

**Service #2: Nursing Management of Persons
Infected with *Mycobacterium tuberculosis* (LTBI) or
Contacts Requiring Window Prophylaxis**

I. Eligible patients

A. Patients with all of the following

- May have a history of exposure to TB
- CXR without findings of active TB disease
- no signs or symptoms suggestive of active TB disease
- a positive TST or IGRA result

B. Patients with all of the following

- a history of exposure to TB
- CXR without findings of active TB disease
- no signs or symptoms suggestive of active TB disease
- a negative TST or IGRA result but is a contact to a TB case/suspect and should be considered for treatment (**window prophylaxis**)
 - Children younger than 5 years of age
 - Immunosuppressed patients, including those with HIV infection

II. Pretreatment evaluation

A. Perform all relevant activities under **procedure #1: Patient Assessment, Education, and Screening Procedures** (personal health history, physical exam, specimen collection, clinical assessment, specimen collection, tuberculosis screening procedures, referral for CXR/medical evaluation, patient education and counseling, signed documents)

B. Before beginning treatment of LTBI, active TB should be ruled out by history, physical examination, CXR, and when indicated, bacteriologic studies. If patient is suspected of having active TB disease, see procedure #4: Nursing Management of Persons with or Suspected to have *Mycobacterium tuberculosis* Disease (Pulmonary and/or Extrapulmonary Disease).

Note: If patient has signs or symptoms of active TB disease, irrespective of CXR findings, consult the treating physician before starting LTBI treatment

C. **Sputum examination is not indicated for most persons** being considered for treatment of LTBI

Exceptions:

- Persons with CXR findings suggestive of prior, healed TB infection should have three consecutive sputum samples, obtained on different days, submitted for AFB smear and culture. Results of sputum smears and cultures must be negative before LTBI is started.
- HIV-infected persons with respiratory symptoms or individuals with untreated extrapulmonary TB disease who are being considered for treatment of LTBI should have sputum specimens submitted for AFB smear and culture, even if the CXR is normal. If results of sputum smears and cultures are negative and respiratory symptoms can be explained by another etiology, then LTBI can be started. If bacteriologic results are negative but the activity or etiology of a radiographic abnormality is questionable, further evaluation should be undertaken. Treatment of LTBI should not be started until active TB has been excluded.

III. Chest X-ray must be obtained and show no evidence of active TB disease before starting LTBI treatment

Note: It is recommended that children less than 5 years of age and preferred that older children and adolescents up to age 18 have both posterior-anterior and lateral views; all others should have at least posterior-anterior views. Other views or additional studies should be done only by order of the treating physician.

- A. If treatment for LTBI is not started within two months of the CXR showing no abnormalities indicative of tuberculosis, a repeat CXR should be examined prior to the start of therapy for LTBI to ensure that TB disease has not developed
- B. For persons at high risk of progressing to TB disease (including those < 1 year of age, those co-infected with HIV, or those receiving immunosuppressive therapy), if treatment for LTBI is not started within one month of the CXR showing no abnormalities indicative of tuberculosis, a repeat CXR should be examined before the start of therapy for LTBI to ensure that TB disease has not developed
- C. If the patient begins to exhibit symptoms suggestive of tuberculosis prior to the start of therapy for LTBI, a repeat CXR should be examined to ensure that TB disease has not developed
- D. If patient refuses treatment (either initially or during treatment course) for LTBI, educate patient on importance of seeking medical evaluation for development of any symptoms suggestive of TB and document refusal in the medical record

IV. **LTBI treatment for contacts of patients with drug-susceptible TB**

- A. For adults, the following regimens are preferred (**in this order**) by the 2012 DSHS Tuberculosis

Expert Panel:

Note: When choosing the best regimen for an individual patient, consideration should also be given to the indications/contraindications for each treatment regimen, resources required for DOT (if INH-RPT selected), and likelihood of patient compliance

- Isoniazid (INH)-Rifapentine (RPT) – see procedure #3: Nursing Management of Persons Treated for LTBI with INH-RPT by DOT Once Weekly for 12 Weeks
- Rifampin (RIF) for 4 months
- INH for 9 months
- INH for 6 months
- INH/RIF for 3 months – Note: This regimen has been used in the UK and Western Europe for some time and is included as recognition of its status as an available alternative and effective LTBI treatment regimen for completeness. If this regimen is considered for use, consult the treating physician and a DSHS-recognized expert TB physician first.
- For patients that were initially started on treatment for active TB disease, 2 months of standard 4 drug treatment with RIF, INH, pyrazinamide (PZA), and ethambutol (EMB) can be considered adequate treatment for LTBI

B. For **adolescents age 12 years and older**, the preferred regimens are the same as adults, with the following exceptions:

- When treating with rifampin alone for LTBI, the length of treatment is 6 months for children and adolescents

C. For **children age 2-11 years old**, the preferred regimens are the same as adults, with the following exceptions:

- When treating with rifampin alone for LTBI, the length of treatment is 6 months for children and adolescents
- INH-RPT can be considered on a case-by-case basis when both 1. The circumstances make the completion of 9 months of daily INH unlikely and 2. The likelihood hazard of TB is great (e.g. recent TB infection in a preschool-aged-child). The number of children in this age range who have received INH-RPT is insufficient for assessing tolerability and efficacy. Consult the treating physician before using.

