

# Diagnosis of Tuberculosis Disease

---

## CONTENTS

<b>Forms Used in this Section .....</b>	<b>4.2</b>
<b>Quick Start Check List .....</b>	<b>4.3</b>
<b>Tuberculosis Screening Guidelines .....</b>	<b>4.6</b>
<b>Introduction .....</b>	<b>4.8</b>
Purpose.....	4.8
Policy .....	4.9
<b>Case Finding .....</b>	<b>4.10</b>
Identifying suspected tuberculosis cases.....	4.10
Follow-up on suspected cases of tuberculosis ..	4.12
<b>Diagnosis of Tuberculosis Disease... ..</b>	<b>4.13</b>
Medical history .....	4.14
Human immunodeficiency virus screening .....	4.16
Physical examination .....	4.17
Tuberculin skin test and interferon gamma release assays.....	4.17
Chest radiography.....	4.18
Bacteriologic examination .....	4.19
<b>Resources and References .....</b>	<b>4.22</b>

## Forms Used in this Section

- [Acknowledgement of TB Counseling](#) (PHSKC)
- [Authorization for Care Coordination](#) (PHSKC)
- [Authorization for Disclosure of Protected Health Information](#) (PHSKC)
- [Chart Audit Tool](#)
- [Civil Detention Flowchart](#)
- [Clinic Record](#) (SHD)
- [Contact Investigation](#)
- [Contact Investigation Instructions](#)
- [Do Not Board \(DNB\) Protocol](#)
- [Home Evaluation](#) (SHD)
- [Home Isolation Agreement](#) (SHD)
- [Isolation Instructions](#) (TPCHD)
- [Isolation Instructions/Spanish](#) (TPCHD)
- [QFT: TB Control Guidelines for Public Health Staff](#) (Thurston County)
- [RVCT Form](#) (CDC)
- [Protocol and Standing Orders](#) (SHD)
- [Public Health Directive \(Adherence\)](#) (PHSKC)
- [Public Health Directive \(Non-Compliance\)](#) (PHSKC)
- [Screening Record](#) (SHD)
- [Tuberculosis Screening Guidelines](#)
- [Voluntary Isolation/Quarantine Agreement](#) (TPCHD)

# Quick Start Check List: Diagnosis of Tuberculosis Disease

This check list is designed to assist public health nurses when evaluating a patient for tuberculosis disease. The tasks below should be performed by licensed nursing, medical, and laboratory staff. This check list requires understanding the instructions in the manual and familiarity with local protocols and standing orders.

Forms can be submitted by fax to the attention of the Washington State TB Services at 360-236-3405 or mail to:

Washington State TB Services

Mailing address: P.O. Box 47837 Olympia, WA 98504

Physical address: 111 Israel Rd SE Tumwater, WA 98501

Tasks for Diagnosis of Tuberculosis Disease	Instructions and Forms
<p><b>Start the initial assessment of the patient within ≤1 business day of the case report</b></p>	<p><b>Instructions:</b></p> <p>Effective TB Interviewing for Contact Investigation</p> <ul style="list-style-type: none"> <li>• <a href="http://www.cdc.gov/tb/publications/guidestoolkits/Interviewing/default.htm">http://www.cdc.gov/tb/publications/guidestoolkits/Interviewing/default.htm</a></li> </ul> <p><b>Forms:</b></p> <ul style="list-style-type: none"> <li>• <a href="#">Home Evaluation</a> (SHD)</li> <li>• <a href="#">Acknowledgement of TB Counseling</a> (PHSKC)</li> <li>• <a href="#">Public Health Directive (Adherence)</a> (PHSKC)</li> <li>• <a href="#">Public Health Directive (Non-Compliance)</a> (PHSKC)</li> <li>• <a href="#">Authorization for Care Coordination</a> (PHSKC)</li> <li>• <a href="#">Authorization for Disclosure of Protected Health Information</a> (PHSKC)</li> <li>• <a href="#">Civil Detention Flowchart</a></li> <li>• <a href="#">Chart Audit Tool</a></li> </ul>
<p><b>Take infection control precautions:</b></p> <ul style="list-style-type: none"> <li><input type="checkbox"/> Isolate the patient, if necessary (if the patient has positive acid-fast bacilli [AFB] sputum smear results and/or cavitary disease)</li> <li><input type="checkbox"/> Advise staff to take personal respiratory precautions, if necessary</li> </ul>	<p><b>Instructions:</b></p> <ul style="list-style-type: none"> <li>• Infection Control (<a href="#">11.1</a>)</li> </ul> <p><b>Forms:</b></p> <ul style="list-style-type: none"> <li>• <a href="#">Letter of Isolation</a> (SHD)</li> <li>• <a href="#">Isolation Instructions</a> (TPCHD)</li> <li>• <a href="#">Isolation Instructions-Spanish</a> (TPCHD)</li> <li>• <a href="#">Voluntary Isolation/Quarantine Agreement</a> (TPCHD)</li> </ul>
<p><b>Evaluate the patient:</b></p> <ul style="list-style-type: none"> <li><input type="checkbox"/> Initiate immediate medical evaluation of patient, if not already done</li> <li><input type="checkbox"/> Assure that a medical evaluation of the patient is <u>completed</u> within 1 week of referral</li> <li><input type="checkbox"/> Gather medical history</li> <li><input type="checkbox"/> Screen for human immunodeficiency virus (HIV)</li> </ul>	<p><b>Instructions:</b></p> <ul style="list-style-type: none"> <li>• <a href="#">Protocol and Standing Orders</a> (SHD)</li> <li>• <a href="#">Tuberculosis Screening Guidelines</a></li> </ul> <p><b>Forms:</b></p> <ul style="list-style-type: none"> <li>• <a href="#">Clinic Record</a> (SHD)</li> <li>• <a href="#">Screening Record</a> (SHD)</li> <li>• <a href="#">Acknowledgement of TB Counseling</a> (PHSKC)</li> </ul>

Tasks for Diagnosis of Tuberculosis Disease	Instructions and Forms
<p><b>Evaluate the patient (continued):</b></p> <ul style="list-style-type: none"> <li><input type="checkbox"/> Conduct a physical examination</li> <li><input type="checkbox"/> Administer, measure, and interpret a Mantoux tuberculin skin test or a IGRA</li> <li><input type="checkbox"/> Order chest radiography</li> <li><input type="checkbox"/> Collect and submit 3 sputum specimens for AFB smear and culture. Obtain specimens 8 to 24 hours apart with one being an early morning specimen</li> <li><input type="checkbox"/> Receive, review and document results of AFB sputum smear tests</li> <li><input type="checkbox"/> Assure that a nucleic acid amplification (NAAT) test is ordered to quickly identify MTB Complex for a patient highly suspicious to have pulmonary tuberculosis.</li> <li><input type="checkbox"/> Reassess information about the patient weekly until drug susceptibility results are available and then at least monthly thereafter</li> <li><input type="checkbox"/> Assess patient for need to restrict travel (do not board)</li> </ul>	<ul style="list-style-type: none"> <li>• <a href="#">Public Health Directive (Adherence)</a> (PHSKC)</li> <li>• <a href="#">Public Health Directive (Non-Compliance)</a> (PHSKC)</li> <li>• <a href="#">Authorization for Care Coordination</a> (PHSKC)</li> <li>• <a href="#">Authorization for Disclosure of Protected Health Information</a> (PHSKC)</li> <li>• <a href="#">Civil Detention Flowchart</a></li> </ul> <p><b>Instructions:</b></p> <ul style="list-style-type: none"> <li>• Laboratory Testing (<a href="#">10.1</a>)</li> <li>• In the WAC, see Chapter 246-101 (Notifiable Conditions) in the Title 246 (Department of Health) at <a href="http://apps.leg.wa.gov/wac/default.aspx?cite=246-101">http://apps.leg.wa.gov/wac/default.aspx?cite=246-101</a></li> </ul> <p>Also, see Notifiable Conditions Guidelines, at <a href="http://www.doh.wa.gov/PublicHealthandHealthcareProviders/NotifiableConditions/Tuberculosis.aspx">http://www.doh.wa.gov/PublicHealthandHealthcareProviders/NotifiableConditions/Tuberculosis.aspx</a></p> <ul style="list-style-type: none"> <li>• <a href="#">Do Not Board Protocol</a></li> </ul>
<p><b>Monitor laboratory test results for culture and drug susceptibility:</b></p> <ul style="list-style-type: none"> <li><input type="checkbox"/> Receive, review and document culture results</li> <li><input type="checkbox"/> Receive, review and document drug susceptibility results as soon as available, usually about four weeks after the patient's initial specimen collection date</li> </ul>	<p><b>Instructions:</b></p> <ul style="list-style-type: none"> <li>• Available Laboratory Tests (Lab Section) (<a href="#">10.8</a>)</li> <li>• The CDC has released "Severe Isoniazid-Associated Liver Injuries Among Persons being Treated for Latent Tuberculosis Infection," available at <a href="http://www.cdc.gov/mmwr/preview/mmwrhtml/m5908a3.htm">http://www.cdc.gov/mmwr/preview/mmwrhtml/m5908a3.htm</a></li> </ul> <p><b>Forms:</b></p> <ul style="list-style-type: none"> <li>• <a href="#">Clinic Record</a> (SHD)</li> <li>• <a href="#">Acknowledgement of TB Counseling</a> (PHSKC)</li> <li>• <a href="#">Public Health Directive (Adherence)</a> (PHSKC)</li> <li>• <a href="#">Public Health Directive (Non-Compliance)</a> (PHSKC)</li> <li>• <a href="#">Authorization for Care Coordination</a> (PHSKC)</li> <li>• <a href="#">Authorization for Disclosure of Protected Health Information</a> (PHSKC)</li> <li>• <a href="#">Civil Detention Flowchart</a></li> </ul>

