**Pneumonia**

**Definition**

Pneumonia is an infection of the pulmonary parenchyma. Despite being the cause of significant morbidity and mortality, pneumonia is often misdiagnosed, mistreated, and underestimated. In the past, pneumonia was typically classified as community-acquired (CAP), hospital-acquired (HAP), or ventilator-associated (VAP). Over the past two decades, however, some persons presenting as outpatients with onset of pneumonia have been found to be infected with the multidrug-resistant (MDR) pathogens previously associated with HAP. Factors responsible for this phenomenon include the development and widespread use of potent oral antibiotics, earlier transfer of patients out of acute-care hospitals to their homes or various lower-acuity facilities, increased use of outpatient IV antibiotic therapy, general aging of the population, and more extensive immune-modulatory therapies. The potential involvement of these MDR pathogens has led to a new category of pneumonia—termed *health care*–*associated pneumonia* (HCAP)—distinct from CAP.

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| |  | **Pathogen** | | | | | --- | --- | --- | --- | --- | | **Condition** | **MRSA** | ***Pseudomonas aeruginosa*** | ***Acinetobacter* spp.** | **MDR Enterobacteriaceae** | | Hospitalization for ≥48 h | X | X | X | X | | Hospitalization for ≥2 days in prior 3 months | X | X | X | X | | Nursing home or extended-care-facility residence | X | X | X | X | | Antibiotic therapy in preceding 3 months |  | X |  | X | | Chronic dialysis | X |  |  |  | | Home infusion therapy | X |  |  |  | | Home wound care | X |  |  |  | | Family member with MDR infection | X |  |  | X | |
| ***Abbreviations:*** MDR, multidrug-resistant; MRSA, methicillin-resistant *Staphylococcus aureus* |
| Pathophysiology  Pneumonia results from the proliferation of microbial pathogens at the alveolar level and the host's response to those pathogens. Microorganisms gain access to the lower respiratory tract in several ways. The most common is by aspiration from the oropharynx. Small-volume aspiration occurs frequently during sleep (especially in the elderly) and in patients with decreased levels of consciousness. Many pathogens are inhaled as contaminated droplets. Rarely, pneumonia occurs via hematogenous spread (e.g., from tricuspid endocarditis) or by contiguous extension from an infected pleural or mediastinal space.  Mechanical factors are critically important in host defense. The hairs and turbinates of the nares capture larger inhaled particles before they reach the lower respiratory tract. The branching architecture of the tracheobronchial tree traps particles on the airway lining, where muco-ciliary clearance and local antibacterial factors either clear or kill the potential pathogen. The gag reflex and the cough mechanism offer critical protection from aspiration. In addition, the normal flora adhering to mucosal cells of the oropharynx, whose components are remarkably constant, prevents pathogenic bacteria from binding and thereby decreases the risk of pneumonia caused by these more virulent bacteria.  When these barriers are overcome or when the microorganisms are small enough to be inhaled to the alveolar level, resident alveolar macrophages are extremely efficient at clearing and killing pathogens. Macrophages are assisted by local proteins (e.g., surfactant proteins A and D) that have intrinsic opsonizing properties or antibacterial or antiviral activity. Once engulfed by the macrophage, the pathogens—even if they are not killed—are eliminated via either the muco-ciliary elevator or the lymphatics and no longer represent an infectious challenge. Only when the capacity of the alveolar macrophages to ingest or kill the microorganisms is exceeded does clinical pneumonia become manifest. In that situation, the alveolar macrophages initiate the inflammatory response to bolster lower respiratory tract defenses. The host inflammatory response, rather than the proliferation of microorganisms, triggers the clinical syndrome of pneumonia. The release of inflammatory mediators, such as interleukin (IL)-1 and tumor necrosis factor (TNF), results in fever. Chemokines, such as IL-8 and granulocyte colony-stimulating factor, stimulate the release of neutrophils and their attraction to the lung, producing both peripheral leukocytosis and increased purulent secretions. *Inflammatory mediators released by macrophages and the newly recruited neutrophils create an alveolar capillary leak* equivalent to that seen in the acute respiratory distress syndrome (ARDS), although in pneumonia this leak is localized (at least initially). Even erythrocytes can cross the alveolar-capillary membrane, with consequent hemoptysis. The capillary leak results in a radiographic infiltrate and rales detectable on auscultation, and hypoxemia results from alveolar filling. Moreover, some bacterial pathogens appear to interfere with the hypoxemic vasoconstriction that would normally occur with fluid-filled alveoli, and this interference can result in severe hypoxemia. Increased respiratory drive in the systemic inflammatory response syndrome (SIRS) leads to respiratory alkalosis. Decreased compliance due to capillary leak, hypoxemia, increased respiratory drive, increased secretions, and occasionally infection-related bronchospasm all lead to dyspnea. If severe enough, the changes in lung mechanics secondary to reductions in lung volume and compliance and the intrapulmonary shunting of blood may cause the patient's death. |

