngeal contents, anaerobic bacteria. Hospital-acquired pneumonia, on the other hand, is more likely to involve *Staphylococcus aureus* and gram-negative aerobic or facultative bacilli, such as *Pseudomonas aeruginosa*, *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus* species, *Enterobacter* spp, *Serratia marcescens*, and *Acinetobacter calcoaceticus*. There is, however, substantial overlap between the flora of community- and hospital-acquired pneumonias.

The oropharynx is the major source of pulmonary bacterial pathogens. Underlying conditions associated with oropharyngeal colonization by gram-negative aerobic or facultative bacilli are shown in Table 1; colonization of healthy individuals is uncommon.2 Recent data suggest that adherence, possibly mediated by pili, of gram-negative bacilli to buccal epithelial cells is an important factor in oropharyngeal colonization. Serveral species of anaerobes that normally reside in the oral cavity, particularly *Bacteroides melaninogenicus*, have been shown to inhibit the growth of a number of potential pulmonary pathogens;4 this bacterial interference may be an important defense against oropharyngeal colonization.

Although the term aspiration pneumonia is used to refer to patients with anaerobic pleuropulmonary infection, it is important to realize that aspiration of oropharyngeal contents is a common occurrence in both healthy and ill persons during sleep4 and is undoubtedly important in the pathophysiology of most cases of bacterial pneumonia regardless of the pathogen. Factors, in addition to sleep, that predispose to aspiration include drug-induced depression of the sensorium, epilepsy, head trauma, cerebrovascular accident, and bulbar or pseudo-bulbar palsy. Community-acquired aspiration pneumonia usually involves anaerobic with or without facultative bacteria, whereas about two thirds of hospital-acquired aspiration pneumonia involve only facultative or aerobic bacteria.6 Because bacteria that proliferate in diseased periodontal tissues are largely anaerobic and are present in extremely high counts, the presence of gingivitis or periodontal disease is an important predisposition to anaerobic pulmonary infection.

Once bacteria have gained access to the normally sterile subglottic region, pneumonia may be averted if the pulmonary clearing mechanisms are intact.1 Endotracheal intubation, tracheostomy, chronic obstructive pulmonary disease, and neurodepressants may render the cough reflex ineffective. Mucociliary

![Table 1](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21283/ on 04/30/2017)
clearance of the airways may be depressed by ethanol, narcotics, chronic airway disease, or recent viral infection. Continuous assisted ventilation may cause large numbers of bacteria to be aerosolized into the respiratory tract. Obstruction of a bronchus (by a foreign body, endobronchial tumor, or extrinsic compression) may also severely impair pulmonary clearing of aspirated bacteria. In addition, conditions such as hypoxia, acidosis, uremia, and therapy with cytotoxic or glucocorticoid agents may impair pulmonary defenses.¹

Bacteremia with secondary seeding of the lung or spread of contiguous infection into the chest cavity are occasional causes of pneumonia.

**Diagnostic Approach**

The *sine qua non* of bacterial pneumonia is the presence of a new pulmonary infiltrate on chest roentgenogram. Although certain findings on chest roentgenogram may suggest specific pathogens (*eg*, bulging of a fissure in *K pneumoniae* pneumonia), these features are neither sensitive nor specific enough to be relied on as a means for making an etiologic diagnosis.

Etiologic diagnosis of pneumonia requires detection of the pathogen; for bacterial pneumonia this is usually achieved by culture. Culture of expectorated sputum is the most frequently used, but least reliable, method. As a coughed sputum specimen passes through the mouth, it becomes contaminated with saliva, which contains approximately $10^6$ bacteria/ml. Virtually all potential bacterial pulmonary pathogens are capable of colonizing the oropharynx; recovery of such organisms from expectorated sputum, therefore, does not necessarily distinguish between infection and colonization. In addition, pathogens detected by means other than sputum culture (*eg*, transtracheal aspiration) may not always be recovered by sputum culture.⁷³ Recent studies have suggested that expectorated sputum should not be cultured unless it contains fewer than ten squamous epithelial cells and greater than 25 leukocytes per low-power field as determined by gram-stain screening.⁹ A similar screening procedure should be applied to sputum specimens obtained by nasotracheal suctioning.

