

Tuberculosis: Common Questions and Answers

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Approximately 10 million people worldwide were infected with tuberculosis (TB) in 2019, resulting in 1.4 million deaths. In the United States that same year, there were nearly 9,000 reported cases of TB disease and up to 13 million people were living with latent TB infection (LTBI), which is an asymptomatic, noncommunicable infection caused by *Mycobacterium tuberculosis*. Without treatment, LTBI will progress to active TB disease in approximately 5% to 10% of affected people. Individuals with symptoms of TB disease warrant testing. The U.S. Preventive Services Task Force recommends testing individuals at increased risk of LTBI with an interferon-gamma release assay or tuberculin skin testing. Because the incidence of LTBI in health care professionals is similar to that of the general population, periodic retesting is not recommended. After a positive test result, chest radiography should be performed and, in patients with suspected pulmonary TB disease, sputum collected for diagnosis. Both suspected and confirmed cases of LTBI and TB disease must be reported to local or state health departments. Preferred treatment regimens for LTBI include isoniazid in combination with rifapentine or rifampin, or rifampin alone for a duration of three and four months, respectively. Treatment of drug-susceptible TB disease includes an eight-week intensive phase with four drugs (isoniazid, rifampin, pyrazinamide, and ethambutol), followed by a continuation phase lasting 18 weeks or more, with two drugs based on susceptibility testing results. Consultation with a TB expert is necessary if there is suspicion or confirmation of drug-resistant TB. (*Am Fam Physician*. 2022;106(3):308-315. Copyright © 2022 American Academy of Family Physicians.)

In 2019, approximately 10 million people worldwide were diagnosed with tuberculosis (TB), an infection caused by *Mycobacterium tuberculosis*, resulting in 1.4 million deaths.¹ In the United States, there were nearly 9,000 reported cases of TB disease in 2019, with up to 13 million people living with latent TB infection (LTBI).² Over the past decade, TB incidence in the United States has decreased by 2% to 3% annually, except in 2020 when the incidence was 20% lower compared with 2019.^{2,3} The COVID-19 pandemic may have affected the reporting of TB incidence in several ways, including underdiagnosis and a true reduction in the incidence of TB.²

TB is caused by inhalation of respiratory droplets containing *M. tuberculosis* from a person with active respiratory disease. The *M. tuberculosis* bacilli multiply in the alveoli and can enter the bloodstream, spreading throughout the body (e.g., brain, larynx, lymph nodes, spine, bone, kidneys). The immune response to TB infection is the

formation of granulomas resulting in LTBI. If the immune system cannot control the infection, the bacilli will multiply and progress to TB disease. Without treatment, LTBI will progress to active TB disease in 5% to 10% of affected people.^{4,5} Risk factors for progression include immunosuppression, diabetes mellitus, intravenous drug use, low body weight, and age younger than five years.⁶

Which Clinical Situations Warrant TB Testing?

The Centers for Disease Control and Prevention and the U.S. Preventive Services Task Force recommend testing people who have symptoms of TB disease or are at increased risk of LTBI (Table 1).⁵⁻¹⁰

EVIDENCE SUMMARY

Testing should be performed in individuals with symptoms of TB disease and in asymptomatic individuals at increased risk of LTBI and progression to TB disease.⁵ Symptoms of TB disease include chronic cough (i.e., lasting three weeks or longer), hemoptysis, chest pain, fever, night sweats, anorexia, fatigue, and unexplained weight loss. People at increased risk include those who were born in, or are former residents of, countries with increased TB prevalence (e.g., immigrants, refugees), those who live or have lived in congregate settings (e.g., homeless shelters, correctional

Additional content is available online.

CME This clinical content conforms to AAFP criteria for CME. See CME Quiz on page 241.

