



Tuberculosis (TB) Management Recommendations: New and Revised!

Revised Treatment Recommendations for Active TB Disease

Revised guidelines for the treatment of TB were presented in the February 15, 2003 issue of the American Journal of Respiratory and Critical Care Medicine. The statement was jointly developed and approved by the Centers for Disease Control and Prevention, the American Thoracic Society, and the Infectious Disease Society of America. These guidelines replace the previous version, published in 1994.

The new guidelines focus on the latest aspects of therapy and include four recommended regimens for treating patients with drug-susceptible TB. A course of therapy consisting of Isoniazid, Rifampin, Ethambutol and Pyrazinamide continues to be the standard initial regimen for persons with suspected active TB.

The guidelines also include sections on:

- Drug interactions
- Management of relapse, treatment failure, and drug resistance
- Organization and supervision of treatment
- Treatment of special populations, including children and adolescents, pregnant women, dialysis patients and those living with HIV
- Drug dosages (including fluoroquinolones)
- Management of side effects
- Extended therapy for patients with delayed response to treatment

Of importance, directly observed therapy (DOT) is designated as “the preferred core management strategy for all patients with tuberculosis.”

*** Revised Centers for Disease Control (CDC) Treatment Guidelines for Active TB Disease**

*** New Local Recommendations for the Management of Pediatric Latent TB Infection (LTBI) and Active TB Disease**

*** New Local Recommendations for the Management of Persons Recently Exposed to Active TB Disease**

*** Revised CDC Guidelines Against the Use of RIF/PZA in the Treatment of LTBI**

Similarly, the guidelines now clearly assign the responsibility for successful treatment of TB – which includes not only prescribing an appropriate regimen, but also ensuring adherence to the regimen through treatment completion – to the private providers and public health programs, rather than to the patient.

First published in 1971, the jointly developed guidelines are intended to advise both public health programs and health care providers in all aspects of the clinical and public health management of TB in the United States.

For a complete copy of the guidelines, please visit www.cdc.gov/mmwr/PDF/rr/rr5211.pdf

Management of Pediatric Latent TB Infection (LTBI) and Active TB Disease

The San Diego Pediatric TB Task Force recently developed guidelines for the management of TB for children living in San Diego County. These guidelines include:

- Screening recommendations for LTBI
- Treatment of LTBI
- Management of contacts of active TB cases
- Diagnosis and treatment of TB disease

To obtain a complete copy of the guidelines, please visit the TB Control website at www.sandiegotbcontrol.org, under *Guidelines and Additional Resources*.

Commonly used agents for the treatment of TB disease in pediatric patients		
	Dosage forms	Daily dose (mg/kg/day)
Isoniazid (INH)	Tablets (100 mg, 300 mg), elixir (10 mg/ml)	10-15 (max 300mg)
Rifampin (RIF)	Capsules (150 mg, 300 mg), liquid can be made from capsules	10-20 (max 600mg)
Pyrazinamide (PZA)	Tablets (500 mg)	15-30 (max 2g)
Ethambutol (EMB)*	Tablets (100 mg, 400 mg)	15-20 (max 1g)

* Ethambutol dosing is recommended to start at 15 mg/kg/day unless bactericidal activity is felt to be necessary.

Local Recommendations for Management of Persons Recently Exposed to Active TB Disease

In 2002, 246 persons in San Diego County were diagnosed with pulmonary TB. Over 1000 individuals were identified as being exposed to these patients, requiring screening and follow up evaluations. Many of these exposed individuals went to their own physicians, who worked in partnership with the TB Program to assure adequate prevention measures were taken. To further assist providers, we have developed guidelines for evaluating recently exposed patients.

Significant exposure to an individual suspected of having active, infectious pulmonary TB is usually defined as at least 4 to 8 hours of continuous or close exposure per week, although less exposure could be significant in some circumstances. Recommendations from the CDC and other authorities on the treatment of TB state that individuals who have been recently exposed should be evaluated for TB infection and disease.

The risk of tuberculosis disease can be reduced when treatment for latent TB infection (LTBI) is initiated early. The tuberculin skin test (TST) may take up to three months to become positive after a person has been infected with tuberculosis. Because of this, treatment is recommended for some exposed person with negative TSTs.

The following chart provides information for clinicians, offering screening and treatment recommendations for persons recently exposed to active, infectious TB.

If you have any questions or comments, please contact our office at (619) 692-8631 and ask for the Nurse of the Day.

Testing and Treatment Recommendations for Individuals Exposed to Active TB Disease

