PREVENTING THE REAL PHANTOM MENACE: TB INFECTION

OREGON REGISTERED 156 cases of tuberculosis disease in 1998, but behind these numbers lurks a much larger phantom menace. An estimated 12,000-37,000 people infected with TB reside in the state. Rates of TB infection are generally proportional to rates of active disease. The case rate for active TB is 2.2 per 100,000 for white, non-Hispanic Oregonians, compared to 48 per 100,000 for Asian/Pacific Islanders, 22 per 100,000 for African Americans, 13 per 100,000 Hispanics and 11 per 100,000 Native Americans. Over half (51%) of the active cases of TB were in foreign-born persons.

TUBERCULIN SKIN TEST (TST)

The Mantoux TST is the time-honored screening method for identifying TB-infected persons; a (time) multi puncture test should not be used for TB screening due to its unreliability. Routine TB screening should be offered to persons with significant TB risk, including foreign-born persons from areas of the world where TB is common (e.g., Asia, Africa, and Latin America), persons with HIV infection or risk factors for HIV, close contacts of a person with infectious TB, persons with certain medical conditions (silicosis, steroid therapy), persons who inject drugs, and residents of long-term-care facilities (e.g., correctional facilities, nursing homes). Groups that are not at high risk for TB should not be screened routinely, because they are more likely to have false-positive reactions and could be given unnecessary preventive therapy.

The TST is an intradermal injection of 0.1 ml (5 tuberculin units) of a purified protein derivative (PPD) from a reference M. tuberculosis strain. The tuberculin solution is placed just below the surface of the skin using a tuberculin syringe with the bevel of the needle facing upwards, creating a 6- to 10-mm wheal (Figure). A trained health-care worker can read the reaction after 48 to 72 hours, recording the diameter of the indurated area (not the erythema) in millimeters (Table). If the patient does not return in 72 hours, a non-reactive "negative" reaction. Fortunately, the TST delayed hypersensitivity response may wane over the years, resulting in a "false negative" reaction. Fortunately, the TST itself may boost the ability to react, revitalizing the immune system's response in persons with TB infection. The second test is performed 1 to 3 weeks after the first; a positive reaction indicates TB infection. Two-step testing is recommended for health-care workers when they are hired. Two-step testing should also be considered for the elderly and for persons with partial immune suppression.

THERAPY OF LATENT TUBERCULOSIS (PREVENTIVE THERAPY)

Ten percent of persons with TB infection will develop active TB disease over the course of their lives. Up to 60% of persons with HIV/TB co-infection will develop TB disease. Therapy of latent tuberculosis, or isoniazid (INH) preventive therapy (IPT) (300 mg daily in adults, 10-15 mg/kg per day in children) reduces the likelihood of developing active TB by 70-80%. The duration of IPT is 6 months for adults and 9 months for children and HIV-positive persons. A recent skin-test converter (defined as a person who develops a positive TST within two years of having had a negative TST) is at much higher risk for developing TB and is a priority for IPT.

Before preventive therapy is started, clinicians should rule out active TB disease and determine the risk for INH-associated side effects. IPT patients should be evaluated monthly for adherence to medications and for evidence of hepatitis and neurotoxicity. As little as 6 mg/day of pyridoxine (vitamin B6) has been shown to prevent INH-associated neuropathy. The risk for INH hepatitis increases with age and underlying liver disease. Liver enzyme tests are done at baseline and every month during therapy for patients at risk for hepatitis. Women, especially black and Hispanic women, may be at increased risk for fatal INH hepatitis, particularly during the postpartum period. Mild, asymptomatic elevations of transaminases occur in 10-20% of persons on INH and often resolve on continued therapy. Liver enzymes exceeding five times normal are significant; INH should be discontin-
ued and the patient evaluated for the cause of hepatitis. When other hepatotoxins are eliminated and the liver enzymes return to normal, INH can be restarted and monitored every two weeks.

INH-intolerant patients should receive rifampin—600 mg per day for 6 months. Close contacts of infectious patients who have INH-resistant TB should also be given rifampin. Since no other regimens have proven efficacy, observation without preventive therapy is reasonable for persons with normal immune systems who have been infected with INH- and rifampin-resistant TB. If the patient is at severe risk for reactivation TB (e.g., persons with HIV infection), preventive therapy should use at least two drugs to which the infecting organism has demonstrated susceptibility. Potential alternative regimens include ethambutol and pyrazinamide (daily for 6 months) or pyrazinamide and a quinolone (daily for 6 months). New, short-course preventive therapy regimens (e.g., rifampin and pyrazinamide for 2 months and rifampin alone for 4 months) show promise.

Adherence to IPT is often difficult due to patient ambivalence about taking medication when they are feeling perfectly well, and to concern about potential side effects of the medication. Completion rates in Oregon are consistently in the 56-65% range for adults, with 84% for children under the age of 15 years completing IPT in 1997. Completion rates for IPT in recent TST converters were slightly better—70% in 1997 compared to 40% in 1996. Directly observed preventive therapy (DOPT) should be considered for patients with especially high risk for reactivation TB and poor adherence potential. INH can be given two times a week at a dosage of 15 mg/kg as directly observed preventive therapy. DOPT is considered the standard of care for children and persons with HIV disease who have TB infection.

Clinicians are encouraged to contact their local health department for additional information on TB screening and preventive therapy. If every TST-positive Oregonian completed a full course of therapy for latent tuberculosis, we would prevent a minimum of 2400 cases of active TB over the next twenty years.