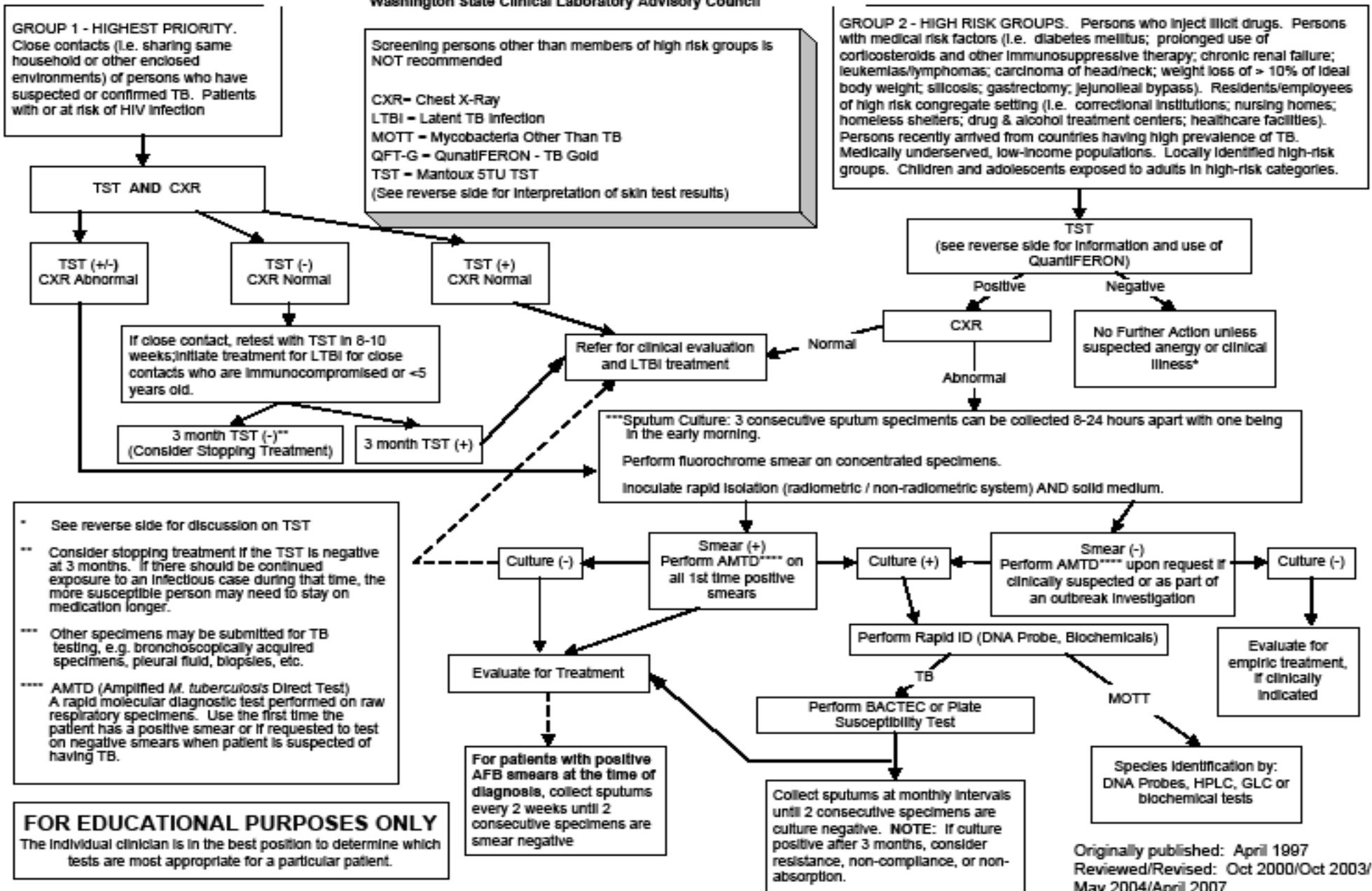
Tasks for Follow up of Patients Diagnosed with Tuberculosis Disease	Instructions and Forms
<p><b>Communicate to Washington State TB program staff:</b></p> <ul style="list-style-type: none"> <li><input type="checkbox"/> Enter information into PHIMS TB within 7 days of the LHJ receiving notification of the suspect OR case</li> <li><input type="checkbox"/> Submit the Contact Investigation form to WA State TB Services within 2 weeks</li> </ul>	<p><b>Forms:</b></p> <ul style="list-style-type: none"> <li>• <a href="#">Contact Investigation</a></li> <li>• <a href="#">Instructions</a></li> </ul>
<p><b>Start the patient on treatment for TB disease</b></p>	<p><b>Instructions:</b></p> <ul style="list-style-type: none"> <li>• Treatment of Disease (<a href="#">5.1</a>)</li> </ul>
<p><b>Manage the case</b></p>	<p><b>Instructions:</b></p> <ul style="list-style-type: none"> <li>• Case Management (<a href="#">8.19</a>)</li> </ul>
<p><b>Conduct the contact investigation</b></p> <ul style="list-style-type: none"> <li><input type="checkbox"/> Submit the TB Contact Investigation Form to WA State TB Services within 2 weeks</li> </ul>	<p><b>Forms:</b></p> <ul style="list-style-type: none"> <li>• <a href="#">Contact Investigation</a></li> <li>• <a href="#">Instructions</a></li> </ul>



The following “Tuberculosis Screening Guidelines” can be used to understand the evaluation process in diagnosing TB disease and LTBI.

