



Treatment of Latent Tuberculosis Infection

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Introduction

Use this chapter to understand and follow national and Idaho guidelines to:

- determine whom to treat for latent tuberculosis infection (LTBI);
- select appropriate treatment regimens and dosages;
- monitor patients for adverse reactions;
- monitor patients' adherence to treatment;
- determine whether and when therapy is completed; and
- provide treatment in special situations, such as when a patient is pregnant or is coinfecting with TB and HIV.

Prevention of TB has major public health implications, and it is essential to identify and treat all those with risk factors for TB disease.¹ LTBI is the presence of *Mycobacterium tuberculosis* organisms (tubercle bacilli) in the body, with no symptoms and no radiographic or bacteriologic evidence of TB disease.² A person with LTBI is noninfectious but can develop active TB disease via reactivation of latent bacilli. Persons with increased risk for developing TB include those who have had recent infection with *M. tuberculosis* and those who have clinical conditions associated with an increased risk for the progression of LTBI to TB disease.

To control and prevent TB, our healthcare resources and efforts in Idaho should be directed to meet the priorities outlined in the 2005 "Controlling Tuberculosis in the United States: Recommendations from the American Thoracic Society, Centers for Disease Control and Prevention, and the Infectious Diseases Society of America." One of the recommended strategies to achieve the goal of reduction of TB morbidity and mortality is the identification and treatment of persons with LTBI at risk for progression to active TB disease.³

Targeted tuberculin testing for LTBI is a strategic component of TB control that identifies persons at high risk for developing active TB who would benefit from treatment of LTBI, if detected. Persons with increased risk for developing TB include those who have had recent infection with *M. tuberculosis* and those who have clinical conditions that are associated with an increased risk of progression from LTBI to active TB.

Healthcare providers must communicate the risks and benefits of treatment to their patients and encourage adherence and treatment completion. Treatment of LTBI is essential to controlling and eliminating TB in the U.S. LTBI treatment substantially reduces the risk that TB infection will progress to disease.⁴ Depending upon adherence and length of treatment, completing treatment for LTBI can reduce the risk of active TB disease by 65–90%.⁵



Whom to Treat

Treatment of latent tuberculosis infection (LTBI) is essential to controlling TB in the United States because it reduces the risk of reactivation and progression to active TB. Targeted testing for LTBI involves testing populations at high risk of TB infection or at high risk of progression to TB disease once infected. Diagnosis of LTBI is described in Chapter 7, “Diagnosis of Latent TB Infection.” If LTBI is diagnosed as a result of targeted testing, treatment for LTBI can be initiated once active TB has been ruled out.

Diagnosis and treatment of LTBI in individuals unlikely to be infected with TB (i.e., those not meeting criteria for targeted testing) involves additional considerations, given the potential for false-positive testing in a population with a lower prevalence of TB. For additional discussion, see ATS/ISDA/CDC guidelines on “Diagnosis of Tuberculosis in Adults and Children,” found here: <https://doi.org/10.1093/cid/ciw694>.



High-risk contacts (children under 5 years of age and immunocompromised individuals) of persons with active TB should be started promptly on treatment for LTBI. For more information, see Chapter 10, “Contact Investigation.”

Several treatment regimens are available for the treatment of LTBI, and providers should discuss treatment options with their patients.⁶



Treatment regimens are discussed in general below. Detailed information on treatment regimens and dosages for LTBI can be found on the CDC website at: <https://www.cdc.gov/tb/topic/treatment/lbti.htm>



For consultation regarding the treatment of LTBI, call the Idaho State TB Program at (208) 334-5939.



Treatment Regimens and Dosages

Treatment of latent tuberculosis infection (LTBI) is an essential part of the strategy to eliminate tuberculosis (TB) in the U.S. Persons considered at increased risk for TB should be offered testing for LTBI and considered for treatment if LTBI is diagnosed.⁷

There are several treatment regimens available for the treatment of LTBI, and providers should discuss options with patients. Persons who are at especially high risk for TB, and either are suspected of nonadherence or are on an intermittent dosing regimen, should be considered for directly observed therapy (DOT). This method of treatment is especially appropriate when a household member is on DOT for TB disease or in institutions and facilities where a staff member can observe treatment.

