Treatment of Tuberculosis Disease

CONTENTS

Introduction

Purpose

The overall goals for treatment of tuberculosis (TB) are to cure the patient and to minimize the transmission of *Mycobacterium tuberculosis* to others. In the 2005 "Controlling Tuberculosis in the United States: Recommendations from the American Thoracic Society, Centers for Disease Control and Prevention, and the Infectious Diseases Society of America," one of the recommended strategies to achieve the goal of reduction of TB morbidity and mortality is the early and accurate detection, diagnosis, and reporting of TB cases, leading to initiation and completion of treatment. Successful treatment of TB has benefits both for the individual patient and for the community in which the patient resides.

Use this section to understand and follow national, California, and San Joaquin County guidelines to do the following:

- Follow basic treatment principles for TB disease.
- Select appropriate treatment regimens, dosages, and duration.
- Monitor patients for side effects and adverse reactions.
- Assess patients' response to treatment.
- Determine completion of therapy.
- Determine the need for post-treatment evaluation.
- Provide treatment in special situations, such as when a patient has drug-resistant TB or TB–human immunodeficiency virus (HIV) coinfection.
- Hospitalize and coordinate hospital discharges of patients with infectious TB.

Policy

Patients with TB disease in San Joaquin County or who move to San Joaquin County with reported TB disease should receive and complete treatment in accordance with the California Department of Public Health/California TB Controllers Association Joint Guidelines: Guidelines for the Treatment of Active Tuberculosis Disease, found at http://www.ctca.org/fileLibrary/file_65.pdf .

Program Standards

1. All confirmed, probable, and suspect active TB patients are offered an HIV test.
2. All patients with confirmed TB disease are started on appropriate therapy within three (3) working days.
3. All patients with suspected TB disease are started on appropriate therapy within five (5) working days.
4. All confirmed, probable, and suspect active TB patients have sputum collected at eight (8) weeks to document culture conversion.

Forms

Confidential Morbidity Report (CMR) form for TB is available on the San Joaquin County Public Health Services website at http://www.sjcphs.org/Disease/documents/cdph110b.pdf?2.

Reporting requirements: **State law requires all confirmed, probable, and suspect cases of TB are to be reported to the SJCPHS within one (1) working day.**

Fax all pertinent medical information to 209-468-8222. Pertinent information includes:

1. TST or IGRA test results
2. History and Physical, Consult, and MD visit notes
3. Radiology reports
4. Bacteriology/microbiology results including any pcr-based test results

Basic Treatment Principles

Follow the basic treatment principles for tuberculosis (TB) disease, as outlined below in Table 1.

Table 1: **BASIC TREATMENT PRINCIPLES FOR TUBERCULOSIS DISEASE**

Phase	Principles
At Start of Treatment	**Patient-centered care and directly observed therapy (DOT).** An adherence plan should tailor treatment and supervision to each patient by considering his or her clinical and social circumstances (patient-centered care), as well as emphasizing DOT.
	Cultural competence. It is imperative to become culturally competent and guide other healthcare providers toward culturally competent healthcare. A culturally competent system acknowledges cultural differences regarding healthcare and incorporates them into all levels of the healthcare delivery system, from policy to provider to patient.
	Human immunodeficiency virus (HIV) testing. HIV testing should be offered to all patients with TB disease.
	Medical supervision. Patients with confirmed or suspected TB disease must be under the medical supervision of a provider who is knowledgeable about TB treatment including medication regimens, side effects, and monitoring.
	Prompt start. Start patients with confirmed TB disease on appropriate therapy within 3 working days. Start patients with suspected TB disease on appropriate treatment within 5 days. It is not necessary to wait for laboratory confirmation.
Regimen During Treatment	**Multiple drugs.** Treatment regimens must contain multiple drugs to which the organism is susceptible. The administration of a single drug or the addition of a single drug to a failing regimen can lead to the development of resistance.
	Single doses. TB medications should be administered together as a single dose rather than in divided doses. A single dose leads to higher, and potentially more effective, peak serum concentrations. Although ingesting the medications with food will delay or moderately decrease the absorption of the medications, the effects are of little clinical significance.
	Pyridoxine to prevent neuropathy. Pyridoxine (Vitamin B-6, 25 mg) is recommended for some individuals receiving isoniazid (INH) as part of their treatment regimen to prevent peripheral neuropathy. It should be used in persons at risk for neuropathy (women who are pregnant or breastfeeding or persons with nutritional deficiency, diabetes, HIV infection, renal failure, or alcoholism).

Phase	Principles
Persistent Positive Cultures	**Evaluation when positive cultures persist.** Monitor for culture conversion at 8 weeks and evaluate patients with persistently positive cultures after 3 months of therapy to identify the cause. Treatment failure is defined as continued or recurrent positive cultures after 4 months of treatment.
At Completion of Treatment	**Completion in terms of the number of doses.** The criteria for treatment completion are based upon the total number of doses taken within a specific time period.

Treatment Regimens and Dosages

Use this information to do the following:

- Identify the appropriate regimen (Table 3).
- Determine the appropriate dosage for each drug (Table 4).
- Determine the duration of treatment/number of doses. While duration of treatment is commonly recommended using time such as 6 months or 9 months, this must be translated into number of DOT doses to determine adequate treatment.

The information in this topic was provided using guidelines for treating tuberculosis (TB) that have been developed by the American Thoracic Society (ATS), Centers for Disease Control and Prevention (CDC), and Infectious Diseases Society of America (IDSA) along with the joint California Department of Public Health (CDPH) and California TB Controllers Association (CTCA) guidelines.

See the “Treatment in Special Situations” topic in this section for information on treatment when there is drug-resistant TB, human immunodeficiency virus (HIV) infection, liver disease, or renal disease; when the patient is taking tumor necrosis factor-alpha (TNF-α) antagonists; where there is culture-negative TB or extrapulmonary TB; when the patient is pregnant or breastfeeding; or when the patient is considered to be of pediatric age (≤ 14 years of age).

Table 2: **ABBREVIATIONS FOR FIRST-LINE DRUGS**

▪ Ethambutol: EMB ▪ Isoniazid: INH ▪ Pyrazinamide: PZA	▪ Rifabutin: RFB ▪ Rifampin: RIF

Regimens

Identify the appropriate regimen for the patient. There are two basic regimens recommended for treating adults with TB caused by organisms that are known or presumed to be susceptible to isoniazid (INH), rifampin (RIF), pyrazinamide (PZA), and ethambutol (EMB).

Both regimens has an initial phase of two months, followed by a choice of options for a continuation phase of either four or seven months. In Table 3: **Drug Regimens for Culture-Positive Pulmonary Tuberculosis Caused by Drug-Susceptible Organisms**, the initial phase is denoted by a number (1 or 2), and the options for the continuation phase are denoted by the respective number and a letter designation (a or b).