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| Pathology  Classic pneumonia evolves through a series of pathologic changes. The initial phase is one of *edema*, with the presence of a proteinaceous exudate—and often of bacteria—in the alveoli. This phase is rarely evident in clinical or autopsy specimens because it is so rapidly followed by a *red hepatization* phase. The presence of erythrocytes in the cellular intra-alveolar exudate gives this second stage its name, but neutrophil influx is more important from the standpoint of host defense. Bacteria are occasionally seen in pathologic specimens collected during this phase. In the third phase, *gray hepatization*, no new erythrocytes are extravasating, and those already present have been lysed and degraded. The neutrophil is the predominant cell, fibrin deposition is abundant, and bacteria have disappeared. This phase corresponds with successful containment of the infection and improvement in gas exchange. In the final phase, *resolution*, the macrophage reappears as the dominant cell type in the alveolar space, and the debris of neutrophils, bacteria, and fibrin has been cleared, as has the inflammatory response.  This pattern has been described best for lobar pneumococcal pneumonia and may not apply to pneumonias of all etiologies, especially viral or *Pneumocystis* pneumonia. In VAP, respiratory bronchiolitis may precede the development of a radiologically apparent infiltrate. **Because of the micro-aspiration mechanism, a bronchopneumonia pattern is most common in nosocomial pneumonias, whereas a lobar pattern is more common in bacterial CAP.** Despite the radiographic appearance, viral and *Pneumocystis* pneumonias represent alveolar rather than interstitial processes.  Community-Acquired Pneumonia  Etiology  The extensive list of potential etiologic agents in CAP includes bacteria, fungi, viruses, and protozoa. Newly identified pathogens include hantaviruses, metapneumoviruses, the coronavirus responsible for severe acute respiratory syndrome (SARS), and community-acquired strains of methicillin-resistant *Staphylococcus aureus* (MRSA). Most cases of CAP, however, are caused by relatively few pathogens (Table 257-2). Although *Streptococcus pneumoniae* is most common, other organisms must also be considered in light of the patient's risk factors and severity of illness. In most cases, it is most useful to think of the potential causes as either "typical" bacterial pathogens or "atypical" organisms. The former category includes *S*. *pneumoniae*, *Haemophilus influenzae*, and (in selected patients) *S*. *aureus* and gram-negative bacilli such as *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*. The "atypical" organisms include *Mycoplasma pneumoniae* and *Chlamydia pneumoniae* (in outpatients) and *Legionella* spp. (in inpatients) as well as respiratory viruses such as influenza viruses, adenoviruses, and respiratory syncytial viruses. Data suggest that a virus may be responsible for up to 18% of cases of CAP that require admission to the hospital. The atypical organisms cannot be cultured on standard media, nor can they be seen on Gram's stain. The frequency and importance of atypical pathogens have significant implications for therapy. These organisms are intrinsically resistant to all β-lactam agents and must be treated with a macrolide, a fluoroquinolone, or a tetracycline. In the ~10–15% of CAP cases that are poly-microbial, the etiology often includes a combination of typical and atypical pathogens.   |  |  | | --- | --- | | |  | | --- | | Table 257-2 Microbial Causes of Community-Acquired Pneumonia, by Site of Care | | | |  | **Hospitalized Patients** | | | --- | --- | --- | | **Outpatients** | **Non-ICU** | **ICU** | | *Streptococcus pneumoniae* | *S. pneumoniae* | *S. pneumoniae* | | *Mycoplasma pneumoniae* | *M. pneumoniae* | *Staphylococcus aureus* | | *Haemophilus influenzae* | *Chlamydia pneumoniae* | *Legionella* spp. | | *C. pneumoniae* | *H. influenzae* | Gram-negative bacilli | | Respiratory viruses*a* | *Legionella* spp. | *H. influenzae* | |  | Respiratory viruses*a* |  | | | *a*Influenza A and B viruses, adenoviruses, respiratory syncytial viruses, parainfluenza viruses. ***Note:*** Pathogens are listed in descending order of frequency |   Anaerobes play a significant role only when an episode of aspiration has occurred days to weeks before presentation for pneumonia. The combination of an unprotected airway (e.g., in patients with alcohol or drug overdose or a seizure disorder) and significant gingivitis constitutes the major risk factor. *Anaerobic pneumonias are often complicated by abscess formation and significant empyemas or parapneumonic effusions*.  *S. aureus* pneumonia is well known to complicate influenza infection. However, MRSA has been reported as the primary etiologic agent of CAP. While this entity is still relatively uncommon**, clinicians must be aware of its potentially serious consequences such as necrotizing pneumonia**. Two important developments have led to this problem: the spread of MRSA from the hospital setting to the community and the emergence of genetically distinct strains of MRSA in the community. The former circumstance is more likely to result in HCAP, whereas the novel community-acquired MRSA (CA-MRSA) strains have infected healthy individuals who have had no association with health care.  Unfortunately, despite a careful history and physical examination as well as routine radiographic studies, the causative pathogen in a case of CAP is difficult to predict with any degree of certainty; in more than one-half of cases, a specific etiology is never determined. Nevertheless, epidemiologic and risk factors may suggest the involvement of certain pathogens (Table 257-3).   |  |  | | --- | --- | | |  | | --- | | Table 257-3 Epidemiologic Factors Suggesting Possible Causes of Community-Acquired Pneumonia | | | | **Factor** | **Possible Pathogen(s)** | | --- | --- | | Alcoholism | *Streptococcus pneumoniae,* oral anaerobes, *Klebsiella pneumoniae, Acinetobacter* spp., *Mycobacterium tuberculosis* | | COPD and/or smoking | *Haemophilus influenzae, Pseudomonas aeruginosa, Legionella* spp.,  *S. pneumoniae, Moraxella catarrhalis, Chlamydia pneumoniae* | | Structural lung disease (e.g., bronchiectasis) | *P. aeruginosa, Burkholderia cepacia, Staphylococcus aureus* | | Dementia, stroke, decreased level of consciousness | Oral anaerobes, gram-negative enteric bacteria | | Lung abscess | CA-MRSA, oral anaerobes, endemic fungi, *M. tuberculosis*, atypical mycobacteria | | Stay in hotel or on cruise ship in previous 2 weeks | *Legionella* spp. | | Local influenza activity | Influenza virus, *S. pneumoniae*, *S. aureus* | | Exposure to bats or birds | *H. capsulatum* | | Exposure to birds | *Chlamydia psittaci* | | Exposure to rabbits | *Francisella tularensis* | | Exposure to sheep, goats, parturient cats | *Coxiella burnetii* | | | ***Abbreviations:*** CA-MRSA, community-acquired methicillin-resistant *Staphylococcus aureus;* |   The risk factors for CAP in general and for pneumococcal pneumonia in particular have implications for treatment regimens. Risk factors for CAP include alcoholism, asthma, immunosuppression, institutionalization, and an age of ≥70 years versus 60–69 years. Risk factors for pneumococcal pneumonia include dementia, seizure disorders, heart failure, cerebrovascular disease, alcoholism, tobacco smoking, chronic obstructive pulmonary disease (COPD), and HIV infection. CA-MRSA pneumonia is more likely in patients with skin colonization or infection with CA-MRSA. Enterobacteriaceae tend to infect patients who have recently been hospitalized and/or received antibiotic therapy or who have comorbidities such as alcoholism, heart failure, or renal failure. *P*. *aeruginosa* is a particular problem in patients with severe structural lung disease, such as bronchiectasis, cystic fibrosis, or severe COPD. Risk factors for *Legionella* infection include diabetes, hematologic malignancy, cancer, severe renal disease, HIV infection, smoking, male gender, and a recent hotel stay or ship cruise. (Many of these risk factors would now reclassify as HCAP some cases that were previously designated CAP.)  Clinical Manifestations  CAP can vary from indolent to fulminant in presentation and from mild to fatal in severity. The various signs and symptoms that depend on the progression and severity of the infection include both constitutional findings and manifestations limited to the lung and associated structures. In light of the pathobiology of the disease, many of the findings are to be expected.  The patient is frequently febrile with tachycardia or may have a history of chills and/or sweats. Cough may be either nonproductive or productive of mucoid, purulent, or blood-tinged sputum. Depending on severity, the patient may be able to speak in full sentences or may be very short of breath. If the pleura is involved, the patient may experience pleuritic chest pain. Up to 20% of patients may have gastrointestinal symptoms such as nausea, vomiting, and/or diarrhea. Other symptoms may include fatigue, headache, myalgias, and arthralgias.  