

# GRANT COUNTY

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# HEALTH DISTRICT

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## Protocol and Standing Orders for Evaluation and Management of Tuberculosis Infection and Disease

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**Effective:** December 1, 2006  
**Signed:** 1/14/08 Dr. Brzezny  
**Modification of 4/23/07 protocol**

**Purpose:** To provide GCHD clinical staff with guidelines for evaluating and managing patients who present for tuberculosis (TB) screening or those with a clinical presentation suspicious for active TB. This document is intended to complement pursuit of medical consultation from the Health Officer where appropriate.

### 1. TB Skin Testing

#### 1.1. TB screening with PPD.

For the purposes of TB skin testing, GCHD shall only use or accept the Mantoux tuberculin skin test of Purified Protein Derivative (PPD). Candidates for TB screening (1.2.) shall be administered PPD in amount of 5 units (0.1 ml) intradermally into the inner surface of the left forearm. Alternative sites include the inner right forearm or the posterior aspect of either trapezius muscle area (intradermally).

PPD solution should not be drawn into the tuberculin syringe any sooner than 15 minutes prior to administration. PPD solution should be stored in the refrigerator when not in use, avoiding freezing of the solution. PPD may be transported in a light protected container for use in field-based testing. An opened vial should be discarded after 30 days.

Skin tests should not be administered on Thursdays unless a specific plan has been established to permit reading over the weekend.

Skin tests should be read by a GCHD clinician, or trained, designated staff, within 48-72 hours of administration with the result recorded in double digits (e.g., 07 mm).

Skin tests may be read up to 96 hours under the following limited circumstances:

- Reasonable efforts to read by 72 hours have failed.
- The observed result is clearly 00 mm induration without erythema or clearly 10 mm induration or greater.

#### 1.2. Candidates for TB Screening

The Grant county Health District promotes a principle of targeted tuberculin testing, within its jurisdiction. This principle identifies persons at high risk for developing tuberculosis who would benefit by treatment of latent tuberculosis infection if detected. Following that principle, targeted tuberculin testing programs should be conducted only among groups at thight risk and discouraged in those at low risk (irrespective of pregnancy status or age). Infected persons who are considered to be at high risk for developing active tuberculosis should be offered treatment of latent tuberculosis infection (irrespective of age or pregnancy status).

Persons with increased risk for developing tuberculosis include those who have had recent infection with *Mycobacterium tuberculosis*, those who have (or are suspected to have) clinical conditions or past history epidemiologically associated with an increased risk for progression of latent tuberculosis infection to active tuberculosis.

Testing is discouraged among persons at lower risk. A flexible approach to identifying high risk groups is recommended. Mandated skin-testing programs (e.g., those that formerly were conducted among teachers and food handlers) should be discouraged unless the targeted groups contain substantial proportions of persons at high risk.

Those identified for testing should be treated if a test turns out a positive result (assuming the targeted tuberculin testing principle has been used). Once a person is recommended for testing that same person should be treated whenever possible if the PPD result is positive (irrespective of age or pregnancy status).

The following groups at high risk for developing active tuberculosis are considered for screening through GCHD:

- Recent close contacts of active cases of infectious tuberculosis
- HIV positive persons
- Persons known to have radiographic evidence suggestive of old, healed TB
- Persons identified by immigration screening to have abnormal chest films suggestive of prior or active TB
- Immigrants or refugees within the last 5 years from high prevalence countries
- Persons who have traveled to high-prevalence regions for  $\geq 6$  months during the preceding 5 years
- Homeless persons
- Injection illicit drug users
- Persons seeking treatment for substance abuse
- Persons with medical conditions that predispose to developing active disease if infected
  - Diabetes mellitus (especially insulin dependent or poorly controlled)
  - Chronic steroid therapy (e.g., equivalent of prednisone 15-20 mg per day for greater than one month)
  - Other immunosuppression (acquired or medically induced)
  - Organ transplant recipients
  - Cancer of the head/neck, lung, hematologic system (e.g., leukemia) or reticuloendothelial system (e.g., lymphoma)
  - End-stage renal disease (i.e., chronic hemodialysis and transplant candidates)
  - Malabsorptive states (e.g., small bowel resection, intestinal bypass)
  - Weight  $< 90\%$  ideal body weight-for-height
  - Silicosis
- Residents of high-risk congregate settings (e.g., correctional facilities, homeless shelters, inpatient facilities)
- Infants, children and adolescents exposed to adults in high-risk categories
- Children younger than 4 years of age
- Any person arranged through discussion with GCHD Health Officer

### 1.3. Employees of high-risk congregate settings.

Employees of high-risk congregate settings are also considered to be at high risk for developing active TB and should be screened by their employer or at the cost of their employer through a community-based provider, unless other arrangements have been made with GCHD Personal Health Director.

### 1.4. Candidates for testing who do not plan to reside in GCHD.

Candidates for testing who do not plan to reside in GCHD for a period adequate to complete screening and treatment, patients who are clinically well and are neither contacts, HIV positive, immunocompromised, refugees nor immigrants may have TB screening deferred until arrival in their

anticipated community of residence. More specifically, such patients planning to move out of the GCHD should only be screened if their current stay in this jurisdiction will exceed four months.

#### 1.5. TB Screening in Pregnancy.

Pregnant women should not be screened unless the managing health care provider plans to treat them during pregnancy, should a latent TB infection be diagnosed. Pregnant candidates for testing would generally be limited to women who meet one of the following criteria:

- Contact with a smear positive case within the preceding 24 months
- HIV positive or immunocompromised status
- Persons undergoing refugee or immigration screening
- Employment in a high-risk occupational setting that is known to serve patients with active TB

Pregnant women who have other medical or epidemiologic indications for screening (e.g., arrival to United States within the preceding 5 years, travel to high-prevalence regions for  $\geq 6$  months), but who lack all of the factors described immediately above, may have skin-testing deferred until the post partum medical evaluation.

