virulent pathogens and the subsequent aspiration of these organisms into the lower respiratory tract. Gastric colonization by gram-negative organisms is enhanced by neutralization of gastric acidity. In the first 5 days of hospitalization, *H. influenzae*, *S. pneumoniae*, and *S. aureus* are often isolated. After this time, *Pseudomonas aeruginosa*, *S. aureus*, anaerobic microbes, *Acinetobacter* species, and various gram-negative enteric bacilli often are the cause of pneumonia. This finding has important therapeutic implications because these organisms are more commonly associated with multidrug antibiotic resistance.

Treatment depends on combined chemotherapy with β-lactam antipseudomonal penicillin or cephalosporin, together with an aminoglycoside or a quinolone. Vancomycin is added if methicillin-resistant *S. aureus* is suspected. A more definitive identification of organisms and their sensitivity to antibiotics is often sought for these patients using more invasive measures, including endotracheal aspirate in intubated patients or flexible fiberoptic bronchoscopy. However, the best predictor of patient outcome with nosocomial pneumonia appears to be adequacy of the initial empirical antibiotic regimen.

For a deeper discussion on this topic, please see Chapter 282, "Prevention and Control of Health Care–Associated Infections," in Goldman-Cecil Medicine, *25th Edition.*

COMPLICATIONS OF PNEUMONIA

Parapneumonic effusion is a neutrophilic exudative effusion adjacent to a lung with pneumonia (E-Fig. 21-2). It has exudative, fibrinopurulent, and organized stages. Depending on the stage, the effusion can resolve with antibiotics alone or may require drainage in addition to antibiotics. As pneumonia progresses, inflammatory edema leaks into the pleural space, first appearing as an uncomplicated effusion (i.e., exudative stage). At this point, the effusion can resolve with antibiotic therapy alone. During the fibrinopurulent and organized stages, the inflammatory process is marked by anaerobic metabolism, cytokine production, fibrin deposition in the pleural space, and thickening of the pleura.

There is no universally accepted definition of *empyema*, but most clinicians include all pleural effusions that are grossly purulent or contain microorganisms identified by a positive Gram stain or culture. Empyema must always be treated with pleural drainage, usually by a chest thoracostomy tube. Highly inflammatory parapneumonic effusions may behave as if they are infected, although microorganisms are never identified. Effusions described as "complicated" parapneumonic effusions are identified clinically by a pH of less than 7.1, a high serum lactate dehydrogenase (LDH) level, and a glucose level of less than 40 mg/dL. Complicated effusions usually require drainage in addition to antibiotic therapy.

The major risk factor for the development of lung abscess is aspiration resulting in a more indolent, polymicrobial infection, usually involving both aerobes and anaerobes. Conditions predisposing patients to aspiration, such as alcoholism, seizures, or stroke, are associated with an increased incidence of lung abscess. Poor dentition increases the anaerobic bacterial load in the mouth and the likelihood of infection after an aspiration event. In trials of empirical therapy for lung abscess, clindamycin showed superiority over penicillin, probably because the incidence of penicillin-resistant anaerobes in lung abscesses is 15% to 20%. Antibiotics should be continued for 6 weeks, and drainage should be reserved for very large abscesses or failure to resolve with antibiotics.

MYCOBACTERIUM TUBERCULOSIS INFECTION

Infection with *M. tuberculosis*, an aerobic, nonmotile, acid-fast rod with niacin production, causes TB. In 2011, the World Health Organization (WHO) Global Surveillance and Monitoring Project estimated 8.7 million new cases of TB per year, 13% of whom are co-infected with HIV. Twelve million cases of the disease existed predominately in Asia and Africa. An estimated 1.4 million individuals die of TB each year, and the global case-fatality rate was 23%, with a rate of 50% in some African countries with high HIV rates. In the United States, TB increased at an alarming rate in the early 1990s as a result of the surge of HIV infection, drug abuse, inner-city poverty, and homelessness.

TB infection occurs when aerosolized, contaminated droplets (expectorated by a diseased person) are inhaled by another individual and droplet nuclei reach an alveolus. This is almost always a latent infection, called *latent tuberculosis infection* (LTBI). If the innate immune system of the host fails to eliminate the latent infection, the bacilli proliferate inside alveolar macrophages and kill the cells.

The infected macrophages produce cytokines and chemokines that attract other phagocytic cells, including monocytes, other alveolar macrophages, and neutrophils, which eventually form a nodular granulomatous structure called the *tubercle*. If the bacterial replication is not controlled, the tubercle enlarges, and the bacilli enter the local draining lymph nodes. This leads to lymphadenopathy, a characteristic manifestation of primary TB. The lesion produced by the expansion of the tubercle into the lung parenchyma and lymph node involvement is called the *Ghon complex*.

The bacilli continue to proliferate until an effective cell-mediated immune response develops, usually 2 to 6 weeks after infection. Failure by the host to mount an effective cell-mediated immune response and tissue repair leads to progressive lung injury. Bacterial products, tumor necrosis factor-α, reactive oxygen intermediates, reactive nitrogen intermediates, and the contents of cytotoxic cells (e.g., granzymes, perforin) can contribute to the development of caseating necrosis that characterizes a tuberculous granuloma (E-Fig. 21-3).

If mycobacterial growth is unchecked, the bacilli may spread hematogenously to produce disseminated TB. Miliary TB is a disseminated form with lesions resembling millet seeds. Bacilli can also spread mechanically by erosion of the caseating lesions into the lung airways. It is at this point that the host becomes infectious to others.

Untreated disseminated TB has a mortality rate of 80%, with the remainder developing chronic disease or recovering spontaneously. The chronic disease is characterized by repeated episodes of spontaneous healing with fibrotic changes around the lesions and tissue breakdown. Healing by complete spontaneous eradication of the bacilli is rare.

Reactivation TB results when the persistent bacteria in a host suddenly proliferate. Only 5% to 10% of patients with no underlying medical problems who become infected develop