



TREATMENT OF LATENT TB INFECTION – 2003

Treatment of latent TB infection (LTBI) is advised for the following:

A. Regardless of age: HIGHEST PRIORITY

1. All household or other close contacts of persons with current pulmonary tuberculosis:

a) High-risk contacts including children under 5 years and immunocompromised individuals (HIV infection, chronic corticosteroids, chemotherapy, etc) should receive treatment for LTBI regardless of tuberculin skin test (TST) reaction if the index case is smear or culture (+) for *M. tuberculosis*:

b) Refer to Contact Investigation Guidelines for other groups

At 3 months, contacts with a negative TST (<5mm) will be retested. If the non-immunocompromised contact is still negative (includes children) and the index case is on TB chemotherapy, treatment of LTBI may be discontinued. Immunocompromised close contacts should complete a full course of treatment regardless of repeat TST results since test results may be unreliable.

2. Tuberculin converters:

Definition of conversion: Increase in the size of the tuberculin reaction by at least 10 mm from less than 10 mm to 10 mm or more within a 2 year period.

3. TST reactors (5mm or greater) with abnormal chest films consistent with dormant tuberculosis that have not had adequate prior therapy.

It is important to exclude current disease by bacteriologic evaluation and/or a review of serial x-rays.

4. All TST reactors (5mm or greater) with HIV infection or at high risk of HIV infection.

Homosexual/bisexual men and injection drug users are at high risk of HIV infection. Unless the HIV test is known to be negative and the patient does not belong to other high-risk groups, they should be encouraged to take INH.

5. TST reactors (10mm or greater) who are newcomers to the U.S. (less than 5 years in U.S.), from areas of the world with a high TB incidence (includes Central and South America, Asia, Philippines, the former Soviet Union, and Africa).

6. TST reactors (10mm or greater) who are injection drug users (HIV testing should be strongly encouraged for all individuals in this group).

7. All TST reactors (10mm or greater) who are homeless or have a transient living arrangement (Note: Because of increased TB disease susceptibility and probability of TB exposure in group settings, HIV testing should be strongly encouraged for all homeless tuberculin reactors).

8. TST reactors with special medical situations of increased risk. These include prolonged corticosteroid therapy (>15mg daily of prednisone or equivalent for 2-4 weeks), immunosuppressive therapy, leukemia or lymphoma, insulin-dependent diabetes, silicosis, post-gastrectomy (especially with weight loss) and renal failure with uremia.

Note: a 5 mm cut point is considered positive for persons who are on immunosuppressive therapy, corticosteroids, or have leukemia or lymphoma. A 10mm cut point should be used for other medical risk groups.

9. All TST reactors (10mm) under 21 years of age.

B. Less than 35 years of age:

1. Foreign-born TST reactors (10mm or greater) living in the U.S. greater than 5 years who come from areas of the world with a high TB incidence (includes Central and South America, Asia, Philippines, the former Soviet Union, and Africa).

2. Post-partum women with significant TST reactions (10mm or greater)

INH is not contraindicated during pregnancy but in general should be delayed until after delivery unless additional risk factors such as HIV infection, being a close contact or recent skin test conversion exists. Nursing is not a contraindication to INH.

3. TST reactors (10mm or greater) for whom the public health consequences of developing tuberculosis disease would be of special importance; i.e. persons who work with small children, such as day care providers, health care providers, teachers, school bus drivers, etc.
4. TST reactors (10mm or greater) who are 21 - 35 years old. As a public health policy, we are not administering INH to this age group without other risk factors. However, if an individual wishes to take INH after reviewing risks and benefits, we will offer the therapy.

C. Contraindications:

1. Known previous adverse reactions INH, rifampin, or pyrazinamide (PZA).
3. Unstable liver disease, with AST greater than 3 times normal. (for INH or PZA only)
3. History of gout when using PZA

D. Recommended Treatment Regimens:

For Dosages, see attached chart on page 4.

