GUIDELINES FROM THE INFECTIOUS DISEASES SOCIETY OF AMERICA

Practice Guidelines for the Treatment of Tuberculosis

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Introduction

The Tuberculosis Committee of the Infectious Disease Society of America, in conjunction with the Division of Tuberculosis Elimination of the Centers for Disease Control and Prevention (CDC), has identified 10 essential recommendations and performance indicators for tuberculosis (TB) care. These include recommendations for treatment of active TB disease and latent TB infection. All 10 of the recommendations are graded “A” (strongly recommended) by the Infectious Disease Society of America–US Public Health Service ranking system. The associated performance indicators are easily measurable and will allow straightforward assessment of the adequacy of TB treatment practices by care providers and organizations. Table 1 shows the specific recommendations, rankings to indicate the strength of each recommendation and the quality of evidence supporting it, and performance indicators.

Rationale for and Explanation of Recommendations

TB is an ancient disease that is common in many developing countries but no longer widespread in the United States. With the advent of managed care and movement of care of patients with TB from specialty public health clinics to primary care providers, more persons with TB are likely to be seen by physicians and health care providers that are unfamiliar with the diagnosis and management of TB. In addition, because of the mode of transmission of Mycobacterium tuberculosis, care of infected patients entails public health obligations that are not relevant to the care of other infectious diseases. Moreover, care providers and health care systems may be unfamiliar with recommendations for TB care. Therefore, the Tuberculosis Committee of the Infectious Disease Society of America, in conjunction with the Division of TB Elimination of the CDC, has identified 10 essential practice recommendations and performance indicators for TB care.

These practice guidelines are principles of treatment for either active TB disease or latent TB infection that should be followed to ensure the best outcome for treatment of patients with TB and for control of TB in the community. The recommendations, which are intended for practitioners, focus on management strategies for the treating clinician; they do not address actions usually taken by public health authorities to limit the spread of TB in the community, such as contact-tracing or maintaining a surveillance system. For each of the recommendations, the relevant literature has been reviewed and is discussed, and the strength of the recommendation is given a ranking of A–E. The quality of the evidence is also ranked (I–III) to allow better understanding of the factual basis for the recommendations (table 2) [1].

Performance indicators are targets for the frequency with which the recommended practices should be followed. These are clearly defined, measurable objectives that are relevant to the recommended practice. Such indicators are useful in evaluating the performance of managed-care plans and other care provider groups with regard to whether minimum performance standards are being met [2]. The benchmark expectation of the frequency with which the recommended practice will be followed has been set in order to allow for variability among sites with regard to the ability to accomplish the action described in the recommendation. Thus, culture diagnosis is not expected as often in children, for whom (compared with adults) an expectorated sputum is more difficult to obtain. Similarly, most programs have found that HIV serologic status cannot always be obtained due to patient refusal; thus, 80% rather than 100% is the proposed benchmark. The performance indicator is calculated as a percentage of the instances the recommendation was actually achieved divided by the instances in which it was applicable.

Recommendations

Below are listed 8 recommendations for the care and treatment of active TB disease and 2 recommendations for the care and treatment of latent TB infection. Each recommendation
Table 1. Specific recommendations, rankings indicating their strength and the quality of evidence supporting them, and performance indicators for treatment of patients with tuberculosis (TB).