D. For children under the age of 2 the preferred regimens are the same as adults, with the following exceptions:

- When treating with rifampin alone for LTBI, the length of treatment is 6 months for children and adolescents
- INH-RPT was not studied in children < 2 y/o so it is contraindicated in this age group

V. **LTBI treatment for contacts of patients with INH-resistant, rifampin-susceptible TB**

A. For adults, rifampin for 4 months is recommended

- B. For children and adolescents, when treating with rifampin alone for LTBI, the length of treatment is 6 months

VI. **LTBI treatment for contacts of patients who are likely to be infected with INH- and rifampin-resistant (MDR)-TB and/or XDR-TB** (a rare type of MDR-TB that is resistant to isoniazid and rifampin, plus any fluoroquinolone and at least one of three injectable second-line drugs i.e., amikacin, kanamycin, or capreomycin) **and** who are at high risk for developing TB: consult with a DSHS-recognized expert TB physician for treatment recommendations and appropriate follow-up

- A. All MDR-TB or XDR-TB contacts with LTBI, whether on treatment of LTBI or not, need to be followed closely with clinical and radiographic evaluation for 2 years, as specified by the DSHS-recognized expert TB physician

- B. If an MDR-TB or XDR-TB contact receives treatment, DOT shall be provided for the following:

- Children <18 years of age
- Those with HIV infection
- Persons who are immunocompromised

VII. **Special considerations** for treatment of LTBI apply to the following populations:

- A. When INH is chosen for treatment of LTBI in persons with **HIV infection** or those with **radiographic evidence of prior Tb**, 9 months rather than 6 months is recommended

- B. Rifampin is generally contraindicated or should be used with caution in **HIV infected patients who are taking protease inhibitors or NNRTIs**

- C. **INH/RPT** is not recommended for the following patients:

- Children aged <2 years
- HIV-infected patients receiving antiretroviral treatment
- Pregnant women or women expecting to become pregnant during treatment
- Patients who have LTBI with presumed INH or RIF resistance

- D. For **pregnant, HIV-negative women**, INH given daily or twice weekly for 9 or 6 months is recommended

- For women at risk of progression of LTBI to disease, especially those who are infected with HIV or who have likely been infected recently, initiation of therapy should not be delayed on the basis of pregnancy alone, even during the first trimester. Consult with the treating

physician.

- For women whose risk for active TB is lower, some experts recommend waiting until after delivery to start treatment. Consult with the treating physician.

VIII. Medication dosages

From: <http://www.cdc.gov/tb/publications/LTBI/treatment.htm>

Drug(s)	Duration	Dose	Frequency	Total Doses
Isoniazid (INH)	9 months	Adult: 5 mg/kg Children: 10-20 mg/kg** Maximum dose: 300 mg	Daily	270
		Adult: 15 mg/kg Children: 20-40 mg/kg** Maximum dose: 900 mg	Twice weekly†	76
	6 months	Adult: 5 mg/kg Children: Not recommended Maximum dose: 300 mg	Daily	180
		Adult: 15 mg/kg Children: Not recommended Maximum dose: 900 mg	Twice weekly†	52
Isoniazid (INH) and Rifapentine (RPT)	3 months	Adults and Children 12 and over: INH* : 15 mg/kg rounded up to the nearest 50 or 100 mg; 900 mg maximum RPT* : 10.0–14.0 kg 300 mg 14.1–25.0 kg 450 mg 25.1–32.0 kg 600 mg 32.1–49.9 kg 750 mg ≥50.0 kg 900 mg maximum	Once weekly†	12
Rifampin (RIF)	4 months	Adult: 10 mg/kg*** Maximum dose: 600 mg	Daily	120

†Intermittent regimens must be provided via directly observed therapy (DOT), i.e., health care worker observes the ingestion of medication.

*Isoniazid (INH) is formulated as 100 mg and 300 mg tablets. Rifapentine (RPT) is formulated as 150 mg tablets in blister packs that should be kept sealed until usage.