Less commonly employed procedures to obtain pulmonary secretions for culture are aspiration or brushing of secretions during fiberoptic bronchoscopy; brushings obtained through an occluded, telescoping cannula during bronchoscopy; percutaneous transtracheal aspiration; direct lung puncture; and open lung biopsy. Culture of bronchial brushings or secretions aspirated via an unoccluded bronchoscopy catheter offers little improvement over expectorated sputum because of contamination during passage through the nasal or oral cavity. The use of a brush inside an occluded, telescoping bronchoscopy catheter may avoid this problem of contamination,¹⁰ but published data are not sufficient to permit definite conclusions. We consider transtracheal aspiration to be superior to the above-mentioned techniques and to be the technique of choice for evaluation of suspected anaerobic infections.¹¹ Direct lung puncture in patients with pneumonia has also been proposed as a means for bacteriologic diagnosis,⁷ but one must be concerned about the reliability of this technique because of the small quantity of material obtained and the possibility of greater risk than with transtracheal aspiration.

Culture of an *appropriately screened* expectorated sputum should be adequate for diagnosis of most community-acquired pneumonias. Transtracheal aspiration should be considered in the seriously ill patient who is unable to produce sputum, who has hospital-acquired pneumonia, or in whom anaerobic pneumonia is suspected. Gram stain of appropriately obtained pulmonary secretions provides immediate, accurate information as regards initial empiric therapy.

Cultures of blood and gram stain and culture of pleural fluid may yield the pulmonary pathogen and are therefore indicated in the patient with suspected bacterial pneumonia.

**Bacterial Pathogens and Therapy**

Common symptoms and signs of bacterial pneumonia are fever, chills or rigors, cough, purulent sputum production, pleurisy, dyspnea, and anorexia. In the case of anaerobic lung abscess or necrotizing pneumonia, symptoms are often present for several weeks before the patient seeks medical care.

 Patients with pneumonia may occasionally fail to respond to that which is considered to be effective therapy; possible causes of such failure are shown in Table 2. Complications of bacterial pneumonia include necrosis of pulmonary parenchyma (necro-

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<tr>
<th>Reasons for Failure or Apparent Failure of Pneumonia to Respond to Antimicrobial Therapy</th>
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<td>Pulmonary infiltrate not of infectious etiology</td>
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<td>Pulmonary infection of nonbacterial etiology</td>
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<td>Bronchial obstruction or foreign body</td>
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<td>Emphyema not adequately drained</td>
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<td>Bacterial pathogen resistant to agent administered</td>
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<td>Suprainfection with resistant organism</td>
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<td>Inadequate dosage or duration of antimicrobial therapy</td>
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<td>Drug fever</td>
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Tizing pneumonia or lung abscess), empyema, bacteremia, metastatic suppuration, pericarditis, and acute and chronic respiratory insufficiency.

Streptococcus pneumoniae: S pneumoniae is by far the most frequent bacterial cause of pneumonia; onset is classically an abrupt shaking chill or rigor, fever, dyspnea, pleuritic pain, and cough productive of rusty sputum. Lobar infiltration is common in adults. Bacteremia occurs in approximately 30 percent of patients with pneumococcal pneumonia and is associated with both metastatic infection and an appreciable increase in mortality.

Aqueous penicillin G (0.6 to 1.2 million units daily) is the agent of choice for uncomplicated pneumococcal pneumonia. S pneumoniae resistant to both penicillin and to many other commonly used antimicrobials have been recovered recently in several countries. Although resistant strains are rare in the United States, susceptibility testing should be performed whenever a suboptimal response to therapy occurs. A safe and effective polyvalent pneumococcal vaccine is now available.

Streptococcus pyogenes: S pyogenes (Group A β-hemolytic Streptococcus) is an occasional cause of epidemic and sporadic pneumonia. Chills tend to be multiple, bronchopneumonia rather than lobar consolidation is typical, and both pleural effusion and empyema are frequent; treatment consists of 2 million units of aqueous penicillin G daily for two weeks or longer.