# TUBERCULOSIS SCREENING GUIDELINES

Washington State Clinical Laboratory Advisory Council



## INTERPRETATION OF TUBERCULIN SKIN-TEST (TST) RESULTS

<p><b>A. <math>\geq 5\text{mm}</math> is positive for:</b></p> <ul style="list-style-type: none"> <li>. Recent close contacts of persons with active TB</li> <li>. Persons with HIV infection</li> <li>. Persons with fibrotic CXR consistent with healed TB</li> <li>. Organ transplant recipients and other immunosuppressed patients</li> </ul>	<p><b>B. <math>\geq 10\text{mm}</math> is positive for persons who do not meet the criteria in (A.) and who belong to one or more of the following:</b></p> <ul style="list-style-type: none"> <li>. Injection-drug users</li> <li>. Persons with other medical conditions reported to increase risk of progressing from latent to active TB (see list in Group 2 box on the reverse side)</li> <li>. Residents/employees of high-risk congregate settings (i.e. correctional institutions, nursing homes, homeless shelters, drug &amp; alcohol treatment centers, healthcare facilities)</li> <li>. Persons recently arrived from countries having high prevalence of TB (e.g. <math>\leq 5</math> years since arrival)</li> <li>. Medically underserved, low-income populations</li> <li>. Locally identified high-risk groups</li> <li>. Children of any age exposed to adults in high-risk categories</li> </ul>	<p><b>C. <math>\geq 15\text{mm}</math> is positive for persons with no risk factors for TB</b></p>
<p><b>ANERGY</b></p> <ul style="list-style-type: none"> <li>. Anergy testing is poorly standardized or can be selective (e.g. anergy or reactivity to mumps or candida may not reliably predict anergy or ability to respond to TST).</li> <li>. Should not be routinely used as part of screening for TB even in HIV infected patients.</li> </ul>	<p><b>BOOSTER EFFECT</b></p> <ul style="list-style-type: none"> <li>. Persons with TB infection may have negative TST when tested many years after infection</li> <li>. Initial TST may stimulate (boost) ability to react to PPD</li> <li>. Positive reactions to subsequent tests may be misinterpreted as new infection</li> <li>. See Two-Step Testing</li> </ul>	<p><b>TWO-STEP TESTING</b></p> <p>For baseline skin testing of adults who will be retested periodically to distinguish boosted reactions from reactions due to new infections:</p> <ul style="list-style-type: none"> <li>. If first test is (+), consider person infected at baseline</li> <li>. If first test (-), give second test 1-3 weeks later</li> <li>. If second test (+), consider person infected at baseline</li> <li>. If second test (-), consider person uninfected at baseline</li> </ul>

**QuantIFERON (QFT):** The Centers for Disease Control and Prevention (CDC) Guidelines for the use of QFT in diagnosing Latent *Mycobacterium tuberculosis* Infection (LTBI) can be found in the Morbidity Mortality Weekly Report (MMWR), January 31, 2003, Volume 52, pages 15-18 (<http://www.cdc.gov/mmwr/PDF/rr/rr5202.pdf>). CDC states that QFT can aid in detecting *M. tuberculosis* infections among certain populations who are at increased risk for LTBI including recent immigrants from countries with a high prevalence of TB infection, injection-drug users, residents and employees of prisons and jails, and healthcare workers that, after their pre-employment assessment, are considered at increased risk for exposure to TB. CDC states that QFT may also be used for military personnel screening, hospital staff and health-care workers whose risk of prior exposure to TB was low, and U.S.-born students at certain colleges and universities. The full text of the CDC document can be found at: <http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5202a2.htm>.

## REFERENCES

1. Centers for Disease Control and Prevention. Targeted Tuberculin Testing and Treatment of Latent Tuberculosis Infection. MMWR 2000; 49:RR-6.
2. American Thoracic Society/CDC. Diagnostic Standards and Classification of Tuberculosis in Adults and Children. Am J Respir Crit Care Med 2000; 161:1376-1395.
3. CDC. Core Curriculum on Tuberculosis. Fourth Edition. DHHS, 2000.
4. ATS/CDC. Treatment of Tuberculosis and Tuberculosis Infection in Adults and Children. Am J Resp Crit Care Med 1994;149:1359-1374.
5. CDC. Guidelines for Using the QuantIFERON-TB Gold Test for Detecting *Mycobacterium tuberculosis* Infection USA. MMWR, Dec. 16, 2006, Vol. 54 (RR15), pages 49-55.
6. American Thoracic Society/CDC/Infectious Diseases Society of America: Treatment of Tuberculosis. 2003. Respir Crit Care Med, vol.167, pp 603-662.

---

# Introduction

## Purpose

Use this section to understand and follow national and Washington State guidelines to do the following:

- Classify patients with tuberculosis (TB) disease and latent TB infection (LTBI).
- Detect suspected cases of TB.
- Know when to report suspected or confirmed cases of TB.
- Diagnose TB disease.

It is important to understand when a person should be evaluated further for TB disease. Not recognizing TB symptoms promptly will lead to delays in treating a TB case—and to more infection, TB disease, and contacts to evaluate.

In the 2005 guideline, “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 early and accurate detection, diagnosis, and reporting of TB cases, leading to initiation and completion of treatment.<sup>1</sup>



Contacts are mentioned within this section, but their evaluation and follow-up and contact investigation are covered in more depth in the Contact Investigation section of the manual ([9.1](#))

Improvement in the detection of TB cases is essential to progress toward elimination of TB in the United States.<sup>2</sup> Case detection includes the processes that lead to the presentation, evaluation, receipt of diagnosis, and reporting of persons with active TB.<sup>3</sup> Detecting and reporting suspected cases of TB are key steps in stopping transmission of *Mycobacterium tuberculosis* because it leads to prompt initiation of effective multiple-drug treatment, which rapidly reduces infectiousness.<sup>4</sup>

TB is commonly diagnosed when a person seeks medical attention for symptoms caused by the disease or a concomitant medical condition. Thus, healthcare providers, particularly those providing primary healthcare to populations at high risk, are key contributors to TB case detection.<sup>5</sup> The majority of pulmonary TB cases continue to be diagnosed at an advanced stage. Earlier diagnosis would result in less individual morbidity and death, greater success in treatment, less transmission to contacts, and fewer outbreaks of TB.<sup>6</sup>

A diagnosis of TB disease is usually based on positive cultures for *M. tuberculosis*. However, TB may also be diagnosed on the basis of clinical signs and symptoms in the absence of a positive culture.

# Policy

In Washington State:

- Persons who show or report signs and symptoms of TB should be evaluated for TB disease as described in the “Diagnosis of Tuberculosis Disease” topic in this section of the manual (4.1) and reported as suspected cases of TB as described in the “Reporting Tuberculosis” topic in the Surveillance section of the manual (2.8).
- Contacts should be evaluated as described in the Contact Investigation section of the manual (9.1)



For roles and responsibilities, refer to the “Roles, Responsibilities, and Contact Information” topic in the Introduction of the manual (1.16).



For more information regarding Protocol and Standing Orders for local health jurisdictions, please see “[Protocol and Standing Orders](#)” located in the **FORMS** section of the manual.



To identify required and recommended forms, refer to the “Quick Start Check List: Diagnosis of Tuberculosis Disease” in this section of the manual or check the **FORMS** section of the manual.

---

# Case Finding

## Identifying Suspected Tuberculosis Cases

The majority of tuberculosis (TB) cases are detected during the medical evaluation of symptomatic illnesses. Persons experiencing symptoms ultimately attributable to TB usually seek care not at a public health TB clinic but rather from other medical practitioners in other healthcare settings.<sup>7</sup> Professionals in the primary healthcare sector, including hospital and emergency department clinicians, should be trained to recognize patients with symptoms consistent with TB.<sup>8</sup>

Be alert for cases of TB among persons who have not sought medical care during evaluation of contacts to patients with pulmonary TB and to other persons with newly diagnosed infection with *Mycobacterium tuberculosis*. Perform screening for TB also during evaluation of immigrants and refugees with Class B1 or Class B2 TB notification status, during evaluations of persons involved in TB outbreaks, and occasionally in working with populations with a known high incidence of TB. Also, screen for TB disease when the risk for TB in the population is high and when the consequences of an undiagnosed case of TB are severe, such as in jails, prisons, and other correctional facilities.<sup>9</sup>

Suspect pulmonary TB and initiate a diagnostic investigation when the historic features, signs, symptoms, and radiographic findings listed in Table 1 occur among adults. The clinical presentation of TB varies considerably as a result of the extent of the disease and the patient's response. **TB should be suspected in any patient who has a persistent cough for more than 2 to 3 weeks, or other compatible signs and symptoms.**<sup>10</sup>

**Note that these symptoms should suggest a diagnosis of TB but are not required. TB should still be considered a diagnosis in asymptomatic patients who have risk factors for TB and chest radiographs compatible with TB.**



All persons who have a chronic cough for more than 2 to 3 weeks<sup>11</sup> should be evaluated and be asked to use a mask or tissue to cover their mouth. Hemoptysis, or coughing up blood, is a serious symptom, and patients who cough up blood should be evaluated as soon as possible. Be sure to have these patients use a mask and tissues.