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TABLE 1

Populations at Increased Risk of TB Infection Who Warrant Testing

Employees of, or residents who live or have lived in, congregate settings (e.g., homeless shelters, correctional facilities, nursing homes)*

Health care workers who have been exposed to a patient with known TB disease*

Infants, children, and adolescents exposed to adults who are known to have latent TB infection or TB disease*

Patients known to have HIV, diabetes mellitus, gastrectomy or jejunioileal bypass, low body weight (< 90% of ideal body weight), silicosis, chronic renal failure, leukemia, or cancer of the head, neck, or lung†

Patients taking active immunosuppressive therapy (e.g., tumor necrosis factor- α antagonists, systemic corticosteroids [15 mg or more of prednisone per day], immunosuppressive drug therapy following organ transplantation)†

People at increased risk of infection because of social determinants, including medically underserved or low-income populations or people who misuse drugs or alcohol*†

People born in or who frequently travel to Mexico, the Philippines, Vietnam, India, China, Haiti, Guatemala, sub-Saharan Africa, or other countries with high rates of TB*

People who have had contact with someone who has tested positive for or is presumed to have TB disease*

People with a history of untreated or inadequately treated TB disease†

People with recent *Mycobacterium tuberculosis* infection (within the past two years)†

TB = tuberculosis.

*—Recommended testing based on risk of exposure to TB infection.

†—Recommended testing based on risk of developing TB disease.

Information from references 5-10.

facilities), and people with known exposure to TB disease.⁵⁻⁷ People from sub-Saharan Africa and Southeast Asia are particularly at risk of LTBI.⁷⁻⁹ People at low risk of getting TB should not be tested because of the low positive predictive value of testing in low-risk populations.^{5,6}

Initial testing is recommended for all health care professionals upon hire or preplacement. Repeat testing is recommended only for known exposure or based on risk assessments of the health care facility and setting.⁶ The incidence of LTBI in health care professionals is similar to that of the general population because of a substantial decline in the annual national TB rate in 2017 compared with previous decades.¹⁰ A screening questionnaire can be

a useful tool in the assessment of health care workers at risk of TB.¹¹

All suspected and confirmed cases of LTBI and TB disease must be reported to local or state health departments. The health department will assist with diagnostic testing, follow-up, and treatment decisions.⁶

What Are the Recommended TB Tests?

Interferon-gamma release assay (IGRA) and tuberculin skin testing (TST) are recommended options in testing for TB in at-risk individuals.⁶

EVIDENCE SUMMARY

IGRA testing requires a blood sample. Two IGRA tests are currently approved for use in the United States: QuantiFERON-TB Gold+ (Qiagen) and T-SPOT.TB (Oxford Immunotec). Both indicate immune sensitization to *M. tuberculosis*.

TST requires an intradermal injection of 0.1 mL of purified protein derivative and is interpreted 48 to 72 hours later. Induration (not erythema) of 15 mm or more is considered positive in patients without risk factors, 10 mm or more is positive for those at low to intermediate risk of progression to TB disease (e.g., past residence in countries where TB disease is common, diabetes, chronic renal failure, alcohol and intravenous drug use, mycobacteriology laboratory workers, age younger than five years, low body weight), and 5 mm or more is positive for patients at increased risk (e.g., immunocompromised, HIV infection, organ transplants, close contact with someone who has a TB infection, clinical or radiographic evidence of current or prior TB infection).^{6-9,12}

Use of TST and IGRA cannot differentiate between LTBI and TB disease or predict the risk of progression from LTBI to TB disease. Chest radiography is indicated when IGRA or TST results are positive.

What Are the Advantages and Disadvantages of TST vs. IGRA?

Advantages of TST include less expense and no need for a laboratory. Disadvantages include the need for more than one visit, trained staff to complete testing, and lower specificity and sensitivity. Advantages of IGRA testing include no requirement for a follow-up visit to interpret results and greater sensitivity and specificity.³² Disadvantages of IGRA testing include cost, and it is not recommended for use in children younger than two years.³² A comparison of TB tests is discussed in Table 2.^{12,13,32}

EVIDENCE SUMMARY

TST is performed without laboratory equipment and is less expensive than IGRA testing, although more personnel time is required. Chronic immunosuppressed states and