In the event such screening does occur in such a “lower”-priority pregnant woman and she is found to have a positive skin test (e.g., 10mm or greater), a posteroanterior chest radiograph (with abdominal shield) should be obtained to assess for evidence of active pulmonary disease. If the radiograph is normal or shows only calcified granulomata or pleural scarring, treatment should be deferred until the second trimester of pregnancy. Further delaying of the treatment must be discussed with the Health Officer on case-by-case basis. If further delaying of the treatment is accepted a repeat chest radiograph should be obtained and reviewed prior to starting treatment for latent TB at later date.

Lab work should be obtained prior to any pregnant woman starting treatment, or if the treatment is started within the 6 weeks after pregnancy (see Table 8.1).

#### 1.6. Classification of the TB skin test result.

All patients screened or evaluated by the GCHD shall be classified based on skin test results pursuant to CDC guidelines set forth in *Core Curriculum on Tuberculosis: What the Clinician Should Know*; USDHHS, CDC, 2000; 4<sup>th</sup> Edition. (Figure 1.)

1.6.1. Congregate setting statements and circumstances will be applied to the time before or during the PPD administration.

1.6.2 A skin test conversion applies to a previously known TB skin test result and shall be defined as the following:

- A documented increase of at least 10 mm induration over the preceding 24 months (e.g., 08 ->18 mm or 00 - >10 mm). Such persons shall be considered PPD-positive, regardless of their placement in the risk matrix above.
- Two-step testing is recommended at baseline for persons undergoing serial testing as part of an institutional or occupational TB control plan. Among such persons having 00mm induration at their first test, a second PPD should be placed 1-3 weeks after the first and read 48-72 hours thereafter. This two-step requirement may be waived for persons who have documentation of a previous skin test result within the preceding 12 months.

Figure 1. TB Skin test results classification

Group	PPD Result			
	00-04 mm	05-09 mm	10-14 mm	15mm+
<ul style="list-style-type: none"> <li>▪ Recent close contact</li> <li>▪ Old, healed TB on CXR</li> <li>▪ HIV infected, or IDU of unknown HIV status</li> <li>▪ Organ transplant recipient</li> <li>▪ Other immunosuppression</li> </ul>	Neg	Pos	Pos	Pos
<ul style="list-style-type: none"> <li>▪ Recent arrivals from high prevalence countries (5 years or less)</li> <li>▪ Injection drug users</li> <li>▪ Residents and employees of high-risk congregate care settings: prisons and jail, nursing homes and other long-term facilities for the elderly, hospitals and other health care facilities, residential facilities for AIDS patients, and homeless shelters</li> <li>▪ Mycobacteriology laboratory personnel</li> <li>▪ Persons with clinical conditions that place them at high risk</li> <li>▪ Children &lt;4 years of age, or children and adolescents exposed to persons in the groups listed above</li> </ul>	Neg	Neg	Pos	Pos
<ul style="list-style-type: none"> <li>▪ All others</li> <li>▪ <i>Note: other than persons required to undergo such testing (e.g., health care workers), such persons should not be tested.</i></li> </ul>	Neg	Neg	Neg	Pos

## 2. Chest-Radiography

### 2.1. Single view (postero-anterior or PA) radiogram

Indications for PA chest radiogram shall include:

- Positive skin test with no chest radiograph since positivity documented
- Household contacts of active pulmonary TB cases
- Reports of class B findings on immigration chest radiographs
- Persons with a productive cough greater than 3 weeks in duration
- End-of-therapy for active TB that included a pulmonary, pleural, or other intrathoracic component (e.g., hilar or mediastinal lymphadenopathy).
- As otherwise directed by Health Officer.

### 2.2. Two-view (2V) radiogram

Indications for 2V radiogram shall include:

- Persons less than 15 years of age.
- Symptoms of TB, specifically: hemoptysis, cough greater than 14 days duration, or cough with fever.
- HIV positive or immunocompromised
- Suspected or reported pleural effusion or hilar adenopathy
- Follow-up of clients with active TB cases under treatment
- Follow-up of clients with past history of active TB
- Contacts (of active TB patients) with prior history of pulmonary diseases, COPD, asthma, etc.
- As otherwise directed by Health Officer.
- Otherwise, chest radiography can be limited to a single, PA view.

### 2.3. Interpretation of chest radiograms

Radiograms of all applicable patients shall be reviewed and interpreted by the Health Officer if a patient will be treated or is being treated directly by GCHD, or if GCHD will issue recommendations about treatment to patient's community health care professional. This rule is irrespective of any previous radiogram readings by another party. GCHD nursing staff may accept the readings of outside health care providers for the purposes of making recommendations on treatment to community-based providers, provided that they make it clear to the consulting provider that GCHD has not directly reviewed the image but has only seen the report. Recommendations made by a GCHD nursing staff shall be discussed with Health Officer at his next on-site visit or sooner whenever deemed appropriate.

2.3.1 X-rays will be evaluated by the Health Officer with respect to TB status only. GCHD communications with healthcare providers and patients will indicate so, and will indicate that other conditions must be evaluated by the patient's health care provider.

### 2.4. Chest radiogram timing

Chest x-ray for asymptomatic patient must be less than 6 months old, or as specified by Health Officer on a case by case basis. Chest x-ray for symptomatic patient must be taken during presence of current symptoms.

## 3. **Sputum Evaluation**

### 3.1. Indication for sputum collection

GCHD staff may request and obtain sputum for Acid-fast Bacilli Smear (AFB) and Culture:

- Among suspected and confirmed cases of active pulmonary TB:
  - Three baseline specimens, each 8-24 hours apart (less than 24 hours applied only when necessary for expediency if 24 hour target can not be met);

If AFB smear of any of the three baseline smears positive then:

- One specimen every 2 weeks until two consecutive smears negative.