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Ranking</th>
<th>Performance indicator</th>
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<tbody>
<tr>
<td>Obtain bacteriologic confirmation and susceptibility testing for patients with TB or suspected of having TB</td>
<td>A-II</td>
<td>90% of adults with or suspected of having TB have 3 cultures for mycobacteria obtained before initiation of antituberculosis therapy (50% of children 0-12 years)</td>
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<td>Place persons with suspected or confirmed smear-positive pulmonary or laryngeal TB in respiratory isolation until noninfectious</td>
<td>A-II</td>
<td>90% of persons with sputum smear-positive TB remain in respiratory isolation until smear converts to negative</td>
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<tr>
<td>Begin treatment of patients with confirmed or suspected TB disease with 1 of the following drug combinations, depending on local resistance patterns: INH + RIF + PZA, or INH + RIF + PZA + EMB, or INH + RIF + PZA + SM</td>
<td>A-III</td>
<td>90% of all patients with TB are started on INH + RIF + PZA + EMB or SM in geographic areas where &gt;4% of TB isolates are resistant to INH</td>
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<tr>
<td>Report each case of TB promptly to the local public health department</td>
<td>A-III</td>
<td>100% of persons with active TB are reported to the local public health department within 1 week of diagnosis</td>
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<tr>
<td>Perform HIV testing for all patients with TB</td>
<td>A-III</td>
<td>80% of all patients with TB have HIV status determined within 2 months of a diagnosis of TB</td>
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<td>Treat patients with TB caused by a susceptible organism for 6 months, using an ATS/CDC-approved regimen</td>
<td>A-I</td>
<td>90% of all patients with TB complete 6 months of therapy within 12 months of beginning treatment</td>
</tr>
<tr>
<td>Reevaluate patients with TB who are smear positive at 3 months for possible nonadherence or infection with drug-resistant bacilli</td>
<td>A-III</td>
<td>90% of all patients with TB who are smear positive at 3 months have sputum culture/susceptibility testing performed within 1 month of the 3-month visit</td>
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<tr>
<td>Add ≥2 new antituberculosis agents when TB treatment failure is suspected</td>
<td>A-II</td>
<td>100% of patients with TB with suspected treatment failure are prescribed ≥2 new antituberculosis agents</td>
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<tr>
<td>Perform tuberculin skin testing on all patients with a history of ≥1 of the following: HIV infection, injection drug use, homelessness, incarceration, or contact with a person with pulmonary TB</td>
<td>A-II</td>
<td>80% of persons in the indicated population groups receive tuberculin skin test and return for reading</td>
</tr>
<tr>
<td>Administer treatment for latent TB infection to all persons with latent TB infection, unless it can be documented that they received such treatment previously</td>
<td>A-I</td>
<td>75% of patients with positive tuberculin skin tests who are candidates for treatment for latent TB infection complete a course of therapy within 12 months of initiation</td>
</tr>
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</table>

**NOTE.** ATS/CDC, American Thoracic Society and Centers for Disease Control and Prevention; EMB, ethambutol; INH, isoniazid; PZA, pyrazamide; RIF, rifampin; SM, streptomycin.

* Explained in table 2.

includes a ranking for its strength and the quality of evidence supporting it, as well as the performance indicators.

**Obtain Specimens for Bacteriologic Confirmation and Susceptibility Testing for Patients with TB or Suspected of Having TB (A-II)**

Adults suspected of having pulmonary TB disease or TB disease at other readily accessible sites should have culture specimens for *M. tuberculosis* obtained from these sites [3]. Culture should be performed on all available specimens from children. Since children aged <10 years often do not produce expectorated sputum, an alternative is an early morning gastric aspirate (or washing with 10–20 mL of sterile water). The expected yield of positive gastric aspirate culture and/or smear in children is 50%, and the procedure can be done on an outpatient basis [4]. Extra efforts should be made to obtain specimens for culture from children when there is no culture-positive index case or where multidrug-resistant TB is suspected. Sputum samples for culture and stain (Ziehl-Neelsen or fluorochrome) are best obtained early in the morning on at least 3 separate days. Standard methods for collection, transportation, concentration, processing, and culturing of specimens have been published elsewhere [5, 6].