Table 3: **DRUG REGIMENS FOR CULTURE-POSITIVE PULMONARY TUBERCULOSIS CAUSED BY DRUG-SUSCEPTIBLE ORGANISMS**

Initial Phase			Continuation Phase			Range of total doses (minimal duration)	Rating* (evidence)†	
Regimen	Drugs	Interval and doses‡ (minimal duration)	Regimen	Drugs	Interval and doses‡ § (minimal duration)		HIV–	HIV+
1	INH RIF PZA EMB	Seven days/week for 56 doses (8 wk) or 5 d/wk for 40 doses (8 wk)¶	1a	INH RIF	Seven days/week for 126 doses (18 wk) or 5 d/wk for 90 doses (18 wk)¶	182–130 (26 wk)	A (I)	A (II)
			1b	INH RIF	Twice weekly for 36 doses (18 wk)	92–76 (26 wk)	A (I)	A (II)#
2	INH RIF PZA EMB	Seven days/week for 14 doses (2 wk), then twice weekly for 12 doses (6 wk) or 5 d/wk for 10 doses (2 wk),¶ then twice weekly for 12 doses (6 wk)	2a	INH RIF	Twice weekly for 36 doses (18 wk)	62–58 (26 wk)	A (II)	B (II)#

Definitions of abbreviations: DOT = directly observed therapy; EMB = ethambutol; INH = isoniazid; HIV = human immunodeficiency virus; PZA = pyrazinamide; RIF = rifampin.

* Definitions of evidence ratings: A = preferred; B = acceptable alternative; C = offer when A and B cannot be given; D = should generally not be offered; E = should never be given.

† Definition of evidence ratings: I = randomized clinical trial; II = data from clinical trials that were not randomized or were conducted in other populations; III = expert opinion.

‡ When DOT is used, drugs may be given 5 days/week and the necessary number of doses adjusted accordingly. Although there are no studies that compare 5 with 7 daily doses, extensive experience indicates this would be an effective practice.

§ Patients with cavitation on initial chest radiograph and positive cultures at completion of 2 months of therapy should receive a 7-month (31 weeks; either 217 doses [daily] or 62 doses [twice weekly]) continuation phase.

¶ Five-day-a-week administration is always given by DOT. Rating for 5 day/week regimens is rated AIII.

Not recommended for HIV-infected patients with CD4+ cell counts <100 cells/microliter.

Adapted from ATS, CDC, IDSA. Treatment of tuberculosis. *MMWR* 2003;52(No. RR-11):

Treatment of TB

For consultation regarding the treatment of TB, contact the TB control program at SJCPHS at 209-468-3828.

Dosages

Once the appropriate regimen has been identified, refer to Table 4 for instructions on dosages for each drug. **First-line antituberculosis medications should be administered together; doses should not be split.** Directly observed therapy (DOT) is the management strategy for all regimens.

Table 4: **DOSES*OF FIRST-LINE ANTITUBERCULOSIS DRUGS FOR ADULTS AND CHILDREN†**

Drug	Preparation	Adults/children	Doses			
			Daily	1x/wk	2x/wk	3x/wk
INH	Tablets (50 mg, 100 mg, 300 mg); elixir (50 mg/5 ml); aqueous solution (100 mg/ml) for intramuscular injection¶	Adults (max.)	5 mg/kg (300 mg)	15 mg/kg (900 mg)	15 mg/kg (900 mg)	15 mg/kg (900 mg)
		Children (max.)	10–15 mg/kg (300 mg)	—	20–30 mg/kg (900 mg)	—
RIF	Capsule (150 mg, 300 mg); powder may be suspended for oral administration; aqueous solution for intravenous injection	Adults‡ (max.)	10 mg/kg (600 mg)	—	10 mg/kg (600 mg)	10 mg/kg (600 mg)
		Children (max.)	10–20 mg/kg (600 mg)	—	10–20 mg/kg (600 mg)	—
RFB	Capsule (150 mg)	Adults‡ (max.)	5 mg/kg (300 mg)	—	5 mg/kg (300 mg)	5 mg/kg (300 mg)
		Children	Appropriate dosing for children is unknown	Appropriate dosing for children is unknown	Appropriate dosing for children is unknown	Appropriate dosing for children is unknown
PZA	Tablet (500 mg, scored)	Adults	20-25 mg/kg (2.0 g)	—	40-50 mg/kg (4.0 g)	35-40 mg/kg (3.0 g)
		Children (max.)	15–30 mg/kg (2.0 g)	—	50 mg/kg (2.0 g)	—
EMB	Tablet (100 mg, 400 mg)	Adults	15–20 mg/kg daily (1.6 g)	—	35-45 mg/kg (4.0 g)	25-30 mg/kg (2.4 g)
		Children§ (max.)	15–20 mg/kg daily (1.0 g)	—	50 mg/kg (2.5 g)	—

Definitions of abbreviations: EMB = ethambutol; FDA = Food and Drug Administration; INH = isoniazid; PZA = pyrazinamide; RFB = rifabutin; RIF = rifampin.

* Dose per weight is based on **ideal body weight**. Children weighing more than 40 kg should be dosed as adults.

† For the purposes of this document, adult dosing begins at the age of 15 years of age or 40 kg weight.

¶ INH is used, but not FDA-approved, for intravenous administration. For intravenous use of INH, please consult with the TB control program at SJCPHS at 209-468-3828.

‡ Dose may need to be adjusted when there is concomitant use of protease inhibitors or nonnucleoside reverse transcriptase inhibitors.

§ The drug can likely be used safely in older children but should be used with caution in children less than 5 years of age, in whom visual acuity cannot be monitored. In younger children, EMB at the dose of 15 mg/kg per day can be used if there is suspected or proven resistance to INH or RIF.

Source: ATS, CDC, IDSA. Treatment of tuberculosis. *MMWR* 2003;52(No. RR-11):4.

Duration of Treatment

The recommended regimens for treating patients with TB caused by drug-susceptible organisms have a duration of six to nine months. Each regimen has an initial phase of two months, followed by a continuation phase of either four or seven months.

Pulmonary TB

The standard duration of treatment for pulmonary TB should be six months. Treatment should be extended to 9 months if:

1. PZA is not taken for the first 8 weeks;

2. There is extensive disease on CXR with cavitation; or

3. The patient is still culture positive after 8 weeks of adequate treatment.

In HIV-negative, culture-negative patients, treatment for four months may be adequate if there is clinical or radiographic improvement and no other etiology identified. However, HIV-infected patients with culture-negative pulmonary TB should be treated for a minimum of six months.

Extrapulmonary TB

The standard duration of treatment for extrapulmonary TB should also be six months. Note that there are two exceptions to the standard six-month duration of treatment.

1. For tuberculous meningitis, the optimal length of therapy has not been established, although some experts recommend nine to twelve months.

2. Treatment for bone or joint TB may need to extend to nine months.

Side Effects and Adverse Reactions

The patient should be monitored by a clinician at least monthly for signs and symptoms of adverse reactions until treatment is completed. If a patient is symptomatic, monitoring may need to occur more frequently. Chemistries and complete blood count (CBC), aspartate aminotransferase (AST)/alanine aminotransferase (ALT), or other tests based on specific drugs should be done as indicated. See Table 6**: Monitoring and Interventions for Side Effects and Adverse Reactions** in this section.

