LATENT TUBERCULOSIS INFECTION (LTI)

PART II: REVISED RECOMMENDATIONS FOR TREATMENT AND FOLLOW-UP

Treatment of latent tuberculosis infection (LTBI) is an essential part of the strategy to eliminate TB in the U.S. In April 2000, the American Thoracic Society and the U.S. Centers for Disease Control and Prevention jointly released updated recommendations for treatment of LTBI. These recommendations were summarized in an earlier Bulletin. In August 2001, reports of adverse reactions caused by the rifampin plus pyrazinamide (RIF&PZA) regimen resulted in revised recommendations. This Bulletin updates and supersedes the previous Bulletin of June 27, 2000.

All persons with LTBI who are at increased risk for active TB should be considered for treatment, regardless of age (See Latent Tuberculosis Infection. Part 1: Diagnosis and Evaluation. Epidemiology Bulletin No. 10 June 6, 2000).

Treatment of LTBI in children and adolescents < 18 years: The only recommended treatment for LTBI in children and adolescents is 9 month of isoniazid (INH) either as daily self-administered therapy or twice weekly as directly observed therapy (DOT). The dose for daily INH is 10-20 mg/kg (maximum 300 mg); for biweekly therapy the dose is 20-40 mg/kg (maximum 900 mg).

Treatment of LTBI in adults: There are four treatment options for treatment of LTBI in adults (Table 1). For non-HIV infected persons with LTBI:
- 9 months of INH remains the gold standard.
- 6 months of INH may be used, although it is less effective than 9 months.
- 4 months of daily rifampin is an acceptable alternative to INH.
- 2 months of daily RIF&PZA may be used if it is unlikely that the patient will complete a longer regimen, does not have risk factors for hepatotoxicity, and can be carefully monitored.

For HIV-infected persons with LTBI:
- Consider 9 months of daily INH for compliant, motivated patients.
- 6 months of INH is acceptable, and will give substantial protection.
- 2 months RIF&PZA remains an acceptable option for HIV-infected patients; previous clinical trials did not show a high risk of severe hepatitis in this group.
- 4 months of RIF is acceptable, especially if infection with INH-resistant M. tuberculosis is suspected. (RIF is generally contraindicated in persons taking protease inhibitors or nonnucleoside transcriptase inhibitors. Rifabutin can be substituted in some cases.)

Pyridoxine supplementation: Persons with conditions where neuropathy is commonly observed, uremia, alcoholism, malnutrition and HIV infection) should receive 50 mg of pyridoxine daily when taking INH. Pregnant women, infants who are breastfeeding and persons with seizure disorders should also receive pyridoxine.

Pregnancy and lactation: The treatment of LTBI in pregnant women is controversial. Some experts prefer to delay treatment until after delivery, however women with HIV infection or who have recently acquired LTBI should begin treatment without delay because both of these factors increase risk of progression to TB disease. The preferred regimen for pregnant women is INH since this drug is not teratogenic, even in the first trimester. Pyridoxine supplementation should be given. Breastfeeding is not contraindicated when the mother is taking INH, however the infant should receive supplemental pyridoxine.

Monitoring treatment: All persons receiving LTBI treatment should be educated about adverse drug reactions and told to stop treatment immediately and contact their provider if side effects develop. Symptoms of adverse reactions include: unexplained anorexia, nausea, vomiting, dark urine, icterus, rash, paresthesias, weakness or fever lasting ≥3 days, abdominal tenderness, easy bruising or bleeding, and arthralgia.
- INH or RIF monotherapy: perform a face-to-face interview and brief physical assessment monthly during treatment. Age ≥35 years is not a criteria for routine laboratory monitoring, however monthly LFTs are indicated for persons with suspected or known liver disease, HIV infection, regular alcohol use, or women who are pregnant or <3 mo postpartum.
- RIF&PZA therapy: perform a face-to-face interview, a brief physical assessment, and routinely draw LFT laboratory studies for every patient at 0, 2, 4 and 6 weeks of treatment.