** The American Academy of Pediatrics recommends an INH dosage of 10-15 mg/kg for the daily regimen and 20-30 mg/kg for the twice weekly regimen.

***In the United States, the recommended regimen for treatment of LTBI in children is a 9-month course of INH. For the treatment of LTBI in infants, children, and adolescents when INH could not be tolerated or the child has had contact with a case patient infected with an isoniazid-resistant but rifamycin-susceptible organism the American Academy of Pediatrics recommends 6 months of daily rifampin (RIF) (180 doses) at a dosage of 10-20 mg/kg.

IX. If treatment for LTBI is recommended,

- A. There must be an appropriate **physician order** on record including name of drug(s), dosage, frequency, route and method of administration (directly observed therapy or self-administered therapy), length of treatment, and maximum number of refills:
- Written order on **TB-400A**, or
 - Written order on a prescription form or physician letterhead, or
 - Verbal order documented in the progress notes
 - All prescriptions and verbal orders must be followed by form TB-400A with the treating physician's signature faxed or mailed within 96 hours
- B. Patient should receive an **initial clinical evaluation and follow-up clinical evaluations** at least monthly with clinical assessment for tuberculosis disease medication toxicity, in the preferred language of the patient or using an interpreter, recorded on form **TB-205**
- This evaluation should include questioning about side effects and a brief physical assessment checking for signs of hepatitis
 - For female patients of childbearing potential: counsel the patient that rifamycins may make hormonal contraceptive methods less effective, encourage the patient to add a back-up barrier method to prevent pregnancy, and emphasize the importance of avoiding pregnancy while on treatment and, for rifapentine, up to two weeks after stopping the medicine
 - Patients should be educated about the symptoms and signs that could be side effects associated with treatment of LTBI and advised to stop treatment and promptly seek medical evaluation when they occur, including: unexplained anorexia, nausea, vomiting, dark urine, icterus, rash, persistent paresthesias of the hands and feet, persistent fatigue, weakness or fever lasting 3 or more days, abdominal tenderness, easy bruising or bleeding, and arthralgia
 - Some experts recommend that INH be withheld if a patient's transaminase level exceeds 3 times the upper limit of normal if associated with symptoms and 5 times the upper limit of normal if the patient is asymptomatic. If this occurs with any medication, consult the treating physician.
 - Patient should be educated regarding signs and symptoms of tuberculosis. If symptoms of active disease occur, stop the medication(s), complete a medical history (TB-202), obtain a chest x-ray, collect 3 sputum samples, at least two of which are obtained in the early morning on consecutive days, and consult the treating physician for medical evaluation. Refer to procedure #4: Nursing Management of Persons with or Suspected to have *Mycobacterium tuberculosis* Disease (Pulmonary and/or Extrapulmonary Disease).
 - Serious adverse reactions that result in hospitalization or death should be reported to the DSHS TB/HIV/STD Unit within two working days on form **EF 12-12274**. Contact the DSHS

TB nurse consultant for instructions, if needed. Adverse reactions resulting in hospitalization or death should also be reported to the CDC Division of Tuberculosis Elimination at 404-639-8401 or LTBIldrugevents@cdc.gov

- Adverse events or medication errors should be reported to the DSHS TB/HIV/STD Unit within five working days on form **EF 12-12274**. Contact the DSHS TB nurse consultant for instructions, if needed. Adverse events should also be reported to FDA MedWatch at <http://www.fda.gov/medwatch>, by submitting a MedWatch Form 3500 (available at http://www.fda.gov/medwatch/safety/FDA-3500_fillable.pdf) or by calling 1-800-FDA-1088.

C. Patients receiving rifamycins should be counseled about the side effects of rifampin, rifapentine, and rifabutin:

- Hepatotoxicity, evidenced by transient asymptomatic hyperbilirubinemia, may occur in 0.6% of persons taking RIF. Hepatitis is more likely when RIF is combined with INH.
- Cutaneous reactions, such as pruritus (with or without a rash), may occur in 6% of persons taking RIF. They are generally self-limited and may not be a true hypersensitivity; continued treatment may be possible. Consult the treating physician if this occurs.
- Rarely, rifamycins can be associated with hypersensitivity reactions, including hypotension, nephritis or thrombocytopenia, and manifested by symptoms such as fever, headache, dizziness/lightheadedness, musculoskeletal pain, petechiae, and pruritus.
- Gastrointestinal symptoms such as nausea, anorexia, and abdominal pain are rarely severe enough to discontinue treatment.
- Orange discoloration of body fluids is expected and harmless, but patients should be advised beforehand. Soft contact lenses and dentures may be permanently stained.
- RIF and RPT interact with a number of drugs, causing drug-drug interactions. They are known to reduce concentrations of methadone, warfarin, hormonal contraceptives, and phenytoin. Women using hormonal contraceptives should be advised to consider an alternative method of contraception (e.g., a barrier method).
- RIF is contraindicated, or should be used with caution, in HIV-infected individuals being treated with certain antiretroviral medications. Substitution of rifabutin for RIF in the 4-month regimen may be considered for such patients. RPT should not be used in HIV-infected persons taking antiretroviral therapy.