Regimens

There are four treatment regimens generally recommended for treatment of LTBI in the United States. These regimens use the drugs isoniazid, rifapentine, and/or rifampin and are prescribed and abbreviated as follows:

- Isoniazid (INH) and Rifapentine (RPT) taken once weekly for 3 months (3HP), often administered by DOT
- Rifampin (RIF) taken daily for 4 months (4R)
- Isoniazid (INH) taken daily (or twice weekly at a higher dose, administered by DOT) for either 6 months (6H) or 9 months (9H)

Information regarding dose and frequency of each regimen can be found on the CDC website at: <https://www.cdc.gov/tb/topic/treatment/ltbi.htm>.

Considerations in Choosing a Regimen

- Shorter treatment regimens have been shown to be effective and safe and have higher rates of completion; when possible, healthcare providers should prescribe the more convenient shorter regimens.⁸ In addition to recommending its use in non-HIV-infected, nonpregnant adults, the CDC has recently updated its recommendations on the use of once-weekly isoniazid and rifapentine (3HP) to include: 1) persons with LTBI aged 2-17 years; 2) persons with LTBI who have HIV infection, including acquired immunodeficiency syndrome (AIDS), and are taking antiretroviral medications that have acceptable drug-drug interactions with rifapentine; and 3) by DOT or self-administered therapy (SAT) in persons aged ≥ 2 years.⁹

The National Tuberculosis Controller Association has issued detailed provider guidance on using the 3HP regimen that can be found on the NTCA website [here](#).

- In general, if circumstances allow, 3HP administered by DOT is the preferred regimen; it is the shortest of the available treatment regimens and, when administered via DOT, provides for the highest level of certainty regarding treatment completion.



- A daily 4-month regimen of rifampin should be considered for persons who cannot complete the 3HP regimen, cannot tolerate isoniazid, or have been exposed to INH-resistant TB.¹⁰
- DOT can be considered for individuals on intermittent (rather than daily) INH regimens and those suspected of nonadherence, particularly if they are at especially high risk for TB disease.¹¹
- See “Treatment in Special Situations” section, below, for information regarding treatment of LTBI in HIV-infected individuals and in women who are pregnant or breastfeeding.
- Additional resources on treatment of LTBI and considerations in choosing a regimen include:
 - CDC publication “Latent Tuberculosis Infection: A Guide for Primary Health Care Providers” found here:
<https://www.cdc.gov/tb/publications/ltbi/pdf/TargetedLTBI.pdf>
 - CDC *Self-Study Modules on Tuberculosis* [DTBE website]. “Module 4: Treatment of Latent Tuberculosis Infection and Tuberculosis Disease” found here:
https://www.cdc.gov/tb/education/ssmodules/pdfs/2017SelfStudy_Module4.pdf



The regimen of rifampin (RIF) and pyrazinamide (PZA) for two months is no longer recommended for treatment of LTBI because of its association with severe liver injury. For more information, see the CDC’s “Update: Adverse Event Data and Revised American Thoracic Society (ATS)/Centers for Disease Control and Prevention (CDC) Recommendations Against the Use of Rifampin and Pyrazinamide for Treatment of Latent Tuberculosis Infection” (MMWR 2003;52[No.31]:735) at <http://www.cdc.gov/mmwr/PDF/wk/mm5231.pdf>.



The use of INH elixir is discouraged as it commonly causes diarrhea and cramping in children. If children have difficulty taking medications, open capsules and crush tablets, and then hide the drugs in soft food or liquids. Possible foods are maple syrup, Nutella, spinach baby food, and chocolate whipped cream. Layer the food and drug on a spoon, and teach the child to take the contents of the spoon without chewing.¹²



For information on information on ordering drugs, see Chapter 15, “Supplies, Materials, and Services.”