During the last 10–15 years, new techniques have been developed that enhance and hasten the direct identification of bacilli in clinical specimens and cultures and that result in more rapid reporting of drug sensitivities. Direct amplification tests, such as Gen-Probe (MTD, San Diego) and Amplicor *M. tuberculosis* test (Roche Diagnostic Systems, Branchburg, NJ) can identify *M. tuberculosis* in acid-fast smear-positive respiratory specimens [7], but culture is still required for susceptibility testing. Mycolic acid analysis by high-performance liquid chromatography (HPLC) is another rapid identification method for clinical mycobacteria isolates [8]. Many community hospitals and virtually all state health departments can perform sensitivity tests on, culture, and identify *M. tuberculosis*. In instances where the microbiology laboratory is limited to using standard media, specimens should be sent to a laboratory that is using more rapid identification methods, such as those that use liquid media [9, 10].

Good TB laboratory diagnostic facilities are available to all clinical sites in the United States. Therefore, the standard of care for adults should be that >90% of adult patients with a clinical diagnosis of TB should be able to have the diagnosis confirmed by culture. Since culture of the organism is a prerequisite for susceptibility testing and susceptibility test results are essential for proper clinical management of TB [11], bac-
tuberculosis through aerosolization of the bacilli in infectious

Isolation until Noninfectious (A-II)

Smear-Positive Pulmonary or Laryngeal TB in Respiratory

Place Persons with Suspected or Confirmed
Smear-Positive Pulmonary or Laryngeal TB in Respiratory
Isolation until Noninfectious (A-II)

Persons with pulmonary or laryngeal TB can transmit *M. tuberculosis* through aerosolization of the bacilli in infectious droplet nuclei that are produced by coughing or sneezing (or speaking or singing in the case of laryngeal TB) [11, 12]. Nosocomial transmission of TB has been clearly documented in a number of investigations and has been associated with close contact with persons with infectious TB and with the performance of certain procedures (e.g., bronchoscopy, endotracheal intubation, suctioning, open-abscess irrigation, autopsy). Sputum induction and aerosol treatments that induce coughing may also increase the potential for transmission of *M. tuberculosis*.

The high risk of transmission to other patients and health care workers mandates that hospitalized persons with suspected or confirmed infectious TB be placed in respiratory isolation until (1) they are determined not to have TB, (2) they are discharged from the hospital, or (3) they are confirmed to be noninfectious. Guidelines for respiratory isolation have been published elsewhere [11]. A patient is considered to be noninfectious when he or she is receiving effective therapy, is improving clinically, and has had negative results for 3 consecutive sputum acid-fast smears collected on different days. Patients who have responded clinically may be discharged to home despite positive smears if their household contacts have already been exposed and these contacts are not at increased risk of TB (infants and immunosuppressed persons are considered at increased risk of acquiring *M. tuberculosis* if exposed). In addition, patients discharged to home with positive smears must agree not to have contact with other susceptible persons.

Determination of the absolute lack of infectiousness of a person with pulmonary or laryngeal TB requires demonstration that cultures are negative. However, since this can take 6 weeks from the time cultures samples are obtained, such a measure is impractical as a performance indicator. Therefore, conversion to negative smear results is used as a surrogate for infectiousness, even though a small risk of transmission may still be present. For the performance indicator, patients are considered to be noninfectious if they have a clinical response to anti-TB chemotherapy and 3 consecutive smear-negative sputum samples that were collected on different days (these days may be consecutive) [11]. All persons with suspected or confirmed respiratory or laryngeal TB should be placed in isolation. However, some patients can be discharged from isolation before smears convert, as in the case where a person returns to a residence where contacts already have positive tuberculin skin test results. Therefore, the performance indicator is set at 90%.

### Table 2. Infectious Disease Society of America–US Public Health Service grading system for ranking recommendations in clinical guidelines.