If AFB smear of baseline specimens negative but culture positive then:

- Two specimens monthly until culture negative, 8-24 hours apart (less than 24 hours applied only when necessary for expediency if 24 hour target can not be met).

When two consecutive specimens become AFB smear and/or culture negative then:

- Two specimens every three months until the end of therapy, 8-24 hours apart (less than 24 hours applied only when necessary for expediency if 24 hour target can not be met).
- As part of screening for HIV-infected patients who are potential candidates for treatment of latent TB infection.
- As otherwise ordered by Health Officer
  - The most common instance under which the Health Officer will order sputum collection is when radiographic abnormalities suggestive of tuberculosis of indeterminate activity (e.g., fibrosis, nodular infiltrates) are found. The typical approach will be to collect three sputa, follow cultures, and repeat the chest radiograph when the cultures are final. At that point the Health Officer will review the patient's TB history and laboratory, clinical, and radiographic information to assign a diagnosis and, when indicated, prescribe treatment.

### 3.2. Rapid amplification test

In some instances, rapid amplification test will be provided by the state laboratory as a surrogate to the sputum result (often significantly sooner than sputum culture). Results of rapid amplification results

will be considered by the Health Officer on case-by-case basis. A positive rapid amplification test result does not always mean active TB infection, however, may aid in making such a determination in conjunction with clinical symptoms and history.

### 3.3. Positive culture susceptibility testing

In the event of positive sputum culture for *M. tuberculosis*, drug susceptibility testing should be performed on an initial positive culture. Drug susceptibility should be repeated on all patients who have positive cultures after 3 months of therapy or as ordered by Health Officer (usually in patients with prior therapy, in contact with drug resistant strains, in patients with resistant strains, etc.)

### 3.4. Other testing methods for active or latent tuberculosis

GCHD recognizes that other tests may be necessary from time to time in order to assess for active or latent tuberculosis. Those can be but are not limited to bronchoalveolar lavage via bronchoscopy, gastric lavage /aspirate, other body tissue sampling, novel testing methods, etc. Utility and applicability of those tests will be determined by the Health Officer on case-by-case basis.

## 4. **Bloodborne pathogen and other tests**

### 4.1. Active TB cases

All active TB infection patients shall be tested for following:

- HIV status as a routine part of their TB care unless they are already known to be HIV infected.
- Hepatitis B and C if high risk for those infections (IV drug users, HIV positive, etc.).
- Baseline liver enzymes, serum creatinine and platelet count unless performed within 4 weeks prior to infection diagnosis.
- Baseline and monthly testing of visual acuity (Snellen chart) and color vision (Ishihara) should be performed or recent test documented when ethambutol (EMB) is to be used for treatment.

### 4.2. Latent or inactive TB cases

Patients undergoing screening or treatment for latent or inactive TB should be screened for HIV testing if they report any of the following

- Men who have sex with other men
- Injection of illicit drugs
- Blood product or transplant recipient 1977-1985
- Exchange of sex for drugs or money
- Sex partner of any of the above
- Sex partner of HIV-infected person

Patients undergoing screening or treatment for latent or inactive TB with epidemiological risks for Hepatitis B or C should be counseled about testing for those infections and may be referred to community-based resources for that testing.

### 4.3. Other provisions for testing

The Health Officer may order additional testing on an individualized basis for other patients undergoing TB evaluation or treatment.

All testing recommendations, patient's intent to test, and test results should be documented in patient's chart. Tests are preferably referred to community-based resources for that testing (i.e. patient's health care facility or consultant).

## 5. Assignment of TB Diagnosis Classification, recommendations and follow up

### 5.1. Classification

All patients evaluated by GCHD shall be assigned a classification diagnosis according to *Core Curriculum on Tuberculosis: What the Clinician Should Know; USDHHS, CDC, 2000; 4<sup>th</sup> Edition. (Figure 2.)*

FIGURE 2. TB classification

Class 0:	Not recently exposed, not infected (or exposed >3 months ago and infection ruled out with follow-up skin testing)
Class I:	Recently exposed, not infected (should become reclassified within 3 months after follow-up skin-testing)
Class II:	Latent infection
Class III:	Confirmed active disease
Class IV:	Old, inactive disease
Class V:	Suspected active disease

### 5.2. Diagnosis assignment timeframe

GCHD shall strive to assign a valid diagnosis to all patients referred for TB evaluation in timely and appropriate fashion. Prior to diagnosis assignment a thorough information gathering shall take place. Health Officer shall review the following non-urgent consults during his regular on-site visits (unless otherwise specified in this policy):

- Charts and radiographs of asymptomatic persons with positive skin tests and radiographs obtained.
- Charts and radiographs of patients whose sputum cultures are final and are awaiting diagnostic classification.
- Charts of patients treated for active disease at least every two months and prior to dismissal.

Any cases defined by this policy as in need of urgent consultation (i.e. new acute TB case, severe side effect) or other consults deemed in need of urgent consultation shall be discussed with Health Officer promptly via phone, Email or in person (at discretion of TB nursing staff).

### 5.3. Evaluation

The Health Officer will evaluate all available information and assign the class diagnosis. This may be delegated to nursing staff interim if the patient is referred in by their primary care provider or another health department with an appropriately documented, positive skin test and a written report of a normal chest radiograph and the patient has neither symptoms nor history of active TB. In these cases, the nurse may designate the patient as “Class II” and proceed with standing orders for therapy. However, efforts should be taken to acquire the chest radiograph for later review (e.g., within 2 weeks) by the Health Officer. The Health officer will later review the case and finalize the recommendation. The Health Officer may be consulted immediately whenever deemed appropriate.