For consultation regarding the treatment of LTBI in persons who have been in contact with an active case of TB that is resistant to drugs in the recommended regimens, contact the Idaho State TB Program at (208) 334-5939.



Side Effects and Adverse Reactions

The patient should be monitored by a registered nurse and/or clinician or case manager monthly for signs and symptoms of adverse reactions until treatment is completed. If a patient is symptomatic, the provider should be consulted and the patient monitored more frequently. Laboratory tests (including basic or comprehensive metabolic profiles, complete blood counts, liver transaminases, or other tests based on specific drugs) may need to be checked periodically. (See Table 4: Monitoring and Interventions for Side Effects and Adverse Reactions.)

As is true with all medications, combination chemotherapy for tuberculosis is associated with a predictable incidence of adverse effects, some mild, some serious.¹³

Adverse effects are fairly common and often manageable. Although it is important to be attuned to the potential for adverse effects, it is at least equally important that first-line drugs not be stopped without adequate justification.¹⁴ However, adverse reactions can be severe, and thus, it is important to recognize adverse reactions that indicate when a drug should not be used. Mild adverse effects can generally be managed with symptomatic therapy; whereas with more severe effects, the offending drug or drugs must be discontinued.¹⁵ In addition, proper management of more serious adverse reactions often requires expert consultation.¹⁶

Monitor patients for side effects and adverse reactions following the basic monitoring steps listed below.

Basic Monitoring Steps

1. All healthcare workers providing treatment for latent tuberculosis infection (LTBI) should be familiar with the American Thoracic Society (ATS)/Centers for Disease Control and Prevention (CDC) guidelines.
 - a. All jurisdictions should follow the national monitoring guidelines identified in the current treatment guidelines for treatment of LTBI, "Targeting Tuberculin Testing and Treatment of Latent Tuberculosis Infection," at <http://www.cdc.gov/mmwr/PDF/rr/rr4906.pdf>
 - b. It is also important to check for guideline updates posted on the CDC's Division of Tuberculosis Elimination home page at <http://www.cdc.gov/TB/> and the list of guidelines by date at https://www.cdc.gov/tb/publications/guidelines/list_date.htm.
2. While on treatment, all patients should be evaluated in person at baseline (before starting treatment) and then monthly for side effects and adverse reactions.



3. The common side effects of and adverse reactions to drugs used to treat for latent TB infection (LTBI) are listed in Table 1: **Some Reactions to Antituberculosis Medications.**
 - a. If a patient reports a potentially serious adverse reaction, or an interaction with another medication the patient is taking, call the patient’s provider immediately or advise the patient to seek emergency care, and alert the state TB program by calling the Idaho State TB Program at (208) 334-5939.
 - b. If a patient reports a potentially less severe side effect, call the patient’s provider immediately and monitor the patient.
4. At every visit, document the following patient information:
 - a. Review of symptoms, side effects, and adverse reactions (and any labs that were drawn)
 - b. Education given
 - c. Refill provided
 - d. Description of any problems encountered and action taken for that visit
 - e. Next appointment

Reporting Reactions

The table below is intended for use by the nurse or epidemiology case manager.

TABLE 1: SOME REACTIONS TO ANTITUBERCULOSIS MEDICATIONS¹⁷

| Potentially Serious Adverse Reactions* | Less Severe Signs and Symptoms* |
|---|--|
| <p>Immediately report the following signs and symptoms or other abnormalities or unexpected events to the patient’s provider. These signs and symptoms suggest side effects, including hepatotoxicity:</p> <ul style="list-style-type: none"> ▪ Jaundice ▪ Dark urine ▪ Vomiting ▪ Abdominal pain ▪ Fever ▪ Visual changes ▪ Rash <p>In consultation with the provider, instruct the patient to stop TB medications until evaluated by the provider.</p> | <p>Report the following signs and symptoms to the patient’s provider within 24 hours:</p> <ul style="list-style-type: none"> ▪ Anorexia ▪ Nausea ▪ Malaise ▪ Peripheral neuropathy: tingling or burning sensation in hands or feet |
| <p>* These lists are not all-inclusive. For a more complete discussion of common adverse effects, refer to the current guidelines for treatment of drug-susceptible TB at: https://academic.oup.com/cid/article/63/7/e147/2196792</p> | |