Streptococcus agalactiae: S agalactiae (group B β-hemolytic Streptococcus) has recently been recognized to cause a variety of infections in adults, including pneumonia with or without bacteremia. Penicillin and ampicillin are active against S agalactiae; uncomplicated pneumonia should be treated with 4 to 6 million units of penicillin per day. Erythromycin should be an adequate substitute for any of the streptococcal pneumonias in the penicillin-allergic patient.

Staphylococcus aureus: S aureus is a relatively common cause of pneumonia and is most often associated with prior pneumonia due to influenza A virus, antecedent staphylococcal bacteremia, endocarditis, or hospitalization. Pulmonary infiltrates are patchy; pleural effusion, empyema, and lung abscess are relatively frequent.

A number of agents are active against S aureus. Those most commonly used for treatment of staphylococcal infections are the penicillinase-resistant penicillins (methicillin, nafcillin, or oxacillin) and the cephalosporins. Because the cephalosporins are relatively frequently associated with Clostridium difficile (pseudomembranous) colitis and other suprainfections, the penicillinase-resistant penicillins are generally preferred therapy for staphylococcal infections. Pneumonia due to "methicillin-resistant" S aureus should be treated with vancomycin because both the penicillins and cephalosporins are usually ineffective. Tube thoracostomy or open surgical drainage of staphylococcal empyemas is almost always needed because of the viscous nature of the empyema fluid and the tendency for loculations to develop rapidly.

Group Y Neisseria meningitidis: N meningitidis was largely ignored as a primary pulmonary pathogen until the mid-1970s. Pneumonia due to meningococcal serogroups other than Y is usually secondary to meningococcemia and has a grave prognosis. In contrast, group Y meningococcal pneumonia is frequently not associated with either meningococcemia or meningitis. Patchy alveolar infiltration is the most common radiologic pattern and pleural effusion occurs in approximately 20 percent of patients. Penicillin G (1.2 million units daily) was highly effective in one large series. It should be recognized, however, that group Y N meningitidis also produces meningitis and fulminating meningococcemia; in such instances the dose of penicillin should be 8 to 24 million units daily.

Branhamella (Neisseria) catarrhalis. B. catarrhalis has been considered to be a harmless commensal of the oral cavity. Although data are extremely limited, this organism is an unquestioned respiratory tract pathogen (Ref 19 and Dr. M.H. Louie et al, unpublished data). Some strains of B catarrhalis produce beta lactamase and may, therefore, be resistant to the penicillins; in such instances therapy with erythromycin, tetracycline, or a cephalosporin may be required to effect cure.

Haemophilus influenzae: Recent reports have emphasized the importance of H influenzae as an adult pulmonary pathogen. Common predisposing factors include chronic obstructive pulmonary disease (both H influenzae and S pneumoniae may colonize the airways of such individuals), ethanol abuse, and antecedent upper respiratory tract infection. Because H influenzae is a small gram-negative coccobacillus, it may easily be overlooked on gram stained smears of respiratory secretions.

Ampicillin (4 to 6 g daily) is the agent of choice for β-lactamase-negative strains of H influenzae. Cefamandole has been recommended as an appropriate agent for β lactamase-producing strains; several recent reports, however, have documented ther-
Bacterial infections of the lung

Legionella pneumophila: In the past five years a new and clinically quite significant pulmonary pathogen, Legionella, has been studied intensively. Although several different species of Legionella have been reported to cause pneumonia, most cases have involved L. pneumophila. Legionellosis may be sporadic or occur in localized outbreaks in institutions such as hotels and hospitals. There are some clinical similarities between legionellosis and Mycoplasma pneumoniae infection. The illness may be gradual in onset; malaise, headache, anorexia, arthralgia, myalgia, and cough are common initial symptoms; recurrent shaking chills, watery diarrhea, nausea, and vomiting are relatively frequent. Cough is initially dry but may become productive of moderate amounts of nonpurulent sputum. Fever is often nonremitting and frequently exceeds 39 to 40°C; relative bradycardia is often noted. Central nervous system manifestations are varied and include both cerebral and cerebellar dysfunction. Liver function abnormalities, and, occasionally, jaundice have been reported. Proteinuria, hematuria, and occasionally severe renal failure have been reported.