Regarding all children <15 years of age, a documented physical examination to rule out signs of active tuberculosis (i.e., examination of heart, lungs, abdomen, and peripheral lymph nodes) prior to initiating therapy for latent TB by patient’s primary care provider should be elicited whenever possible and documented (i.e. “exam normal”) in patient’s chart.

### 5.4. Recommendations and follow up

When recommendations by Health Officer are made following shall take place:

- 5.4.1. For all patients with class diagnosis “Class II, IV” (i.e. latent or inactive TB):

**If treatment IS recommended** then the single sheet copy of the GCHD recommendations should be forwarded back to patient's health care provider (or source of the referral to the GCHD) for further treatment. Patient shall be contacted about the treatment recommendations and need to follow up with their health care provider for treatment initiation. In the initial phase of this policy (referrals made during year 2003) all patients in this group prescribed treatment will be contacted at three, six and nine months period after therapy recommendations and compliance with treatment will be documented. The patient's health care provider will be notified if treatment recommendations are not followed.

**If treatment IS NOT recommended** patient and patient's health care provider are informed and case closed.

5.4.2. For all patients with class diagnosis of "Class I, III, V" (i.e. contact in need of further reclassification, active or suspected active TB):

Patient and patient's health care provider shall be informed about class diagnosis and GCHD shall assume primary responsibility for further case management (which may include but should not be limited to DOT, consults, etc.). An active TB case within GCHD jurisdiction can be treated by a third party only with explicit agreement from the Health Officer and with GCHD supervision. Thus, the responsibility for successful treatment of active TB within the GCHD jurisdiction shall lie with the GCHD or designated private providers in consultation with GCHD, rather than the patient.

#### 5.5. Active extrapulmonary tuberculosis

In most instances, active extrapulmonary tuberculosis presents minimal risk to the public health. GCHD will continue to provide assistance, consultations, referrals, case investigations and others as deemed appropriate on order of Health Officer. The basic principles that underlie the investigation, evaluation and treatment of pulmonary tuberculosis also apply to extrapulmonary forms of the disease with preferred 6-9 month regimen duration. The only exception is tuberculous meningitis with preferred 9-12 months of therapy. In general, GCHD will encourage and seek that extrapulmonary tuberculosis patients are cared for by community health care providers.

5.5.1. If extrapulmonary case exhibits no cough or other respiratory symptoms, including shortness of breath, and chest x-ray is negative, initially 3 consecutive sputa should be obtained.

## 6. **General Standing Orders for TB Therapy:**

### 6.1. "Class II" TB diagnosis

Latent (Class II) TB will typically be recommended isoniazid (INH) for 9 months or rifampin (RIF) for 4 months, provided no contraindications exist. In rare instances, isoniazid may be offered by GCHD nursing staff to qualified patients when Health Officer is not available immediately and if diagnosis is not in doubt (i.g. transfer from other LHJ, etc.; *see section 5. above*). Health Officer shall review the case at soonest possible date, but no later than two weeks. Contacts of INH-resistant patients should routinely be considered for a 2-month PZA+RIF regimen (alternatively RIF for 4 months). Contacts of active TB who are HIV-positive should routinely be considered for a 2-month PZA + rifamycin regimen.

A 9-month regimen of INH is the preferred regimen for the treatment of latent TB infection. A 6-month regimen also provides substantial protection and has been shown to be superior to placebo in both HIV-negative and HIV-positive persons. In some situations, treatment for 6 months rather than 9 months may provide a more favorable outcome from a cost-effectiveness standpoint. Thus, based on local conditions, a 6-month course may be preferred by the provider. **However, a 6-month regimen is not indicated for clients who are contacts of an active TB case, HIV-infected persons, those with fibrotic lesions on chest radiographs, or children.**

Both 9-month and 6-month regimens may be given intermittently, (i.e., twice weekly). **When isoniazid is given intermittently, it should be administered *only* as directly observed therapy (DOT).**

## 6.2. “Class IV” TB diagnosis

Old, inactive (Class IV) TB therapy will be individualized and ordered by the Health Officer, but in most cases will consist of isoniazid for 9 months or rifampin for 4 months.

## 6.3. Isoniazid for “Class II” and “Class IV”

6.3.1.A minimum of 270 doses administered within 12 months (9 months regimen) shall be considered optimal treatment for both HIV positive and negative adults and children. In the context of treatment for latent infection or inactive disease, the choice of daily self-administered vs. twice weekly observed is delegated to the nursing staff. The following patients should be prioritized for twice-weekly observed therapy over patients who lack these characteristics:

- Recent close contacts of smear positive cases
- Old, inactive TB
- Previous history of non-adherence to treatment
- Homelessness
- Substance abuse
- Severe mental health disorders (e.g., poorly controlled psychotic illnesses)
- Frequent or recent incarceration
- Patients with complex medical problems or taking multiple medications
- Patients with considerable language and cultural barriers to adherence
- Other patients who’s social, medical, or behavioral circumstances raise reasonable concern about adherence.

6.3.2. A course of INH for 6 months (180 doses within a period of 9 months) is reserved for certain low risk LTBI cases at the discretion of the health officer. This is not appropriate for HIV infected, for children, or for those with fibrotic lesions on x-ray.

## 6.4. Rifampin for “Class II” and “Class IV”

A minimum of 120 doses administered within 6 months (4 months regimen) shall be considered optimal second line treatment for both HIV positive and negative adults and children with exception of pregnant women.

## 6.5. Suspected (“Class V”) and confirmed (“Class III”) active TB

Treatment regimen will be individualized and ordered by the Health Officer. In general, treatment should not start prior to Health Officer consultation.