TABLE 2

Comparison of Tuberculosis Tests

Test characteristic	Tuberculin skin test	QuantiFERON-TB Gold+	T-SPOT.TB
Format	Purified protein derivative injected intradermally; patient must return in 48 to 72 hours for results	Enzyme-linked immunosorbent assay using whole blood; processed within 16 hours	Enzyme-linked immunosorbent spot test using peripheral blood mononuclear cells; processed in eight to 24 hours (up to 32 hours if T-Cell Xtend is used)
Measurement	Size of skin induration	Interferon-gamma level	Interferon-gamma level
Sensitivity (%)	68.9	94.1	95.6
Specificity (%)	59	97.3	97.1
Positive likelihood ratio	1.68	34.85	32.97
Negative likelihood ratio	0.595	0.029	0.030
Results affected by BCG vaccination?	Yes	No	No
Pros	Lower cost	High specificity Objective results	High specificity Objective results Only reacts to <i>Mycobacterium tuberculosis</i> , not other mycobacterial strains
Cons	Requires at least two separate visits Affected by BCG vaccination status False-negative risk if recent live vaccination Subjective results Misreading of skin test results	Cost Availability Not recommended for children younger than two years*	Cost Availability Potential for improper handling and processing Not approved for children younger than two years* Different reactivity criteria in the United States, Canada, Europe

BCG = bacillus Calmette-Guérin.

*—Guidelines from the Centers for Disease Control and Prevention and the American Thoracic Society state five years and older, but the American Academy of Pediatrics guidelines state two years and older.³²

Information from references 12, 13, and 32.

receiving immunizations with live vaccines within four weeks of TST placement may cause a false-negative result. Reliability of TST is dependent on clinician technique and experience.¹³

IGRA testing is more convenient for the patient because no return visit is necessary. IGRA test results are objective and not affected by reader variability. IGRA testing is not susceptible to a false-positive result in recipients of the bacillus Calmette-Guérin vaccine, but it does have a false-negative risk similar to that of TST performed in immunosuppressed persons.^{12,14} For a century, the bacillus

Calmette-Guérin vaccine has been used in many parts of the world (i.e., Mexico, South America, Africa, Asia, and Western Europe) in the general population to prevent TB infection.¹⁵ It is also used in special populations in North America, Eastern Europe, and Australia.

How Is TB Disease Distinguished From LTBI?

People with LTBI are asymptomatic. People with TB disease will often have suggestive symptoms, an abnormal result on chest radiography, and a positive sputum smear or culture. Table 3 shows a comparison of LTBI and TB disease.⁶

EVIDENCE SUMMARY

People with LTBI are asymptomatic, noninfectious, and have chest radiography without findings suggestive of TB disease. Those with TB disease are symptomatic and often contagious. Manifestations of TB disease may include respiratory and constitutional symptoms, abnormal results on chest radiography, and positive sputum smear or culture.

In addition to chest radiography, three sputum specimens for acid-fast bacilli smear microscopy, diagnostic nucleic acid amplification test, and cultures are required in patients with suspected pulmonary TB disease. When extrapulmonary TB is suspected, the specimen should be obtained from the site of infection (e.g., lymph node, urine, pleural fluid, cerebrospinal fluid, bone marrow). Additional testing for drug susceptibility is completed on all positive cultures.¹² New methods for whole genome sequencing of *M. tuberculosis* samples are now widely used in areas of the world with limited resources for laboratory-based culture testing. These tests have similar sensitivity to cultures and provide information about genetic mutations that predict drug resistance.¹⁶

What Are the Standard Treatment Recommendations for LTBI?

There are three preferred regimens for the treatment of LTBI: isoniazid plus rifapentine (Priftin), rifampin alone, or isoniazid plus rifampin. Alternative treatment options involve isoniazid monotherapy.^{17,18} Table 4 summarizes the preferred and alternative treatment options for LTBI.^{14,17,18} Standard treatment recommendations are modified if a patient has been exposed to someone with drug-resistant TB.

EVIDENCE SUMMARY

All cases of LTBI and TB disease should be reported to local or state health departments, which can provide valuable resources for contact tracing and support to ensure completion of treatment. Guidelines preferentially recommend three- to four-month drug regimens, all of which include a rifamycin-based medication, rather than the previous standard of six or nine months of monotherapy with isoniazid.¹⁸ The Centers for Disease Control and Prevention recommends initiating treatment of LTBI after excluding the possibility of TB disease.¹⁷ The current treatment guidelines consider the benefits to patients and the public, the complexity of the regimens, potential for toxicity, and costs. Based on these considerations and the quality of evidence, three preferred regimens emerged: (1) 12 weeks of isoniazid plus rifapentine once per week; (2) four months of rifampin once per day; and (3) three months of isoniazid plus rifampin once per day.

Drug-drug interactions, especially with rifampin, may limit the ability to use shorter, preferred options. Alternative regimens use single-drug isoniazid, in a once per day or twice per week dosage for six or nine months. Intermittent regimens must be given under direct observation.

