

TB Elimination

Treatment Options for Latent Tuberculosis Infection

Introduction

Treatment of latent tuberculosis (TB) infection (LTBI) is essential to controlling and eliminating TB in the United States, because it substantially reduces the risk that TB infection will progress to TB disease. The Centers for Disease Control and Prevention (CDC) and the United States Preventive Services Task Force (USPSTF) recommend testing populations that are at increased risk for TB infection. Once the diagnosis of LTBI has been made, health care providers must choose the most appropriate and effective treatment regimen, and make every effort to ensure those persons complete the entire course of treatment for LTBI.

However, if exposed to and infected by a person with multidrug-resistant TB (MDR TB) or extensively drug-resistant TB (XDR TB), preventive treatment may not be an option.

Pretreatment Evaluation

To decide whether an individual who has a positive tuberculin skin test (TST) or interferon gamma release assay (IGRA) result is a candidate for treatment of LTBI

- Determine the benefits of treatment by evaluating the individual's risk for developing TB disease
- Assess the person's level of commitment to completion of treatment and resources available to ensure adherence

Once the decision is made to treat an individual for LTBI, the health care provider must establish rapport with the patient and

- Discuss benefits and risks of treatment
- Review possible medication side effects or drug interactions
- Emphasize importance of adherence
- Identify potential barriers to adherence
- Establish a plan to ensure adherence

Table 1: **Candidates for the Treatment of Latent TB Infection**

Groups Who Should be Given High Priority for Latent TB Infection Treatment	
People who have a positive IGRA result or a TST reaction of 5 or more millimeters	People who have a positive IGRA result or a TST reaction of 10 or more millimeters
<ul style="list-style-type: none"> • HIV-infected persons • Recent contacts of a TB case • Persons with fibrotic changes on chest radiograph consistent with old TB • Organ transplant recipients • Persons who are immunosuppressed for other reasons (e.g., taking the equivalent of >15 mg/day of prednisone for 1 month or longer, taking TNF-α antagonists) 	<ul style="list-style-type: none"> • Recent immigrants (< 5 years) from high-prevalence countries • Injection drug users • Residents and employees of high-risk congregate settings (e.g., correctional facilities, nursing homes, homeless shelters, hospitals, and other health care facilities) • Mycobacteriology laboratory personnel • Children under 4 years of age, or children and adolescents exposed to adults in high-risk categories

Persons with no known risk factors for TB may be considered for treatment of LTBI if they have either a positive IGRA result or if their reaction to the TST is 15 mm or larger. However, targeted TB testing programs should only be conducted among high-risk groups. All testing activities should be accompanied by a plan for follow-up care for persons with TB infection or disease.



Choosing the Most Effective Regimen

Treatment of LTBI should be initiated after the possibility of TB disease has been excluded. Persons suspected of having TB disease should receive the recommended multidrug regimen for treatment of disease until the diagnosis is confirmed or ruled out.

Consultation with a TB expert is advised if the known source of TB infection has drug-resistant TB.

Table 2. Latent TB Infection Treatment Regimens

Drugs	Duration	Interval	Minimum doses
Isoniazid	9 months	Daily	270
		Twice weekly*	76
Isoniazid	6 months	Daily	180
		Twice weekly*	52
Isoniazid & Rifapentine	3 months	Once weekly*	12
Rifampin	4 months	Daily	120

*Use Directly Observed Therapy (DOT).

Note: Due to the reports of severe liver injury and deaths, CDC recommends that the combination of rifampin (RIF) and pyrazinamide (PZA) should generally not be offered for the treatment of latent TB infection.

Although regimens are broadly applicable, there are modifications that should be considered under special circumstances (e.g., HIV infection, suspected drug resistance, pregnancy, or treatment of children). Table 2 lists the current recommended regimens. Refer to *Targeted Tuberculin Testing and Recommendations for Use of an Isoniazid–Rifapentine Regimen with Direct Observation to Treat Latent Mycobacterium tuberculosis Infection* for detailed information about the treatment of LTBI.

Isoniazid (INH)

The standard treatment regimen for LTBI is nine months of daily INH. This regimen is very effective and is the preferred regimen for HIV-infected people taking antiretroviral therapy, and children aged 2–11 years of age.

