11. Here, it is enough to emphasize that a transbronchial lung biopsy might provide the only tissue available for diagnosis. Since the amount of tissue is small, necrosis and granulomatous vasculitis might not be present. Rather, the diagnostically important features are capillaritis and scattered, poorly formed granulomas (unlike those of sarcoidosis, which are rounded and well-defined).

Pulmonary Infections

Respiratory tract infections are more frequent than infections of any other organ and account for the largest number of workdays lost in the general population. The vast majority are upper respiratory tract infections caused by viruses (common cold, pharyngitis), but bacterial, viral, mycoplasmal, and fungal infections of the lung (pneumonia) still account for an enormous amount of morbidity and are the eighth leading cause of death (responsible for 2.3% of all deaths) in the United States. Pneumonia can be very broadly defined as any infection of the lung parenchyma.

Pulmonary anti-microbial defense mechanisms are described in Chapter 8. Pneumonia can result whenever these local defense mechanisms are impaired or the systemic resistance of the host is lowered. Factors that affect resistance in general include chronic diseases, immunologic deficiency, treatment with immunosuppressive agents, and leukopenia. The local defense mechanisms of the lung can be compromised by many factors, including:

- *Loss or suppression of the cough reflex* as a result of coma, anesthesia, neuromuscular disorders, drugs, or chest pain (may lead to *aspiration* of gastric contents)
- *Injury to the mucociliary apparatus* by either impairment of ciliary function or destruction of ciliated epithelium, due to cigarette smoke, inhalation of hot or corrosive gases, viral diseases, or genetic defects of ciliary function (e.g., the immotile cilia syndrome)
- *Accumulation of secretions* in conditions such as cystic fibrosis and bronchial obstruction
- *Interference with the phagocytic* or bactericidal action of alveolar macrophages by alcohol, tobacco smoke, anoxia, or oxygen intoxication
- *Pulmonary congestion and edema*

Defects in innate immunity (including neutrophil and complement defects) and humoral immunodeficiency typically lead to an increased incidence of infections with pyogenic bacteria. Germline mutations in MyD88 (an adaptor for several TLRs that is important for activation of the transcription factor NFκB) are also associated with destructive bacterial (pneumococcal) pneumonias. On the other hand, cell-mediated immune defects (congenital and acquired) lead to increased infections with intracellular microbes such as mycobacteria and herpesviruses as well as with microorganisms of very low virulence, such as *Pneumocystis jiroveci*.

Several other points should be emphasized. First, to paraphrase the French physician Louis Cruveilhier in 1919 (during the Spanish flu epidemic), "flu condemns, and additional infection executes". This is particularly true in debilitated patients. For example, the most common cause of death in viral influenza epidemics is superimposed bacterial pneumonia. Second, although the portal of entry for most bacterial pneumonias is the respiratory tract, hematogenous seeding of the lungs from another organ may occur and may be difficult to distinguish from primary pneumonia. Finally, many patients with chronic diseases acquire terminal pneumonia while hospitalized *(nosocomial infection)*. Bacteria common to the hospital environment may have acquired resistance to antibiotics; opportunities for spread are increased; invasive procedures, such as intubations and injections, are common; and bacteria may contaminate equipment used in respiratory care units.

Pneumonia is classified by the specific etiologic agent, which determines the treatment, or, if no pathogen can be isolated (which occurs in about 50% of cases), by the clinical setting in which the infection occurs. The latter considerably narrows the list of suspected pathogens, providing a guide for empirical antimicrobial therapy. As Table 15-7 indicates, pneumonia can arise in seven distinct clinical settings ("pneumonia syndromes"), and the implicated pathogens are reasonably specific to each category.

Community-Acquired Bacterial Pneumonias

Community-acquired acute pneumonia refers to lung infection in otherwise healthy individuals that is acquired from the normal environment (in contrast to hospital acquired pneumonia). It may be bacterial or viral. Clinical and radiologic features are usually insensitive in differentiating between them. Several newer biomarkers have been developed to identify patients with bacterial infection and to define their prognosis. Of these, C-reactive protein and procalcitonin, both acute-phase reactants produced primarily in the liver, are significantly elevated in bacterial more than in viral infections.

Often, the bacterial infection follows an upper respiratory tract viral infection. Bacterial invasion of the lung parenchyma causes the alveoli to be filled with an inflammatory exudate, thus causing consolidation ("solidification") of the pulmonary tissue. Many variables, such as the specific etiologic agent, the host reaction, and the extent of involvement, determine the precise form of pneumonia. Predisposing conditions include extremes of age, chronic diseases (congestive heart failure, COPD, and diabetes), congenital or acquired immune deficiencies, and decreased or absent splenic function (sickle cell disease or postsplenectomy, which puts the patient at risk for infection with encapsulated bacteria such as pneumococcus).

Streptococcus pneumoniae

***Streptococcus pneumoniae*, or *pneumococcus*, is the most common cause of community-acquired acute pneumonia.** Examination of Gram-stained sputum is an important step in the diagnosis of acute pneumonia. The presence of numerous neutrophils containing the typical gram-positive, lancet-shaped diplococci supports the diagnosis of pneumococcal pneumonia, but it must be remembered that *S. pneumoniae* is a part of the endogenous flora in 20% of adults, and therefore false-positive results may be obtained. Isolation of pneumococci from blood cultures is more specific but less sensitive (in the early phase of illness, only 20% to 30% of patients have positive blood cultures).