Isoniazid with rifapentine taken once per week for 12 weeks results in better adherence and is as safe and effective in treating LTBI as taking isoniazid once per day for nine months, which has a completion rate of less than 60%.¹⁹⁻²² In patients who have increased risk of progression to TB disease, taking rifampin once per day for four months was not inferior to taking isoniazid monotherapy for

TABLE 3

Comparison of Latent TB Infection vs. TB Disease

Feature	Latent TB infection	TB disease
Symptoms	None	Cough of at least three weeks' duration, hemoptysis, weight loss, fever, night sweats
Infectivity	Noninfectious	Infectious
Tuberculin skin test	Positive (may take two to eight weeks after exposure to react)	Positive
Interferon-gamma release assay	Positive (may take two to eight weeks after exposure to react)	Positive
Sputum acid-fast bacilli smear and body fluid cultures	Negative	Positive or negative
Chest radiography	Usually normal	May show abnormal findings consistent with TB disease
Management	Should consider treatment for all, especially in people at increased risk of progression to TB disease Does not require isolation	Requires drug treatment regimen May need isolation

TB = tuberculosis.

Information from reference 6.

TABLE 4

Treatment Options for Latent Tuberculosis Infection

Priority	Drug	Cost*	Dosing for adults and children 12 years and older	Dosing for children two to 11 years of age	Frequency and duration
Preferred	Isoniazid† plus rifapentine‡ (Priftin)	Isoniazid: \$5 for 12 300-mg tablets	15 mg per kg	25 mg per kg	Isoniazid (rounded up to the nearest 50 mg or 100 mg) and rifapentine, once weekly for three months
		Rifapentine: NA (\$60) for 12 150-mg tablets	10.0 kg to 14.0 kg (22.1 lb to 30.9 lb), maximum dose: 300 mg 14.1 kg to 25.0 kg (31.1 lb to 55.1 lb), maximum dose: 450 mg 25.1 kg to 32.0 kg (55.3 lb to 70.6 lb), maximum dose: 600 mg 32.1 kg to 49.9 kg (70.8 lb to 110.0 lb), maximum dose: 750 mg ≥ 50.0 kg (110.2 lb), maximum dose: 900 mg		
Preferred	Rifampin§	\$70 for 120 300-mg capsules	10 mg per kg, maximum dose: 600 mg	15 mg to 20 mg per kg, maximum dose: 600 mg	Daily for four months
Preferred	Isoniazid plus rifampin	Isoniazid: \$15 for 90 300-mg tablets	5 mg per kg, maximum dose: 300 mg	10 mg to 20 mg per kg,¶ maximum dose: 300 mg	Daily for three months
		Rifampin: \$60 for 90 150-mg capsules	10 mg per kg, maximum dose: 600 mg	15 mg to 20 mg per kg, maximum dose: 600 mg	
Alternative	Isoniazid	\$15 for 90 300-mg tablets	5 mg per kg, maximum dose: 300 mg	10 mg to 20 mg per kg,¶ maximum dose: 300 mg	Daily for six months
			15 mg per kg, maximum dose: 900 mg	20 mg to 40 mg per kg,¶ maximum dose: 900 mg	Twice weekly for six months**
			5 mg per kg, maximum dose: 300 mg	10 mg to 20 mg per kg,¶ maximum dose: 300 mg	Daily for nine months
			15 mg per kg, maximum dose: 900 mg	20 mg to 40 mg per kg,¶ maximum dose: 900 mg	Twice weekly for nine months**

NA = not available.

*—Estimated lowest GoodRx price for treatment (varies per patient). Actual cost will vary with insurance and by region. Generic price listed first; brand name in parentheses. Information obtained at <https://www.goodrx.com> (accessed May 30, 2022; zip code 26505).

†—Isoniazid is formulated as 100-mg and 300-mg tablets.

‡—Rifapentine is formulated as 150-mg tablets in blister packs that should be kept sealed until use.

§—Rifampin is formulated as 150-mg and 300-mg capsules.

||—The American Academy of Pediatrics acknowledges that some experts use rifampin at 20 mg to 30 mg per kg for the daily regimen when prescribing for infants and toddlers.¹⁴

¶—The American Academy of Pediatrics recommends 10 mg to 15 mg per kg for the once per day regimen and 20 mg to 30 mg per kg for the twice per week regimen of isoniazid.