Findings on physical examination vary with the degree of pulmonary consolidation and the presence or absence of a significant pleural effusion. An increased respiratory rate and use of accessory muscles of respiration are common. Palpation may reveal increased or decreased tactile fremitus, and the percussion note can vary from dull to flat, reflecting underlying consolidated lung and pleural fluid, respectively. Crackles, bronchial breath sounds, and possibly a pleural friction rub may be heard on auscultation. The clinical presentation may not be so obvious in the elderly, who may initially display new-onset or worsening confusion and few other manifestations. Severely ill patients may have septic shock and evidence of organ failure. Diagnosis When confronted with possible CAP, the physician must ask two questions: Is this pneumonia, and, if so, what is the likely etiology? The former question is typically answered by clinical and radiographic methods, whereas the latter requires the aid of laboratory techniques. Clinical Diagnosis The differential diagnosis includes both infectious and noninfectious entities such as acute bronchitis, acute exacerbations of chronic bronchitis, heart failure, pulmonary embolism, and radiation pneumonitis. The importance of a careful history cannot be overemphasized. For example, known cardiac disease may suggest worsening pulmonary edema, while underlying carcinoma may suggest lung injury secondary to irradiation.  Unfortunately, the sensitivity and specificity of the findings on physical examination are less than ideal, averaging 58% and 67%, respectively. Therefore, chest radiography is often necessary to differentiate CAP from other conditions. Radiographic findings may include risk factors for increased severity (e.g., cavitation or multi-lobar involvement). Occasionally, radiographic results suggest an etiologic diagnosis. For example, pneumatoceles suggest infection with *S*. *aureus*, and an upper-lobe cavitating lesion suggests tuberculosis. CT is rarely necessary but may be of value in a patient with suspected post-obstructive pneumonia caused by a tumor or foreign body. For outpatients, the clinical and radiologic assessments are usually all that is done before treatment for CAP is started since most laboratory results are not available soon enough to influence initial management significantly. In certain cases, the availability of rapid point-of-care outpatient diagnostic tests can be very important (e.g., rapid diagnosis of influenza virus infection can prompt specific anti-influenza drug treatment and secondary prevention). Etiologic Diagnosis The etiology of pneumonia usually cannot be determined solely on the basis of clinical presentation; instead, the physician must rely upon the laboratory for support. Except for the 2% of CAP patients who are admitted to the intensive care unit (ICU), no data exist to show that treatment directed at a specific pathogen is statistically superior to empirical therapy. The benefit of establishing a microbial etiology can therefore be questioned, particularly in light of the cost of diagnostic testing. However, a number of reasons can be advanced for attempting an etiologic diagnosis. Identification of an unexpected pathogen allows narrowing of the initial empirical regimen that decreases antibiotic selection pressure, lessening the risk of resistance. Pathogens with important public safety implications such as *Mycobacterium tuberculosis* and influenza virus, may be found in some cases. Finally, without culture and susceptibility data, trends in resistance cannot be followed accurately, and appropriate empirical therapeutic regimens are harder to devise. Gram's Stain and Culture of Sputum The main purpose of the sputum Gram's stain is to ensure that a sample is suitable for culture. However, Gram's staining may also identify certain pathogens (e.g., *S*. *pneumoniae*, *S*. *aureus*, and gram-negative bacteria) by their characteristic appearance. To be adequate for culture, a sputum sample must have >25 neutrophils and <10 squamous epithelial cells per low-power field. The sensitivity and specificity of the sputum Gram's stain and culture are highly variable. Even in cases of proven bacteremic pneumococcal pneumonia, the yield of positive cultures from sputum samples is ≥50%.  