**TABLE 1: WHEN TO SUSPECT PULMONARY TUBERCULOSIS IN ADULTS<sup>12</sup>**

<b>Historic Features</b>	<ul style="list-style-type: none"> <li>• Exposure to a person with infectious tuberculosis (TB)</li> <li>• Positive test result for <i>Mycobacterium tuberculosis</i> infection</li> <li>• Presence of risk factors, such as immigration from a high-prevalence area, human immunodeficiency virus (HIV) infection, homelessness, or previous incarceration</li> <li>• Diagnosis of community-acquired pneumonia that has not improved after 7 days of treatment<sup>†,13</sup></li> </ul>
<b>Signs and Symptoms Typical of TB</b>	<ul style="list-style-type: none"> <li>• Prolonged coughing (≥2–3 weeks) with or without production of sputum that might be bloody (hemoptysis)<sup>§,14</sup></li> <li>• Chest pain<sup>15</sup></li> <li>• Chills<sup>16</sup></li> <li>• Fever</li> <li>• Night sweats</li> <li>• Loss of appetite<sup>17</sup></li> <li>• Weight loss</li> <li>• Weakness or easy fatigability<sup>18</sup></li> <li>• Malaise (a feeling of general discomfort or illness)<sup>19</sup></li> </ul>
<b>Chest Radiograph: Immunocompetent patients</b>	<ul style="list-style-type: none"> <li>• Classic findings of TB are upper-lobe opacities, frequently with evidence of contraction fibrosis and cavitation<sup>¶</sup></li> </ul>
<b>Chest Radiograph: Patients with advanced HIV infection</b>	<ul style="list-style-type: none"> <li>• Lower-lobe and multilobar opacities, hilar adenopathy, or interstitial opacities might indicate TB</li> </ul>
<p>† Patients treated with levofloxacin or moxifloxacin may have a clinical response when TB is the cause of the pneumonia.</p> <p>§ Do <b>not</b> wait until sputum is bloody to consider a productive cough a symptom of TB. Sputum produced by coughing does <b>not</b> need to be bloody to be a symptom of TB.</p> <p>¶ These features are not specific for TB, and, for every person in whom pulmonary TB is diagnosed, an estimated 10–100 persons are suspected on the basis of clinical criteria and must be evaluated.</p>	

Source: Adapted from: ATS, CDC, IDSA. Controlling tuberculosis in the United States: recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America. *MMWR* 2005;54(No. RR-12):33.

## Extrapulmonary Tuberculosis

If a patient has a positive tuberculin skin test or interferon gamma release assay (IGRA), consider signs and symptoms of extrapulmonary TB. See Available Laboratory Tests, Table 2 ([10.8](#)) for labs within Washington State that perform IGRA testing.

## Follow-up on Suspected Cases of Tuberculosis

When a suspected case of TB is identified, the following should be done:



In the WAC, see Chapter 246-101 (Notifiable Conditions) in the Title 246 (Department of Health) at <http://apps.leg.wa.gov/wac/default.aspx?cite=246-101>

Also, see Notifiable Conditions Guidelines, at <http://www.doh.wa.gov/PublicHealthandHealthcareProviders/NotifiableConditions/Tuberculosis.aspx>



When a suspected case of pulmonary TB is identified, refer to Table 2: Guidelines for the Evaluation of Pulmonary Tuberculosis in Adults in Five Clinical Scenarios in the “Diagnosis of Tuberculosis Disease” topic in this section. This table presents guidelines for the initial steps of TB case detection in five clinical scenarios encountered by providers of primary health care, including those serving in medical emergency departments.<sup>20</sup>



To formally report a suspected case of TB, see the “Reporting Tuberculosis” topic in the Surveillance section of the manual ([2.8](#)).



The patient should be masked and immediately excluded from the workplace or placed in airborne infection isolation (AII) until confirmed noninfectious. For more information, see the “Isolation” topic in the Infection Control section of the manual ([11.15](#)).



Laboratories must report positive smears and positives cultures, and primary healthcare providers should report suspected or confirmed cases of TB to the local health jurisdiction, as specified in the “Reporting Tuberculosis” topic in the Surveillance section of the manual ([2.8](#)). Prompt reporting allows the local health jurisdiction to organize treatment and case management services and to initiate a contact investigation as quickly as possible.<sup>21</sup>



Within 48 hours of suspect identification, administer a tuberculin skin test (TST) or perform an interferon gamma release assay (IGRA) and/or provide a chest radiograph (if these activities had not already been completed). Evaluate the patient for TB disease as specified in the “Diagnosis of Tuberculosis Disease” topic in this section of the manual ([4.1](#)).



For more information regarding Protocol and Standing Orders for local health jurisdictions, please see the “[Protocol and Standing Orders](#)” form in the **FORMS** section of the manual.

---

# Diagnosis of Tuberculosis Disease

Consideration of tuberculosis (TB) disease as a possible diagnosis is the first step that must be taken before further evaluation, diagnosis, and management can occur. The diagnosis of TB disease is often overlooked because of the failure to consider it among possible diagnoses. While a definitive diagnosis may involve the addition of laboratory and radiographic findings, a high degree of suspicion can be based on epidemiology, medical history, and physical examination. In considering TB disease, it is also important to consider factors that may affect the typical presentation of TB, such as the patient's age, nutritional status, and coexisting diseases.

An individual who is suspected of having TB disease requires a complete medical evaluation, including the following:

- Medical history, including exposure, symptoms, previous treatment for TB, and risk factors
- Human immunodeficiency virus (HIV) screening
- Physical examination
- Tuberculin skin test (TST) or interferon gamma release assay (IGRA)
- Chest radiography
- Bacteriologic examination

When a suspected case of pulmonary TB is identified, refer to Table 2 for guidelines for the initial steps of TB case detection in five clinical scenarios encountered by providers of primary healthcare, including those serving in medical emergency departments.<sup>22</sup>



In the WAC, see Chapter 246-101 (Notifiable Conditions) in the Title 246 (Department of Health) at

<http://apps.leg.wa.gov/wac/default.aspx?cite=246-101>

Also, see Notifiable Conditions Guidelines, at

<http://www.doh.wa.gov/PublicHealthandHealthcareProviders/NotifiableConditions/Tuberculosis.aspx>

**TABLE 2: GUIDELINES FOR THE EVALUATION OF PULMONARY TUBERCULOSIS IN ADULTS IN FIVE CLINICAL SCENARIOS<sup>23</sup>**

Patient and Setting	Recommended Evaluation
Any patient with a cough of ≥2–3 weeks' duration	Chest radiograph: If suggestive of tuberculosis (TB)*, collect 3 sputum specimens for acid-fast bacilli (AFB) smear microscopy, culture, and nucleic acid amplification (NAA).
Any patient at high risk for TB with an unexplained illness, including respiratory symptoms of ≥2–3 weeks' duration†	Chest radiograph: If suggestive of TB, collect 3 sputum specimens for AFB smear microscopy, culture, and NAA (available at PHL)
Any patient with human immunodeficiency virus (HIV) infection and unexplained cough or fever	Chest radiograph, and collect 3 sputum specimens for AFB smear microscopy, culture, and NAA (available at PHL)
Any patient at high risk for TB with a diagnosis of community-acquired pneumonia who has not improved after 7 days of treatment†	Chest radiograph, and collect 3 sputum specimens for AFB smear microscopy, culture, and NAA (available at PHL)
Any patient at high risk for TB with incidental findings on chest radiograph suggestive of TB even if symptoms are minimal or absent†§	Review of previous chest radiographs, if available, 3 sputum specimens for AFB smear microscopy, NAA (available at PHL), and culture
<p>* Opacities with or without cavitation in the upper lobes or the superior segments of the lower lobes.<sup>24</sup></p> <p>† See Table 2: Persons at High Risk for Tuberculosis Infection and Progression to Tuberculosis Disease.</p> <p>§ Chest radiograph performed for any reason, including targeted testing for latent TB infection and screening for TB disease.</p>	

Source: Adapted from: ATS, CDC, IDSA. Controlling tuberculosis in the United States: recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America. *MMWR* 2005;54(No. RR-12):33.

