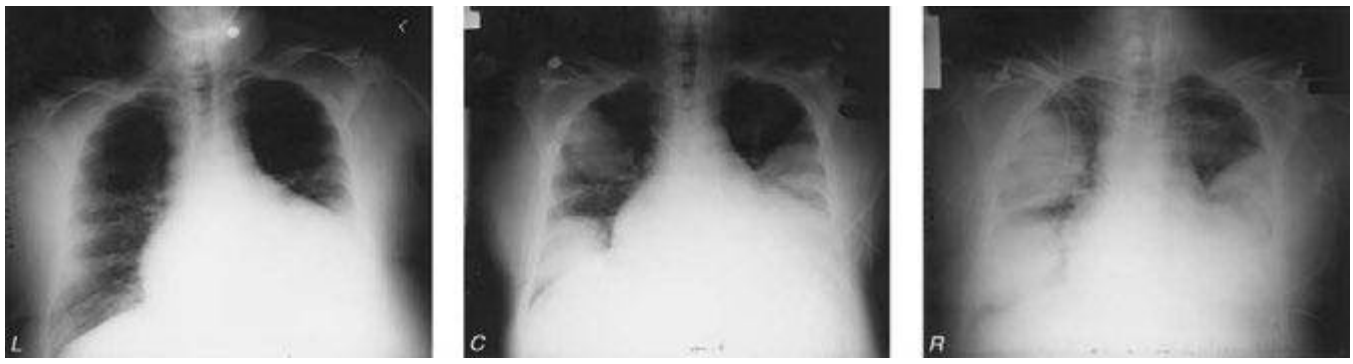

FIGURE 184-1 Chest radiographic findings in a 52-year-old man who presented with pneumonia subsequently diagnosed as Legionnaires' disease. The patient was a cigarette smoker with chronic obstructive pulmonary disease and alcoholic cardiomyopathy; he had received glucocorticoids. *Legionella pneumophila* was identified by direct fluorescent antibody staining and culture of sputum. ***Left:*** Baseline chest radiograph showing long-standing cardiomegaly. ***Center:*** Admission chest radiograph showing new rounded opacities. ***Right:*** Chest radiograph taken 3 days after admission, during treatment with erythromycin.

DIAGNOSIS

Given the nonspecific clinical manifestations of Legionnaires' disease and the high mortality rates for untreated Legionnaires' disease, *Legionella* testing—especially the *Legionella* urinary antigen test—is recommended for all patients with pneumonia, including patients with ambulatory pneumonia and hospitalized children. *Legionella* cultures should be made more widely available because the urinary antigen test can diagnose only *L. pneumophila* serogroup 1. Hospitals in which the drinking water is known to be colonized with *Legionella* species should have *Legionella* cultures routinely available.

The diagnosis of Legionnaires' disease requires special microbiologic tests (Table 184-2). The sensitivity of bronchoscopy specimens is similar to that of sputum samples for culture on selective media; if sputum is not available, bronchoscopy specimens may yield the organism. Bronchoalveolar lavage fluid gives higher yields than bronchial wash specimens. Thoracentesis should be performed if pleural effusion is found, and the fluid should be evaluated by direct fluorescent antibody (DFA) staining, culture, and the antigen assay designed for use with urine.

Stains Gram's staining of material from normally sterile sites, such as pleural fluid or lung tissue, occasionally suggests the diagnosis; efforts to detect *Legionella* in sputum by Gram's staining typically reveal numerous leukocytes but no organisms. When they are visualized, the organisms appear as small, pleomorphic, faint, gram-negative bacilli. *L. micdadei* organisms can be detected as weakly or partially acid-fast bacilli in clinical specimens.

The DFA stain is rapid and highly specific but is less sensitive than culture because large numbers of organisms are required for microscopic visualization. This test is more likely to be positive in advanced than in early disease.

Culture The definitive method for diagnosis of *Legionella* infection is isolation of the organism from respiratory secretions, although culture for 3–5 days is required. Antibiotics added to the medium suppress the growth of competing flora from nonsterile sites, and dyes color the colonies and assist in identification. The use of multiple selective BCYE media is necessary for maximal sensitivity. When culture plates are overgrown with other microflora, pretreatment of the specimen with acid or heat can markedly improve the yield. *L. pneumophila* is often isolated from sputum that is not grossly or microscopically purulent; sputum containing more than 25 epithelial cells per high-power field (a finding that classically suggests contamination) may still yield *L. pneumophila*.

Antibody Detection Antibody testing of both acute- and convalescent-phase sera is necessary. A fourfold rise in titer is diagnostic; 12 weeks are often required for the detection of an antibody response. A single titer of 1:128 in a patient with pneumonia constitutes circumstantial evidence for Legionnaires' disease. The CDC uses a titer of 1:256 as presumptive evidence for Legionnaires' disease. Serology is of use primarily in epidemiologic studies. The specificity of serology for *Legionella* species other than *L. pneumophila* is uncertain; there is cross-reactivity within *Legionella* species and with some gram-negative bacilli. Serology is used as the criterion for the diagnosis of Pontiac fever.

Urinary Antigen The assay for *Legionella* soluble antigen in urine is second only to culture in terms of sensitivity and is highly specific. A rapid immunochromatographic assay is commercially available (BinaxNOW; Alere, Waltham, MA). This assay is relatively inexpensive and easy to perform. Its drawback is that the urinary antigen test is reliable only for *L. pneumophila* serogroup 1, which causes ~80% of *Legionella* infections. Cross-reactivity with other *L. pneumophila* serogroups and other *Legionella* species has been detected in up to 22% of urine samples from patients with culture-proven cases. Antigen in urine is detectable 3 days after the onset of clinical disease and disappears over 2 months; positivity can be prolonged when patients receive glucocorticoids. The test is not affected by antibiotic administration.

Molecular Methods DFA stains can identify a number of *Legionella* species. Both polyclonal and monoclonal antibody stains are commercially available. Polymerase chain reaction (PCR) with DNA probes is being applied in-house in selected hospitals but is not yet commercially available. PCR has proven somewhat useful in the identification of *Legionella* from environmental water specimens. Epidemiologic links cannot easily be made with PCR because the infecting pathogen is not available for molecular subtyping.

Procalcitonin can be used as an indicator of severity of illness in patients in ICUs. Clinical response to antibiotics can be monitored by procalcitonin levels.

TREATMENT *LEGIONELLA* INFECTION

Because *Legionella* is an intracellular pathogen, antibiotics that can attain high intracellular concentrations are most likely to be effective. The dosages for various drugs used in the treatment of *Legionella* infection are listed in Table 184-3.

The macrolides (especially azithromycin) and the respiratory quinolones are now the antibiotics of choice and are effective as monotherapy. Compared with erythromycin, the newer macrolides have superior in vitro activity, display greater intracellular activity, reach higher concentrations in respiratory secretions and lung tissue, and have fewer adverse effects. The pharmacokinetics of the newer macrolides and quinolones also allow once- or twice-daily dosing. Quinolones are the preferred antibiotics for transplant recipients because both macrolides and rifampin interact pharmacologically with cyclosporine and tacrolimus. Retrospective uncontrolled studies have shown that complications of pneumonia are fewer and clinical response is more rapid in patients receiving quinolones than in those receiving macrolides. Initial therapy should be given by the