**—Ingestion of intermittent regimens must be directly observed by health care personnel.

Information from references 14, 17, and 18.

nine months because of equivalent effectiveness, improved adherence, and safety.²³

What Is the Standard Treatment Regimen for TB Disease?

Treatment of TB disease is typically done in consultation with the local public health department. Standard treatment for drug-susceptible TB disease includes an eight-week intensive phase with isoniazid, rifampin, pyrazinamide, and

ethambutol, and is followed by a three- to four-month continuation phase with isoniazid and rifampin (Table 5).²⁴

EVIDENCE SUMMARY

Empiric treatment of TB disease begins with a regimen of four drugs. The preferred course of therapy for treating adults and children with TB disease known or believed to be drug-susceptible consists of an eight-week intensive phase using isoniazid, rifampin, pyrazinamide, and ethambutol.²⁴

TABLE 5

Treatment Options for Drug-Susceptible Tuberculosis Disease

Intensive phase drugs*	Dosage† (minimum duration)	Continuation phase drugs	Dosage†‡ (minimum duration)	Comments‡§
Isoniazid, rifampin, pyrazinamide, and ethambutol	Seven days per week for 56 doses (8 weeks) or Five days per week for 40 doses (8 weeks)	Isoniazid and rifampin	Seven days per week for 126 doses (18 weeks) or Five days per week for 90 doses (18 weeks)	Preferred regimen for patients with newly diagnosed pulmonary tuberculosis
Isoniazid, rifampin, pyrazinamide, and ethambutol	Seven days per week for 56 doses (8 weeks) or Five days per week for 40 doses (8 weeks)	Isoniazid and rifampin	Three times per week for 54 doses (18 weeks)	Preferred alternative regimen for situations in which frequent direct observation therapy during continuation phase is difficult
Isoniazid, rifampin, pyrazinamide, and ethambutol	Three times per week for 24 doses (8 weeks)	Isoniazid and rifampin	Three times per week for 54 doses (18 weeks)	Use regimen with caution in patients with HIV and cavitary disease; missed doses can lead to treatment failure, relapse, and acquired drug resistance
Isoniazid, rifampin, pyrazinamide, and ethambutol	Seven days per week for 14 doses, then twice per week for 12 doses	Isoniazid and rifampin	Twice per week for 36 doses (18 weeks)	Do not use twice per week regimens in patients with HIV, cavitary disease, or a positive acid-fast bacilli smear; if doses are missed then therapy is equivalent to once weekly, which is inferior

Note: Regimens are listed in order of preferred treatment and greatest effectiveness. Regimens for treating tuberculosis disease have an intensive phase of two months, followed by a continuation phase of either four or seven months for a total of six or nine months of treatment. The use of once per week therapy with isoniazid, 900 mg, and rifapentine (Priftin), 600 mg, in the continuation phase is not generally recommended but may be considered in situations when directly observed therapy is difficult to achieve more than once per week. This regimen should not be used in patients with HIV or cavitation on chest radiography.

*—Other combinations may be appropriate in certain circumstances.

†—When directly observed therapy is used, drugs may be given five days per week and the necessary number of doses should be adjusted accordingly. Although there are no studies that compare five with seven daily doses, extensive experience indicates this would be an effective practice. Directly observed therapy should be used when drugs are administered less than seven days per week.

‡—Based on expert opinion, patients with cavitation on initial chest radiography and positive sputum cultures at completion of two months of intensive phase therapy should receive seven months (31 weeks) of continuation phase therapy.

§—Vitamin B₆ (pyridoxine), 25 mg to 50 mg per day, is given with isoniazid to all patients at risk of neuropathy (e.g., pregnant patients; breastfeeding infants; patients with HIV, diabetes mellitus, alcoholism, malnutrition, chronic renal failure, advanced age). For patients with peripheral neuropathy, experts recommend increasing pyridoxine dosage to 100 mg per day.

||—Some U.S. tuberculosis control programs have administered intensive phase regimens five days per week for 15 doses (three weeks), then twice per week for 12 doses.

Adapted with permission from Nahid P, Dorman SE, Alipanah N, et al. Official American Thoracic Society/Centers for Disease Control and Prevention/Infectious Diseases Society of America clinical practice guidelines: treatment of drug-susceptible tuberculosis. Clin Infect Dis. 2016; 63(7):e150.