Gram stain of pulmonary secretions usually reveals scant polymorphonuclear leukocytes and no bacteria (the organism, a gram-negative bacillus, stains quite poorly in clinical specimens with gram's reagents). The chest roentgenogram initially reveals patchy alveolar infiltration; subsequent spread of infiltration to the ipsilateral or contralateral lung is frequent. Consolidation is also frequent, and pleural effusion is present in most patients, whereas cavitation is uncommon.

Etiologic diagnosis can be made either by culture or by demonstration of the organism in pulmonary secretions or pleural fluid by immunofluorescence. Diagnosis by culture is somewhat limited by the lack of a highly selective medium for culture of sputum and by slow growth of the organism. Limitations of immunofluorescence include occasional cross-reactivity with other pulmonary pathogens and the need for multiple antiseras directed against the various serogroups and species of Legionella. Serology is not of diagnostic value in the acute phase of illness. Diagnosis must often be made and therapy instituted on the basis of a suggestive clinical presentation.

Erythromycin is currently the agent of choice for treatment of Legionella infections. Initially it should be given intravenously (4 g daily) in the seriously ill patient, and therapy should last for at least three weeks to avoid relapse. Tetracycline plus rifampin appears to be an acceptable alternative combination when erythromycin is contraindicated. Beta-lactam antimicrobials, chloramphenicol, clindamycin, and aminoglycosides are ineffective.

Aerobic and facultative gram-negative bacilli: Hospital-acquired pneumonias often involve gram-negative bacilli; they usually develop in association with immunosuppressive therapy, aspiration, mechanical ventilation, or as a consequence of bacteremia; and often have a high mortality rate. The most commonly reported pathogens have been mentioned above.

A great deal of confusion exists in the literature regarding the pathogenesis of gram-negative bacillary pneumonia. Without doubt, it may occur as a sequela of either bacteremia or accidental nebulization of bacteria into the airways. Many reports of gram-negative bacillary pneumonia, however, are attributed to oropharyngeal aspiration and have been diagnosed only by sputum culture. When the clinical setting is consistent with aspiration, the possibility of mixed anaerobic and facultative or aerobic infection should always be considered. Lorber and Swenson recovered anaerobes (usually in association with facultative or aerobic organisms) from eight of 23 cases of hospital-acquired aspiration pneumonia. Bartlett and Finegold reported 143 cases of anaerobic pleuropulmonary infections (35 percent of which were hospital-acquired) and were able to recover facultative or aerobic bacteria from 64 percent of pneumonias, 29 percent of necrotizing pneumonias, 42 percent of lung abscesses, and 40 percent of empyemas. Nonanaerobes recovered were S. aureus, various Streptococcus species, and several species of pathogenic facultative or aerobic gram-negative bacilli. Moreover, they noted that 58 of 102 cultures of expectorated sputum yielded potential pathogens that were not detected by other techniques, such as transtracheal aspiration.

These data indicate that anaerobic pulmonary infections frequently involve gram-negative bacilli, that gram-negative bacillary pneumonia often involves anaerobes, and that sputum culture is not adequate for evaluation of such cases.

We believe that transtracheal aspiration (or other techniques that bypass the oral cavity) should be performed, whenever possible, in cases of complicated pneumonia. Gram stain and culture (aerobic and anaerobic) of pulmonary secretions obtained by transtracheal aspiration would provide important data both for initiation and subsequent modification of therapy. If transtracheal aspiration is not feasible, then sputum should be gram-stained, screened as outlined earlier, and cultured aerobic-
ly; empiric coverage for anaerobes should be added to the coverage given for facultative and aerobic organisms.