As is true with all medications, combination chemotherapy for tuberculosis is associated with a predictable incidence of adverse effects, some mild, some serious.

Adverse effects are fairly common and often manageable. Although it is important to be attuned to the potential for adverse effects, it is at least equally important that first-line drugs not be stopped without adequate justification. However, adverse reactions can be severe, and thus, it is important to recognize adverse reactions that indicate when a drug should not be used. Mild adverse effects can generally be managed with symptomatic therapy; with more severe effects, the offending drug or drugs must be discontinued. Proper management of more serious adverse reactions often requires expert consultation.

Monitor patients for side effects and adverse reactions following the basic monitoring steps listed below.

Basic Monitoring Steps

1. All healthcare workers providing treatment for TB disease should be familiar with the American Thoracic Society (ATS)/Centers for Disease Control and Prevention (CDC) guidelines.
   - **a.** All jurisdictions should follow the national monitoring guidelines identified in the current guidelines for treatment of TB, “Treatment of Tuberculosis” (*MMWR* 2003;52[No. RR-11]) at http://www.cdc.gov/mmwr/PDF/rr/rr5211.pdf .
   - **b.** It is also important to check for guideline updates posted on the CDC’s Division of Tuberculosis Elimination home page at http://www.cdc.gov/tb/ and the list of guidelines by date at http://www.cdc.gov/tb/pubs/mmwr/Maj_guide/List_date.htm.
2. While on treatment, all patients should be evaluated in person at baseline (before starting treatment) and then at least monthly for side effects and adverse reactions.

3. The common side effects of and adverse reactions to drugs used to treat for TB disease are listed below in Table 5: **Reporting Reactions to Antituberculosis Medications**. Educate patients to stop the medicine and promptly report any of the symptoms or signs listed in Table 5 or any unexplained illness to the prescribing provider immediately.
4. If you suspect that an antituberculosis drug may be causing a particular side effect or adverse reaction:
   a. Refer to Table 6: **Monitoring and Interventions for Side Effects and Adverse Reactions**.
   b. Consult with the SJCPHS TB program by calling 209-468-3828.
5. If you suspect that an antituberculosis drug may be interacting with other medications that the patient is taking, ensure that the provider is notified and also notify SJCPHS TB Program. More information can be found on pages 45–47 in the "Treatment of Tuberculosis" (*MMWR* 2003;52[No. RR-11]) at http://www.cdc.gov/mmwr/PDF/rr/rr5211.pdf .
6. Document the following patient information and fax to PHS TB Control Program (209) 468-8222:
   a. Review of symptoms, test results, side effects, and adverse reactions
   b. Education given
   c. Refill provided
   d. Description of any problems encountered and action taken for that visit
   e. Next appointment

Reporting Reactions

The patient should be instructed to report to the provider the side effects and adverse reactions listed below in Table 5.

Table 5: **REPORTING REACTIONS TO ANTITUBERCULOSIS MEDICATIONS**

Potentially Serious Adverse Reactions*	Less Severe Signs and Symptoms*
These signs and symptoms suggest side effects, including hepatotoxicity and require immediate medical attention: ▪ Jaundice ▪ Dark urine ▪ Vomiting ▪ Abdominal pain ▪ Fever ▪ Ototoxicity ▪ Visual changes ▪ Vestibular changes ▪ Marked clinical rash Instruct the patient to stop TB medications until evaluated by the provider.	Report the following signs and symptoms within 24 hours: ▪ Anorexia ▪ Nausea ▪ Malaise ▪ Peripheral neuropathy: tingling or burning sensation in hands or feet ▪ Rashes
* These lists are not all-inclusive. Second-line drugs are not included. For a complete list, refer to the current guidelines for treatment of TB, "Treatment of Tuberculosis" (*MMWR* 2003;52[No. RR-11]), at http://www.cdc.gov/mmwr/PDF/rr/rr5211.pdf .	

Source: California Department of Public Health (CDPH)/California Tuberculosis Controllers Association (CTCA). TB case management—core components. *CDPH/CTCA Joint Guidelines* [CTCA Web site]. Nov 2011. Available at: http://www.ctca.org/fileLibrary/file_238.pdf. Accessed July 2, 2015.

Monitoring for Side Effects and Adverse Reactions by Antituberculosis Drug

Refer to Table 6**: Monitoring and Interventions for Side Effects and Adverse Reactions** to do the following:

- Identify the side effects and adverse reactions associated with particular antituberculosis drugs
- Determine how to monitor for side effects and adverse reactions

Table 6: **MONITORING AND INTERVENTIONS FOR SIDE EFFECTS AND ADVERSE REACTIONS**

Anti-tuberculosis Drug	Side Effects/ Adverse Reactions	Monitoring	Comments
Isoniazid (INH)	▪ Rash ▪ Hepatic enzyme elevation ▪ Hepatitis ▪ Peripheral neuropathy ▪ Mild central nervous system effects	Clinical monitoring monthly Liver function tests (aspartate aminotransferase [AST], alanine aminotransferase [ALT], and serum bilirubin) at baseline Repeat measurements if ▪ Baseline results are abnormal ▪ Patient is pregnant, in the immediate postpartum period, or at high risk for adverse reactions ▪ Patient has symptoms of adverse reactions ▪ Patient has underlying liver disease including viral hepatitis ▪ Patient has a history of alcoholism	Hepatitis risk increases with age and alcohol consumption. Pyridoxine (vitamin B6, 10–25 mg/d) might prevent peripheral neuropathy and central nervous system effects. Serum concentrations of phenytoin, disulfiram (Antabuse), and carbamazepine may be increased in persons taking INH. Measure serum concentrations of phenytoin and carbamazepine in patients receiving INH (with or without rifampin), and adjust the dose if necessary.

Anti-tuberculosis Drug	Side Effects/ Adverse Reactions	Monitoring	Comments
Rifampin (RIF)	▪ Rash ▪ Gastrointestinal upset ▪ Hepatitis ▪ Fever ▪ Bleeding problems ▪ Thrombocytopenia ▪ Renal failure ▪ Flu-like symptoms ▪ Orange-colored body fluids (secretions, urine, tears)	Complete blood count, platelets, and liver function tests (aspartate aminotransferase [AST], alanine aminotransferase [ALT], and serum bilirubin) at baseline Repeat measurements if ▪ Baseline results are abnormal ▪ Patient has symptoms of adverse reactions ▪ Patient is pregnant, in the immediate postpartum period, or at high risk for adverse reactions ▪ Patient has underlying liver disease including viral hepatitis ▪ Patient has a history of alcoholism	There are a number of drug interactions with potentially serious consequences. Significant interactions with methadone, birth control hormones, and many other drugs. Contraindicated or should be used with caution when administered with protease inhibitors (PIs) and nonnucleoside reverse transcriptase inhibitors (NNRTIs). Reduces levels of many drugs (e.g., PIs, NNRTIs, methadone, dapsone, ketoconazole, coumadin derivatives, hormonal contraceptive, digitalis, sulfonylureas, diazepam, ß-blockers, anticonvulsants, and theophylline). For more information, refer to “Section 7: Drug Interactions” on page 45 in “Treatment of Tuberculosis” at http://www.cdc.gov/mmwr/PDF/rr/rr5211.pdf . Because information regarding rifamycin drug interactions is evolving rapidly, consult the CDC’s Division of Tuberculosis “News and Updates” Web page at http://www.cdc.gov/tb/ to obtain the most up-to-date information. Colors body fluids orange. May permanently discolor soft contact lenses.