If susceptibility testing confirms sensitivity of the *M. tuberculosis* isolate to both isoniazid and rifampin, ethambutol can be stopped, completing the intensive phase with isoniazid, rifampin, and pyrazinamide.

The intensive phase is followed by a four-month continuation phase consisting of isoniazid plus rifampin.²⁴ Vitamin B₆ (pyridoxine) should be given with isoniazid to people at risk of neuropathy (e.g., pregnant patients; breastfeeding infants; older adults; patients with HIV, diabetes, alcoholism, malnutrition, or chronic renal failure). The

preferred frequency of dosing is once per day; however, directly observed therapy five days a week is an acceptable alternative to seven days per week of self-administered therapy.

Baseline and monthly follow-up evaluations are recommended. The results of acid-fast bacilli smears and cultures determine the duration of the continuation phase and, therefore, are critical to appropriate management. Acid-fast bacilli smears and cultures should be obtained monthly until two consecutive specimens are negative. Additional

information on monitoring and adverse effects of TB therapy is provided in *eTable A*.

Interruptions in TB therapy can impact treatment, such as extending the duration. Experience with SARS-CoV-2 infection in patients with LTBI and TB disease remains limited, but it is anticipated that they may have poorer treatment outcomes, especially if TB therapy is interrupted. Patients who have TB should be vaccinated for and follow precautions to be protected from COVID-19 while continuing TB therapy as prescribed.²⁵

The treatment of drug-resistant isolates of *M. tuberculosis* is more complex and includes additional molecular and phenotypic diagnostic tests to determine susceptibilities, the use of second-line drugs, and prolonged treatment durations. The World Health Organization recommendations are rapidly changing the modern treatment of TB disease with the use of fluoroquinolones for isoniazid resistance and newer medications such as bedaquiline (Sirturo) or delamanid (Delyba; not available in the United States) in cases of rifampin resistance.^{1,26} A TB expert should be consulted when there is suspicion or confirmation of drug-resistant TB disease.²⁷ Recommendations in special populations (i.e., patients with HIV, extrapulmonary TB, culture-negative pulmonary TB, advanced age, renal or hepatic disease, or who are pregnant or breastfeeding) are beyond the scope of this review.

This article updates previous articles on this topic by Jerant, et al.,²⁸ Potter, et al.,²⁹ Inge and Wilson,³⁰ Hauck, et al.,³¹ and Hartman-Adams, et al.⁴

Data Sources: The primary resource used to identify literature was PubMed. Search terms included *Mycobacterium tuberculosis*, latent tuberculosis infection, TB disease, TST, IGRA testing for TB, and treatment of TB. Essential Evidence Plus and article reference lists were reviewed to identify further sources. The search included meta-analyses and reviews. The Centers for Disease Control and Prevention website was also searched using the terms above. Search dates: July 26, 2021; August 6, 2021; August 22, 2021; January 2, 2022; and May 30, 2022.

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SORT: KEY RECOMMENDATIONS FOR PRACTICE

Clinical recommendation	Evidence rating	Comments
Screening for LTBI is recommended in individuals at increased risk. ⁵	B	U.S. Preventive Services Task Force recommendation
Interferon-gamma release assay and tuberculin skin testing are the preferred methods of testing for TB in at-risk individuals. ⁶	C	CDC recommendation
Preferred treatment regimens for LTBI are three to four months in duration. ¹⁸	C	National Tuberculosis Controllers Association and CDC recommendation
In active, drug-susceptible TB disease, four drugs (i.e., isoniazid, rifampin, pyrazinamide, and ethambutol) should be used for an intensive phase of eight weeks. This is followed by a continuation phase of four months with two drugs based on susceptibility test results (i.e., isoniazid and rifampin). ²⁴	C	American Thoracic Society, CDC, and Infectious Diseases Society of America recommendation

CDC = Centers for Disease Control and Prevention; LTBI = latent tuberculosis infection; TB = tuberculosis.

A = consistent, good-quality patient-oriented evidence; **B** = inconsistent or limited-quality patient-oriented evidence; **C** = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to <https://www.aafp.org/afpsort>.

