reactivation disease in their lifetimes. Although immunosuppression is clearly associated with reactivation TB, it is not clear what host factors specifically maintain the infection in a latent state for many years and what triggers the latent infection to become overt.

The diagnosis of latent TB infection depends on a positive tuberculin test result, which indicates previous infection but not necessarily active disease. The standard Mantoux test is an intradermal injection of 0.1 mL (5 tuberculin units) of purified protein derivative (PPD) tuberculin in the skin of the forearm. The injection site is evaluated 48 to 72 hours later. The reading is based on the diameter of the indurated or swollen area.

Patients are at high risk for active TB early after tuberculin conversion, and treatment is recommended for LTBI. QuantiFERON-TB Gold (QFT-G) has been approved by the U.S. Food and Drug Administration (FDA) for the diagnosis of LTBI and TB. It uses the enzyme-linked immunosorbent assay (ELISA) for two proteins in *M. tuberculosis* (i.e., ESAT6 and CFP10). Because these proteins are absent from all bacillus Calmette-Guérin (BCG) vaccine strains, this test does not produce false-positive results in people with previous BCG vaccinations. Other advantages to QFT-G are that the results are available within 24 hours without the need for a second visit and without reading biases or errors. However, QFT-G sensitivity for LTBI may be less than the tuberculin skin test (TST). It is also limited in differentiating infection associated with TB disease or LTBI, similar to the TST. Differentiation is based on suggestive symptoms, radiographs, and sputum samples. Negative QFT-G results cannot exclude the absence of infection in patients with TB signs and symptoms, patients who are HIV positive, or those who are severely immunosuppressed.

The risk for active disease is 5% within 2 years of exposure and another 5% per year thereafter. HIV-infected patients are an exception and have a 40% risk for active disease within several months of conversion. The current recommendations about what constitutes a positive PPD test result take into account the degree of clinical suspicion for LTBI (Table 21-2). Typical treatment of LTBI is 5 mg/kg/day to a maximum dose of 300 mg/day of isoniazid for 9 months (Adult).

Treatment of patients suspected of having active disease includes at least four drugs: 5 mg/kg/day of isoniazid, 10 mg/kg/day of rifampin; 15 to 20 mg/kg/day ethambutol; and 15 to 30 mg/kg/day of pyrazinamide. Treatment should be considered before a formal diagnosis is made. Factors suggesting active disease include exposure to active TB, pulmonary symptoms, and cavitary disease seen on imaging studies. If the diagnosis of TB is confirmed, the drugs are continued for 2 months, barring adverse reactions to drug therapy. After 2 months, the regimen can be tailored, depending on drug-sensitivity studies, and continued for another 4 months with at least two active drugs. Rates of drug-resistant TB are increased in certain populations (e.g., recent immigrants from high-prevalence TB areas, homeless people).

Resistance is detected in 9% of patients who have not received previous therapy and in 22.8% of those with prior treatment. In patients with drug-resistant TB, treatment should include at least three drugs that have not been administered before and to which the organism is susceptible in vitro. Treatment should continue for at least 18 to 24 months. Direct observation of therapy is recommended to ensure compliance.

**TABLE 21-2 PROPHYLAXIS AGAINST TUBERCULOSIS IN ADULTS**

| PPD TEST RESULT* | PROPHYLAXIS INDICATED REGARDLESS OF AGE | OTHER INDICATIONS FOR PROPHYLAXIS |
|---|---|---|
| ≥5 mm | Close contacts recently diagnosed with TB<br>HIV positive or HIV risk factors<br>Fibrotic changes on chest radiograph<br>Patients with organ transplants | No risk factors |
| ≥10 mm | Diabetes mellitus<br>Immunosuppression<br>Hematologic malignancy<br>Injection drug use<br>Renal failure<br>Malnutrition | PPD increased >10 mm within 2 yr<br>Native of high-prevalence country<br>High-risk ethnic minorities<br>Residents and staff of long-term care facilities |
| ≥15 mm | PPD increased >15 mm within 2 yr | No risk factors |

HIV, Human immunodeficiency virus; PPD, purified protein derivative of tuberculin; TB, tuberculosis.

*After 48 to 72 hours, evaluation of the injection site is based on the diameter of the indurated or swollen area.

*For a deeper discussion on this topic, please see Chapter 324, "Tuberculosis," in* Goldman-Cecil Medicine, *25th Edition.*

## PNEUMOCYSTIS PNEUMONIA

*Pneumocystis jiroveci* pneumonia (PCP), formerly called *Pneumocystis carinii* pneumonia, is an opportunistic fungus that occurs mainly in malnourished, premature infants and in adults with hematologic malignancy undergoing chemotherapy in the era before acquired immunodeficiency syndrome (AIDS). However, its incidence rose significantly in the late 1980s and 1990s in patients with AIDS with low $CD4^+$ lymphocyte counts (<250 cells/$mm^3$).

Patients may complain of nonproductive cough, fever, dyspnea, and weight loss. The symptoms are slowly progressive over weeks in patients infected with HIV. Oral candidiasis, an increased serum LDH level, an increased A-a oxygen gradient, and a decreased $CD4^+$ count are independent predictors of HIV-related PCP.

The chest radiograph may show diffuse, bilateral interstitial infiltrates, but the chest radiograph may be clear for up to 15% of patients (E-Fig. 21-4). High-resolution computed tomography (HRCT) is more sensitive, with a diagnostic accuracy of 94% for PCP. Other findings include isolated infiltrates, cavitary lesions, nodular masses, pneumothorax, and a miliary pattern. Hilar and mediastinal adenopathy are rare. Identifying the organism in sputum, which is effective in 60% to 85% of patients, helps with diagnosis. Bronchoscopy with bronchoalveolar lavage can increase the yield (86%), especially if a transbronchial biopsy is included (98% to 100%).

Prophylaxis can be provided by oral sulfamethoxazole-trimethoprim or aerosolized pentamidine. For pneumonia, the