<table>
<thead>
<tr>
<th>Category, grade</th>
<th>Definition</th>
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<tbody>
<tr>
<td>Strength of recommendation</td>
<td></td>
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<tr>
<td>A</td>
<td>Good evidence to support a recommendation for use</td>
</tr>
<tr>
<td>B</td>
<td>Moderate evidence to support a recommendation for use</td>
</tr>
<tr>
<td>C</td>
<td>Poor evidence to support a recommendation</td>
</tr>
<tr>
<td>D</td>
<td>Moderate evidence to support a recommendation against use</td>
</tr>
<tr>
<td>E</td>
<td>Good evidence to support a recommendation against use</td>
</tr>
<tr>
<td>Quality of evidence</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>Evidence from at least 1 properly randomized, controlled trial</td>
</tr>
<tr>
<td>II</td>
<td>Evidence from at least 1 well designed clinical trial without randomization, from cohort or case-control analytic studies (preferably from &gt;1 center), from multiple time-series studies, or from dramatic results in uncontrolled experiments</td>
</tr>
<tr>
<td>III</td>
<td>Evidence from opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees</td>
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This recommendation is based on the risk of treating unsuspected drug-resistant TB when initiating therapy for a person whose isolate has an unknown susceptibility pattern. It is assumed that if the local prevalence of isolates resistant to isoniazid is above a certain threshold, a fourth drug should be added to avoid selecting for further resistance [13]. An arbitrary 4% threshold is recommended, such that when ≥4% of TB isolates in an area are resistant to isoniazid, the usual 3-drug regimen should be augmented with a fourth drug, either ethambutol or streptomycin. When the results of susceptibility tests
are available, and the isolate can be shown to be susceptible to isoniazid, rifampin, and pyrazinamide, then the fourth drug may be discontinued when the patients are receiving daily or twice weekly therapy [13].

Clinicians should be aware of the patterns of susceptibility that can be expected in their geographic area. In the United States in 1997, 33 states, representing 84% of the US population, had $\geq 4\%$ of isolates that were resistant to isoniazid [14]. Thus, the recommended initial regimen for most of the United States is 4-drug therapy. Exceptions are as follows: (1) patients who have recently acquired disease from a contact with a strain of *M. tuberculosis* that is known to be susceptible to isoniazid, rifampin, and pyrazinamide, or (2) patients whose susceptibility results are available at the time of initiation of therapy and are infected with a susceptible organism; these patients may safely be treated with isoniazid/rifampin/pyrazinamide for the first 8 weeks of therapy [12]. Since such cases are uncommon, the performance indicator has been set for at least 90% of patients to receive 4 drugs in areas where isoniazid resistance rates are $\geq 4\%$ and 3 drugs in areas where isoniazid resistance rates are $< 4\%$.

**Report Each Case of TB Promptly to the Local Public Health Department (A-III)**

Reporting cases of TB to public health authorities serves several functions: it allows public health investigators to perform contact and source case investigations to determine if other cases of untreated, infectious TB are present in the community; it allows monitoring of adherence to therapy by patients with TB who might otherwise continue to spread TB in the community; it allows identification of infected contacts and administration of treatment of latent TB infection to eligible candidates; and it permits record-keeping and surveillance to determine if public health TB control efforts are achieving their goal of preventing the spread of TB [13]. To allow health departments to perform these functions adequately, prompt notification of cases of TB disease by clinicians and hospitals is essential. It is preferable to report suspected cases (suspected on the basis clinical diagnosis or the presence of acid-fast bacilli in clinical specimens) before definitive culture confirmation of TB disease.

As early as 1878, Congress authorized the US Marine Hospital Service (later, the Public Health Service) to collect reports on various communicable diseases. TB disease is now reportable in all states and territories, although the specific reporting requirements (such as the time within which cases should be reported) varies. A list of nationally notifiable diseases can be found on World Wide Web site for the Council of State and Territorial Epidemiologists (http://www.cste.org). In some areas, TB infection may also be reportable in certain circumstances (e.g., in children), but clinicians should consult their local and state regulations to determine which requirements pertain in their area.

TB should be reported promptly so that patients are not lost to follow-up after they are discharged from the hospital. The health department should be notified as soon as TB is suspected and well before the patient is discharged from the hospital; this allows the patient to be visited before being discharged, which helps ensure continuity of care. For outpatients who are diagnosed with TB, reporting should be prompt to ensure optimal health department monitoring and follow-up. Thus, the performance indicator for reporting is set at an expectation that 100% of confirmed cases be reported within 1 week of establishing the diagnosis.