In the rare instance where the Health Officer cannot be reached for verbal orders and a patient is a confirmed case (e.g., transfer from other LHJ) or is referred by their private health care provider for treatment of active disease, GCHD nursing staff may do the following:

- Obtain all applicable and pertinent medical records
- Take a TB and medical history
- Get a new chest film if one has not been done in the preceding 30 days
- Collect two additional sputum specimens
- Assure blood and other tests (*see section 4. above, and section 8. below*)
- Place PPD if not already done
- If the patient is clinically ill or is smear positive on more than one specimen, start isoniazid, rifampin, pyrazinamide, ethambutol, po, and daily pyridoxine (unless contraindications exist) and obtain Health Officer consultation within 2 working days for ongoing orders.
- If the patient is neither ill nor smear positive, wait to start medications until Health Officer consultation is obtained.

All active cases shall receive **treatment under direct observation (DOT)**. In cases where this is not the method of supervision, the alternative method of supervision (e.g., monthly or weekly pill counts, use of DOT extenders) and circumstances leading to its choice (e.g., provider refusal, schedule conflicts) should be clearly documented in the chart and reviewed with the Health Officer.

#### 6.6. Treatment regimens for active pulmonary TB

In general, GCHD shall treat active TB in two phases: initiation and continuation phase

##### 6.6.1. Initiation phase (first two months)

Regimen I (preferred): INH+PZA+RIF+EMB daily for 2 months

Regimen II: INH+PZA+RIF+EMB daily for 2 weeks followed by 2 times weekly for 6 weeks

Regimen III: INH+PZA+RIF+EMB three times a week for 2 months

Exceptions: EMB may be excluded from the regimen if the organism is known from the testing to be sensitive to INH and RIF.

##### 6.6.2. Continuation phase (latter 4 months)

Regimen I: INH+RIF daily for 18 weeks

Regimen II: INH+RIF twice weekly for 18 weeks

Regimen III: INH+RIF three times a week for 18 weeks

Regimen IV: INH+rifapentine once a week (reserved only for patients with HIV negative status, AFB negative status after 2 months, without cavitations on any radiogram).

- Exceptions:
1. Additional 12 weeks of treatment shall always be added to all patients with findings of cavitations on any radiogram or with positive cultures after initiation phase.
  2. Additional 12 weeks of Regimen I or II should be added if PZA is not included in initial regimen for any reason (resistance of the organism, allergy, etc.)
  3. Culture negative patients with active pulmonary TB shall be treated identically as culture positive patients in initial phase. However, their continuation phase with Regimens I, II or III may be shortened by 8 weeks. Approximately 17% of all active pulmonary TB are culture negative.
  4. In pregnant women PZA can be excluded from the treatment regimens provided duration of the continuation phase is extended by 12 weeks.
  5. Clients with active pulmonary TB who are AFB negative and culture negative and who show clinical improvement may be treated with shorter duration of DOT as determined by the Health Officer.

#### 6.7 Interruptions of active TB therapy

In general, any initial phase regimen of therapy that has lapsed in excess of 14 days must be restarted de novo. In general, any continuation phase regimen of therapy that has lapsed in excess of 3 months must be restarted de novo. If de novo regimen must be started sputum cultures and sensitivity testing must be repeated. Indications for repeat chest radiograph in patients who have lapsed or failed to start treatment shall include:

- Symptoms of TB
- Intercurrent illness with productive cough lasting  $\geq 2$  weeks
- Lapse greater than three months (since last dose or, if never started, since last chest radiograph)
- Intercurrent delivery of an infant

**Interruptions in therapy are discussed with Health Officer in all instances.**

### 6.8. Completion of active TB therapy

Treatment for active TB is considered complete when all of following has occurred:

- Patient is clinically stable and improved
- Appropriately obtained cultures and AFB smears are negative (as defined above)
- Total number of doses taken has been counted and found adequate and in concert with prescribed regimen (for example, 6-month daily INH means at least 180 doses of INH)

### 6.9. Use of pyridoxine in active or latent TB

Pyridoxine should be routinely administered to the following patients receiving isoniazid, regardless of whether the Health Officer has ordered it:

- Diabetes mellitus
- Seizure disorder, anti-seizure medication, anti-psychotic medication, or other conditions associated with lowered seizure threshold
- Conditions associated with chronic malabsorption
- Chronic renal failure
- Alcoholism
- Pregnancy
- Weight <90% of ideal
- Age >65

Pyridoxine can be recommended to all patients receiving INH, or to breastfed infants of mothers receiving INH.

## 7. **Standing Orders for Drug Dosing**

When the Health Officer orders drugs to be dosed “per standing orders,” use the tables in Appendix 2 to administer correct doses of medications. Verbal or written orders from the Health Officer always supersede standing orders.

Weigh children <13 years monthly and all other patients every 3 months, then adjust dose, if necessary. If a weight change calls for a *reduction* in dosage, hold the patient at the previous (higher) dosage and notify the Health Officer for consultation.

**Seek Health Officer consultation if standing orders conflict with the health professional's judgment.**

## 8. **Monitoring Therapy:**

### 8.1. Clinical and laboratory evaluation

Routine baseline and follow-up laboratory monitoring can be eliminated in most persons with latent tuberculosis infection, except for those with HIV infection, pregnant women (or those in the immediate postpartum period), and persons with chronic liver disease or those who use alcohol regularly.

