State of Alaska Epidemiology **Bulletin**

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Tuberculosis Treatment Update: Did the Patient Really Swallow All Those Pills?

Over the past decade, recommendations for the treatment of tuberculosis (TB) have undergone several important modifications. These changes have been driven by both a significant rise in incidence of TB in the U.S. and by a dramatic increase in multi-drug resistant *M. tuberculosis* (MDR-TB). Previous *Bulletins* from the Section of Epidemiology have reported Alaska's own unique problems with tuberculosis. [1, 2] This *Bulletin* addresses updated recommendations for TB treatment. The goal for Alaska is to reduce the occurrence of isoniazid (INH) resistance and to improve TB treatment completion rates.

Initial Treatment of Active Tuberculosis:
The treatment of tuberculosis requires at least two active agents to prevent the development of drug resistance. In the 1980's, the three-drug regimen of INH, rifampin and pyrazinamide allowed a shorter six month treatment course and more rapid conversion of the sputum to culture negative status. Two years ago, the Centers for Disease Control and Prevention (CDC) recommended the use of four drug therapy in areas of the country where INH resistance exceeded 4%.[3] Over the past 5 years, 5% of Alaska's *M. tuberculosis* isolates were resistant to INH. **A recent CDC review of Alaska's TB program recommended that "initial four-drug regimens be used routinely for all suspected and confirmed patients in the state."**

The four-drug regimen will benefit Alaska by 1) protecting the effectiveness of INH and rifampin, the two most important anti-tuberculosis agents available and 2) more rapidly clearing culture positive sputums.[3] In addition, the four-drug regimen is more likely to prevent relapse in patients failing to complete their treatment than patients who receive only three drugs. **The Section of Epidemiology recommends the use of INH, rifampin, pyrazinamide and ethambutol for initial treatment of all persons with suspected or active tuberculosis (Table I).**

Directly Observed Therapy (DOT):
The combination of the long course of treatment, the number of pills (7 to 12 pills daily), and early improvement of symptoms makes noncompliance a major problem. Interrupted therapy and failure to complete the treatment course are ingredients for relapse and the appearance of MDR-TB. DOT is a valuable tool to assure that patients take their TB drugs as prescribed. A designated person observes the patient swallow his or her TB medications at each dose for the duration of therapy. Most often DOT is witnessed by a health care professional or a DOT aide. The DOT observer may also be a teacher, social service provider, safety officer, or employer. The patient may come to a clinic or doctor's office or the DOT provider may meet the patient at work, home, school or some other mutually agreed upon location. In some cases, incentives such as bus tokens, temporary housing, meal or gas vouchers may be useful to augment DOT's success; this is especially true later in the treatment course. The Sections of Epidemiology and Nursing have modest resources for incentives to encourage patients to remain compliant.

Health care professionals have consistently been unsuccessful in predicting their patients' compliance with medical treatment regimens. "Age, sex, religion, education, race...socioeconomic status... psychiatric disease, alcoholism, drug addiction, substance abuse and homelessness do not predict noncompliance."[4] Several independent investigators have documented both a decrease in drug resistance and a decrease in relapse of TB as a result of implementing DOT. **The Section of Epidemiology recommends DOT for all patients receiving treatment for active tuberculosis.**

Summary:
The Section of Epidemiology recommends DOT combined with four-drug therapy as the standard treatment for confirmed and suspected cases of tuberculosis. After an initial 2 weeks of daily treatment, most patients can successfully be continued on the twice weekly regimen in Table I. Therapy is modified as soon as drug susceptibility results are available in culture confirmed cases. In culture negative cases, an evaluation should be made regarding the possibility of drug resistant TB before the remainder of the treatment course is planned.

1. State of Alaska. Tuberculosis Threatens Rural Alaskans. *Bulletin* 1994;No. 25:Oct 25.

2. State of Alaska. Village Tuberculosis Outbreaks - Update. *Bulletin* 1995;No 8:Mar 9.

3. CDC. Initial Therapy for Tuberculosis in the Era of Multidrug Resistance: recommendations of the Advisory Council for the Elimination of Tuberculosis. *MMWR* 1993;42 (RR-7):1-8.

4. Weis SE, Slocum PC, et. al. The effect of directly observed therapy on the rates of drug resistance and relapse in tuberculosis. *N Engl J Med* 1993; 330: 1179-84.)

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Table I. Dosage Recommendation for the Initial Treatment of Tuberculosis in Children and Adults

	Daily Dose		Twice-Wk Dose		Thrice-Wk Dose	
Drugs	**Children**	**Adults**	**Children**	**Adults**	**Children**	**Adults**
Isoniazid (mg/kg)	10-20 Max 300 mg	5 Max 300 mg	20-40 Max 900 mg	15 max Max 900 mg	20-40 Max 900 mg	15 max Max 900 mg
Rifampin (mg/kg)	10-20 Max 600 mg	10 Max 600 mg	10-20 Max 600 mg	10 Max 600 mg	10-20 Max 600 mg	10 Max 600 mg
Pyrazinamide (mg/kg)	15-30 Max 2g	15-30 Max 2g	50-70 Max 4g	50-70 Max 4g	50-70 Max 3g	50-70 Max 3g
Ethambutol + (mg/kg)	15-25	15-25	50	50	25-30	25-30
Streptomycin (mg/kg)	20-40 Max 1g	15 Max 1g	25-30 Max 1.5g	25-30 Max 1.5g	25-30 Max 1.5g	25-30 Max 1.5g

Ethambutol is usually not recommended for children whose visual acuity cannot be monitored (< 8 yr of age). However, it should be considered with organisms that are resistant to other drugs but susceptible to ethambutol.