## Medical History

The clinician should interview patients to document their medical histories. A written record of a patient's medical history should include the following:

- Exposure to infectious TB
- Symptoms of TB disease (as listed in Table 1: When to Suspect Pulmonary Tuberculosis in Adults, Table 2: Guidelines for the Evaluation of Pulmonary Tuberculosis in Adults in Five Clinical Scenarios, and Table 3: Symptoms of Tuberculosis Disease)
- Previous TB infection or disease
- Risk factors
- Recent medical encounters (e.g., going to the emergency department for pneumonia)
- Previous antibiotic therapy

## 1. Exposure to infectious TB:

### Ask patients if they have spent time with someone with infectious TB.

Question patients about whether they know of any contact in the recent or distant past with persons diagnosed with pulmonary or laryngeal TB. It is important to note that patients often refer to latent TB infection (LTBI) as TB disease. Be aware that most persons become infected with *Mycobacterium tuberculosis* without knowing they were exposed. Clinicians should also consider demographic factors that may increase a patient's risk for exposure to TB disease and drug-resistant TB, such as country of origin, age, ethnic or racial group, occupation, and residence in congregate settings (such as a jail, homeless shelter, or refugee camp).

## 2. Symptoms of TB Disease:

### Ask patients about their symptoms.

Although TB disease does not always produce symptoms, most patients with TB disease have one or more symptoms that led them to seek medical care. When symptoms are present, they usually have developed gradually and been present for weeks or even months. Occasionally, however, TB is discovered during a medical examination for an unrelated condition, such as ruling out a cancer diagnosis (e.g., through a chest radiograph given to patients before surgery).

The symptoms in Table 3 below may be caused by other diseases, but they should prompt the clinician to suspect TB disease. For historic features and chest radiograph results that should raise suspicion of pulmonary TB disease, refer to Table 1: When to Suspect Pulmonary Tuberculosis in Adults.

TABLE 3: SYMPTOMS OF TUBERCULOSIS DISEASE<sup>25</sup>

Pulmonary	General: Pulmonary and Extrapulmonary	Extrapulmonary
<ul style="list-style-type: none"><li>• Coughing</li><li>• Coughing up sputum or blood</li><li>• Pain in the chest when breathing or coughing</li></ul>	<ul style="list-style-type: none"><li>• Chills<sup>26</sup></li><li>• Fever</li><li>• Night sweats</li><li>• Loss of appetite<sup>27</sup></li><li>• Weight loss</li><li>• Weakness or easy fatigability<sup>28</sup></li><li>• Malaise (a feeling of general discomfort or illness)<sup>29</sup></li></ul>	<ul style="list-style-type: none"><li>• The symptoms depend on part of body affected by tuberculosis (TB) disease</li><li>• TB of the spine may cause pain in the back.</li><li>• TB of the kidney may cause blood in the urine.</li><li>• Meningeal TB may cause headaches or psychiatric symptoms.</li><li>• Lymphatic TB may cause swollen and tender lymph nodes, often at the base of the neck.</li><li>• Pleural</li><li>• Laryngeal</li></ul>

Source: Adapted from: ATS, CDC, IDSA. Controlling tuberculosis in the United States: recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America. *MMWR* 2005;54(No. RR-12):33.

### 3. Previous Latent TB Infection or TB Disease:

Ask patients whether they have ever been diagnosed with or treated for TB infection or disease.

- **Patients who have had TB disease before** should be asked when they had the disease and how the disease was treated. Ask how many pills were taken per day (to determine what treatment regimen was used and whether they received injections). If the regimen prescribed was inadequate or if the patient did not follow the recommended treatment, TB may recur, and it may be resistant to one or more of the drugs used.
- **Patients known to have a positive skin test reaction or positive Interferon Gamma Release Assay (IGRA)** probably have TB infection. If they were infected within the past two years, they are at high risk for TB disease if certain immunosuppressive conditions exist or if immunosuppressive therapies are being taken. For persons previously skin tested, an increase in induration of 10 mm within a two-year period is classified as a conversion to positive or positive Interferon Gamma Release Assay (IGRA).

### 4. Risk Factors for Developing TB Disease:

Determine whether patients have any conditions or behaviors that are risk factors for developing TB disease.

## Human Immunodeficiency Virus Screening

Voluntary counseling and testing for human immunodeficiency virus (HIV) is recommended for all patients with TB. HIV counseling and testing has also been recommended for contacts of persons with TB.<sup>30</sup>

The Centers for Disease Control and Prevention (CDC) recommends the following:

- HIV screening for patients in all health-care settings after the patient is notified that testing will be performed unless the patient declines (opt-out screening).
- Routine HIV testing for persons suspected of having TB disease and contacts to TB patients.
- Persons at high risk for HIV infection should be screened for HIV at least annually<sup>31</sup>



New HIV testing, counseling, and partner services rules offer flexibility to health care providers and local health jurisdictions. Please visit

<http://www.doh.wa.lcl/YouandYourFamily/IllnessandDisease/HIVAIDS/Prevention/InformationforProviders.aspx> for more information.

## Physical Examination

A physical examination is an essential part of the evaluation of any patient. It cannot be used to confirm or rule out TB, but it can provide valuable information about the patient's overall condition; other factors, such as human immunodeficiency virus (HIV) infection, which may affect how TB is manifested; and the presence of extrapulmonary TB.<sup>32</sup>

## Tuberculin Skin Test and Interferon Gamma Release Assays (IGRA)

Use the Mantoux tuberculin skin test (TST) or an interferon gamma release assay (IGRA) to test for *M. tuberculosis* infection. Note that for patients with a previous documented positive TST reaction, a TST is not necessary. However, an IGRA can be done if there is suspicion that the TST result was a false positive. Additional tests, such as chest radiography and bacteriologic examination, are required to confirm TB disease.<sup>33</sup>

Blood assay for *Mycobacterium tuberculosis* (BAMT) is a general term referring to recently developed in vitro diagnostic tests that assess for the presence of infection with *M. tuberculosis*. This term includes, but is not limited to IGRAs. The IGRAs currently approved by the Food and Drug Administration (FDA) and available on the market are QuantiFERON<sup>®</sup>-TB Gold in-tube (QFT<sup>™</sup>), QuantiFERON<sup>®</sup>-TB test (QFT), QuantiFERON<sup>®</sup>-TB Gold test (QFT-G) and the T-SPOT<sup>®</sup>.TB test, which can be used in all circumstances in which the TST is used. IGRA usually can be used in place of the TST.<sup>34</sup> Other cytokine-based immunoassays are under development and may also become useful in the diagnosis of *M. tuberculosis* infection. Future FDA-licensed products, in combination with Centers for Disease Control and Prevention (CDC)-issued recommendations, may provide additional diagnostic alternatives.<sup>35</sup>

The advantages of IGRA, compared with the TST, are that results can be obtained after a single patient visit, and that, because it is a blood test performed in a qualified laboratory, the variability associated with skin test reading can be eliminated.<sup>36</sup> In addition, the IGRA test appears to be less affected by past bacille of Calmette-Guérin (BCG) vaccination than the TST and may eliminate the unnecessary treatment of patients with BCG-related false-positive results.<sup>37</sup> However, the IGRA test has practical limitations that include the need to draw blood and to ensure its receipt in a qualified laboratory in time for testing. For IGRA tests, the blood must be incubated with the test antigens less than 12 hours after collection, while the lymphocytes are viable.<sup>38</sup> (Note: When newer IGRA tests are available, this time frame may differ.)

For both the TST and IGRA, additional tests, such as chest radiography and bacteriologic examination, are required to confirm TB disease.<sup>39</sup>

Persons with a positive TST result, regardless of signs and symptoms, should be evaluated for TB disease before LTBI is diagnosed. At a minimum, a chest radiograph should be examined for abnormalities consistent with TB disease.<sup>40</sup>

A negative TST does not rule out TB disease<sup>41</sup>—as many as 20% of patients with TB disease have a negative TST reaction.<sup>42</sup> A negative TST result should not be used alone to exclude *M.*

*tuberculosis* infection in persons with symptoms or signs suggestive of TB disease. Medical evaluation of such persons should include a history and physical examination, chest radiograph, bacteriologic studies, serology for human immunodeficiency virus (HIV), and, when indicated, other tests or studies.<sup>43</sup>



For more information on the Mantoux TST, see the Diagnosis of Latent Tuberculosis Infection section of the manual ([6.1](#)).