Some patients, particularly elderly individuals, may not be able to produce an appropriate expectorated sputum sample. Others may already have started a course of antibiotics that can interfere with culture results at the time a sample is obtained. Inability to produce sputum can be a consequence of dehydration, and the correction of this condition may result in increased sputum production and a more obvious infiltrate on chest radiography. For patients admitted to the ICU and intubated, a deep-suction aspirate or broncho-alveolar lavage sample (obtained either via bronchoscopy or non-bronchoscopically) has a high yield on culture when sent to the microbiology laboratory as soon as possible. Blood Cultures The yield from blood cultures, even when samples are collected before antibiotic therapy, is disappointingly low. Only ~5–14% of cultures of blood from patients hospitalized with CAP are positive, and the most frequently isolated pathogen is *S*. *pneumoniae*. Since recommended empirical regimens all provide pneumococcal coverage, a blood culture positive for this pathogen has little, if any, effect on clinical outcome. However, susceptibility data may allow narrowing of antibiotic therapy in appropriate cases. Because of the low yield and the lack of significant impact on outcome, blood cultures are no longer considered *de rigueur* for all hospitalized CAP patients. Certain high-risk patients—including those with neutropenia secondary to pneumonia, asplenia, or complement deficiencies; chronic liver disease; or severe CAP—should have blood cultured. Antigen Tests Two commercially available tests detect pneumococcal and certain *Legionella* antigens in urine. The test for *L*. *pneumophila* detects only serogroup 1, but this serogroup accounts for most community-acquired cases of Legionnaires' disease. The sensitivity and specificity of the *Legionella* urine antigen test are as high as 90% and 99%, respectively. The pneumococcal urine antigen test is also quite sensitive and specific (80% and >90%, respectively). Although false-positive results can be obtained with samples from pneumococcus-colonized children, the test is generally reliable. Both tests can detect antigen even after the initiation of appropriate antibiotic therapy. Other antigen tests include a rapid test for influenza virus and direct fluorescent antibody tests for influenza virus and respiratory syncytial virus; the latter tests are only poorly sensitive. Polymerase Chain Reaction Polymerase chain reaction (PCR) tests, which amplify a microorganism's DNA or RNA, are available for a number of pathogens, including *L*. *pneumophila* and mycobacteria. In addition, a multiplex PCR can detect the nucleic acid of *Legionella* spp., *M*. *pneumoniae*, and *C*. *pneumoniae*. However, the use of these PCR assays is generally limited to research studies. In patients with pneumococcal pneumonia, an increased bacterial load documented by PCR is associated with an increased risk of septic shock, need for mechanical ventilation, and death. Such a test could conceivably help identify patients suitable for ICU admission. Serology A fourfold rise in specific IgM antibody titer between acute- and convalescent-phase serum samples is generally considered diagnostic of infection with the pathogen in question. In the past, serologic tests were used to help identify atypical pathogens as well as selected unusual organisms such as *Coxiella burnetii*. Recently, however, they have fallen out of favor because of the time required to obtain a final result for the convalescent-phase sample. Treatment: Community-Acquired Pneumonia Site of Care  The cost of inpatient management exceeds that of outpatient treatment by a factor of 20, and hospitalization accounts for most CAP-related expenditures. Thus the decision to admit a patient with CAP to the hospital has considerable implications. Certain patients clearly can be managed at home, and others clearly require treatment in the hospital, but the choice is sometimes difficult. Tools that objectively assess the risk of adverse outcomes, including severe illness and death, can minimize unnecessary hospital admissions. There are currently two sets of criteria: the Pneumonia Severity Index (PSI), a prognostic model used to identify patients at low risk of dying; and the CURB-65 criteria, a severity-of-illness score.  To determine the PSI, points are given for 20 variables, including age, coexisting illness, and abnormal physical and laboratory findings. On the basis of the resulting score, patients are assigned to one of five classes with the following mortality rates: class 1, 0.1%; class 2, 0.6%; class 3, 2.8%; class 4, 8.2%; and class 5, 29.2%. Clinical trials demonstrate that routine use of the PSI results in lower admission rates for class 1 and class 2 patients. Patients in classes 4 and 5 should be admitted to the hospital, while those in class 3 should ideally be admitted to an observation unit until a further decision can be made.  