Isoniazid (INH) and Rifapentine (RPT) Regimen

The 12-dose regimen of INH and RPT does not replace other recommended LTBI treatment regimens; it is another effective regimen option for otherwise healthy patients aged ≥ 12 years who have predictive factor for greater likelihood of TB developing, which includes recent exposure to contagious TB, conversion from negative to positive on an indirect test for infection (i.e., interferon- γ release assay or tuberculin test), and radiographic findings of healed pulmonary TB.

This regimen is not recommended for

- Children younger than 2 years old,
- People with HIV/AIDS who are taking antiretroviral treatment,
- People presumed to be infected with INH or RIF-resistant *M. tuberculosis*, and
- Pregnant women or women expecting to become pregnant within the 12-week regimen.

Adverse Drug Reactions

Patients on treatment for LTBI should be instructed to report any signs and symptoms of adverse drug reactions to their health care provider, including

- Unexplained anorexia, nausea or vomiting, dark urine*, or icterus
- Persistent paresthesia of hands or feet
- Persistent weakness, fatigue, fever, or abdominal tenderness
- Easy bruising or bleeding

*Advise patients taking RIF or RPT that they will notice a normal orange discoloration of body fluids, including urine and tears. Contact lenses may be permanently stained.

Obtain a list of patient's current medications to avoid drug interactions. Some interactions to note:

- INH increases blood levels of phenytoin (Dilantin) and disulfiram (Antabuse)
- RIF and RPT decrease blood levels of many drugs including oral contraceptives, warfarin, sulfonureas, and methadone
- RIF and RPT are contraindicated in HIV-infected individuals being treated with protease inhibitors (PIs) and most nonnucleoside reverse transcriptase inhibitors (NNRTIs)

Monitoring During Treatment

Baseline and routine laboratory monitoring during treatment of LTBI are indicated only when there is a history of liver disease, HIV infection, pregnancy (or within 3 months post delivery), or regular alcohol use. Baseline hepatic measurements of serum AST, ALT, and bilirubin are used in the situations mentioned above and to evaluate symptoms of hepatotoxicity. Laboratory testing should be performed to evaluate possible adverse reactions that occur during the treatment regimen.

Clinical monitoring, including a brief physical examination, should occur at monthly visits to assess adherence, rationale for treatment, and to identify signs or symptoms of adverse drug reactions.

CDC collects reports of all severe adverse events (e.g., liver injury, metabolic acidosis, anaphylaxis, seizure, severe dermatitis) leading to hospitalization or death of a person receiving treatment for LTBI. Report these adverse events to the Division of Tuberculosis Elimination by sending an email to LTBIdrugevents@cdc.gov.

<http://www.cdc.gov/tb>

Additional Information

1. ATS/CDC. Targeted tuberculin testing and treatment of latent TB infection. (PDF) *MMWR* 2000;49(No. RR- 6). <http://www.cdc.gov/MMWR/PDF/rr/rr4906.pdf>
2. USPSTF. Latent Tuberculosis Infection: Screening Recommendation. <http://www.uspreventiveservicestaskforce.org/Page/Document/UpdateSummaryDraft/latent-tuberculosis-infection-screening>
3. CDC. Recommendations for Use of an Isoniazid–Rifapentine Regimen with Direct Observation to Treat Latent *Mycobacterium tuberculosis* Infection. *MMWR* 2011; 60:1650–1653. http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6048a3.htm?s_cid=mm6048a3_w
4. CDC. Update: Adverse Event Data and Revised American Thoracic Society/CDC Recommendations Against the Use of Rifampin and Pyrazinamide for Treatment of Latent Tuberculosis Infection. *MMWR* 2003; 52 (No. 31). <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5231a4.htm>
5. Updated Guidelines for the Use of Rifamycins for the Treatment of Tuberculosis Among HIV-Infected Patients Taking Protease Inhibitors or Nonnucleoside Reverse Transcriptase Inhibitors. *MMWR* 2004; 53 (No. 2). <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5302a6.htm>
6. Latent Tuberculosis Infection: A Guide for Primary Health Care Providers. <http://www.cdc.gov/tb/publications/LTBI/default.htm>
7. Targeted Tuberculosis (TB) Testing and Treatment of Latent TB Infection (slide set). <http://www.cdc.gov/tb/publications/slidesets/LTBI/default.htm>
8. Treatment of Latent Tuberculosis Infection: Maximizing Adherence. <http://www.cdc.gov/tb/publications/factsheets/treatment/LTBIadherence.htm>
9. CDC Division of Tuberculosis Elimination website <http://www.cdc.gov/tb>