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TUBERCULOSIS

eTABLE A

Monitoring and Adverse Effects of Drugs Used in the Treatment of Tuberculosis

Drug	Clinical monitoring	Adverse effects
Ethambutol	Baseline and monthly visual acuity testing (Snellen chart) and color discrimination (Ishihara color test)	Cutaneous reactions, retrobulbar optic neuritis, peripheral neuritis
Fluoroquinolones (levofloxacin, moxifloxacin [Avelox])	No monitoring recommended	Arthropathy and tendinopathy, dizziness, gastrointestinal upset, headache, insomnia, photosensitivity, pruritus, QT prolongation, rash, tremulousness
Isoniazid	Routine monitoring is not generally recommended* Liver function tests should be followed closely and performed more often in patients with preexisting liver disease or symptoms†	Asymptomatic elevation of liver transaminase levels, diarrhea, drug-induced hepatitis, hypersensitivity reactions (e.g., fever, hemolytic anemia, rash, Stevens-Johnson syndrome), lupus-like syndrome, mild central nervous system effects, monoamine poisoning, peripheral neuropathy
Pyrazinamide	Liver function testing in patients with liver disease Routine serum uric acid measurement may serve as a marker for adherence	Acute gout, asymptomatic hyperuricemia, dermatitis, drug-induced hepatitis, gastrointestinal upset, mild anorexia, non-gouty polyarthralgia, transient morbiliform rash
Rifabutin (Mycobutin)	No routine monitoring tests are required Drug interactions may require monitoring of therapeutic concentrations	Gastrointestinal upset, hepatotoxicity, influenza-like syndrome, neutropenia, orange discoloration of body fluids, polyarthralgias, pseudojaundice (i.e., skin discoloration with normal bilirubin), rash, thrombocytopenia, uveitis
Rifampin	No routine monitoring tests are required Drug interactions may require monitoring of rifabutin therapeutic concentrations	Drug-induced hepatitis, fever, immune reconstitution inflammatory syndrome in people with HIV, influenza-like symptoms, orange discoloration of body fluids, pruritus, rash, thrombocytopenia, transient hyperbilirubinemia
Rifapentine	No routine monitoring tests are required Drug interactions may require monitoring of rifabutin therapeutic concentrations	Red secretions, similar to adverse effects of rifampin, staining of contact lenses

CDC = Centers for Disease Control and Prevention.

*—Baseline laboratory testing is not routinely indicated for all patients (including older patients). It is indicated for patients with HIV infection or a history of chronic liver disease (e.g., hepatitis B or C, alcoholic hepatitis, cirrhosis), patients who are pregnant or no more than three months postpartum, or those who consume alcohol regularly. Testing may be considered on an individual basis, particularly for patients taking medications for chronic conditions.

†—Developing abnormal liver function does not require discontinuation. Liver transaminase elevations greater than five times can occur in 10% to 20% of patients. Elevations usually return to normal even with continued drug therapy, a phenomenon known as hepatic adaptation.

Information from:

Centers for Disease Control and Prevention. Tuberculosis (TB). Accessed June 2, 2022. <https://www.cdc.gov/tb/default.htm>

Nahid P, Dorman SE, Alipanah N, et al. Official American Thoracic Society/Centers for Disease Control and Prevention/Infectious Diseases Society of America clinical practice guidelines: treatment of drug-susceptible tuberculosis. Clin Infect Dis. 2016;63(7):e147-e195.

Precautions

Renal dose adjustments may be needed because of primary renal clearance of drug

Antacids and divalent cations decrease absorption

Renal dose adjustments if creatinine clearance < 30 mL per minute per 1.73 m² (0.50 mL per second per m²)

Hepatitis risk increases with age, viral hepatitis, alcohol consumption, and pregnancy and postpartum

Vitamin B₆ (pyridoxine) may be added to prevent peripheral neuropathy and central nervous system effects

Potential drug interactions with phenytoin (Dilantin) and disulfiram

No renal dose adjustment needed

Renal dose adjustments needed because of drug metabolite accumulation

No renal dose adjustment needed

May cause substantial drug interactions from induction of hepatic microsomal enzymes, including oral contraceptives, methadone, warfarin (Coumadin)

Caution in patients with HIV receiving protease inhibitors or nonnucleoside reverse transcriptase inhibitors

False-positive opiate results

No renal dose adjustment needed

May cause substantial drug interactions caused by induction of hepatic microsomal enzymes

No renal dose adjustment needed