X. Directly observed therapy (DOT)

A. Any regimen that is given intermittently (including INH/RPT) should be given only under DOT

B. Other patients to be considered for DOT, as resources permit:

- Those with the highest priority for DOT (those at the highest risk of progression from latent to active TB):

- Persons with HIV infection
 - Young children who are contacts of infectious patients with pulmonary TB
 - Household contacts of patients receiving DOT for active TB
 - Treatment observed by staff members in certain facilities (such as schools and homeless shelters)
- C. For patients receiving DOT, in the event of evacuation, re-establish contact, as soon as possible. Confirm location and reinstitute DOT or transfer to new jurisdiction for continuation of treatment.
- D. Document doses of medications given by DOT on form **TB-206** (or form **TB-206A for INH-RPT** use)

XI. Laboratory testing

- A. Baseline laboratory testing and laboratory monitoring during treatment is **not** routinely indicated for all patients at the start of treatment for LTBI
- B. Exceptions:** Patients who should have baseline hepatic measurements of AST, ALT and bilirubin include
- Initial evaluation suggests a liver disorder
 - HIV infection
 - Pregnant women or women in the immediate postpartum period (within 3 months of delivery)
 - Regular alcohol use
 - Persons with a history of liver disease
 - Others at risk for chronic liver disease
- C. Consider testing on an individual basis for older persons or patients who are taking other medications for chronic medical conditions, as ordered by the treating physician
- D. If baseline liver function studies exceed the normal range, consult the treating physician. Do not give the medication(s) until approved by the treating physician.
- E. Active hepatitis and end-stage liver disease are relative contraindications to the use of INH. Consult the treating physician if patient has active hepatitis or end-stage liver disease before starting ANY medication.
- F. Routine laboratory monitoring during treatment is indicated for**
- Persons whose baseline liver function tests are abnormal
 - Other persons at risk for hepatic disease (history of liver disease, HIV infection, HBV, HCV or other chronic hepatitis, sexual or household contact with individuals chronically infected with viral hepatitis, chronic hemodialysis, receipt of clotting factors prior to 1987, pregnant or less than 3 months post-partum, jaundice, substance abuse, taking other potentially

hepatotoxic medications, other chronic medical conditions such as DM, CHF, or chronic kidney disease)

G. Laboratory testing may also be indicated for the evaluation of possible adverse effects that occur during the course of treatment, as ordered by the treating physician

- Obtain liver function studies on the same day, if possible
- Do not restart medication without a physician's order

XII. When INH is used (including INH-RPT) , **pyridoxine supplementation** should be given to the following:

- A. Pregnant women
- B. Breastfeeding infants
- C. Patients with diets likely to be deficient in pyridoxine
- D. Patients who are at risk for developing paresthesias (such as HIV/AIDS, alcohol use, diabetes mellitus)
- E. Patients who experience paresthesias while taking INH

XIII. **Completion of therapy** is based on total number of doses administered – not on duration of therapy alone

- A. 9 months of INH = 270 doses, at minimum, administered within 12 months
- B. 6 months of INH = 180 doses, at minimum, administered within 9 months
- C. 9 months of twice-weekly INH = 76 doses, at minimum, administered within 12 months
- D. 6 months of twice-weekly INH = 52 doses, at minimum, administered within 9 months
- E. 4 months of rifampin = 120 doses, at minimum, administered within 6 months
- F. INH/RPT = 11 or 12 doses within 16 weeks; doses must be separated by ≥ 72 hours to be counted

XIV. Interruptions of therapy

- A. When reinstating therapy for patients who have interrupted treatment, obtain a new order from

the treating physician stating whether to continue the regimen originally prescribed or restart the entire regimen if interruptions were frequent or prolonged enough to preclude completion of treatment as recommended

- B. In either situation, when therapy is restored after an interruption of more than two months, a medical examination and CXR to rule out active TB disease is indicated

XV. Other treatment notes

- A. Refer patients for other medical and social services as appropriate
- B. If a physician orders to withhold treatment of LTBI, educate patients about TB infection and disease and advise patient to seek medical evaluation immediately if any signs or symptoms of TB develop