Source: Adapted from California Department of Health Services (CDHS)/California Tuberculosis Controllers Association (CTCA) Joint Guidelines TB Case Management: Core Components, 2011. Available here: https://ctca.org/wp-content/uploads/2018/11/ctca_case_management_5_.pdf. Accessed December 10, 2018.



Remember that any serious adverse event associated with a medication should be reported to FDA MedWatch. More information about what and how to report can be found on the FDA MedWatch website found here: <https://www.fda.gov/Safety/MedWatch/default.htm>.

Checking for Side Effects or Adverse Reactions to an Antituberculosis Drug

Refer to Table 2: Monitoring and Interventions for Side Effects and Adverse Reactions to:

- identify the side effects and adverse reactions associated with particular antituberculosis drugs;
- determine how to monitor for side effects and adverse reactions.



TABLE 2: MONITORING AND INTERVENTIONS FOR SIDE EFFECTS AND ADVERSE REACTIONS^{18, 19, 20}

| Antituberculosis Drug | Side Effects/ Adverse Reactions | Monitoring | Comments |
|------------------------|---|---|--|
| <p>Isoniazid (INH)</p> | <ul style="list-style-type: none"> ▪ Rash ▪ Hepatic enzyme elevation ▪ Hepatitis ▪ Peripheral neuropathy ▪ Mild central nervous system effects | <p>Clinical monitoring monthly</p> <p>Liver function tests (aspartate aminotransferase [AST], alanine aminotransferase [ALT], and serum bilirubin) at baseline in selected cases (human immunodeficiency virus [HIV] infection, history of liver disease or risks for chronic liver disease, alcoholism, and pregnancy or the immediate postpartum period)</p> <p>Repeat measurements if</p> <ul style="list-style-type: none"> ▪ Baseline results are abnormal ▪ Patient is pregnant, in the immediate postpartum period, or at high risk for adverse reactions ▪ Patient has symptoms of adverse reactions | <p>Hepatitis risk increases with age and alcohol consumption.</p> <p>Pyridoxine (vitamin B6, 10–25 mg/d) might prevent peripheral neuropathy and central nervous system effects.</p> <p>INH inhibits several CYP isoenzymes and can therefore increase the concentrations of some medications including phenytoin, carbamazepine, certain benzodiazepines (e.g., diazepam, triazolam), warfarin, and others. The treating provider may want to consider consultation with a clinical pharmacist or use of a web-based drug interaction program to determine whether specific drug-drug interactions exist and if medication dosages need to be adjusted.</p> |