Patient	Risk	Initial TST	Additional Exams	If initial and repeat TST is negative	If initial or repeat TST is positive
Child (0-3 years of age)	Able to progress rapidly from primary infection to disseminated disease, including meningitis.	Place a Mantoux method tuberculin skin test (TST) and read in 48-72 hours.	Regardless of TST results, evaluate the child with clinical and CXR exams.	If active disease has been ruled out and the TST, by the Mantoux method, is 0-4mm: <ul style="list-style-type: none"> • Start Tx for presumptive LTBI. • Repeat TST three months after contact with the infectious patient has ended. • If the repeat TST remains 0-4 mm, discontinue Tx. 	If initial or repeat TST is 5 mm or greater and active disease has been ruled out: <ul style="list-style-type: none"> • Initiate or continue LTBI Tx • If using Isoniazid (INH), the recommended treatment course is 9 months.
Immunocompromised Individual <ul style="list-style-type: none"> • HIV-positive persons • Patients receiving immunosuppressive therapy (equiv. to $\geq 15\text{mg/day}$ Of prednisone for ≥ 1 month) 	Able to rapidly progress from primary infection to disseminated disease. May be unable to develop a positive TST reaction even if infected.	Place a Mantoux method TST and read in 48-72 hours.	Regardless of TST results, evaluate the patient with clinical and CXR exams.	If active disease has been ruled out, and the TST, by the Mantoux method, is 0-4mm: <ul style="list-style-type: none"> • Start Tx for presumptive LTBI. • Repeat TST three months after contact with the infectious patient has ended. • If the repeat TST remains 0-4 mm, re-evaluate continuation of therapy in consideration of the patient's level of exposure, current immune status, and final results of the suspected source case's evaluation. 	If initial or repeat TST is 5 mm or greater and active disease has been ruled out: <ul style="list-style-type: none"> • Initiate or continue LTBI Tx • If using Isoniazid (INH), the recommended treatment course is 9 months.
All Other Individuals	Risk of progressing from TB infection to TB disease is high within the first two years after becoming infected.	Place a Mantoux method TST and read in 48-72 hours.	Regardless of TST results, evaluate the patient for any signs or symptoms of TB disease.	If the patient has no signs or symptoms of active TB disease and the TST, by the Mantoux method, is 0-4 mm: <ul style="list-style-type: none"> • Tx for presumptive LTBI <i>need not</i> be started. • Repeat TST three months after contact with the infectious patient has ended. • If the repeat TST remains 0-4 mm, no further action is needed. 	If initial or repeat TST is 5 mm or greater and active disease has been ruled out: <ul style="list-style-type: none"> • Evaluate person for LTBI Tx • If using Isoniazid (INH), the recommended treatment course is 9 months. • Must have a CXR prior to LTBI Tx.
A contact with a documented positive TST prior to current exposure	Reinfection possible, but minimal risk in immunocompetent contacts.	Ensure past TST was intradermal (Mantoux) and $\geq 10\text{mm}$ induration is documented.	Obtain CXR to rule out current disease.	Note: Patient may be a candidate for treatment of LTBI based on pre-existing TB infection, not related to the recent exposure. Patient may be a candidate for treatment based on other co-morbid conditions or when transmission risk is particularly high.	

**Revised CDC Recommendations Against the Use of Rifampin/Pyrazinamide (RZ)
for the Treatment of Latent TB Infection (LTBI)**

In the 2000 CDC statement, “Targeted Tuberculin Testing and Treatment of Latent Tuberculosis Infection,” the 2-month Rifampin-Pyrazinamide (RZ) regimen was introduced as a short course alternative to 9 months of Isoniazid (INH). However, due to reports of severe liver injury and deaths, the CDC now recommends **against the use of RZ for treatment of LTBI.**

Based on reports of severe adverse reactions following recommendation of the regimen, the CDC conducted a retrospective analysis for the period Jan 2000-June 2002. TB Programs in all 50 states and 12 big cities were contacted and all responded. A total of 7,737 patients were reported to have started on the RZ regimen for LTBI. There were 204 patients (26.4 per 1000 starts) who discontinued RZ due to aspartate aminotransferase (AST) levels greater than five times the upper limit of normal, and 146 (18.9 per 1000 starts) who discontinued due to symptoms of hepatitis. Thirty cases were hospitalized secondary to severe liver injury, of whom 7 (23%) died.

The rates of hospitalization and death during the survey period were 3.0 and 0.9 per 1000 RZ starts, respectively. Studies since 1991 involving over one million persons treated with INH for LTBI have reported hospitalization rates of 0.1-0.2 (median 0.15) and mortality rates of 0-0.3 (median 0.04) per 1000 starts, far below the rates seen in the brief experience with the RZ regimen.

Please note that the recommendation does not extend to the appropriate use of Rifampin and Pyrazinamide as part of a multi-drug regimen for the treatment of active TB disease. A four-drug regimen of INH, Rifampin, Ethambutol, and Pyrazinamide continues to be the standard initial regimen for persons with suspected or confirmed active TB disease.

For the full text of the CDC Recommendations against the use of RZ for treatment of LTBI, please see MMWR 52 (31); 735-739, Aug 8, 2003 or visit www.cdc.gov/mmwr/preview/mmwrhtml/mm5231a4.htm

Treatment Regimens for Latent TB Infection (LTBI) in Adults			
Drugs	Duration (months)	Interval	Dosage
Isoniazid (INH)	9 (preferred regimen)	Daily	5mg/kg: Max 300mg
		Twice weekly (if fully observed)	15mg/kg: Max 900mg
INH	6 (if 9-month regimen cannot be offered)	Daily	5mg/kg: Max 300mg
		Twice weekly (if fully observed)	15mg/kg: Max 900mg
RIF	4-6 (if INH cannot be used)	Daily or twice weekly	10mg/kg: Max 600mg

<u>San Diego TB Control</u>	
TB Reporting:	619-692-8610
General TB Education:	619-692-8627
Clinic Appointment:	619-692-5565
Medical Questions:	619-692-8631, and ask for the Nurse of the Day
TB Website:	www.sandiegotbcontrol.org