diameter (in millimeters) of induration; the diameter of erythema is not considered. In some persons, TST reactivity wanes with time but can be recalled by a second skin test administered ≥1 week after the first (i.e., two-step testing). For persons periodically undergoing the TST, such as health care workers and individuals admitted to long-term-care institutions, initial two-step testing may preclude subsequent misclassification of those who have boosted reactions as TST converters. The cutoff for a positive TST (and thus for treatment) is related both to the probability that the reaction represents true infection and to the likelihood that the individual, if truly infected, will develop TB. Table 202-5 suggests possible cutoff by risk group. Thus, positive reactions for persons with HIV infection, recent close contacts of infectious cases, organ transplant recipients, previously untreated persons whose chest radiograph shows fibrotic lesions consistent with old TB, and persons receiving drugs that suppress the immune system are defined as an area of induration ≥5 mm in diameter. A 10-mm cutoff is used to define positive reactions in most other at-risk persons. For persons with a very low risk of developing TB if infected, a cutoff of 15 mm is used. (Except for employment purposes where longitudinal screening is anticipated, the TST is not indicated for these low-risk persons.) A positive IGRA is based on the manufacturers' recommendations; however, good clinical practice requires that epidemiologic and clinical factors also guide the decision to implement treatment for LTBI and that active TB be definitively excluded before the initiation of chemoprophylaxis.

Some TST- and IGRA-negative individuals are also candidates for treatment. Once an appropriate clinical evaluation has excluded active TB, infants and children who have come into contact with infectious cases should be treated for presumed LTBI. HIV-infected persons who have been exposed to an infectious TB patient should receive treatment regardless of the TST result. Any HIV-infected candidate for LTBI treatment must be screened carefully to exclude active TB, which would necessitate full treatment. The use of a clinical algorithm based on four symptoms (current cough, fever, weight loss, and night sweats) helps to define which HIV-infected person is a candidate for LTBI treatment. The absence of all four symptoms tends to exclude active TB. The presence of one of the four symptoms, on the other hand, warrants further investigation for active TB before treatment of LTBI is started. Although administering a TST is prudent, this test is not an absolute requirement—given the logistical challenges—among people living with HIV in high-TB-incidence and low-resource settings.

Before treatment of LTBI begins, it is mandatory to carefully exclude active TB. Several regimens can be used to treat LTBI. The most widely used is that based on isoniazid alone at a daily dose of 5 mg/kg (up to 300 mg/d) for 9 months. On the basis of cost-benefit analyses and concerns about feasibility, a 6-month period of treatment is currently recommended by the WHO, especially in highly TB-endemic countries. Isoniazid can be administered intermittently (twice weekly) at a dose of 15 mg/kg (up to 900 mg) but only as directly observed therapy. An alternative regimen for adults is 4 months of daily rifampin. A 3-month regimen of daily isoniazid and rifampin is used in some countries (e.g., the United Kingdom) for both adults and children who are known not to have HIV infection. A previously recommended regimen of 2 months of rifampin and pyrazinamide has been associated with serious or even fatal hepatotoxicity and now is generally not recommended. The rifampin-containing regimens should be considered for persons who are likely to have been infected with an isoniazid-resistant strain. A recent clinical trial showed that a regimen of isoniazid (900 mg) and rifapentine (900 mg) given once weekly for 12 weeks is as effective as the standard 9-month isoniazid regimen. This regimen was associated with higher treatment completion (82% vs 69%) and less hepatotoxicity (0.4% vs 2.7%) than isoniazid alone, although the rate of permanent discontinuation due to an adverse event was higher (4.9% vs 3.7%).

Currently, the isoniazid–rifapentine regimen is not recommended for children <2 years of age, people living with HIV infection who are receiving ART, or pregnant women. Rifampin and rifapentine are contraindicated in HIV-infected individuals receiving protease inhibitors and most NNRTIs. (Efavirenz is the safest agent in this class of antiretrovirals for simultaneous administration with a rifamycin.) Clinical trials to assess the efficacy of long-term isoniazid administration (i.e., for at least 3 years) among people living with HIV in high-TB-transmission settings have shown that this regimen can be more effective than 9 months of isoniazid and is therefore recommended under those circumstances. Isoniazid should not be given to persons with active liver disease. All persons at increased risk of hepatotoxicity (e.g., those abusing alcohol daily and those with a history of liver disease) should undergo baseline and then monthly assessment of liver function. All patients should be carefully educated about hepatitis and instructed to discontinue use of the drug immediately should any symptoms develop. Moreover, patients should be seen and questioned monthly during therapy about adverse reactions and should be given no more than a 1-month supply of drug at each visit. Treatment of LTBI among persons likely to have been infected by a multidrug-resistant strain is a challenge because no regimens have yet been tested in clinical trials. Close observation for early signs of disease is one option; consultation with a TB expert is advised.

It may be more difficult to ensure compliance when treating persons with LTBI than when treating those with active TB. If family members of active cases are being treated, compliance and monitoring may be easier. When feasible, supervised therapy may increase the likelihood of completion. As in active cases, the provision of incentives may also be helpful.

PRINCIPLES OF TB CONTROL

The highest priority in any TB control program is the prompt detection of cases and the provision of short-course chemotherapy to all TB patients under proper case-management conditions, including directly observed therapy. In addition, screening of high-risk groups, including immigrants from high-prevalence countries, migratory workers, prisoners, homeless individuals, substance abusers, and HIV-seropositive persons, is recommended. TST-positive high-risk persons should be treated for LTBI as described above. Contact investigation is an important component of efficient TB control. In the United States and other countries worldwide, a great deal of attention has been given to the transmission of TB (particularly in association with HIV infection) in institutional settings such as hospitals, homeless shelters, and prisons. Measures to limit such transmission include respiratory isolation of persons with suspected TB until they are proven to be noninfectious (at least by sputum AFB smear negativity), proper ventilation in rooms of patients with infectious TB, use of ultraviolet irradiation in areas of increased risk of TB transmission, and periodic screening of personnel who may come into contact with known or unsuspected cases of TB. In the past, radiographic surveys, especially those conducted with portable equipment and miniature films, were advocated for case finding. Today, however, the prevalence of TB in industrialized countries is sufficiently low that "mass miniature radiography" is not cost-effective.

In high-prevalence countries, most TB control programs have made remarkable progress in reducing morbidity and mortality since the mid-1990s by adopting and implementing the strategy promoted by the WHO. Between 2000 and 2013, 37 million lives were saved, and since 1995, 61 million TB cases have been successfully treated. The essential elements of good TB care and control (the DOTS strategy) are (1) political commitment with increased and sustained financing; (2) case detection through quality-assured bacteriology (starting with examination of sputum from patients with cough of >2–3 weeks' duration); (3) administration of standardized short-course chemotherapy, with direct supervision and patient support; (4) an effective drug supply and management system; and (5) a monitoring and evaluation system, with impact measurement (including assessment of treatment outcomes—e.g., cure, completion of treatment without bacteriologic proof of cure, death, treatment failure, and default—in all cases