| Antituberculosis Drug | Side Effects/ Adverse Reactions | Monitoring | Comments |
|-----------------------|--|--|---|
| <p>Rifampin (RIF)</p> | <ul style="list-style-type: none"> ▪ Rash ▪ Gastrointestinal upset ▪ Hepatitis ▪ Fever ▪ Bleeding problems ▪ Thrombocytopenia ▪ Renal failure ▪ Flu-like symptoms ▪ Orange-colored body fluids (secretions, urine, tears) | <p>Clinical monitoring monthly</p> <p>Complete blood count and liver function tests (aspartate aminotransferase [AST], alanine aminotransferase [ALT], and serum bilirubin) at baseline in selected cases (human immunodeficiency virus [HIV] infection, history of liver disease or risks for chronic liver disease, alcoholism, and pregnancy or the immediate postpartum period)</p> <p>Repeat measurements if</p> <ul style="list-style-type: none"> ▪ Baseline results are abnormal ▪ Patient has symptoms of adverse reactions | <p>There are several drug interactions with potentially serious consequences. Significant interactions occur with methadone, hormonal contraceptives, antiretroviral agents, and many other drugs. The treating provider may want to consider consultation with a clinical pharmacist or use of a web-based drug interaction program to determine whether specific drug-drug interactions exist and if medication dosages need to be adjusted.</p> <p>For more information, refer to "Table 8. Clinically Significant Drug-Drug Interactions Involving the Rifamycins" in <i>Official American Thoracic Society/Centers for Disease Control and Prevention/Infectious Diseases Society of America Clinical Practice Guidelines: Treatment of Drug-Susceptible Tuberculosis</i> at https://academic.oup.com/cid/article/63/7/e147/2196792</p> <p>Because information regarding rifamycin drug interactions is evolving rapidly, consult the CDC's Division of Tuberculosis "News and Updates" Web page at http://www.cdc.gov/tb/default.htm to obtain the most up-to-date information.</p> <p>Colors body fluids orange.</p> <p>May permanently discolor soft contact lenses.</p> |



| Antituberculosis Drug | Side Effects/ Adverse Reactions | Monitoring | Comments |
|--------------------------|--|--|---|
| <p>Rifapentine (RPT)</p> | <ul style="list-style-type: none"> ▪ Rash ▪ Gastrointestinal upset ▪ Hepatitis ▪ Fever ▪ Bleeding problems ▪ Thrombocytopenia ▪ Renal failure ▪ Flu-like symptoms ▪ Orange-colored body fluids (secretions, urine, tears) | <p>Clinical monitoring monthly</p> <p>Complete blood count and liver function tests (aspartate aminotransferase [AST], alanine aminotransferase [ALT], and serum bilirubin) at baseline in selected cases (human immunodeficiency virus [HIV] infection, history of liver disease or risks for chronic liver disease, alcoholism, and pregnancy or the immediate postpartum period)</p> <p>Repeat measurements if</p> <ul style="list-style-type: none"> ▪ Baseline results are abnormal ▪ Patient has symptoms of adverse reactions | <p>Drug interactions involving RPT are being investigated and are likely to be similar to those of rifampin. RPT is an inducer of multiple hepatic enzymes and therefore may increase metabolism of co-administered drugs that are metabolized by these enzymes.</p> <p>Rifapentine decreases levels of beta blockers, estrogen containing oral contraceptives, calcium channel blockers, hydrocodone and methadone (potentially causing opioid withdrawal symptoms), some corticosteroids, all statins but less so with pravastatin, medications used for treatment of HCV infection, etc. Drug-drug interactions with RPT are extensive, consult with a tuberculosis expert and/or pharmacist first.</p> <p>For more information, refer to "Table 8. Clinically Significant Drug-Drug Interactions Involving the Rifamycins" in <i>Official American Thoracic Society/Centers for Disease Control and Prevention/Infectious Diseases Society of America Clinical Practice Guidelines: Treatment of Drug-Susceptible Tuberculosis</i> at https://academic.oup.com/cid/article/63/7/e147/2196792</p> <p>Because information regarding rifamycin drug interactions is evolving rapidly, consult the CDC's Division of Tuberculosis "News and Updates" Web page at http://www.cdc.gov/tb/default.htm to obtain the most up-to-date information.</p> <p>Body fluids turn orange or red in color.</p> <p>May permanently discolor soft contact lenses.</p> |



Adherence

Monitor patients for adherence to self-administered latent tuberculosis infection (LTBI) treatment regimens monthly throughout treatment.²¹ It is difficult to identify who will and who will not be adherent.²² If patients do not take medicine as directed, the effectiveness of the regimen decreases, and the patient will be at greater risk of progressing to disease in the future and of infecting others.