Anti-tuberculosis Drug	Side Effects/ Adverse Reactions	Monitoring	Comments
Rifabutin (RFB)	▪ Rash ▪ Hepatitis ▪ Fever ▪ Thrombocytopenia ▪ Orange-colored body fluids (secretions, urine, tears) With increased levels of RFB: ▪ Severe arthralgias ▪ Uveitis ▪ Leukopenia	Complete blood count, platelets, and liver function tests (aspartate aminotransferase [AST], alanine aminotransferase [ALT], and serum bilirubin) at baseline Repeat measurements if ▪ Baseline results are abnormal ▪ Patient has symptoms of adverse reactions ▪ Patient is pregnant, in the immediate postpartum period, or at high risk for adverse reactions Use adjusted daily dose of RFB and monitor for decreased antiretroviral activity and for RFB toxicity if RFB taken concurrently with protease inhibitors (PIs) or nonnucleoside reverse transcriptase inhibitors (NNRTIs)	Although drug interactions are less problematic with RFB, they still occur and close monitoring is required. Contraindicated for HIV-infected patients taking hard-gel saquinavir or delavirdine; caution is also advised if RFB is administered with soft-gel saquinavir. Similar to rifampin but less potent of an inducer, rifabutin reduces levels of many drugs (e.g., PIs, NNRTIs, methadone, dapsone, ketoconazole, coumadin derivatives, hormonal contraceptive, digitalis, sulfonylureas, diazepam, ß-blockers, anticonvulsants, and theophylline). When used with efavirenz, the daily dose of RFB should be increased from 300 mg to 450 mg or 600 mg. May permanently discolor soft contact lenses.

Anti-tuberculosis Drug	Side Effects/ Adverse Reactions	Monitoring	Comments
Pyrazinamide (PZA)	▪ Gastrointestinal upset ▪ Hepatitis ▪ Rash ▪ Photosensitive dermatitis ▪ Hyperuricemia ▪ Joint aches ▪ Gout (rare)	Clinical monitoring at weeks 2, 4, and 8 Baseline measurements of uric acid Liver function tests (aspartate aminotransferase [AST], alanine aminotransferase [ALT], and serum bilirubin) at baseline Repeat measurements if ▪ Baseline results are abnormal ▪ Patient has symptoms of adverse reactions ▪ Patient is pregnant, in the immediate postpartum period, or at high risk for adverse reactions ▪ Patient has underlying liver disease including viral hepatitis ▪ Patient has a history of alcoholism	Treat hyperuricemia only if patient has symptoms. Might make glucose control more difficult in persons with diabetes. Serum uric acid measurements are not recommended as a routine but may serve as a surrogate marker for compliance.

Anti-tuberculosis Drug	Side Effects/ Adverse Reactions	Monitoring	Comments
Ethambutol (EMB)	▪ Optic neuritis (pre-existing optic neuritis is a contraindication) ▪ Rash	Baseline tests of visual acuity (Snellen chart) and color discrimination (Ishihara tests) At each monthly visit, patients should be questioned regarding possible visual disturbances, including blurred vision or scotomata Monthly testing of visual acuity and color discrimination is recommended for ▪ Patients taking doses >20 mg/kg ▪ Patients receiving EMB for >2 months ▪ Patients with renal insufficiency	Optic neuritis may be unilateral; check each eye separately. Patients should be instructed to contact their physician or public health clinic immediately if they experience a change in vision. EMB should be discontinued immediately and permanently if there are any signs of visual toxicity.

Definitions of abbreviations: ALT = alanine aminotransferase; AST = aspartate aminotransferase; EMB = ethambutol; HIV = human immunodeficiency virus; INH = isoniazid; NNRTIs = nonnucleoside reverse transcriptase inhibitors; PZA = pyrazinamide; PIs = protease inhibitors; RFB = rifabutin; RIF = rifampin; RPT = rifapentine.

Sources: CDC. Targeted tuberculin testing and treatment of latent tuberculosis infection. *MMWR* 2000;49 (No. RR-6):26–29, 38–39; ATS, CDC, IDSA. Treatment of tuberculosis. *MMWR* 2003;52(No. RR-11):19–25; CDC. Update: Adverse event data and revised American Thoracic Society/CDC recommendations against the use of rifampin and pyrazinamide for treatment of latent tuberculosis infection—United States. *MMWR* 2003;52(No. 31):735–736; CDC.

Response to Treatment

For consultation regarding a patient's response to treatment, contact the TB control program at SJCPHS at 209-468-3828.

For patients whose sputum cultures are positive before treatment, the best way to measure the effectiveness of therapy is to obtain specimens for culture every two weeks until the cultures convert to negative. Patients with multidrug-resistant tuberculosis (MDR-TB) should have cultures performed monthly for the entire course of treatment.

In some cases, a patient may not be able to produce a sputum specimen after two months of treatment. If culture conversion is not able to be documented at two months, duration of treatment will be determined by the TB Controller.

Radiographic evaluations during treatment are of less importance than sputum evaluation. However, a chest radiograph at two months of treatment is important to assess response to treatment and another chest radiograph at completion of treatment provides a baseline for comparison with future films.

Patients whose cultures have not become negative or whose symptoms do not resolve despite two months of therapy should be evaluated for potential drug-resistant disease, malabsorption, or failure to adhere to the regimen.

If drug susceptibility results show resistance to any of the first-line drugs or if the patient remains symptomatic or smear- or culture-positive after two months, contact the TB control program at SJCPHS at 209-468-3828 immediately.

In patients with negative sputum cultures before treatment, the major indicators of response to therapy are the chest radiograph and clinical evaluation. The intervals at which chest radiography should be repeated depend on the clinical circumstances and the differential diagnoses that are being considered but usually should be no more than every two months. If the radiograph does not improve after the patient has received two months of treatment, the abnormality may be the result of either previous (not current) TB or another process.

Completion of Therapy

The San Joaquin County TB controller determines the appropriate length of treatment for all cases of active tuberculosis. A full course of therapy (completion of treatment) is determined more accurately if the total number of doses ingested is taken into account, as well as the duration of therapy. If there are no interruptions in drug administration, six months is usually the minimum duration of treatment and accurately indicates the amount of time in which drugs are given. However, in human immunodeficiency virus (HIV)-negative, culture-negative patients, treatment for four months may be adequate if there is clinical or radiographic improvement and no other etiology identified.