For more information on IGRAs and the QuantiFERON<sup>®</sup>-TB Gold (QFT-G) Test, see the CDC's "Guidelines for Using the QuantiFERON<sup>®</sup>-TB Gold Test for Detecting *Mycobacterium tuberculosis* Infection, United States" (*MMWR* 2005;54[No. RR-15]) at <http://www.cdc.gov/mmwr/pdf/rr/rr5415.pdf>.

CDC released new Interferon Gamma Release Assays (IGRA) guidelines on June 25, 2010, "Updated Guidelines for Using Interferon Gamma Release Assays to Detect *Mycobacterium tuberculosis* Infection — United States, 2010" (*MMWR* 2010; 59 [No. RR-5];1-25) at <http://www.cdc.gov/mmwr/PDF/rr/rr5905.pdf>.

CDC has also developed the Interferon-Gamma Release Assays (fact sheet) that will assist you in learning more about IGRAs.

<http://www.cdc.gov/tb/publications/factsheets/testing/IGRA.htm>



For more information regarding QFT healthcare worker guidelines see [QFT: TB Control Guidelines for Public Health Staff](#) (Forms Section).



Find answers to common questions posed by healthcare professionals on the use of QFT at

<http://www.cellestis.com/IRM/Company/ShowPage.aspx?CPID=1588&EID=60701344>.

## Chest Radiography

A posterior-anterior radiograph of the chest is the standard view used for the detection and description of chest abnormalities in adults. In some instances, other views (e.g., lateral, lordotic) or additional studies (e.g., computed tomography [CT] scans) may be necessary.



Children younger than 5 years of age should receive posterior-anterior and lateral radiographs.<sup>44</sup>

Certain abnormalities on chest radiographs are suggestive, but are not diagnostic, of TB. In pulmonary TB, radiographic abnormalities are often seen in the apical and posterior segments of the upper lobe or in the superior segments of the lower lobe. However, lesions may appear anywhere in the lungs and may differ in size, shape, density, and presence or absence of cavitation, especially in HIV-infected and other immunosuppressed persons.

In HIV-infected persons, pulmonary TB may present atypically on the chest radiograph. For example, TB may cause opacities without cavities in any lung zone, or it may cause mediastinal or hilar lymphadenopathy with or without accompanying opacities and/or cavities. In HIV-infected persons, almost any abnormality on a chest radiograph may indicate TB. In fact, the radiograph of an HIV-infected person with TB disease may even appear entirely normal.<sup>45</sup>



For more information on chest radiography, see the Curry International Tuberculosis Center's *Radiographic Manifestations of Tuberculosis: A Primer for Clinicians* (2006) at <http://www.currytbcenter.ucsf.edu/radiographic/>

## Bacteriologic Examination

Refer to Table 4 below to determine the types of specimens needed to assist in the diagnosis of TB.

**TABLE 4: SPECIMENS FOR DIAGNOSING TUBERCULOSIS DISEASE**

Suspected Diagnosis	Specimen Needed
<b>Pulmonary or laryngeal tuberculosis (TB)</b>	<p>Sputum (phlegm from deep in the lungs) samples for smear and culture examination.</p> <p>If a diagnosis of pulmonary TB cannot be established from sputum smear, other procedures may be necessary, including nucleic acid amplification (NAA), bronchoscopy, and gastric aspiration in children.</p>
<b>Extrapulmonary TB</b>	<p>Depending on the anatomical site, other clinical specimens are necessary, such as:</p> <ul style="list-style-type: none"> <li>• Urine</li> <li>• Cerebrospinal fluid</li> <li>• Pleural fluid</li> <li>• Pus or other aspirated fluid</li> <li>• Biopsy specimens</li> <li>• Blood</li> </ul>

Refer to Table 5 below for information on the bacteriologic tests used to diagnose TB.

**TABLE 5: BACTERIOLOGIC TESTS USED IN DIAGNOSING TUBERCULOSIS DISEASE<sup>46</sup>**

Test	Description	Laboratory Turnaround Times
<b>Acid-Fast Bacilli (AFB) Smear</b>	<ul style="list-style-type: none"> <li>Provides the physician with a preliminary confirmation of the diagnosis. It usually is the first bacteriologic evidence of the presence of mycobacteria in a clinical specimen.</li> <li>If positive, gives a semiquantitative estimate of the number of bacilli being excreted (which is of vital clinical and epidemiologic importance in assessing the patient's infectiousness).</li> </ul>	<ul style="list-style-type: none"> <li>Within 24 hours from receipt of specimen in the laboratory.<sup>47</sup></li> </ul>
<b>Nucleic Acid Amplification (NAA) Assay<sup>48</sup></b>	<ul style="list-style-type: none"> <li>A test done on sputum specimens for the direct and rapid identification of the <i>Mycobacterium tuberculosis</i> complex.</li> <li>Allows for the amplification of specific target sequences of nucleic acids that will be detected by a nucleic acid probe.</li> <li>Does not replace the need for routine AFB smear and culture.<sup>49</sup></li> </ul>	<ul style="list-style-type: none"> <li>Within 2-3 working days from receipt of specimen in the laboratory.<sup>50,51</sup></li> </ul>
<b>Culture</b>	<ul style="list-style-type: none"> <li>Usually necessary for species identification of all clinical specimens suspected of containing mycobacteria.</li> <li>Is required for drug susceptibility testing and genotyping.</li> </ul>	<ul style="list-style-type: none"> <li>Mycobacterial growth detection: within 14 days from specimen collection</li> <li>Identification of mycobacteria: within 21 days from specimen collection<sup>52,53</sup></li> </ul>
<b>Drug Susceptibility Testing</b>	<ul style="list-style-type: none"> <li>For first-line drugs: Is performed on initial isolates of all patients to identify an effective antituberculosis regimen.</li> <li>For both first-line and second-line drugs: Is repeated on interim isolates when a patient remains culture-positive after 3 months of treatment.<sup>54,55</sup></li> </ul>	<ul style="list-style-type: none"> <li>First-line drugs: within 30 days from specimen collection.</li> <li>Second-line drugs: within 4 weeks from date of request.<sup>56,57</sup></li> </ul>
<b>Drug Resistance Screening by Sequencing (DRSS)</b>	<ul style="list-style-type: none"> <li>Allows rapid confirmation of MDR TB through the identification of genetic mutations associated with RIF and INH resistance – MDR case. Also the DRSS examines the genetic loci that are associated with resistance to the most effective second-line drugs, fluoroquinolones (FQ) and the injectables amakacin (AMK), kanamycin (KAN) and capreomycin (CAP) will be examined.<sup>58</sup></li> </ul>	<ul style="list-style-type: none"> <li>DRSS results are available within 3-4 business days from the receipt of specimen at the WA PHL laboratory.</li> <li>DRSS is a presumptive test and needs to be confirmed by traditional susceptibility testing. WA PHL performs confirmation for the First line drugs (up to 14 days MTBC identification) and Second line drug (28 days from the receipt of the specimen [reference cultures] or MTBC identification).</li> </ul>

Sources: ATS, CDC, IDSA. Controlling tuberculosis in the United States: recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America. *MMWR* 2005;54(No. RR-12):19; and Tenover, R., et al. The resurgence of tuberculosis: is your laboratory ready? *Journal of Clinical Microbiology* 1993:767–770.

Laboratories must report positive smears or positive cultures within **2 business days**, and primary healthcare providers should report **immediately** suspected and confirmed cases of TB to the local health jurisdictions, as specified in the “Reporting Tuberculosis” topic in the Surveillance section ([2.8](#)). See [WAC 246-101](#). Prompt reporting allows the health department to organize treatment and case management services and to initiate a contact investigation as quickly as possible.<sup>59</sup>



For information on reporting, see the “Reporting Tuberculosis” topic in the Surveillance section of the manual ([2.8](#)).



For information on process for collecting specimens see the “Specimen Collection” topic in the Laboratory section of the manual ([10.13](#)).



In the WAC, see Chapter 246-101 (Notifiable Conditions) in the Title 246 (Department of Health) at <http://apps.leg.wa.gov/wac/default.aspx?cite=246-101>

Also, see Notifiable Conditions Guidelines, at <http://www.doh.wa.gov/PublicHealthandHealthcareProviders/NotifiableConditions/Tuberculosis.aspx>



The Curry International Tuberculosis Center has developed a web presentation on “Practical Solutions for TB Infection Control: Infectiousness and Isolation” available at <http://www.currytbcenter.ucsf.edu/tbicweb/>



For laboratory ([10.8](#)) services available at the Washington State Public Health Laboratory, contact TB Laboratory Supervisor at 206-418-5474.