Monthly Assessment of Adherence

At each visit, the clinician should assess adherence by doing the following:

1. Ask patients how many doses they have missed since their last refill. If patients are asked, "Did you take all your pills last month?" the natural inclination is to agree and say "yes" even if they did not.
2. Have patients bring their bottle of medicine to the refill appointment and count how many pills are left.
3. If adherence problems are identified, include patients in the problem-solving process.
 - a. Ask patients why they think that doses are missed and what could be done better: change the time of day, the location where they keep or take their pills, etc.
 - b. Find out if there are barriers to obtaining refills in a timely manner that could be corrected.
 - c. Review with patients what they believe is their risk of developing tuberculosis (TB) if medicine is not taken. Provide education again as needed.
 - d. Mutually agree on a plan to improve adherence.
 - e. Praise patients for cooperation.
4. If adherence seems to be good, praise patients.



For information on what to include in a patient education session, see Chapter 12, "Patient Education."



Completion of Therapy

Completion of therapy is based on the total number of doses administered, not on the duration of therapy alone. When patients have had lapses in therapy but are still able to complete the recommended number of doses in the allotted time period, encourage them to complete therapy.

Assess patients who will not complete appropriate therapy within the time frame specified to determine whether or not to restart treatment. If the decision is made to retreat the patient, then restart the entire regimen and follow recommended treatment plan of therapy. Also, consider whether the patient will have better success with a different regimen (eg, 3HP by DOT, if they don't remember to take their pills).

Specific factors to consider when determining whether to restart treatment include the following:

- Individual's risk for developing tuberculosis (TB) disease. Generally, the higher their risk, the more urgent it is to complete LTBI treatment. For example, someone recently infected with TB, young children, and persons infected with HIV are at higher risk of progressing to active TB.
- Total number of doses of latent tuberculosis infection (LTBI) treatment administered. Generally, if an individual has completed most of the treatment course, there is less benefit to starting over. For example, someone who has completed at least 6 months of INH can be considered "complete" although their risk of developing future active TB is not as low as if they had completed a 9-month regimen.
- Patient adherence issues (previous attempts at completion, willingness to continue, etc.). Generally, if a patient is very unmotivated, it will not be more productive to try again, and persistent, inadequate exposure to medication might encourage the development of drug resistance.



Give nonadherent patients at very high risk of developing TB disease every opportunity to complete treatment for LTBI. Consider intermittent directly observed therapy and the use of incentives and enablers.²³



Treatment of LTBI in contacts of active TB cases is considered a priority in TB control activities. Make every effort to assure completion of treatment in contacts.

Table 3 describes the duration of therapy, the number of doses that patients are required to take, and the time frame within which the total number of doses must be administered, in order for therapy to be considered complete.

TABLE 3: RECOMMENDED REGIMENS FOR COMPLETION OF THERAPY²⁴

| Regimen | Age | Duration of Therapy | Number of Doses | Must be Administered Within |
|---------------------|--------------------------|---------------------|-----------------|-----------------------------|
| INH daily | Adult and child | 9 months | 270 | 12 months |
| INH daily | Adult | 6 months | 180 | 9 months |
| INH twice weekly | Adult and child | 9 months | 76 | 12 months |
| INH twice weekly | Adult | 6 months | 52 | 9 months |
| RIF daily | Adult and child | 4 months | 120 | 6 months |
| RPT/INH once weekly | Adult and child ≥2 years | 12 weekly doses | 12* | 16 weeks |

Definitions of abbreviations: INH = isoniazid, RIF = rifampin, RPT = rifapentine.
*In rare circumstances when 12 doses cannot be completed, 11 once-weekly doses within a 16-week period can be considered completion of therapy.