For consultation regarding the treatment of tuberculosis (TB) in a patient with negative cultures, contact the TB control program at SJCPHS at 209-468-3828.

In some cases, either because of drug toxicity or nonadherence to the treatment regimen, the specified number of doses cannot be administered within the targeted period. In such cases, the goal is to deliver the specified number of doses within a recommended maximum time. For example, for a six-month daily regimen, the total doses should be administered within nine months of beginning treatment. If treatment is not completed within this period, the patient needs to be assessed to determine the appropriate action to take, such as continuing treatment for a longer duration or restarting treatment from the beginning.

Treating a patient for a defined duration, without accounting for the number of doses taken, can result in undertreatment.

Interruptions in treatment may have a significant effect on the duration of therapy. Reinstitution of treatment must take into account the extensiveness of the disease (e.g., cavitary versus noncavitary disease on chest radiograph, smears and cultures, immunologic status), the point in time when the interruption occurred, and the duration of the interruption. In general, the earlier in treatment and the longer the duration of the interruption, the more serious the effect and the greater the need to restart therapy from the beginning.

For consultation regarding completion of therapy or considerations for retreatment, contact the TB control program at SJCPHS at 209-468-3828.

Post-Treatment Evaluation

Routine follow-up after completion of therapy is not necessary for patients with a satisfactory and prompt bacteriologic response to a six- or nine-month regimen that included both isoniazid and rifampin.

The table below describes the clinician's responsibilities at completion of therapy for cases in which the organisms are drug-susceptible and drug-resistant.

Table 7: **CLINICIAN'S RESPONSIBILITIES AT COMPLETION OF THERAPY**

Drug Susceptibility	Clinician's Actions
Drug-susceptible organisms	Instruct the patient to promptly report the development of any symptoms, particularly prolonged cough, fever, or weight loss.
Organisms resistant to isoniazid, rifampin, or both	Individualize follow-up evaluation.

For consultation regarding post-treatment evaluation, contact the TB control program at SJCPHS at 209-468-3828.

Treatment in Special Situations

Treatment of tuberculosis (TB) in the following situations requires a high level of expertise or close consultation with an expert to provide appropriate management:

- Drug-resistant TB
- Diabetes
- Human immunodeficiency virus (HIV) infection
- Alcoholism
- Liver disease
- Renal insufficiency and end-stage renal disease
- TB associated with tumor necrosis factor-alpha (TNF-α) antagonists
- Culture-negative pulmonary TB
- Extrapulmonary TB
- Pregnancy and breastfeeding
- TB in children

For consultation regarding treatment in the following situations, contact the TB control program at SJCPHS at 209-468-3828.

Drug-Resistant Tuberculosis

Treatment of TB caused by drug-resistant organisms should be provided by, or in close consultation with, an expert in the management of these difficult situations. **Second-line regimens often represent the patient's last hope for being cured and inappropriate management can have life-threatening consequences.**

A patient with a strain of *Mycobacterium tuberculosis* resistant to both isoniazid (INH) and rifampin (RIF) has multidrug-resistant TB (MDR-TB). Refer MDR-TB patients immediately to a specialist or seek consultation with a specialized treatment center.

Acquired drug resistance usually develops when an inadequate drug regimen is prescribed (e.g., inappropriate drugs or insufficient dosage) or when there is a combined failure of both the patient and the provider to ensure that an adequate regimen is taken. A patient with acquired drug resistance may transmit his or her strain to others, who may then develop primary drug-resistant TB.

Resources

- ATS, CDC, IDSA. “Treatment of Tuberculosis” *(MMWR* 2003;52[No. RR-11]:11-12, 68–70). Available at: http://www.cdc.gov/mmwr/PDF/rr/rr5211.pdf .
- CDC. “Multidrug-Resistant Tuberculosis (MDR TB)” (Accessed June 2, 2014). Available at: http://www.cdc.gov/tb/publications/factsheets/drtb/mdrtb.htm.
- CDC. “Extensively Drug-Resistant Tuberculosis (XDR TB)” (Accessed June 2, 2014). Available at: http://www.cdc.gov/tb/publications/factsheets/drtb/xdrtb.htm.
- Curry International Tuberculosis Center and California Department of Public Health, 2011: Drug-Resistant Tuberculosis: A Survival Guide for Clinicians, Second Edition. Available at: http://www.currytbcenter.ucsf.edu/products/drug-resistant-tuberculosis-survival-guide-clinicians-2nd-edition.

Diabetes

Diabetes triples the risk of developing TB. Consequently, rates of TB are higher in people with diabetes than in the general population, and diabetes is a common comorbidity in people with TB.

People with diabetes are also:

- More likely to not have negative sputum cultures at two months of treatment
- More likely to have low rifampin levels
- More likely to have hepatotoxicity during treatment
- Three times more likely to relapse
- Four-five times more likely to die during treatment

Diabetes can worsen the clinical course of TB and TB can worsen the glycemic control in people with diabetes. Individuals with both conditions thus require careful clinical management.

- Rifampin levels are likely to be low in diabetics. Low levels are associated with higher body weight and poor glucose control. Consider checking rifampin levels for slow conversion of sputum. Rifampin raises blood glucose levels and lowers blood levels of sulfonylureas and thiazolidinediones. As a result, blood glucose control may worsen during treatment.
- INH-related peripheral neuropathy is more common in diabetics. All diabetics should take Vitamin B6 while taking INH.
- PZA and Ethambutol need adjustment for renal impairment. Check creatinine prior to dosing.

Monitor diabetes control closely at onset and at end of treatment. Attempt to achieve optimal glycemic control to improve TB treatment outcome.

Human Immunodeficiency Virus Infection

Management of HIV-related TB is complex and requires expertise in the management of both HIV disease and TB. Because HIV-infected patients often take numerous medications, some of which interact with antituberculosis medications, clinicians are strongly encouraged to consult with experts who treat HIV-related TB.

It is especially important to use directly observed therapy (DOT) and other adherence-promoting strategies with patients with HIV-related TB.

Patients with advanced HIV (CD4 counts less than 100) should be treated with daily or three times weekly therapy in both the initial and continuation phase.

Patients with HIV-related TB may experience a temporary exacerbation of symptoms, signs, or radiographic manifestations (paradoxical reactions) of TB while receiving antituberculosis treatment.