---

# Resources and References

## Resources

- ATS, CDC, IDSA. “Diagnostic Standards and Classification of Tuberculosis in Adults and Children” (*Am J Respir Crit Care Med* 2000;161[4 Pt 1]). Available at: <http://www.cdc.gov/tb/publications/PDF/1376.pdf> .
- CDC. *Self-Study Modules on Tuberculosis* (Division of Tuberculosis Elimination Web site; 1999). Available at: <http://www.cdc.gov/tb/education/ssmodules/default.htm> .
- CDC. *Core Curriculum on Tuberculosis (2011)* (Division of Tuberculosis Elimination Web site; updated November 2011). Available at: <http://www.cdc.gov/tb/pubs/corecurr/default.htm>.
- Tenover, R., et al. “The Resurgence of Tuberculosis: Is Your Laboratory Ready?” (*Journal of Clinical Microbiology* 1993;767–770).

## References

---

- <sup>1</sup> ATS, CDC, IDSA. Controlling tuberculosis in the United States: recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America. *MMWR* 2005;54(No. RR-12):15. Available at <http://www.cdc.gov/mmwr/PDF/rr/rr5412.pdf>
- <sup>2</sup> ATS, CDC, IDSA. Controlling tuberculosis in the United States: recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America. *MMWR* 2005;54(No. RR-12):32.
- <sup>3</sup> ATS, CDC, IDSA. Controlling tuberculosis in the United States: recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America. *MMWR* 2005;54(No. RR-12):32.
- <sup>4</sup> ATS, CDC, IDSA. Controlling tuberculosis in the United States: recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America. *MMWR* 2005;54(No. RR-12):15.
- <sup>5</sup> ATS, CDC, IDSA. Controlling tuberculosis in the United States: recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America. *MMWR* 2005;54(No. RR-12):15–16.
- <sup>6</sup> ATS, CDC, IDSA. Controlling tuberculosis in the United States: recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America. *MMWR* 2005;54(No. RR-12):32.
- <sup>7</sup> ATS, CDC, IDSA. Controlling tuberculosis in the United States: recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America. *MMWR* 2005;54(No. RR-12):32.
- <sup>8</sup> ATS, CDC, IDSA. Controlling tuberculosis in the United States: recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America. *MMWR* 2005;54(No. RR-12):32.
- <sup>9</sup> ATS, CDC, IDSA. Controlling tuberculosis in the United States: recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America. *MMWR* 2005;54(No. RR-12):34.
- <sup>10</sup> ATS, CDC, IDSA. Controlling tuberculosis in the United States: recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America. *MMWR* 2005;54(No. RR-12):33.
- <sup>11</sup> ATS, CDC, IDSA. Controlling tuberculosis in the United States: recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America. *MMWR* 2005;54(No. RR-12):33.
- <sup>12</sup> ATS, CDC, IDSA. Controlling tuberculosis in the United States: recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America. *MMWR* 2005;54(No. RR-12):33; CDC. Medical evaluation. In: Chapter 5: diagnosis of TB. *Core Curriculum on Tuberculosis (2000)* [Division of Tuberculosis Elimination Web site]. Updated November 2001. Available at: <http://www.cdc.gov/tb/education/corecurr/index.htm>; CDC. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care settings, 2005. *MMWR* 2005;54(No. RR-17):11; ATS, CDC, IDSA. Diagnostic standards and classification of tuberculosis in adults and children. *Am J Respir Crit Care Med*. 2000;161:1378; CDC. Module 3: diagnosis of tuberculosis infection and disease. *Self-Study Modules on Tuberculosis* [Division of Tuberculosis Elimination Web site]. 1999:3. Available at: <http://www.cdc.gov/tb/education/ssmodules/default.htm>.
- <sup>13</sup> ATS, CDC, IDSA. Controlling tuberculosis in the United States: recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America. *MMWR* 2005;54(No. RR-12):33.
- <sup>14</sup> ATS, CDC, IDSA. Controlling tuberculosis in the United States: recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America. *MMWR* 2005;54(No. RR-12):33.

- 
- <sup>15</sup> CDC. Medical evaluation. In: Chapter 5: diagnosis of TB. *Core Curriculum on Tuberculosis (2000)* [Division of Tuberculosis Elimination Web site]. Updated November 2001. Available at: <http://www.cdc.gov/tb/education/corecurr/index.htm>; and CDC. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care settings, 2005. *MMWR* 2005;54(No. RR-17):11.
- <sup>16</sup> CDC. Medical evaluation. In: Chapter 5: diagnosis of TB. *Core Curriculum on Tuberculosis (2000)* [Division of Tuberculosis Elimination Web site]. Updated November 2001. Available at: <http://www.cdc.gov/tb/education/corecurr/index.htm>; and CDC. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care settings, 2005. *MMWR* 2005;54(No. RR-17):11.
- <sup>17</sup> ATS, CDC, IDSA. Diagnostic standards and classification of tuberculosis in adults and children. *Am J Respir Crit Care Med* 2000;161:1378; CDC. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care settings, 2005. *MMWR* 2005;54(No. RR-17):11; and CDC. Medical evaluation. In: Chapter 5: diagnosis of TB. *Core Curriculum on Tuberculosis (2000)* [Division of Tuberculosis Elimination Web site]. Updated November 2001. Available at: <http://www.cdc.gov/tb/education/corecurr/index.htm>.
- <sup>18</sup> CDC. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care settings, 2005. *MMWR* 2005;54(No. RR-17):11; and ATS, CDC, IDSA. Diagnostic standards and classification of tuberculosis in adults and children. *Am J Respir Crit Care Med* 2000;161:1378.
- <sup>19</sup> CDC. Module 3: diagnosis of tuberculosis infection and disease. *Self-Study Modules on Tuberculosis* [Division of Tuberculosis Elimination Web site]. 1999:3. Available at: <http://www.cdc.gov/tb/education/ssmodules/default.htm>; and CDC. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care settings, 2005. *MMWR* 2005;54(No. RR-17):11.
- <sup>20</sup> ATS, CDC, IDSA. Controlling tuberculosis in the United States: recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America. *MMWR* 2005;54(No. RR-12):33.
- <sup>21</sup> CDC. Diagnostic microbiology. In: Chapter 5: diagnosis of TB. *Core Curriculum on Tuberculosis (2000)* [Division of Tuberculosis Elimination Web site]. Updated November 2001. Available at: <http://www.cdc.gov/tb/education/corecurr/index.htm>.
- <sup>22</sup> ATS, CDC, IDSA. Controlling tuberculosis in the United States: recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America. *MMWR* 2005;54(No. RR-12):33.
- <sup>23</sup> ATS, CDC, IDSA. Controlling tuberculosis in the United States: recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America. *MMWR* 2005;54(No. RR-12):33.
- <sup>24</sup> Daley CL, Gotway MB, Jasmer RM. *Radiographic manifestations of tuberculosis: a primer for clinicians*. San Francisco, CA: Curry International Tuberculosis Center; 2003:1–30.
- <sup>25</sup> CDC. The medical history. In: Module 3: diagnosis of TB infection and disease. *Self-Study Modules on Tuberculosis* [Division of Tuberculosis Elimination Web site]. 1999:12. Available at: <http://www.cdc.gov/tb/education/ssmodules/default.htm>.
- <sup>26</sup> CDC. Medical evaluation. In: Chapter 5: diagnosis of TB. *Core Curriculum on Tuberculosis (2000)* [Division of Tuberculosis Elimination Web site]. Updated November 2001. Available at: <http://www.cdc.gov/tb/education/corecurr/index.htm>; and CDC. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care settings, 2005. *MMWR* 2005;54(No. RR-17):11.
- <sup>27</sup> ATS, CDC, IDSA. Diagnostic standards and classification of tuberculosis in adults and children. *Am J Respir Crit Care Med* 2000;161:1378; CDC. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care settings, 2005. *MMWR* 2005;54(No. RR-17):11; and CDC. Medical evaluation. In: Chapter 5: diagnosis of TB. *Core Curriculum on Tuberculosis (2000)* [Division of Tuberculosis Elimination Web site]. Updated November 2001. Available at: <http://www.cdc.gov/tb/education/corecurr/index.htm>.
- <sup>28</sup> CDC. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care settings, 2005. *MMWR* 2005;54(No. RR-17):11; and ATS, CDC, IDSA. Diagnostic standards and classification of tuberculosis in adults and children. *Am J Respir Crit Care Med* 2000;161:1378.
- <sup>29</sup> CDC. Module 3: diagnosis of TB infection and disease. *Self-Study Modules on Tuberculosis* [Division of Tuberculosis Elimination Web site]. 1999:3. Available at: <http://www.cdc.gov/tb/education/ssmodules/default.htm>; and CDC. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care settings, 2005. *MMWR* 2005;54(No. RR-17):11.
- <sup>30</sup> ATS, CDC, IDSA. Controlling tuberculosis in the United States: recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America. *MMWR* 2005;54(No. RR-12):51.
- <sup>31</sup> CDC. Revised Recommendations for HIV Testing of Adults, Adolescents, and Pregnant Women in Health-Care Settings. *MMWR* 2006;55(No. RR-14):1–17.
- <sup>32</sup> CDC. Medical evaluation. In: Chapter 5: diagnosis of TB. *Core Curriculum on Tuberculosis (2000)* [Division of Tuberculosis Elimination Web site]. Updated November 2001. Available at: <http://www.cdc.gov/tb/education/corecurr/index.htm>. Accessed January 10, 2012; and Colorado Department of Public Health and Environment. *Tuberculosis Manual* [Colorado Department of Public Health and Environment Web site]. 2004:3-1. Available at: <http://www.cdphe.state.co.us/dc/TB/tbman.html>. Accessed January 10, 2012.
- <sup>33</sup> CDC. Guidelines for using the QuantiFERON<sup>®</sup>-TB Gold test for detecting *Mycobacterium tuberculosis* infection, United States. *MMWR* 2005;54(No. RR-15):52.
- <sup>34</sup> CDC. Guidelines for using the QuantiFERON<sup>®</sup>-TB Gold test for detecting *Mycobacterium tuberculosis* infection, United States. *MMWR* 2005;54(No. RR-15):52.
- <sup>35</sup> CDC. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care settings, 2005. *MMWR* 2005;54(No. RR-17):4.

