State of Alaska Epidemiology

Bulletin

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LATENT TUBERCULOSIS INFECTION (LTBI)
Part II: 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.[1] These recommendations are summarized in this *Bulletin*. Information about the diagnosis and evaluation of LTBI is found in an earlier *Bulletin*.[2]

Change in nomenclature: The terminology, treatment of LTBI, replaces potentially confusing terminology such as "preventive therapy" or "chemoprophylaxis."

> ***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 I: Diagnosis and Evaluation. Epidemiology Bulletin No. 10 June 26, 2000.).*

Treatment of LTBI in children and adolescents £18 years: The only recommended regimen for treatment of LTBI in children and adolescents is a 9-month course 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 regimens available to treat LTBI in adults. A rating system is used to rank the strength of each regimen; the designation "A" indicates a preferred regimen, "B" is an acceptable alternative, and "C" indicates an alternative that should be used only when an "A" or "B" regimen cannot be given (Table 1).

Nine months of daily isoniazid (INH) is preferred. Prospective, randomized trials in HIV-negative persons found that the maximal benefit is likely achieved by 9 months of therapy. Although not as effective as 9 months, a 6 month regimen of INH also gives substantial protection for both HIV-negative and HIV-positive adults. Both 9 and 6 month regimens may be given twice weekly if directly observed therapy (DOT) is used.

A 2 month regimen of rifampin (RIF) plus pyrazinamide (PZA) is an acceptable alternative for HIV-negative adults and a preferred regimen for HIV-positive adults. Twice-weekly treatment with RIF plus PZA for 2 to 3 months can be considered if "A" or "B" regimens cannot be used; intermittent treatment should be given using DOT.

Rifampin, daily for 4 months, is an acceptable alternative for either HIV-positive or HIV-negative persons, especially if infection with INH-resistant M. tuberculosis is suspected.

Pyridoxine supplementation: Persons with conditions where neuropathy is common (diabetes, 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.

HIV co-infection: When INH is used to treat LTBI in a person with HIV infection, 9 mo. of therapy is recommended. RIF is generally contraindicated in persons taking protease inhibitors or nonnucleoside reverse transcriptase inhibitors. For HIV-infected persons taking these medications, rifabutin can be substituted in some cases. Detailed information about treating LTBI in HIV-positive persons can be found in the following publications:

- Prevention and treatment of tuberculosis among patients infected with human immunodeficiency virus: principles of therapy and revised recommendations. *MMWR* 1998;47(no. RR-20)
- Notice to Readers: Updated guidelines for the use of rifabutin or rifampin for the treatment and prevention of tuberculosis in HIV-infected persons taking protease inhibitors or nonnucleoside reverse transcriptase inhibitors. *MMWR* 2000;49:184-9

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: Persons receiving treatment for LTBI should be educated about adverse drug reactions and told to stop treatment and contact their provider if adverse reactions develop. Symptoms of adverse reactions include: unexplained anorexia, nausea, vomiting, dark urine, icterus, rash, paresthesia, weakness or fever lasting ≥3 days, abdominal tenderness, easy bruising or bleeding, and arthralgia.

An interview and brief physical assessment should be conducted monthly during INH or RIF monotherapy. The RIF plus PZA regimen should be monitored at 2, 4 and 8 weeks. Routine laboratory tests are indicated only for those with suspected or known liver disease, HIV infection, regular alcohol use, or who are pregnant or recently pospartum (3 mo.). *Age ≥35 years is no longer a criteria for laboratory monitoring*. Withhold treatment if transaminase levels exceed 3 times the upper limit of normal in symptomatic persons or 5 times the upper limit of normal in asymptomatic persons.

Referennces:

1 Targeted tuberculin testing and treatment of latent tuberculosis infection. *Am J Respir Dis* 2000;161:S221-S247.
Available at http://www.cdc.gov/nchstp/tb/

2. Section of Epidemiology. Latent Tuberculosis Infection (LTBI). Part I: Diagnosis and Evaluation. *Epidemiology Bulletin* No. 10, June 26, 2000.
Available at http://www.epi.hss.state.ak.us/bulletins/i_tuberc.htm

Table 1: Treatment options for latent tuberculosis infection (LTBI) in adults

Drugs	Duration (months)	Interval	Rating* HIV -	Rating* HIV +	Medication dose
Isoniazid (INH)	9	Daily Twice weekly	A B	A B	*Daily*: INH 5 mg/kg (max. 300 mg) *Twice weekly*: INH 15 mg/kg (max. 900 mg) using DOT**
Isoniazid (INH)	6	Daily Twice weekly	B B	C C	As above
Rifampin (RIF) +	2	Daily	B	A	*Daily*: RIF 10 mg/kg (max. 600 mg) + PZA 15-20 mg/kg (max. 2 gm)
Pyrazinamide (PZA)	2-3	Twice weekly	C	C	*Twice weekly*: RIF 10 mg/kg (max. 600 mg) + PZA 50 mg/kg (max. 4 gm) using DOT**
Rifampin (RIF)	4	Daily	B	B	*Daily*: RIF 10 mg/kg (max. 600 mg)

*Rating scale: A=preferred; B=alternative to A; C=acceptable if A and B can't be given.
**DOT = directly observed therapy

(Contributed by Beth Funk, MD, MPH, Section of Epidemiology.)