Resources

- ATS, CDC, IDSA. “Treatment of Tuberculosis” (*MMWR* 2003;52[No. RR-11]:9, 50–55). Available at: http://www.cdc.gov/mmwr/PDF/rr/rr5211.pdf .
- ATS, CDC. “Notice to Readers: Updated Guidelines for the Use of Rifamycins for the Treatment of Tuberculosis among HIV-infected Patients Taking Protease Inhibitors or Nonnucleoside Reverse Transcriptase Inhibitors” (*MMWR* 2004;53[No. 2]:37). Available at: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5302a6.htm .
- CDC. *Self-Study Modules on Tuberculosis*. Available at: http://www.cdc.gov/tb/education/ssmodules/default.htm.
- CDC. “Treatment of Drug-Susceptible TB in HIV-Infected Persons” (Accessed June 2, 2014). Available at: http://www.cdc.gov/tb/publications/factseries/tbandhiv_eng.htm .
- CDC. “Guidelines for the Prevention and Treatment of Opportunistic Infections Among HIV-exposed and HIV-Infected Children” (*MMWR* 2009; 58[No. RR-11]). Available at: http://www.cdc.gov/mmwr/pdf/rr/rr5811.pdf .
- CDC. “Guidelines for the Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents” (*MMWR* 2009; 58[No. RR-4]). Available at: http://www.cdc.gov/mmwr/pdf/rr/rr5804.pdf .

Alcoholism

Alcohol-Related Treatment Complications

Risk of drug-induced liver injury and nonadherence complicate health interventions for patients who are diagnosed with TB disease or latent tuberculosis infection (LTBI) and who also are known or suspected to have an alcohol use disorder, who drink heavily, or who regularly consume alcohol.

In several important ways related to tuberculosis and its treatment, alcohol consumption increases health risks and can complicate the treatment of patients.

- **Immunosuppression:** Persons who use alcohol may be at increased risk for acquiring or developing TB, but given the many other potential risk factors that commonly occur among such persons, alcohol use has been difficult to identify as a separate risk factor for TB. However, studies have shown that "alcohol consumption is a major risk factor for infection with opportunistic bacterial, viral, fungal, and parasitic pathogens."
- **Liver injury and death**: Drug-induced liver injury "may occur with all currently recommended regimens for the treatment of …LTBI". In the treatment of TB disease, "the crucial efficacy of isoniazid, and particularly rifampin, warrants their use and retention, if at all possible, even in the face of preexisting liver disease." However, it is not fully understood yet how antituberculosis medications cause drug-induced liver injury. For persons taking isoniazid, an association of hepatitis was found with alcohol consumption, with rates being fourfold higher among persons consuming alcohol daily than among those who did not drink alcohol. When a patient has hepatic disease, the risk of drug accumulation and drug-induced hepatitis is increased. However, with more frequent laboratory and clinical monitoring, isoniazid may be used in patients with stable hepatic disease. Transient asymptomatic hyperbilirubinemia may occur in patients taking rifampin or rifapentine, and more severe clinical hepatitis may also occur. Hepatitis is more common when rifampin is given with isoniazid than when rifampin is given alone or with drugs other than isoniazid. Pyrazinamide has slightly lower rates of hepatotoxicity than isoniazid or rifampin, but pyrazinamide can cause liver injury that may be severe and prolonged.

  To prevent and manage drug-induced liver injury, the American Thoracic Society recommends the following systematic steps: consideration of benefits and risks in selecting patients and regimens, careful and thorough staff and patient education, ready access to care, good communication between providers, and clinical and biochemical monitoring.
- **Nonadherence to treatment:** Patients who do not complete treatment for TB disease risk relapse, development of drug-resistant TB, serious illness, and possible death. Barriers to adherence may be patient related, such as conflicting health beliefs, alcohol or drug dependence, or mental illness, or they may be system related, such as lack of transportation, inconvenient clinic hours, and lack

of interpreters. It is more difficult for patients who have an alcohol use disorder to adhere to therapy. In a prospective study of 224 patients, “noncompliance was significantly associated with homelessness and alcoholism.” In a study of 237 patients in the Russian Federation undergoing DOTS treatment for TB disease, “substance abuse was identified as the only factor that was strongly associated with non-adherence…These results suggest that DOTS programmes [sic] might be more likely to achieve TB control targets if they include interventions aimed at improving adherence by diagnosing and treating substance abuse concurrently with standard TB therapy.” DOTS programs that have explicitly offered substance abuse treatment have reported better outcomes that those that have not. In South Carolina, joint treatment programs to treat patients with TB who have alcohol and substance abuse problems were used in conjunction with incentives, enablers, and a process of increasing restrictions (health department warnings, then court-ordered directly observed therapy, then involuntary confinement) as needed to address noncompliance. This combination of strategies was associated with an increase in overall completion of antituberculosis therapy and a decrease in new cases between 1986-1991.

Liver Disease

Management of TB in patients with unstable or advanced liver disease is difficult. The likelihood of drug-induced hepatitis may be greater in these patients. The implications of drug-induced hepatitis for patients with marginal hepatic reserve are potentially serious, even life-threatening. Also, fluctuations in the biochemical indicators of liver function (with/without symptoms) related to the preexisting liver disease confound monitoring for drug-induced hepatitis.

Safe Treatment Guidelines

In 2006, the American Thoracic Society (ATS) issued “An Official ATS Statement: Hepatotoxicity of Antituberculosis Therapy.” These recommendations at http://www.thoracic.org/statements/resources/tb-opi/hepatotoxicity-of-antituberculosis-therapy.pdf on page 947 for guidance for the safe treatment of TB Disease are:

> **Regimen selection.** The crucial efficacy of isoniazid, and particularly rifampin, warrants their use and retention, if at all possible, even in the face of preexisting liver disease. Several regimens are recommended if baseline serum ALT is more than three times the upper limit of normal (ULN), and TB is not believed to be the cause:
>
> 1. Treatment without pyrazinamide might utilize isoniazid and rifampin for 9 months with ethambutol until drug susceptibility testing of the *M. tuberculosis* isolate is completed.

2. In patients with cirrhosis, rifampin and ethambutol, with levofloxacin, moxifloxacin, gatifloxacin, or cycloserine, for 12 to 18 months may be considered.

3. For patients with encephalopathic liver disease, ethambutol combined with a fluoroquinolone, cycloserine, and capreomycin or aminoglycoside for 18 to 24 months may be an option. However, these regimens have not been tested systematically.

4. Some providers avoid aminoglycosides in severe, unstable liver disease due to concerns about renal insufficiency, or bleeding from injected medication in patients with thrombocytopenia and/or coagulopathy.

Clinical monitoring

1. Face-to-face monthly assessments and patient education for adverse drug events are essential.

2. Directly observed treatment (DOT) enhances treatment adherence and monitoring.

3. The World Health Organization and the International Union Against Tuberculosis and Lung Disease (IUATLD) recommend only clinical monitoring in patients with TB in low-income countries.

Baseline testing and monitoring

1. Baseline measurements of serum transaminases, bilirubin, alkaline phosphatase, and creatinine, and a blood platelet count are recommended for all adults beginning treatment for TB disease.

2. For patients with preexisting severe liver disease, some clinicians also recommend periodic measurement of prothrombin time and INR to assess hepatic synthetic function.

3. Routine measurements during treatment are recommended when baseline abnormalities are present and for patients who chronically consume alcohol, take other potentially hepatotoxic medications, or who have viral hepatitis or history of liver disease, HIV infection, or prior TB drug-induced liver injury (DILI).

4. In patients with abnormal baseline transaminases, the range of their prior fluctuations may be of assistance in interpreting results of biochemical monitoring of treatment.