The CURB-65 criteria include five variables: 🡺confusion (C);  🡺urea >7 mmol/L (U);  🡺respiratory rate ≥30/min (R);  🡺blood pressure, systolic ≤90 mmHg or diastolic ≤60 mmHg (B); and  🡺age ≥65 years (65). Patients with a score of 0, among whom the 30-day mortality rate is 1.5%, can be treated outside the hospital. With a score of 2, the 30-day mortality rate is 9.2%, and patients should be admitted to the hospital. Among patients with scores of ≥3, mortality rates are 22% overall; these patients may require admission to an ICU. Antibiotic Resistance Antimicrobial resistance is a significant problem that threatens to diminish our therapeutic armamentarium. Misuse of antibiotics results in increased antibiotic selection pressure that can affect resistance locally or even globally by clonal dissemination. For CAP, the main resistance issues currently involve *S*. *pneumoniae* and CA-MRSA.    S. Pneumoniae  In general, pneumococcal resistance is acquired  (1) by direct DNA incorporation and remodeling resulting from contact with closely related oral commensal bacteria,  (2) by the process of natural transformation, or  (3) by mutation of certain genes.  The cutoff for penicillin susceptibility in pneumonia has recently been raised from a minimal inhibitory concentration (MIC) of ≤0.6 µg/mL to an MIC of ≤2 µg/mL. Cutoffs for intermediate resistance have been raised to 4 µg/mL (from 0.1–1 µg/mL) and ≥8 µg/mL (from ≥2 µg/mL), respectively. These changes in susceptibility thresholds have resulted in a dramatic decrease in the proportion of pneumococcal isolates considered non-susceptible. For meningitis, MIC thresholds remain at the former levels. Fortunately, resistance to penicillin appeared to plateau even before the change in MIC thresholds. Pneumococcal resistance to β-lactam drugs is due solely to low-affinity penicillin-binding proteins. Risk factors for penicillin-resistant pneumococcal infection include recent antimicrobial therapy, an age of <2 years or >65 years, attendance at day-care centers, recent hospitalization, and HIV infection.  In contrast to penicillin resistance, resistance to macrolides is increasing through several mechanisms. *Target*-*site modification* is caused by ribosomal methylation in 23S rRNA encoded by the *ermB* gene, resulting in resistance to macrolides, lincosamides, and streptogramin B–type antibiotics. This MLSB phenotype is associated with high-level resistance, with typical MICs of ≥64 µg/mL. The *efflux mechanism* encoded by the *mef* gene (*M phenotype*) is usually associated with low-level resistance (MICs, 1–32 µg/mL). These two mechanisms account for ~45% and ~65%, respectively, of resistant pneumococcal isolates in the United States. High-level resistance to macrolides is more common in Europe, whereas lower-level resistance seems to predominate in North America. Although clinical failures with macrolides have been reported, many experts think that these drugs still have a role to play in the management of pneumococcal pneumonia in North America.  Pneumococcal resistance to fluoroquinolones (e.g., ciprofloxacin and levofloxacin) has been reported. Changes can occur in one or both target sites (topoisomerases II and IV); changes in these two sites usually result from mutations in the *gyrA* and *parC* genes, respectively. The increasing number of pneumococcal isolates that, although still testing susceptible to fluoroquinolones, already have a mutation in one target site is of concern. Such organisms may be more likely to undergo a second step mutation that will render them fully resistant to fluoroquinolones. In addition, an efflux pump may play a role in pneumococcal resistance to fluoroquinolones.  Isolates resistant to drugs from three or more antimicrobial classes with different mechanisms of action are considered MDR. The propensity for an association of pneumococcal resistance to penicillin with reduced susceptibility to other drugs such as macrolides, tetracyclines, and trimethoprim-sulfamethoxazole, is also of concern. In the United States, 58.9% of penicillin-resistant pneumococcal isolates from blood are also resistant to macrolides.  The most important risk factor for antibiotic-resistant pneumococcal infection is use of a specific antibiotic within the previous 3 months. Therefore, a patient's history of prior antibiotic treatment is a critical factor in avoiding the use of an inappropriate antibiotic. |

