Chapter 9. Tuberculosis

Background

Tuberculosis (TB) is a significant cause of morbidity and mortality in HIV-infected patients. The risk of developing active TB in patients with HIV disease if infected with *Mycobacterium tuberculosis* may be as high as 10 percent each year compared to a 10 percent lifetime risk in immunocompetent hosts. Treatment of latent TB is effective in HIV-infected patients with a positive TB test and will decrease the likelihood of active TB.

TB may present with extrapulmonary manifestations in advanced HIV disease, and cutaneous anergy (lack of reactivity to skin tests) is more common in this context. Diagnosis may be delayed because of these characteristics. Multidrug-resistant (MDR) strains, which are problematic to treat, have become common in some parts of the country.

Screening

Screening for latent TB should be part of the initial assessment of HIV-infected patients and repeated annually in high-risk individuals if the test result is negative. Testing options include a skin test (PPD) [purified protein derivative, intermediate strength, 5TU] or interferon-gamma release assay (IGRA).

The PPD is administered intracutaneously and read at 48-72 hours. The routine use of control agents, such as candida, tetanus toxoid, and mumps, is not recommended because of their lack of standardization. A positive test in an HIV-infected patient is defined as 5 mm or more of induration (measured across the forearm). A history of prior BCG administration should not affect the interpretation of PPD results.

The IGRA is an *in vitro* blood test of cell-mediated immune response to *M. tuberculosis*. It is highly specific and not affected by BCG vaccination status of the patient. CDC guidelines state that IGRA can be used in lieu of the PPD in all situations. However, it is preferred in patients with a history of BCG administration and in those in whom a repeat visit for PPD reading is difficult.

Repeat PPD testing is recommended in HIV-infected patients with a baseline CD4 cell count less than 200/mm^3 who had a negative result if it increases above this threshold on antiretroviral therapy.

Treatment of Latent TB

Antimicrobial therapy is recommended for HIV-infected patients regardless of age with any of the following:

- Positive PPD or positive interferon-gamma release assay
- History of a positive PPD and no documentation of a standard course of prophylaxis
- Recent exposure to active pulmonary TB

Antimicrobial therapy is not generally recommended in HIV-infected persons with anergy who have historical risk factors for TB exposure, such as injection-drug use, alcoholism, homelessness, incarceration, living in shelter or institution, and originating from a country endemic for TB.

A chest x-ray should be performed on all patients with a positive PPD or IGRA before initiating antimicrobial prophylaxis to rule out active pulmonary TB. If extrapulmonary disease is suspected clinically, the appropriate additional diagnostic evaluation should also be completed.

Isoniazid (INH) 300 mg po qd given with pyridoxine 50 mg po qd *or* 900 mg twice per week given with pyridoxine 50 mg po qd (directly observed therapy [DOT]) is the standard prophylactic regimen. Treatment is continued for nine months. Alternative regimens, which include rifampin (RIF) 600 mg po qd for four months *or* INH 300 mg po qd and RIF 600 mg po qd for three months, are generally avoided in HIV-infected patients on antiretroviral therapy because of concern about drug interactions.

Hepatotoxicity to INH is uncommon in patients younger than 35 years old but increases with advancing age. Other common side effects include fever and rash. The drug should be discontinued if clinical stigmata of hepatitis develop or if liver transaminases increase to $\geq$ 5 times baseline.

Infectious disease consultation is recommended in the prophylaxis of MDR TB strains.

Treatment of Active TB

A four-drug regimen is preferred for initial empiric treatment of TB pending culture and sensitivity results. The combination of INH, RIF or another rifamycin, ethambutol, and pyrazinamide is given for 8 weeks, after which INH and RIF alone are continued if the organism is sensitive to these drugs. The total duration of treatment is generally 6 months for pulmonary TB and 6-12 months for extrapulmonary TB. DOT is preferred over conventional management whenever possible. All patients with INH-resistant or RIF-resistant isolates, as well as persons with a history of nonadherence, should receive DOT.

The presence of active TB requires immediate initiation of antimicrobial treatment. All HIV-infected patients with active TB should be treated with antiretroviral therapy. In patients with a CD4 cell count $\leq 50/mm^3$, antiretroviral therapy should be started within 2-4 weeks of initiating TB treatment. In patients with higher CD4 counts, antiretroviral therapy can be delayed for up to 4-12 weeks depending upon the specific clinical circumstances (see DHHS guidelines for more information).

Rifampin, an important component of combination therapy for TB, cannot be given with many protease inhibitors and non-nucleoside reverse transcriptase inhibitors (see Chapter 3). In some instances, rifabutin can be substituted for it.

Susceptibility tests should be performed on the initial TB isolate and on any isolate obtained at three months post-treatment.

Antimicrobial drug resistance should be considered if there has been prior ineffective or intermittent treatment or if there is a history of exposure to TB strains from Central or South America, Africa, or the Far East.

Infectious disease consultation is recommended in the treatment of active TB.