5. Some providers prefer to monitor ALT in women or older adults being treated for TB disease.

Interventions for hepatotoxicity

1. The first-line anti-TB drugs, especially rifampin, should not be discontinued for mild gastrointestinal complaints, which may be relatively frequent in the initial weeks of anti-TB treatment.

2. If serum transaminase concentrations are more than five times the ULN (with or without symptoms) or more than three times the ULN with jaundice and/or hepatitis symptoms, then potentially hepatotoxic medications should be stopped immediately and the patient evaluated promptly.

3. Serologic tests for hepatitis A, B, and C viruses should be obtained, and the patient should be evaluated for biliary disease, use of alcohol, and other hepatotoxic drugs.

4. Some experts recommend interrupting treatment for lesser increases in patients with cirrhosis or encephalopathy.

5. If indicated, until the specific cause of abnormalities can be determined, clinicians should treat with at least three anti-TB agents that are less likely to cause hepatotoxicity.

Rechallenge

1. After ALT returns to less than two times the ULN, rifampin may be restarted with or without ethambutol.

2. After 3 to 7 days, isoniazid may be reintroduced, subsequently rechecking ALT.

3. If symptoms recur or ALT increases, the last drug added should be stopped.

4. For those who have experienced prolonged or severe hepatotoxicity, but tolerate reintroduction with rifampin and isoniazid, rechallenge with pyrazinamide may be hazardous. In this circumstance, pyrazinamide may be permanently discontinued, with treatment extended to 9 months. Although pyrazinamide can be reintroduced in some milder cases of hepatotoxicity, the benefit of a shorter treatment course likely does not outweigh the risk of severe hepatotoxicity from pyrazinamide rechallenge.

For all patients with preexisting liver disease, frequent clinical and laboratory monitoring should be performed to detect drug-induced hepatic injury.

Resources

- ATS, CDC, IDSA. “Treatment of Tuberculosis” (*MMWR* 2003;52[No. RR-11]:11, 65). Available at: http://www.cdc.gov/mmwr/PDF/rr/rr5211.pdf .

For consultation regarding patients with preexisting liver disease, contact the TB control program at SJCPHS at 209-468-3828.

Renal Insufficiency and End-Stage Renal Disease

Treatment Complications

Renal insufficiency complicates the management of TB because some antituberculosis medications are cleared by the kidneys. Management may be further complicated by the removal of some antituberculosis agents via hemodialysis. Thus, some alteration in dosing antituberculosis medications is commonly necessary in patients with renal insufficiency and end-stage renal disease (ESRD) receiving hemodialysis.

Creatinine Clearance

Dosing recommendations are based on patients’ creatinine clearance. In patients having a reduced creatinine clearance (but not less than 30 ml/minute), standard doses should be used, but measurement of serum concentrations should be considered to avoid toxicity.

Dosing Recommendations

For patients having a creatinine clearance of less than 30 ml/minute or for patients receiving hemodialysis, the following adjustments to conventional dosing are recommended.

Table 8: **DOSING RECOMMENDATIONS FOR ADULT PATIENTS WITH REDUCED RENAL FUNCTION AND FOR ADULT PATIENTS RECEIVING HEMODIALYSIS**

Drug	Change in Frequency?	Recommended dose and frequency for patients with creatinine clearance <30 ml/min or for patients receiving hemodialysis
Isoniazid	No change	300 mg once daily, or 900 mg 3 times per week
Rifampin	No change	600 mg once daily, or 600 mg 3 times per week
Pyrazinamide	Yes	25–35 mg/kg per dose 3 times per week (not daily)
Ethambutol	Yes	15–25 mg/kg per dose 3 times per week (not daily)
Moxifloxacin	No	400 mg/dose daily†
Levofloxacin	Yes	750–1,000 mg per dose 3 times per week (not daily)
Cycloserine	Yes	250 mg once daily, or 500 mg/dose 3 times per week*
Ethionamide	No change	250-500 mg/dose daily
Linezolid	No change	600 mg/dose daily
p-Aminosalicylic acid	No change	8-12 g/day, divided into two-three times per day
Streptomycin	Yes	12–15 mg/kg per dose 2 or 3 times per week (not daily)
Capreomycin	Yes	12–15 mg/kg per dose 2 or 3 times per week (not daily)
Kanamycin	Yes	12–15 mg/kg per dose 2 or 3 times per week (not daily)
Amikacin	Yes	12–15 mg/kg per dose 2 or 3 times per week (not daily)

* The appropriateness of 250-mg daily doses has not been established. There should be careful monitoring for evidence of neurotoxicity. (See Section 3 of the "Treatment of Tuberculosis" guidelines.)

† No adjustment in dose is needed for those with low creatinine clearance or those on hemodialysis. No adjustment in dosing frequency is needed, but it may be given three times per week to facilitate administration.

Standard doses are given unless there is intolerance. The medications should be given after hemodialysis on the day of hemodialysis. Monitoring of serum drug concentrations should be considered to ensure adequate drug absorption, without excessive accumulation, and to assist in avoiding toxicity.

Data currently are not available for patients receiving peritoneal dialysis. Until data become available, begin with doses recommended for patients receiving hemodialysis and verify adequacy of dosing, using serum concentration monitoring.

Source: Curry International Tuberculosis Center and California Department of Public Health, 2012: Tuberculosis Drug information Guide, 2nd edition.

- **Rifampin** and **isoniazid** are metabolized by the liver, so conventional dosing may be used in the setting of renal insufficiency.
- Supplemental dosing is not necessary for **isoniazid, rifampin,** or **ethambutol**. If **pyrazinamide** is given after hemodialysis, supplemental dosing is not required.
- A longer interval between doses with three times a week administration is recommended for **pyrazinamide** and **ethambutol**.
- Doses of **streptomycin, kanamycin, amikacin,** and **capreomycin** must be adjusted in patients with renal failure, and the dosing interval should be increased. In general, the dose should not be reduced because the drugs exhibit concentration dependent bactericidal action, and smaller doses may reduce drug efficacy.
- **Ethionamide** requires no dose adjustment.
- Twice daily dosing (4 g) of **p-Aminosalicylic acid (PAS)** should be adequate if the granule formulation is used. Its metabolite, acetyl-PAS, is substantially removed by hemodialysis.
- **Cycloserine** requires an increase in the dosing interval to avoid accumulation between hemodialysis sessions; the drug should be given after hemodialysis to avoid underdosing.
- The **fluoroquinolones** undergo some degree of renal clearance that varies from drug to drug. For example, levofloxacin undergoes greater renal clearance than moxifloxacin. It should be noted that the fluoroquinolone dosing recommendations for end-stage renal disease provided by the manufacturers were developed for treating pyogenic bacterial infections. These recommendations may not be applicable to the treatment of tuberculosis in patients with end-stage renal disease.

Administration of Drugs Immediately After Hemodialysis

Administration of all antituberculosis drugs immediately after hemodialysis will facilitate DOT (three times per week) and avoid premature removal of the drugs.