It is recommended that patients are clinically evaluated for adherence, tolerance, and adverse effects by their primary care provider or GCHD (whichever applies) based on section 4 recommendations and in concert with following schedule:

Regimen	Clinical Evaluation	Other Evaluation
INH /RIF for Class II or IV	Baseline, monthly and prn	<p>ALT, AST, and total bilirubin at baseline if:</p> <ul style="list-style-type: none"> <li>Chemical dependency</li> <li>Chronic hepatitis</li> <li>Other liver disease</li> <li>Multiple medications</li> <li>Pregnant or within six weeks after pregnancy</li> </ul> <p>In these patients, the plan for follow-up or additional biochemical testing, if any, could be individualized through patient's health care provider.</p> <p>ALT, AST, total bilirubin (and others) later if: symptoms of hepatitis</p>
Other treatment regimens (e.g., active disease)	Baseline, monthly <u>or other appropriate interval</u> , and prn	Comprehensive metabolic panel and complete blood count with platelets and differential at baseline. The plan for follow-up laboratory testing, if any, will be individualized through Health Officer consultation and orders.

Medications like INH or Rifampin can be continued in asymptomatic patients with LFT's <5 times normal (ALT around 200); in those instances LFT's should be continued once or twice a week. For a continued upward trend, the medication should be discontinued, and LFT's checked in 2 weeks.

## 8.2. Monitored side effects

Patients should be educated about the adverse effects of TB medications and told to hold their medications and call the clinic immediately if such effects develop. "TB medications side effect sheet"(Appendix 1.) should be used to document occurrence of side effects. In particular, following signs and symptoms are to be discussed with patients and documented if present:

- Hepatotoxicity (isoniazid, rifampin, pyrazinamide, ethionamide): nausea, vomiting, right upper quadrant pain, anorexia, jaundice, bilirubinuria, acholic stools
- Gastritis (rifampin, fluoroquinolones, para-amino salicylate): severe epigastric pain, nausea, vomiting
- Hypersensitivity (any): rash, fever, swelling of the tongue or lips
- Neurologic (isoniazid, ethionamide): headache (severe, persistent), parasthesiae
- Visual (ethambutol, isoniazid, ethionamide): visual changes (loss of acuity, loss of color discrimination)
- Vestibular (streptomycin, other aminoglycosides and capreomycin): tinnitus, loss of hearing, vertigo, loss of balance
- Musculoskeletal (pyrazinamide or fluoroquinolones): gout, arthralgias, tendon pain or rupture
- Hematologic (rifampin): easy bruising, bleeding gums, blood in stools

## 8.3. Methods of monitoring

Patients receiving antituberculous medications should be monitored.

### 8.3.1. "Latent" or "inactive" TB treatment monitoring

GCHD recommends that monthly monitoring of persons undergoing treatment for latent or inactive infection be done. With discretion from patient's health care provider, that may usually be done by telephone, unless patient requires specimen collection for laboratory evaluation or other elements in the patients social, medical, or behavioral circumstances make such history-taking reasonably likely to be unreliable. Administration or dispensing of medication should cease for any patient who is more than two months overdue for monitoring. Chart should be held open for up to three months, before dismissing the case and closing the file. Prior to such closure, 3 attempts, including written attempt to engage the patient, should be conducted and documented in the chart. Face-to-face contact for monitoring should occur at least every 2 months, and is encouraged prior to the client receiving the last month's medication.

### 8.3.2. Active TB treatment monitoring

All patients with active disease must be seen for monitoring and /or exam in person at least monthly by GCHD nursing staff or with GCHD notification and approval, by patient's (community) health care provider who is managing their TB disease. Administration or dispensing of medication should cease for any patient who is more than two weeks overdue for monitoring. The chart should then be referred for further consultation to the Health Officer in timely fashion.

When patients will be going to Mexico for either short or long time periods, a Binational referral form should be filled out and forwarded to the State DOH TB control program.

### 8.4. Monitored symptoms or values requiring Health Officer consultation

Medications should be held (if applicable) and Health Officer (or health care provider when applicable) immediately notified if any treated patient develops:

- Icterus
- Severe nausea and vomiting (e.g.,  $\geq 2$  times per day for  $> 3$  days)
- Other overt clinical evidence of hepatitis
- Transaminases  $> 3$  times upper limit of normal and symptoms consistent with hepatitis
- Any transaminase elevation above 5 times normal
- Other critical laboratory abnormalities (e.g., platelets  $< 25K$ , WBC  $< 2500/ul$ )
- Gout
- Tendon pain or rupture (if on fluoroquinolones)
- Overt bleeding manifestations (e.g., purpura, petechiae, bleeding gums, hemorrhage)
- Anaphylactic or anaphylactoid reaction reported
- Hospitalization due to TB medications in latent infection
- Hospitalization for any reason among active cases

Medications should be held (if applicable) Health Officer (or health care provider when applicable) notified within 48 hours if any treated patient develops:

- New suspected case (mail radiographs and key chart contents)
- Persistent, severe headache
- Persistent mild or moderate nausea and vomiting
- Paresthesias
- Non-urticarial rash
- Visual changes
- Vestibular changes
- Other adverse effect symptoms not of an emergent nature which still merit prompt attention
- Hospitalization for reasons unrelated to TB or TB treatment among persons with latent infection

Medication should be continued and chart (or faxed key contents) should be submitted to Health Officer (or health care provider when applicable) for review within 96 hours if any of treated patients develops:

- Transaminases greater than upper limit of normal, but not meeting more urgent criteria set forth above
- Other (non-critical) laboratory abnormalities
- Other adverse effect symptoms not of an urgent nature

## 9. Contact Investigation

Contact investigations should be individualized by the TB public health nurse/case manager in consultation with the Health Officer. The following general guidelines should be taken into consideration.