**Perform HIV Testing for All Patients with TB within 2 Months of the Diagnosis of TB (A-III)**

Persons with HIV infection and TB usually can be treated with standard anti-TB regimens with good results, although in some cases, prolonged therapy may be warranted [15]. Patients with TB and HIV may also have more rapid resolution of their TB if the HIV infection is treated concurrently [15]. Therefore, it is important for clinicians to be aware of the HIV status of their patients with TB. Testing of persons with TB for infection with HIV is an important intervention point for counseling and testing for HIV infection, and for administration of antiretroviral therapy and prophylaxis for opportunistic infections. Since treatment of HIV may require protease inhibitors or nonnucleoside reverse transcriptase inhibitors and TB therapy for persons receiving these drugs may preclude the use of rifampin, this may lead to alteration of the anti-TB regimen.

In the United States, 14% of persons with TB in 1993–1994 also were reported to have AIDS, and in some areas, HIV infection is seen in as many as 58% of patients with TB [16, 17]. While the rate of coinfection varies widely among different geographic areas, clinicians are poor predictors of which patients are likely to have HIV infection. Therefore, HIV testing is recommended for and should be offered to all patients with newly diagnosed TB. However, because not all patients will accept HIV serologic testing, 80% rather than 100% is the proposed performance indicator.

**Treat Patients with TB for 6 Months Total Duration, Using an American Thoracic Society (ATS)/CDC–Approved Regimen (A-I)**

In the treatment of disease caused by *M. tuberculosis* susceptible to all agents, a 6-month course of treatment is effective and well tolerated [12]. Isoniazid and rifampin are used throughout the entire course of therapy, with pyrazinamide added during the first 2 months. Only patients with miliary, meningeal, or bone and joint disease require longer therapy (12
months) [12]. ATS and CDC have evaluated and recommend any of 3 different treatment schedules (daily or twice- or thrice-weekly dosing) [12]. Thus, in most cases, 1 of these 3 treatment regimens should be used. When patients cannot tolerate 1 of the agents, substitutions can be made, but an expert in the treatment of TB should be consulted.

ATS and CDC recommend that TB caused by an isoniazid-resistant organism can be treated with 6 month’s administration of rifampin, ethambutol, and pyrazinamide; however, a longer regimen is needed to treat TB caused by M. tuberculosis resistant to rifampin, and expert consultation is recommended. TB caused by isolates resistant to both isoniazid and rifampin require at least 18–24 months of therapy and should be treated by experts in the treatment of multidrug-resistant TB [18].

Nonadherence to anti-TB therapy is the main reason for treatment failure and the development of drug-resistant strains of M. tuberculosis [13, 19]. Therefore, it has been recommended that all patients with TB be treated by directly observed therapy (DOT), in which ingestion of medications is observed by a responsible person. Rates of drug-resistant TB and relapse are decreased in communities where DOT is used [20]. Moreover, clinicians are poor at predicting which patients will adhere to a course of therapy [19]. If it is not possible to treat all patients with direct observation, efforts should be made to offer DOT to patients who are at high risk for treatment failure, such as patients with drug-resistant disease, injection drug users, alcoholics, and homeless persons.

Despite the best efforts of the clinician, some patients may not complete the 6-month regimen in the first 6 months of treatment. To account for gaps in therapy, which may occur because of drug intolerance or nonadherence, the performance indicator is for 90% of patients with TB caused by a drug-susceptible isolate to complete a course within 12 months of initiation of treatment.

**Reevaluate Patients with TB Who Are Smear-Positive at 3 Months for Possible Nonadherence or Infection with Drug-Resistant Bacilli (A-III)**

Response to anti-TB therapy should be assessed by monitoring clinical symptoms and sputum smears and cultures. If clinical improvement is not seen or if smear and culture results continue to be positive or convert from negative to positive after initiation of anti-TB therapy, treatment failure should be suspected. Smears and cultures usually become negative by 3 months. Continued positive smears and cultures at or after 3 months should prompt a reevaluation of the patient and the regimen.