Sources: CDC. Targeted tuberculin testing and treatment of latent tuberculosis infection. MMWR 2000;49(No. RR-6):26–27; CDC. Chapter 5: Treatment for LTBI. Core Curriculum on Tuberculosis (2013) [DTBE Web site]. Available at: <https://www.cdc.gov/tb/education/corecurr/pdf/chapter5.pdf>. Accessed December 5, 2018; American Academy of Pediatrics. Tuberculosis. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. *Red Book: 2018 Report of the Committee on Infectious Diseases*. American Academy of Pediatrics; 2018; 829-853.



For consultation regarding completion of therapy and considerations to examine when restarting treatment in noncompliant patients, contact the Idaho State TB Program at (208) 334-5939.



For more information on adherence strategies for different developmental stages, see Appendix C in the New Jersey Medical School National Tuberculosis Center’s Management of Latent Tuberculosis Infection in Children and Adolescents: A Guide for the Primary Care Provider (2004) at: <http://www.umdnj.edu/globaltb/downloads/products/PediatricGuidelines.pdf>.



Treatment in Special Situations

Human Immunodeficiency Virus and Latent Tuberculosis Infection



Treatment of latent tuberculosis infection (LTBI) in a person with human immunodeficiency virus (HIV) infection can be extremely complicated. Before treatment is initiated, contact the Idaho State TB Program at (208) 334-5939 for consultation.

HIV infection is the strongest known risk factor for the progression of LTBI to tuberculosis (TB) disease. HIV-infected persons with LTBI are 100 times more likely to progress to TB disease than are those patients without HIV infection. Coinfected HIV and LTBI patients have a 5 to 10 percent yearly risk of developing TB disease. Patients with only LTBI have a 10 percent lifetime risk of developing TB disease (0.1% risk per year).



High-risk contacts (children less than 5 years of age or individuals who are immunocompromised) should be started on treatment for latent TB infection as soon as possible after exposure, sometimes even before infection is confirmed. For more information, see Chapter 10, "Contact Investigation."

Resources

(For easy access to references, hyperlinks are provided for online references in the list below.)

- CDC. "TB and HIV Guidelines" (DTBE Web site, accessed December 2018) at https://www.cdc.gov/tb/publications/guidelines/hiv_aids.htm
- ATS, CDC. "Targeted Tuberculin Testing and Treatment of Latent Tuberculosis Infection" (MMWR 2000;49[No. RR-6]:33) at: <http://www.cdc.gov/mmwr/PDF/rr/rr4906.pdf>
- CDC. "Prevention and Treatment of Tuberculosis among Patients Infected with Human Immunodeficiency Virus: Principles of Therapy and Revised Recommendations" (MMWR 1998;47[No. RR-20) at: <http://www.cdc.gov/mmwr/PDF/rr/rr4720.pdf>
- CDC. "Updated Guidelines for the Use of Rifabutin or Rifampin for the Treatment and Prevention of Tuberculosis among HIV-infected Patients Taking Protease Inhibitors or Nonnucleoside Reverse Transcriptase Inhibitors" (MMWR 2000;49[No. 9]:185) at <http://www.cdc.gov/mmwr/PDF/wk/mm4909.pdf>
- Francis J. Curry National Tuberculosis Center. Online course "TB Prevention in the HIV-infected Patient: Screening, Testing, and Treatment of Latent TB Infection" at <https://www.currytbcenter.ucsf.edu/products/tb-prevention-hiv-infected-patient-screening-testing-and-treatment-latent-tb-infection>



Pregnancy and Breastfeeding

Treatment for most pregnant women with LTBI can be delayed until after delivery. However, if the pregnant woman is HIV-infected or a recent contact of an active case, immediate treatment should be considered.²⁵ INH daily or twice weekly (using DOT) is the preferred regimen for pregnant women. Supplementation with 10-25 mg/d of pyridoxine (vitamin B6) is recommended.²⁶ Note that there is a potential for increased risk of hepatotoxicity during pregnancy and the first 2-3 months of the post-partum period.²⁷ Consult and coordinate care with the patient's obstetric provider.