### 9.1. Smear positive pulmonary cases

- All household and analogous contacts should have a history, PPD (if no positive skin test previously documented), and chest radiograph conducted.
- Those with negative skin tests (<05 mm) should have a repeat skin test applied 12 weeks after contact with the infectious case was broken (either by quarantine or cessation of infectiousness following initiation of therapy).
- In most cases, the Health Officer will initiate treatment for latent TB infection among children (especially those <5 years of age) and immunocompromised contacts, pending the outcome of the second skin test. Detection of any induration among such contacts during the first or second round of skin testing is cause for seeking Health Officer consultation.
- Additional investigation and testing in work, leisure, and other environments should be managed on a case-by-case basis in consultation with the Health Officer.
- Contacts of active pulmonary cases under age 4 should have a 2-view chest film and history at the time of the first TST, and receive LTBI treatment until the second TST (after 8-10 weeks from last exposure) is negative (those with positive TST results should be treated accordingly).

### 9.2. Smear negative pulmonary cases

- All household and analogous contacts should have a history and PPD (if no previous positive skin test previously documented) conducted.
- Those with negative skin tests (<05 mm) should have a repeat skin test applied 12 weeks after contact with the infectious case was broken (either by quarantine or cessation of infectiousness following initiation of therapy).
- In some cases, the Health Officer may order chest radiography among vulnerable close contacts (e.g., <5 years of age, immunocompromised), pending the outcome of the second skin test. Detection of any induration among such contacts during the first or second round of skin testing is cause for seeking Health Officer consultation.
- Additional investigation and testing in work, leisure, and other environments usually is unnecessary, but when considered should be managed on a case-by-case basis in consultation with the Health Officer.

### 9.3. Extrapulmonary cases

- No specific contact investigation is necessary, but household and analogous long-term contacts should be referred to their primary care provider or GCHD for skin testing.
- At the case managing nurse's discretion, more extensive contact follow-up may be undertaken

### 9.4. Pediatric cases

- When active TB is found in a child <5 years of age, efforts should be taken to identify an infectious case in the child's environment.
- In most cases this will include history, PPD, and chest radiograph for household, extended family members with frequent contact, and other analogous contacts.
- Pursuit of a source case beyond these groups is rarely productive and should be considered only in consultation with the Health Officer.
- Management of infants born to mothers with active TB disease and other close contacts under 6 months of age: consult Health Officer

## Grant County Health District

### ANTI-TUBERCULOSIS AGENT SIDE-EFFECT REPORT

**Patient:** \_\_\_\_\_ **Birthdate:** \_\_\_\_\_

**Patient's phone No.:** \_\_\_\_\_

**Date and Time of Report:** \_\_\_\_\_

**Person(s) reported to:** \_\_\_\_\_

**Duration and Severity of side effect:** \_\_\_\_\_

**Past Medial History:** \_\_\_\_\_

**Alcohol use** (circle one):                      **NO**                      **YES (how often: \_\_\_\_\_)**                      **UNKNOWN**

**Substance abuse** (circle one):                      **NO**                      **YES (how often: \_\_\_\_\_)**                      **UNKNOWN**

**Diagnosis** (circle one):                      **CLASS**                      **I**                      **II**                      **III**                      **IV**                      **V**

**Medications and Side Effects** (circle all that apply):

<p><b>INH (Isoniazid)</b></p> <p>GENERAL: Weakness, Fatigue, Fever, Headache Drowsiness</p> <p>EYE: Blurry vision, Pain, Yellowing (jaundice)</p> <p>GI: Nausea, Vomiting, Epigastric Distress, Loss of Appetite</p> <p>SKIN: Rash, Itching, Jaundice</p> <p>NEURO: Numbness, Tingling, Twitching, Pain (extremities)</p> <p>OTHER: Urine Discoloration (brown or dark) Decreased Urine Output</p>	<p><b>RIF (Rifampin)</b></p> <p>GENERAL: Flu-like symptoms (fatigue, muscle</p> <p>GI: Nausea, Vomiting, Diarrhea, Loss of appetite, Abdominal pain</p> <p>SKIN: Rash, Itching, Easy bruising, Yellowing (jaundice)</p> <p>NEURO: Headache, Drowsiness, Dizziness, Mental Confusion</p> <p>OTHER: Reduced effectiveness of oral Contraceptives, Shock, Discoloration of Body Fluids, Visual Disturbances</p>
<p><b>PZA (Pyrazinamide)</b></p> <p>GENERAL: Fever, Malaise, Hepatitis</p> <p>EYE: Yellowing (jaundice)</p> <p>GI: Nausea, Vomiting, Diarrhea, Loss of appetite, Pain in upper abdomen</p> <p>JOINTS &amp; MUSCLES: Pain, Swelling</p> <p>SKIN: Rash, Itching, Jaundice, Photosensitivity</p> <p>OTHER: Dysuria, Gout</p>	<p><b>EMB (Ethambutol)</b></p> <p>GI: Anorexia, Nausea, Vomiting, Abdominal Pain</p> <p>EYE: Blurry vision, Decreased Visual Acuity, Pain</p> <p>EAR: Hearing Loss, Loss of Balance</p> <p>OTHER: Headache, Dizziness, Mental Confusion, Malaise, Peripheral Neuritis, Joint Pain, Rash, Fever, Gout</p>

**Action Taken:**

**Signed:** \_\_\_\_\_ **Dated:** \_\_\_\_\_

## **APPENDIX 2**

### **TB Drug Dosing Tables**

Definitions:

- Adults: Persons 18 years old or more.
- Children: Persons 17 years old or less.
- Twice weekly: To be administered on a Monday/Thursday (preferred) or Tuesday/Friday schedule

## ISONIAZID (For Treatment of Latent or Active Disease)

### Isoniazid:

**Pediatric daily dosing (10-20 mg/kg po [up to 300 mg] daily)**

Wt range (kg)	Wt range (lb)	Daily Dose (mg)
<3	<6	consult physician
3-4	6-9	50
5-9	10-19	100
10-14	20-29	200
≥15	≥30	300