The 2 most common reasons for treatment failure are nonadherence with therapy and infection with drug-resistant bacilli. Determining if a patient has been nonadherent with therapy may be difficult. While certain groups of patients, such as injection drug users, alcoholics, and homeless persons, are more likely to be nonadherent than others, there is no reliable method of predicting which patients will not adhere to therapy. Administration of medications by DOT is the only way to eliminate the possibility of nonadherence [21]. If nonadherence is suspected, DOT is essential and should be instituted immediately. Notification of the health department is important for the rare cases in which detention may be needed to ensure adherence to TB treatment.

Failure of therapy because the bacilli are drug resistant is also a concern in patients whose smears or cultures do not clear after 3 months. Persons who have a history of TB treatment or were born in areas of the world where there is a high prevalence of drug-resistant strains of M. tuberculosis have an increased risk of TB caused by drug-resistant organisms [22]. In addition, persons who are nonadherent with therapy are at increased risk for emergence of drug-resistant strains of M. tuberculosis because they may have been treated with mono-therapy. When there is suspicion of treatment failure secondary to drug resistance, repeat culture and susceptibility testing should be done to determine if drug resistance has been acquired since the initial isolate was evaluated.

Evaluation for nonadherence and drug resistance should be undertaken in all patients with pulmonary TB whose sputum smears have not converted to smear-negative status after 3 months of therapy. Evaluation should include a second culture and a second susceptibility test, consideration of DOT, and consultation with experts in the treatment of TB. Since some patients may not promptly return for evaluation, the performance indicator is set at 90% within 1 month, but all such patients should receive evaluation. Patients who have negative smears but positive cultures at 3 months should be similarly evaluated; however, evaluation of these patients is not expected to be accomplished within the 1-month time frame since cultures are often not completed by that time.

**Add Two or More New Anti-TB Agents When TB Treatment Failure Is Suspected (A-II)**

Response to anti-TB therapy should be assessed by monitoring clinical symptoms and sputum smears and cultures. If there is not a clinical response or if smear and culture results continue to be positive, treatment failure should be suspected. Drug resistance can be confirmed by obtaining specimens for culture and drug susceptibility testing, but confirmation of drug resistance can take as long as 6 weeks. Since it may be detrimental to wait 6 weeks before altering the therapeutic regimen, additional drugs may need to be added without complete information about the resistance pattern. In such a situation, it is difficult to know which drug(s) to stop, and there is a tendency to add 1 drug to the existing regimen to minimize adherence and intolerance problems [23]. However, such a strategy
runs a high risk of adding 1 good drug to several that are not effective, resulting in de facto monotherapy. By the time the error is recognized, resistance to the new drug is likely to have emerged, compounding the problem. For this reason, a single drug should never be added to a failing regimen. Adding ≥2 drugs to a failing regimen minimizes the chance of creating further drug resistance, and a therapeutic disaster.

If drug resistance is suspected or confirmed, ≥2 drugs to which the infecting organism is susceptible or likely to be susceptible should be added to the treatment regimen. The treatment regimen must always include ≥2 drugs to which the organism is susceptible. When the susceptibility pattern is not yet known, every effort should be made to include several drugs to which the isolate is likely to be susceptible. If disease caused by a drug-resistant organism requires treatment with second-line anti-TB agents, use of ≥3 drugs is recommended [18, 24]. Consultation with an expert in the treatment of TB is advised when addressing these issues.

The performance indicator is for the regimen prescribed by the clinician and is independent of the actions of the patient. For this reason, a 100% standard is expected. There are no circumstances in which addition of a single drug to a regimen that is failing would be acceptable.

