

**1016** develop a specific antibody response, with subsequent resistance to *Legionella* challenge. However, antibodies neither enhance lysis by complement nor inhibit intracellular multiplication within phagocytes.



The genome of *L. pneumophila* has been sequenced. A broad range of membrane transporters within the genome are thought to optimize the use of nutrients in water and soil.

Some *L. pneumophila* strains are clearly more virulent than others, although the precise factors mediating virulence remain uncertain. For example, although multiple strains may colonize water-distribution systems, only a few cause disease in patients exposed to water from these systems. At least one surface epitope of *L. pneumophila* serogroup 1 is associated with virulence. Monoclonal antibody subtype mAb2 has been linked to virulence. *L. pneumophila* serogroup 6 is more commonly involved in hospital-acquired Legionnaires' disease and is especially likely to be associated with a poor outcome.

#### CLINICAL AND LABORATORY FEATURES

**Pontiac Fever** Pontiac fever is an acute, self-limiting, flu-like illness with an incubation period of 24–48 h. Pneumonia does not develop. Malaise, fatigue, and myalgias are the most common symptoms, occurring in 97% of cases. Fever (usually with chills) develops in 80–90% of cases and headache in 80%. Other symptoms (seen in fewer than 50% of cases) include arthralgias, nausea, cough, abdominal pain, and diarrhea. Modest leukocytosis with a neutrophilic predominance is sometimes detected. Complete recovery occurs within a few days; antibiotic therapy is unnecessary. A few patients may experience lassitude for some weeks after recovery. The diagnosis is established by antibody seroconversion. Pontiac fever due to *L. longbeachae* has been reported in individuals exposed to potting soil.

**Legionnaires' Disease (Pneumonia)** Legionnaires' disease is often included in the differential diagnosis of "atypical pneumonia," along with pneumonia due to *C. pneumoniae*, *Chlamydia psittaci*, *Mycoplasma pneumoniae*, *Coxiella burnetii*, and some viruses. The clinical similarities among "atypical" pneumonias include a nonproductive cough with a low frequency of grossly purulent sputum. The clinical manifestations of Legionnaires' disease are usually more severe than those of most "atypical" pneumonias. The course and prognosis of *Legionella* pneumonia more closely resemble those of bacteremic pneumococcal pneumonia than those of pneumonia due to other "atypical" pathogens. Patients with community-acquired Legionnaires' disease are significantly more likely than patients with pneumonia of other etiologies to be admitted to an intensive care unit (ICU) on presentation.

The incubation period for Legionnaires' disease is usually 2–10 days, although slightly longer incubation periods have been documented. Fever is almost universal. In one observational study, 20% of patients had temperatures in excess of 40°C (104°F). The symptoms and signs may range from a mild cough and a slight fever to stupor with widespread pulmonary infiltrates and multisystem failure. The mild cough of Legionnaires' disease is only slightly productive. Sometimes the sputum is streaked with blood. Chest pain—either pleuritic or nonpleuritic—can be a prominent feature and, when coupled with hemoptysis, can lead to an incorrect diagnosis of pulmonary embolism. Shortness of breath is reported by one-third to one-half of patients. Gastrointestinal difficulties are often pronounced; abdominal pain, nausea, and vomiting affect 10–20% of patients. Diarrhea (watery rather than bloody) is reported in 25–50% of cases. The most common neurologic abnormalities are confusion or changes in mental status; however, the multitudinous neurologic symptoms reported range from headache and lethargy to encephalopathy. Nonspecific symptoms—malaise, fatigue, anorexia, and headache—are reported early in the illness. Myalgias and arthralgias are uncommon but are prominent in a few patients. Upper respiratory symptoms, including coryza, are rare.

Relative bradycardia has been overemphasized as a useful diagnostic finding; it occurs primarily in older patients with severe pneumonia. Rales are detected by chest examination early in the course, and evidence of consolidation is found as the disease progresses. Abdominal examination may reveal generalized or local tenderness.

**TABLE 184-1 CLINICAL CLUES SUGGESTIVE OF LEGIONNAIRES' DISEASE**

Diarrhea
High fever (>40°C; >104°F)
Numerous neutrophils but no organisms revealed by Gram's staining of respiratory secretions
Hyponatremia (serum sodium level <131 mg/dL)
Failure to respond to $\beta$ -lactam drugs (penicillins or cephalosporins) and aminoglycoside antibiotics
Occurrence of illness in an environment in which the potable water supply is known to be contaminated with <i>Legionella</i>
Onset of symptoms within 10 days after discharge from the hospital (hospital-acquired legionellosis manifesting after discharge or transfer)

Although the clinical manifestations often considered classic for Legionnaires' disease may suggest the diagnosis (Table 184-1), prospective comparative studies have shown that clinical manifestations are generally nonspecific and that Legionnaires' disease is not readily distinguishable from pneumonia of other etiologies. In a review of 13 studies of community-acquired pneumonia, clinical manifestations that occurred significantly more often in Legionnaires' disease included diarrhea, neurologic findings (including confusion), and a temperature of >39°C. Hyponatremia, elevated values in liver function tests, and hematuria also occurred more frequently in Legionnaires' disease. Other laboratory abnormalities include creatine phosphokinase elevation, hypophosphatemia, serum creatinine elevation, and proteinuria.

Sporadic cases of Legionnaires' disease appear to be more severe than outbreak-associated and hospital-acquired cases, presumably because their diagnosis is delayed. Results of the German CAPNETZ Study showed that, among cases of community-acquired *Legionella* pneumonia, ambulatory patients were as common as hospitalized patients.

**Extrapulmonary Legionellosis** Because the portal of entry for *Legionella* is the lung in virtually all cases, extrapulmonary manifestations usually result from bloodborne dissemination from the lung. *Legionella* has been identified in lymph nodes, spleen, liver, or kidneys in autopsied cases. Sinusitis, peritonitis, pyelonephritis, skin and soft tissue infection, septic arthritis, and pancreatitis have developed predominantly in immunosuppressed patients. The most severe sequela, neurologic dysfunction, is rare but can be debilitating. The most common neurologic deficits in the long term—ataxia and speech difficulties—result from cerebellar dysfunction.

We speculate that cardiac abnormalities in patients without pneumonia are caused by *Legionella*-contaminated water entering through an intravenous site, chest tube, or surgical wound, with subsequent seeding of a prosthetic valve, the myocardium, or the pericardium. This scenario is supported by cases occurring at Stanford University Hospital in which sternal wound infections and prosthetic valve endocarditis due to *L. pneumophila* were observed. The source was a sink in the postoperative surgical recovery ward.

**Chest Radiography** Virtually all patients with Legionnaires' disease have abnormal chest radiographs showing pulmonary infiltrates at the time of clinical presentation. In a few cases of hospital-acquired disease, fever and respiratory tract symptoms have preceded the radiographic appearance of the infiltrate. Radiologic findings are nonspecific. Pleural effusion is evident in 28–63% of patients on hospital admission. In immunosuppressed patients, especially those receiving glucocorticoids, distinctive rounded nodular opacities may be seen; these lesions may expand and cavitate (Fig. 184-1). Likewise, abscesses can occur in immunosuppressed hosts. The progression of infiltrates and pleural effusion on chest radiography despite appropriate antibiotic therapy within the first week is common, and radiographic improvement lags behind clinical improvement by several days. Complete clearing of infiltrates requires 1–4 months. Computed tomography (CT) is more sensitive than chest radiography, may show more extensive disease, and should be performed if fever persists during treatment with presumably effective antibiotics (Fig. 184-2).