Monitoring of Serum Drug Concentrations

It is important to monitor serum drug concentrations in persons with renal insufficiency who are taking cycloserine, ethambutol, or any of the injectable agents to minimize dose-related toxicity, while providing effective doses.

Clinicians also should be aware that patients with end-stage renal disease may have additional clinical conditions, such as diabetes mellitus with gastroparesis, that may affect the absorption of the antituberculosis drugs, or they may be taking concurrent medications that interact with these drugs. Under these circumstances a careful clinical and pharmacologic assessment is necessary, and, in selected cases, serum drug

concentration measurements may be used to assist in determining the optimum dose of the antituberculosis drugs.

Finally, data currently do not exist for patients receiving peritoneal dialysis. Because the drug removal mechanisms differ between hemodialysis and peritoneal dialysis, it cannot be assumed that all of the recommendations in Table 8 will apply to peritoneal dialysis. Such patients may require close monitoring, including measurements of the serum concentrations of the antituberculosis drugs.

Culture-Negative Pulmonary Tuberculosis

A diagnosis of TB should not be ruled out if *M. tuberculosis* cannot be isolated from persons suspected of having pulmonary TB on the basis of clinical features and chest radiographic examination. Alternative diagnoses should be carefully considered and further appropriate diagnostic studies undertaken in persons with apparent culture-negative TB.

A diagnosis of culture-negative pulmonary TB can be made if all the following conditions are met:

- Initial acid-fast bacilli (AFB) smears and cultures are negative.
- Clinical or radiographic response occurs within two months of initiation of therapy.
- No other diagnosis has been established.

After the initial phase (first two months), continue treatment with an additional two months of isoniazid and rifampin during the continuation phase to complete a total of four months of treatment. However, HIV-infected patients with culture-negative pulmonary TB should be treated for a minimum of six months.

For consultation regarding the treatment of TB in a patient with negative cultures, contact the TB control program at SJCPHS at 209-468-3828.

Resources

- ATS, CDC, IDSA. “Treatment of Tuberculosis” (*MMWR* 2003;52[No. RR-11]:10, 61). Available at: http://www.cdc.gov/mmwr/PDF/rr/rr5211.pdf .

Extrapulmonary Tuberculosis

The basic principles for treating pulmonary TB also apply to extrapulmonary forms of the disease. The addition of corticosteroids is recommended for patients with TB pericarditis and TB meningitis. Recommendations concerning duration of therapy are as follows:

- Use a six-month course of therapy for TB involving any site. **Exceptions:** For bone or joint TB, use a six- to nine-month regimen. For the meninges, use a nine- to twelve-month regimen.

- Consider prolonging therapy for patients with TB in any site that is slow to respond.

Note: **Affected lymph nodes may enlarge while patients are receiving appropriate therapy or after treatment has ended without any evidence of bacteriologic relapse. On occasion, new nodes can appear during or after treatment as well.**

For consultation to discuss length of treatment, contact the TB control program at SJCPHS at 209-468-3828.

Resources

- ATS, CDC, IDSA. "Treatment of Tuberculosis" (*MMWR* 2003;52[No. RR-11]:10, 56–61). Available at: http://www.cdc.gov/mmwr/PDF/rr/rr5211.pdf .
- Division of Tuberculosis Elimination. *Fact Sheets* (Accessed June 2014). Available at: http://www.cdc.gov/tb/publications/factsheets/general.htm.
- CDC.*Self-Study Modules on Tuberculosis*. Available at: http://www.cdc.gov/tb/education/ssmodules/default.htm.

Pregnancy and Breastfeeding

Because of the risk of TB to the fetus, treatment in pregnant women should be initiated whenever the probability of maternal disease is moderate to high. The initial treatment regimen should consist of isoniazid (INH), rifampin (RIF), pyrazinamide (PZA), and ethambutol (EMB). Although these drugs cross the placenta, they do not appear to have teratogenic effects.

Breastfeeding should not be discouraged in women being treated with first-line antituberculosis agents because the small concentrations of drugs in breast milk do not produce toxicity in the nursing newborn. Conversely, drugs in breast milk should not be considered an effective treatment for TB in a nursing infant.

Pyridoxine supplementation (25 mg/day) is recommended for all women taking INH who are either pregnant or breastfeeding.

Resources

- ATS, CDC, IDSA. "Treatment of Tuberculosis" (*MMWR* 2003;52[No. RR-11]:11, 62–63). Available at: http://www.cdc.gov/mmwr/PDF/rr/rr5211.pdf .
- CDC. *Self-Study Modules on Tuberculosis*. Available at: http://www.cdc.gov/tb/education/ssmodules/default.htm.
- American Academy of Pediatrics. In: Pickering LK, Baker CJ, Kimberlin DW, Long SS, eds. *Red Book: 2012 Report of the Committee on Infectious Diseases*. 29th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2012 (Red Book® Online Web site). Available at: http://www.aapredbook.org .

Tuberculosis in Children

For TB treatment, a pediatric patient is a person 14 years of age and younger.

Because of the high risk of disseminated TB in infants and children 4 years of age and younger, treatment should be started as soon as the diagnosis of TB is suspected.

The following recommendations have been developed for children:

- Regimens recommended for infants, children, and adolescents with TB are generally the same as those for adults.
- Duration of treatment in children is six months.
  Exception: For disseminated disease and TB meningitis, use a nine- to twelve-month regimen. For other exceptions, refer to "Duration of Treatment" in the "Treatment Regimens and Dosages" topic in this section.
- Directly observed therapy (DOT) should always be used in treating children.

Due to the difficulty of isolating *M. tuberculosis* in a child with pulmonary TB, the choice of drugs for the child is frequently guided by the drug susceptibility test results of the presumed source case. If drug-resistant TB is suspected or the source case isolate is not available, specimens for microbiological evaluation should be obtained via early morning gastric aspiration, bronchoalveolar lavage, or biopsy.

Resources

- ATS, CDC, IDSA. "Treatment of Tuberculosis" (*MMWR* 2003;52[No. RR-11]:9–10, 55–56). Available at: http://www.cdc.gov/mmwr/PDF/rr/rr5211.pdf .
- CDC. *Self-Study Modules on Tuberculosis*. Available at: http://www.cdc.gov/tb/education/ssmodules/default.htm.
- Francis J. Curry National Tuberculosis Center. *Pediatric Tuberculosis: An Online Presentation*. Available at: http://www.nationaltbcenter.ucsf.edu/pediatric_tb/ .
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Resources and References

Resources

- ATS, CDC, IDSA. “Treatment of Tuberculosis” (*MMWR* 2003;52[No. RR-11]). Available at: http://www.cdc.gov/mmwr/PDF/rr/rr5211.pdf .
- CDC. *Core Curriculum on Tuberculosis: What the Clinician Should Know (2013).* Available at: http://www.cdc.gov/tb/education/corecurr/default.htm
- CDC. *Self-Study Modules on Tuberculosis*. Available at: http://www.cdc.gov/tb/education/ssmodules/default.htm.