1. INH is prescribed for 9 months for:
 - children under age 15,
 - immunocompromised reactors (especially HIV seropositive persons)
2. The 2 month regimen of daily rifampin/PZA may be prescribed to:
 - HIV infected individuals [*rifabutin may be substituted for rifampin if the HIV patient is on protease inhibitors (PIs) or non-nucleoside reverse transcriptase inhibitors (NNRTIs)*]

At the TB Clinic physician's discretion: (must be under TB Control DOT program)

- homeless (prioritize TST converters and contacts)
 - incarcerated patients
3. Persons with abnormal chest films consistent with dormant tuberculosis may be treated with 4 months of the multi-drug regimen of rifampin /INH or 9 months of INH alone
 4. Other groups will receive 6 months of INH

E. Vitamin B6:

The routine use of B6 is recommended only for persons at high risk of developing peripheral neuropathy: persons with diabetes, uremia, chronic alcoholism, severe malnutrition, HIV infection, pregnant women and the aged.

F. BCG:

In most situations prior BCG history will be ignored when considering INH recommendations. Reactions over 10 mm are unusual several years after vaccination. If BCG has been given within 1 year of the tuberculin skin test, the PPD can be repeated after 1 year has passed before deciding on treatment.

G. Monitoring:

1. Baseline liver function tests (AST, Alkaline phosphatase and total bilirubin) are required only for individuals with:
 - known liver disease
 - alcoholism
 - injection drug use
 - HIV infection
 - those placed on any multi-drug regimen (INH/RIF for 4 months, RIF/PZA for 2 months)
2. Complete blood count, creatinine, and uric acid at baseline and monthly are required for those placed on the 2-month rifampin/PZA regimen.
3. If baseline results are abnormal, repeat measurements should be obtained monthly until documented stable or if the patient has symptoms of adverse reactions.
4. For individuals on the 2-month rifampin/PZA regimen, serum aminotransferase and bilirubin should be repeated at 2, 4 and 6 weeks of treatment.

DRUGS FOR LATENT TUBERCULOSIS INFECTION (LTBI)

Drug	Supplied	Dose/frequency	Duration	Side Effects	Monitoring	Comments
Isoniazid (INH):	Tabs: 300mg 100mg Susp: 50mg/5ml Inj: 100mg/ml	<u>Adults:</u> 300mg daily or 900mg 2X weekly <u>Children:</u> 10 – 15mg/kg daily (>20kg = 300mg) or 20-30mg/kg 2 X weekly	<u>Adults:</u> 6 months (180 doses) <u>Children, HIV infected, immuno-compromised or has CXR consistent with old inactive TB :</u> 9 months (270 doses)	Hepatitis; peripheral neuropathy; mild CNS effects; skin rash; increased Dilantin levels.	LFTs (not routine) unless known or suspected liver disease or other hepatotoxic drugs used concurrently.	Give pyridoxine 25mg/day to prevent neuropathy in elderly, D.M., nutritionally deficient, renal disease, pregnancy, HIV, alcoholics.
Rifampin (RIF):	Caps: 300mg 150mg	<u>Adults:</u> 10mg/kg up to 600mg PO daily <u>Children:</u> 10 – 20mg/kg up to 600mg PO (use RIF only when INH cannot be used because of toxicity or INH drug resistance)	<u>Adults:</u> 4 months (120 doses) when used w/ INH) <u>HIV+ adults only:</u> 2 months (60 doses) when used w/ PZA	Orange discoloration of secretions; cholestatic or hepatocellular hepatitis; febrile (flu-like) reaction; induces hepatic enzymes, drug interactions; thrombocytopenia; skin rash.	LFTs (not routine) unless known or suspected liver disease or other hepatotoxic drugs used concurrently. Baseline CBC.	Warn patient about orange discoloration of urine and other body secretions. Discoloration of contact lens. Induces hepatitis microsomal enzymes.
Rifabutin:	Caps: 150mg	<u>Adults only:</u> 5 mg/kg up to 300mg daily	As for rifampin	As for rifampin except hepatic enzyme induction less; risk of uveitis when used with macrolides, PI's and azole antifungal agents.	As for rifampin.	As for rifampin.
Pyrazinamide (PZA):	Tabs: 500mg scored	<u>Adults only:</u> 15 – 20mg/kg PO	<u>HIV+ adults only:</u> 2 months (60 doses) when used w/ RIF	Hepatitis; GI upset; hyperuricemia; arthralgias; photosensitive dermatitis.	LFTs and uric acid at start of therapy and LFTs every 2 weeks when used with rifampin.	Dose adjustment needed for renal disease. Safety not established in pregnancy.