Perform Tuberculin Skin Testing on All Patients with a History of One or More of the Following: HIV Infection, Injection Drug Use, Homelessness, Incarceration, or Contact with a Person with Pulmonary TB (A-II)

Tuberculin skin testing with purified protein derivative using the Mantoux method is an effective means of identifying persons with active or latent TB [15, 25]. Criteria for a positive test are detailed in reference [3]. In general, a 5-mm diameter reaction is considered positive for recent contacts of a person with active TB, HIV-infected persons, persons with other immunosuppression, and persons with a chest radiograph suggestive of an old case of TB; a 10-mm diameter reaction is considered positive for recent arrivals from countries where the prevalence of TB is high, injection drug users, children <4 years old, and persons whose medical or social condition puts them at increased risk for exposure to TB or for progression to TB disease; a 15-mm diameter reaction is considered positive in persons with no known risks for exposure to TB or for progression to TB disease; a 20-mm diameter reaction is considered positive in persons with no known risks for exposure to TB or for progression to TB disease. Skin testing should be done in all persons from groups at high risk for latent TB infection (those with a history of injecting drug use, homelessness, incarceration, or contact with a person with pulmonary TB) [25].

Infection with HIV is the strongest risk factor known for progression of latent infection with M. tuberculosis to active disease, and reactivation rates for those with M. tuberculosis and HIV infection are estimated to be 7%–10% per year [15, 25]. HIV-infected persons who become newly infected with M. tuberculosis have an increased risk of developing active TB disease, often with rapid progression. Tuberculin skin testing is not recommended in persons without risk factors for TB; in such persons the risk of a false-positive test outweighs the possible benefit of identification of latent TB infection [26].

Skin testing is simple and has few side effects. The largest drawback is the need for the patient to return in 48–72 h to have the test read. Self-reported reading is not reliable; use of trained readers is recommended [3]. Since some patients may fail to return for reading, a performance indicator of 80% is expected.

Administer Treatment to All Persons with Latent TB Infection Unless Prior Treatment of Latent TB Can Be Documented (A-I)

Treatment of latent TB infection (formerly known as preventive therapy) is effective in preventing TB disease in persons who have positive tuberculin skin tests and who are at risk for reactivated TB [15, 25]. Thus, its use is strongly recommended. The recommended regimens are 9 months of isoniazid or 2 months of rifampin plus pyrazinamide; an alternate though less strongly recommended regimen is 4 months of rifampin [15, 26, 27]. For children, isoniazid for 9 months is the only recommended regimen. Randomized prospective trials support the use of treatment of latent TB infection in HIV-infected and HIV-uninfected persons [15, 26]. Rifampin is not recommended for use in pregnant women, and isoniazid use in persons aged >35 years may have increased toxicity. Therefore, decisions about which treatment regimen to administer need to be individualized.

Persons with a high likelihood of developing active TB include those with HIV infection and a positive skin test (or HIV-infected persons who are close contacts to persons with infectious TB, regardless of skin test results), persons with tuberculin skin test results that have converted from negative to positive within the past 2 years, tuberculin skin test–positive contacts of persons with active TB, tuberculin skin test–positive persons with immunosuppressive conditions, and some tuberculosis skin test–positive persons who were born in a country with a high prevalence of TB [15, 25]. Persons who have received BCG may have positive skin test results without latent TB infection, but most experts believe that such persons are still likely to benefit from treatment of latent TB infection since many will have latent TB and no currently available test can distinguish true-positive from false-positive skin test reactivity [3]. All persons for whom treatment of latent TB infection is considered should have their history should be taken and a chest radiograph and a physical examination performed to exclude active TB before treatment of latent TB infection is initiated.

Ensuring completion of treatment of latent TB infection is difficult; many patients are reluctant to take medication when they are asymptomatic, and maintaining treatment adherence for 9 months is particularly challenging. A recent report showed 68% adherence with a 12-month isoniazid regimen and 80%
adherence with a 2-month rifampin/pyrazinamide regimen [28]. Therefore, a performance indicator of 75% completion within the year after initiation of treatment is expected.

References