- 
- <sup>36</sup> CDC. Guidelines for using the QuantiFERON-TB Gold test for detecting *Mycobacterium tuberculosis* infection, United States. *MMWR* 2005;54(No RR-15):52.
- <sup>37</sup> CDC. Guidelines for using the QuantiFERON-TB Gold test for detecting *Mycobacterium tuberculosis* infection, United States. *MMWR* 2005;54(No RR-15):50.
- <sup>38</sup> CDC. Guidelines for using the QuantiFERON-TB Gold test for detecting *Mycobacterium tuberculosis* infection, United States. *MMWR* 2005;54(No RR-15):52.
- <sup>39</sup> CDC. Guidelines for using the QuantiFERON<sup>®</sup>-TB Gold test for detecting *Mycobacterium tuberculosis* infection, United States. *MMWR*. 2005; 54 (No. RR-15):52.
- <sup>40</sup> CDC. Guidelines for using the QuantiFERON<sup>®</sup>-TB Gold test for detecting *Mycobacterium tuberculosis* infection, United States. *MMWR* 2005;54(No. RR-15):52.
- <sup>41</sup> ATS, CDC, IDSA. Treatment of tuberculosis. *MMWR* 2003;52(No. RR-11):3.
- <sup>42</sup> CDC. Module 3: diagnosis of TB infection and disease. *Self-Study Modules on Tuberculosis* [Division of Tuberculosis Elimination Web site]. 1999:13. Available at: <http://www.cdc.gov/tb/education/ssmodules/default.htm>. Accessed January 10, 2012.
- <sup>43</sup> CDC. Guidelines for using the QuantiFERON-TB Gold test for detecting *Mycobacterium tuberculosis* infection, United States. *MMWR*. 2005;54(No. RR-15):52.
- <sup>44</sup> CDC. Targeted tuberculin testing and treatment of latent tuberculosis infection. *MMWR* 2000;49(No. RR-6):25.
- <sup>45</sup> CDC. Medical evaluation. In: Chapter 5: diagnosis of TB. *Core Curriculum on Tuberculosis (2000)* [Division of Tuberculosis Elimination Web site]. Updated November 2001. Available at: <http://www.cdc.gov/tb/education/corecurr/index.htm> . Accessed January 10, 2012.
- <sup>46</sup> ATS, CDC, IDSA. Controlling tuberculosis in the United States: recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America. *MMWR* 2005;54(No. RR-12):19; and Tenover, R., et al. The resurgence of tuberculosis: is your laboratory ready? *Journal of Clinical Microbiology* 1993:767–770.
- <sup>47</sup> ATS, CDC, IDSA. Controlling tuberculosis in the United States: recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America. *MMWR* 2005;54(No. RR-12):19; and Tenover, R., et al. The resurgence of tuberculosis: is your laboratory ready? *Journal of Clinical Microbiology* 1993:767–770.
- <sup>48</sup> ATS, CDC, IDSA. Controlling tuberculosis in the United States: recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America. *MMWR* 2005;54(No. RR-12):19.
- <sup>49</sup> ATS, CDC, IDSA. Diagnostic standards and classification of tuberculosis in adults and children. *Am J Respir Crit Care Med* 2000;161:1384.
- <sup>50</sup> ATS, CDC, IDSA. Controlling tuberculosis in the United States: recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America. *MMWR* 2005;54(No. RR-12):19; and Tenover, R., et al. The resurgence of tuberculosis: is your laboratory ready? *Journal of Clinical Microbiology* 1993:767–770.
- <sup>51</sup> CDC. National plan for reliable tuberculosis laboratory services using a systems approach—recommendations from CDC and the Association of Public Health Laboratories Task Force on Tuberculosis Laboratory Services. *MMWR* 2005;54(No. RR-6):3.
- <sup>52</sup> ATS, CDC, IDSA. Controlling tuberculosis in the United States: Recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America. *MMWR* 2005;54(No RR-12):19; and Tenover, R., et al. The resurgence of tuberculosis: is your laboratory ready? *Journal of Clinical Microbiology* 1993:767–770.
- <sup>53</sup> CDC. National plan for reliable tuberculosis laboratory services using a systems approach - recommendations from CDC and the Association of Public Health Laboratories Task Force on Tuberculosis Laboratory Services. *MMWR* 2005;54(No. RR-6):2.
- <sup>54</sup> Tenover, R., et al. The resurgence of tuberculosis: is your laboratory ready? *Journal of Clinical Microbiology* 1993:769; and ATS, CDC, IDSA. Treatment of tuberculosis. *MMWR* 2003;52(No. RR-11):38.
- <sup>55</sup> ATS, CDC, IDSA. Treatment of tuberculosis. *MMWR* 2003;52(No. RR-11):12.
- <sup>56</sup> ATS, CDC, IDSA. Controlling tuberculosis in the United States: Recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America. *MMWR* 2005;54(No RR-12):19; and Tenover, R., et al. The resurgence of tuberculosis: is your laboratory ready? *Journal of Clinical Microbiology* 1993:767–770.
- <sup>57</sup> CDC. National plan for reliable tuberculosis laboratory services using a systems approach - recommendations from CDC and the Association of Public Health Laboratories Task Force on Tuberculosis Laboratory Services. *MMWR* 2005;54(No. RR-6):2.
- <sup>58</sup> CDC. Laboratory User Guide: Molecular Detection of Drug Resistance (MDDR) in *Mycobacterium tuberculosis* Complex by DNA Sequencing, 2009. Available at <http://www.cdc.gov/tb/topic/Laboratory/guide.htm>. Accessed January 10, 2012.
- <sup>59</sup> CDC. Diagnostic microbiology. In: Chapter 5: diagnosis of TB. *Core Curriculum on Tuberculosis (2000)* [Division of Tuberculosis Elimination Web site]. Updated November 2001. Available at: <http://www.cdc.gov/tb/education/corecurr/index.htm>. Accessed January 10, 2012.