General Considerations

In addition to appropriate antimicrobial therapy, certain general considerations apply in dealing with CAP, HCAP, or HAP/VAP. Adequate hydration, oxygen therapy for hypoxemia, and assisted ventilation when necessary are critical to the success of therapy. Patients with severe CAP who remain hypotensive despite fluid resuscitation may have adrenal insufficiency and may respond to glucocorticoid treatment. Immunomodulatory therapy in the form of drotrecogin alfa (activated) should be considered for CAP patients with persistent septic shock and APACHE II scores of ≥25, particularly if the infection is caused by *S*. *pneumoniae*. The value of other forms of adjunctive therapy, including glucocorticoids, statins, and angiotensin-converting enzyme inhibitors, remains unproven in the management of CAP.

Failure to Improve

Patients who are slow to respond to therapy should be reevaluated at about day 3 (sooner if their condition is worsening rather than simply not improving), and a number of possible scenarios should be considered. A number of noninfectious conditions can mimic pneumonia, including pulmonary edema, pulmonary embolism, lung carcinoma, radiation and hypersensitivity pneumonitis, and connective tissue disease involving the lungs. If the patient has CAP and treatment is aimed at the correct pathogen, the lack of response may be explained in a number of ways. The pathogen may be resistant to the drug selected, or a sequestered focus (e.g., a lung abscess or empyema) may be blocking access of the antibiotic(s) to the pathogen. The patient may be getting either the wrong drug or the correct drug at the wrong dose or frequency of administration. It is also possible that CAP is the correct diagnosis but that an unsuspected pathogen (e.g., CA-MRSA, *M*. *tuberculosis*, or a fungus) is the cause. Nosocomial superinfections—both pulmonary and extra-pulmonary—are possible explanations for failure to improve or worsening. In all cases of delayed response or deteriorating condition, the patient must be carefully reassessed and appropriate studies initiated. These studies may include such diverse procedures as CT and bronchoscopy.

# Complications

As in other severe infections, common complications of severe CAP include respiratory failure, shock and multi-organ failure, coagulopathy, and exacerbation of comorbid illnesses. Three particularly noteworthy conditions are metastatic infection, lung abscess, and complicated pleural effusion. Metastatic infection (e.g., brain abscess or endocarditis), although unusual, deserves immediate attention by the physician, with a detailed workup and proper treatment. Lung abscess may occur in association with aspiration or with infection caused by a single CAP pathogen such as CA-MRSA, *P*. *aeruginosa*, or (rarely) *S*. *pneumoniae*. Aspiration pneumonia is typically a mixed poly-microbial infection involving both aerobes and anaerobes. In either scenario, drainage should be established, and antibiotics that cover the known or suspected pathogens should be administered. A significant pleural effusion should be tapped for both diagnostic and therapeutic purposes.

If the fluid has a pH of <7, a glucose level of <2.2 mmol/L, and a lactate dehydrogenase concentration of >1000 U/L or if bacteria are seen or cultured, then the fluid should be drained; a chest tube is usually required.

{ **Exudative pleural effusion: Fulfills one or more of the following**

## LIGHT’S CRITERIA

🡺 Pleural protein-to-serum protein ratio > 0.5,

🡺 Pleural LDH-to-serum LDH ratio >0.6, or

🡺 Pleural LDH (lactate dehydrogenase) is above 2/3 of upper normal serum level}

# Health Care–Associated Pneumonia

HCAP represents a transition between classic CAP and typical HAP. The definition of HCAP is still in some degree of flux because of a lack of large-scale studies. Several of the studies that are available have been limited to patients with culture-positive pneumonia. In these studies, the incidence of MDR pathogens in HCAP was as high as or higher than in HAP/VAP. MRSA in particular was more common in HCAP than in traditional HAP/VAP. Conversely, prospective studies in non-tertiary-care centers have found a low incidence of MDR pathogens in HCAP.

The patients at greatest risk for HCAP are not well defined. Patients from nursing homes are not always at elevated risk for infection with MDR pathogens. Careful evaluation of nursing home residents with pneumonia suggests that their risk of MDR infection is low if they have not recently received antibiotics and are independent in most activities of daily living. Conversely, nursing home patients are at increased risk of infection with influenza virus and other atypical pneumonia pathogens. Undue concern about MDR pathogens occasionally results in a failure to cover atypical pathogens in treating nursing home patients. In addition, patients receiving home infusion therapy or undergoing chronic dialysis are probably at particular risk for MRSA pneumonia but may not be at greater risk for infection with *Pseudomonas* or *Acinetobacter* than are other patients who develop CAP.

In general, the management of HCAP due to MDR pathogens is similar to that of MDR HAP/VAP. This topic will therefore be covered in subsequent sections on HAP and VAP. The prognosis of HCAP is intermediate between that of CAP and VAP and is closer to that of HAP.