Breastfeeding is not contraindicated when the mother is taking INH. Pyridoxine supplementation is recommended for nursing women. Guidelines differ regarding the need for pyridoxine supplementation in the breastfed infants of women taking INH.^{28,29} Consult with the infant's pediatrician to determine if pyridoxine supplementation if needed.

Resources and References

Resources

(For easy access to references, hyperlinks are provided for online references in the list below.)

Whom to Treat

- CDC. "Targeted Tuberculin Testing and Treatment of Latent Tuberculosis Infection" (MMWR 2000;49[No. RR-6]) at: <http://www.cdc.gov/mmwr/PDF/rr/rr4906.pdf>
- CDC. Core Curriculum on Tuberculosis (2013) at <https://www.cdc.gov/tb/education/corecurr/index.htm>

Treatment Regimens and Dosages

- CDC. "Targeted Tuberculin Testing and Treatment of Latent Tuberculosis Infection" (MMWR 2000;49[No. RR-6]) at: <http://www.cdc.gov/mmwr/PDF/rr/rr4906.pdf>
- CDC. "Update of Recommendations for Use of Once-Weekly Isoniazid-Rifapentine Regimen to Treat Latent Mycobacterium tuberculosis Infection" MMWR 2018;67:723-726 at: <https://www.cdc.gov/mmwr/volumes/67/wr/pdfs/mm6725a5-H.pdf>
- CDC. "Update: Adverse Event Data and Revised American Thoracic Society (ATS)/Centers for Disease Control and Prevention (CDC) Recommendations Against the Use of Rifampin and Pyrazinamide for Treatment of Latent Tuberculosis Infection" (MMWR 2003;52[No. 31]) at http://www.cdc.gov/tb/pubs/mmwr/mmwr_updates.htm
- CDC. Core Curriculum on Tuberculosis (2013) at: <https://www.cdc.gov/tb/education/corecurr/index.htm>

Side Effects and Adverse Reactions

- CDC. "Targeted Tuberculin Testing and Treatment of Latent Tuberculosis Infection" (MMWR 2000;49[No. RR-6]:26–29, 38–39) at <http://www.cdc.gov/mmwr/PDF/rr/rr4906.pdf>



- National Tuberculosis Controllers Association, National Tuberculosis Nurse Coalition. *Tuberculosis Nursing: A Comprehensive Guide to Patient Care* [under revision and not available as of December, 2018]
- CDC. Module 4: “Treatment of Latent Tuberculosis Infection and Tuberculosis Disease (Self-Study Modules on Tuberculosis, 2016) at https://www.cdc.gov/tb/education/ssmodules/pdfs/2017SelfStudy_Module4.pdf

Adherence

- CDC. Module 6: “Managing Tuberculosis Patients and Improving Adherence” (Self-Study Modules on Tuberculosis, 2014) at <https://www.cdc.gov/tb/education/ssmodules/pdfs/Module6v2.pdf>

This module is entirely devoted to assessing and promoting adherence. It covers the many areas that need to be addressed, such as:

- Case management: assigning responsibility to the healthcare worker
- Communication and problem-solving skills
- Education of the patient
- Using interpreters when needed
- Using incentives (rewards) and enablers (things that remove barriers to patients)
- Using DOT

References

- ¹ CDC. Treatment of latent tuberculosis infection: maximizing adherence. *TB Fact Sheets* [DTBE Web site]. April 2005:1. Available at: <http://www.cdc.gov/tb/pubs/tbfactsheets/LTBIadherence.htm>. Accessed February 1, 2007.
- ² CDC. Summary. In: Chapter 6: treatment of LTBI. *Core Curriculum on Tuberculosis (2000)* [DTBE Web site]. November 2001. Available at: <http://www.cdc.gov/tb/pubs/corecurr/index.htm>. Accessed July 3, 2006.
- ³ ATS, CDC, IDSA. Controlling tuberculosis in the United States: Recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America. *MMWR* 2005;54(No. RR-12):15.
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