### Isoniazid:

**Pediatric twice weekly dosing (20-40 mg/kg po [up to 900 mg] twice weekly)**

Wt range (kg)	Wt range (lb)	Twice Weekly Dose (mg)
<3	<6	consult physician
3-5	6-11	100
6-9	12-19	200
10-12	20-26	300
13-15	27-33	400
16-18	34-39	500
19-21	40-46	600
22-25	47-55	700
26-28	56-61	800
≥29	≥62	900

### Isoniazid:

**Adult daily dosing (5 mg/kg po [up to 300 mg] daily)**

Wt range (kg)	Wt range (lb)	Daily Dose (mg)
<40	<88	consult physician
40-48	88-105	200
≥49	≥106	300

### Isoniazid:

**Adult twice weekly dosing (15 mg/kg po [up to 900 mg] twice weekly)**

Wt range (kg)	Wt range (lb)	Twice Weekly Dose (mg)
<40	<88	consult physician
40-42	88-92	600
43-48	93-105	700
49-55	106-121	800
>55	>121	900

## RIFAMPIN (For Treatment of Latent or Active Disease)

When Rifampin is used to treat latent TB infection, it is only used on a daily basis, not twice weekly.

Twice weekly dosing with Rifampin is for treatment of active TB *only*.

### Rifampin:

Pediatric daily and twice-weekly dosing (10-20 mg/kg po [up to 600 mg] daily or twice weekly)

Wt range (kg)	Wt range (lb)	Daily or Twice-weekly Dose (mg)
<8	<17	consult physician
8-13	17-28	150
14-22	28-48	300
23-35	49-77	450
>35	>77	600

### Rifampin:

Adult daily and twice-weekly dosing (10 mg/kg po [up to 600 mg] daily or twice weekly)

Wt range (kg)	Wt range (lb)	Daily or Twice-weekly Dose (mg)
<40	<88	consult physician
40-48	88-105	450
>48	>105	600

See accompanying American Thoracic Society Information for potential drug-drug interactions involving rifamycins.

## PYRAZINAMIDE “PZA” (For Treatment of Active Disease)

**Pyrazinamide:**

**Daily dosing (15-30 mg/kg po for adults; 15-20 mg/kg for children [both up to max. 2000 mg] daily)**

Wt range (kg)	Wt range (lb)	Daily Dose (mg) RANGE
<10	<22	consult physician
10-15	22-33	150-450 (child – 300 max)
16-25	34-55	240-750 (child – 500 max)
26-35	56-77	390-1050 (child – 700 max)
36-45	78-99	540-1350 (child – 900 max)
46-55	100-121	690-1650 (child – 1100 max)
56-65	122-143	840-1950 (child – 1300 max)
66-75	144-165	990-2000 (child – 1500 max)
>75	>165	2000

**Pyrazinamide:**

**Twice weekly dosing (50-70 mg/kg po twice weekly)**

Wt range (kg)	Wt range (lb)	Twice Weekly Dose (mg) RANGE
<7	<15	consult physician
7-10	15-20	350-700
10-14	21-31	500-980
15-18	32-40	750-1260
19-22	41-48	950-1540
23-29	49-64	1150-2030
30-36	65-79	1500-2520
37-44	80-97	1850-3080
45-54	98-119	2250-3780
55-62	120-136	2750-4340
>62	>136	3100-4340

## ETHAMBUTOL (For Treatment of Active Disease)

### Ethambutol:

Daily dosing (15-25 mg/kg po daily)

Wt range (kg)	Wt range (lb)	Daily Dose (mg)
<4	<8	consult physician
4-7	8-15	100
8-13	16-28	200
14-20	29-44	300
21-26	45-57	400
27-32	58-70	500
33-40	71-88	600
41-46	89-101	700
47-52	102-114	800
53-66	115-145	1000
67-80	146-176	1200
81-105	177-231	1600
106-130	232-286	2000
>130	>286	2400

### Ethambutol:

Twice weekly dosing (50 mg/kg po twice weekly)

Wt range (kg)	Wt range (lb)	Twice Weekly Dose (mg)
<2	<4	consult physician
2-3	4-6	100
4-5	7-11	200
6-7	12-15	300
8-9	16-19	400
10-11	20-24	500
12-13	25-28	600
14-15	29-33	700
16-17	34-37	800
18-22	38-48	1000
23-27	49-59	1200
29-36	60-79	1600
37-44	80-97	2000
45-52	98-114	2400
53-60	115-132	2800
61-68	133-150	3200
69-76	151-167	3600
77-85	168-187	4000
86-93	188-204	4400
93-100	204-220	4800
>100	>220	consult physician

# PYRIDOXINE

## (Recommended in Treatment of Latent or Active Disease)

Pyridoxine is recommended for use during treatment for either latent or active disease. It should be especially considered in cases involving pediatric (excluding infants), pregnant or breastfeeding clients, as well as those on multiple medications or with co-morbid conditions that place the client at a higher risk for adverse effects of anti-tuberculous medications.

### Pyridoxine:

Daily dosing (preferred for but not limited to daily antituberculous therapy)

Age group	Dose (mg po qd)
Prepubescent children	Consult physician
Adolescents and adults	25 mg
Pregnant or lactating women	50mg

### Pyridoxine:

Twice weekly dosing (preferred for but not limited to biweekly antituberculous therapy)

Age group	Dose (mg po twice weekly)
Prepubescent children	consult physician
Adolescents and adults	50 mg

Addenda: Request for Health Officer Consultation form  
Rifamycin interaction pages 639-640, ATS documents American Journal of Critical Care Medicine,  
Vol 167  
Wisconsin TB Program FAQ's about Pyridoxine  
DHHS letter regarding Civil Surgeons technical instructions