

## TREATMENT OF LATENT TUBERCULOSIS INFECTION

- I. **Treatment of latent tuberculosis infection (LTBI) with isoniazid greatly reduces the risk of developing tuberculosis in persons infected with TB bacilli**
  - A. Clinical studies on preventive isoniazid (INH) have demonstrated an average reduction in tuberculosis (TB) risk of 60%
    1. Those with high levels of adherence (meaning few missed daily doses) had over 90% protection
    2. 12 months of INH was found most protective (93%) compared to a 6-month course (69%)
    3. Analysis of costs/benefits and the difficulty of patients completing a 12-month course led to the current recommendations
  - B. Who needs treatment for LTBI?
    1. **Highest risk groups** (for developing TB disease once infected)
      - a. persons with **known HIV infection** (have 100 times normal risk)
      - b. **close contacts of active TB cases** *regardless of age*
      - c. **recent “converters”** (skin test has changed to positive PPD within the previous two years) *regardless of age*
      - d. persons with **certain medical conditions**, such as injecting drug use (HIV-negative), diabetes mellitus (especially if taking insulin), prolonged courses of corticosteroid medication, any other immune-suppressive treatment (such as cancer therapy)
    2. **PPD-positive persons** who are at increased risk of TB
      - a. foreign-born persons from high-prevalence countries
      - b. homeless or shelter residents
      - c. persons in congregate living situations
      - d. injection drug users
      - e. children <4 years
    3. **Close contacts of an infectious TB case**, especially children and HIV (+) contacts, should be given INH preventively, *if first PPD is negative*. Usually INH is given preventively until the second PPD at 12 weeks is negative and the active case is no longer infectious. This treatment is called window period prophylaxis
    4. Changes in CDC guidelines (April 2000)
      - a. eliminate the 35 year old cut-off for treatment of LTBI

C. Recommended regimens for treatment of LTBI

Drug	Frequency and Duration	Comments
Isoniazid	Daily or twice weekly for 9 months	DOT for twice weekly regimens
Isoniazid	Daily or twice weekly for 6 months	DOT for twice weekly regimens Not indicated for HIV infected persons
Rifampin plus pyrazinamide	Daily for 2 months	Rifabutin may be substituted in patients receiving PIs or NNRTIs*
Rifampin plus pyrazinamide	Twice weekly for 2-3 months	Rifabutin may be substituted in patients receiving PIs or NNRTIs* DOT for twice weekly regimens
Rifampin	Daily for 4 months	For persons who cannot tolerate pyrazinamide

DOT - directly observed therapy, PIs = protease inhibitors, NNRTIs = non-nucleoside reverse transcriptase inhibitors

\*Rifabutin should not be used with ritonavir, hard-gel saquinavir, or delavirdine. When used with other PIs or NNRTIs, dose adjustment of rifabutin may be necessary.

1. INH daily for 9 months is preferred, although 6 months is acceptable. May also be given bi-weekly when directly-observed by health care staff
2. Rifampin and pyrazinamide (RIF/PZA) daily for 2 months is another option for treatment of LTBI
3. Another alternative regimen with RIF alone is useful for contacts to INH-resistant TB cases

D. Pyridoxine (B6)

1. Concurrent pyridoxine therapy should be given to patients with risk factors for developing peripheral neuropathy:
  - a. diabetes mellitus
  - b. uremia
  - c. alcoholics
  - d. malnutrition
  - e. HIV infection
  - f. advanced age
2. Also given in pregnancy and to patients with a history of a seizure disorder

E. Monitoring for toxicity

NOTE: most people can tolerate INH, with monitoring

1. All adults and children on INH or an alternate regimen should be seen at least monthly *face-to-face* by a licensed health professional
2. Patients should be questioned about any symptoms suggesting liver damage or other adverse effect (nausea, vomiting, jaundice, unusual fatigue, numbness of hands or feet, skin rashes)
3. Patients must be taught about these possible reactions and advised to report any of them immediately to their health care provider
4. Only one month of INH tablets should be given at a time
5. Baseline and monthly liver function tests (LFT, AST) are recommended (CDC April 2000) for:
  - a. HIV-infected persons
  - b. pregnant women
  - c. postpartum women of color (African American and Hispanic women have a greater risk of hepatitis)
  - c. persons with excessive alcohol intake or suspected liver disease
  - d. anyone who develops symptoms of possible toxicity while taking TB medication

NOTE: these are changes from prior recommendations

6. INH-associated hepatitis (liver toxicity)

- a. is related to *age*:

<u>age</u>	<u>hepatitis</u>	
<20 years	0.0%	(0 cases/1000)
20 – 34	0.3%	(3 cases/1000)
35 – 49	1.2%	(12 cases/1000)
50 – 64	2.3%	(23 cases/1000)
>64	0.8%	(8 cases /1000)

- b. most cases of hepatitis during treatment for LTBI occur within the first 3 months

NOTE: INH raises liver function tests mildly in 10 – 20% of patients, which resolves as therapy continues