An aminoglycoside is usually given for treatment of gram-negative bacillary pneumonia; in addition, a broad-spectrum penicillin, such as carbenicillin or ticarcillin, is often added for dual coverage of 
Pseudomonas aeruginosa and, occasionally, for other gram-negative bacilli. The newer cephalosporins, such as cefoxitin and cefotaxime (and others that are currently under investigation), are often active against gram-negative bacilli, but should not be relied on (as a single agent) until susceptibility has been established in the laboratory. Therapy for anaerobes that may be involved in hospital-acquired (aspiration) pneumonia is outlined below.

Anaerobic pulmonary infection: This type of infection is almost invariably polymicrobial and usually involves several species of anaerobic bacteria, often in association with one or more facultative organisms. Three distinct types of anaerobic pulmonary infections (pneumonia, necrotizing pneumonia and lung abscess) have been described; all may be accompanied by empyema. The most important clinical clues, in addition to the presence of necrotizing pneumonia or abscess on chest roentgenogram, are conditions that predispose to impaired consciousness, periodontal disease, lower cranial nerve dysfunction, mechanical obstruction of an airway, and foul-smelling sputum. Unfortunately, foul sputum is present in only about one half of cases.

Anaerobes most frequently isolated from pleuropulmonary infections are usually penicillin-susceptible and include members of the 
Bacteroides melaninogenicus-Bacteroides asaccharolyticus group, 
Fusobacterium nucleatum, Peptococcus species, and 
Peptostreptococcus species. Anaerobes that are more resistant to antimicrobials, such as 
Bacteroides fragilis and other species of Bacteroides, may be encountered in ~15 percent of cases. The most frequently encountered facultative or aerobic bacteria in mixed infections are 
S aureus, S pneumoniae, H influenzae, and facultative or aerobic gram-negative bacilli; one or more of these organisms is present in one-third to one half of anaerobic pleuropulmonary infections. Empyema involving anaerobes invariably requires drainage by either tube thoracostomy or an open surgical procedure.

Penicillin is usually effective for treatment of anaerobic pleuropulmonary infection and is initially given in a daily dose of 6 to 10 million units or more. Once signs and symptoms of toxicity have abated, therapy may be given by the oral route. Anaerobic pneumonia responds rather promptly to therapy, whereas lung abscess and necrotizing pneu-

monia may require six to ten weeks or longer of therapy to effect a cure. Carbenicillin, ticarcillin, and cefoxitin are also active against most clinically significant anaerobes except 5 to 10 percent of the 
B fragilis group; these antimicrobials do not appear to possess any advantage over penicillin G in most cases of anaerobic pulmonary infection, however. Clindamycin is an effective substitute in the patient with penicillin allergy. In the patient with life-threatening infection, it may be prudent to administer an agent such as clindamycin or metronidazole (both preferably supplemented with penicillin G), or chloramphenicol in order to provide coverage for 
B fragilis and other resistant anaerobes.

Miscellaneous Causes of Bacterial Pneumonia

Several additional species of bacteria are rare causes of primary pneumonia. These include 
Bacillus anthracis, Francisella tularensis, Pseudomonas pseudomallei, and Yersinia pestis.

Nocardia asteroides causes pneumonia, often cavitary, particularly in patients who are diabetic, alcoholic, or immunosuppressed. Nocardia infections tend to extend to the pleura and chest wall and to metastasize to the brain. A sulfonamide, such as sulfadiazine, is the agent of choice for pulmonary nocardiosis and should be given for a minimum of six weeks to avoid relapse. Minocycline, erythromycin, ampicillin, trimethoprim, and possibly amikacin and cycloserine may also be useful in combination with a sulfonamide. Empyema and metastatic foci require surgical drainage.

Summary

Bacterial infection of the lung is an important cause of morbidity and mortality in adults and usually develops as a consequence of aspiration of bacteria that colonize the oropharynx. The etiologic agent of pneumonia may be diagnosed incorrectly, particularly when a "routine" sputum culture is relied on for diagnosis.

Recent studies have demonstrated that 
S agalactiae, B catarrhalis, Group Y N meningitidis, H influenzae, and Legionella sp are important pulmonary pathogens in adults.

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