

# Diagnosis of Tuberculosis Disease

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# 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. Required and recommended forms are available on the CDEpi Resource Page for Public Health. For more information on these forms, contact us at 406-444-0273.

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> Section 9: Case Management Topics: Quick Start Check List, Initial Assessment</p>
<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> Section 16: Infection Control Topics: Estimating infectiousness, Who Should Use a Mask or Respirator, Airborne Infection Isolation in a Healthcare Facility, Residential Settings</p> <p><b>Recommended Form:</b></p> <ul style="list-style-type: none"> <li>▪ “Home Isolation Agreement” (if the patient is isolated at home)</li> </ul>
<p><b>Evaluate the patient:</b></p> <ul style="list-style-type: none"> <li><input type="checkbox"/> Assure that a medical evaluation of the patient is completed 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> <li><input type="checkbox"/> Conduct a physical examination</li> <li><input type="checkbox"/> Administer, measure, and interpret a Mantoux tuberculin skin test (or a QuantiFERON®-TB Gold test)</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 results of AFB sputum smear tests</li> </ul>	<p><b>Instructions:</b> Section 5: Diagnosis of Tuberculosis Disease Topic: Diagnosis of Tuberculosis Disease</p> <p>Section 7: Diagnosis of Latent Tuberculosis Infection Topics: Administration, Measurement, and Interpretation of the Tuberculin Skin Test</p> <p>Section 11: Laboratory Services Topics: Specimen Collection, Specimen Shipment</p> <p><b>Recommended Forms:</b></p> <ul style="list-style-type: none"> <li>▪ “TB Diagnostic Referral Form”</li> <li>▪ “Bacteriology Data Sheet”</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"/> Assure that a nucleic acid amplification (NAA) test is ordered, if an NAA test is needed to quickly confirm diagnosis of tuberculosis (TB) for a patient with positive AFB sputum smear results</li> <li><input type="checkbox"/> Reassess information about the patient weekly until drug susceptibility results are available or for 2 months after the case report, whichever is longer</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 culture results</li> <li><input type="checkbox"/> Receive and review drug susceptibility results 1 to 2 months after the patient's initial sputum collection date</li> </ul>	<p><b>Instructions:</b></p> <p>Section 5: Diagnosis of Tuberculosis Disease Topic: Diagnosis of Tuberculosis Disease</p> <p>Section 7: Diagnosis of Latent Tuberculosis Infection Topics: Administration, Measurement, and Interpretation of the Tuberculin Skin Test</p> <p>Section 11: Laboratory Services Topics: Specimen Collection, Specimen Shipment</p> <p><b>Recommended Form:</b></p> <ul style="list-style-type: none"> <li>▪ "Bacteriology Data Sheet"</li> </ul>
Tasks for Follow up of Patients Diagnosed with Tuberculosis Disease	Instructions and Forms
<p><b>Communicate to Montana TB program staff:</b></p> <ul style="list-style-type: none"> <li><input type="checkbox"/> Send the written "Confirmed/Suspected Report of TB Disease" to the Montana TB Program within 7 days of the case report</li> </ul>	<p><b>Instructions:</b></p> <p>Section 2: Surveillance Topic: Required Reports from Local Health Agencies</p> <p><b>Required Form:</b></p> <ul style="list-style-type: none"> <li>▪ "Confirmed/Suspected Report of TB Disease"</li> </ul>
<p><b>Start the patient on treatment for TB disease</b></p>	<p><b>Instructions:</b></p> <p>Section 6: Treatment of Tuberculosis Disease Topic: Quick Start Check List</p>
<p><b>Manage the case</b></p>	<p><b>Instructions:</b></p> <p>Section 9: Case Management Topic: Quick Start Check List</p>
<p><b>Conduct the contact investigation</b></p>	<p><b>Instructions:</b></p> <p>Section 10: Contact Investigation Topic: Quick Start Check List</p>

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# Introduction

## Purpose

Use this section to understand and follow national and Montana guidelines to

- 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; and
- 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. For information on treatment, refer to the Treatment of Tuberculosis Disease section.

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. Positive cultures for *M. tuberculosis* confirm the diagnosis of TB; however, TB may also be diagnosed on the basis of clinical signs and symptoms in the absence of a positive culture.

## Policy

In Montana:

- 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 and reported as suspected cases of TB as described in the “Reporting Tuberculosis” topic in the Surveillance section.
- Contacts should be evaluated as described in the Contact Investigation section.



For roles and responsibilities, refer to the “Roles, Responsibilities, and Contact Information” topic in the Introduction.

## Forms



Required and recommended forms are available on the CDEpi Resource Page for Public Health. For more information on these forms, contact us at 406-444-0273.

# Tuberculosis Classification System

The system for classifying tuberculosis (TB) is based on how the infection and disease develop in the body. Use this classification system to help track the status of TB in your patients and to allow comparison with other reporting areas.

TABLE 1: TUBERCULOSIS CLASSIFICATION SYSTEM<sup>7</sup>

Class	Type	Description
0	<ul style="list-style-type: none"> <li>▪ No tuberculosis (TB) exposure</li> <li>▪ Not infected</li> </ul>	<ul style="list-style-type: none"> <li>▪ No history of exposure</li> <li>▪ Negative reaction to the tuberculin skin test (TST) or interferon gamma release assay (IGRA)</li> </ul>
1	<ul style="list-style-type: none"> <li>▪ TB exposure</li> <li>▪ No evidence of infection</li> </ul>	<ul style="list-style-type: none"> <li>▪ History of exposure</li> <li>▪ Negative reaction to the TST or IGRA</li> </ul>
2	<ul style="list-style-type: none"> <li>▪ TB infection</li> <li>▪ No disease</li> </ul>	<ul style="list-style-type: none"> <li>▪ Positive reaction to the TST or IGRA</li> <li>▪ Negative bacteriologic studies (if done)</li> <li>▪ No clinical, bacteriologic, or radiographic evidence of TB disease</li> </ul>
3	<ul style="list-style-type: none"> <li>▪ TB disease</li> <li>▪ Clinically active</li> </ul>	<ul style="list-style-type: none"> <li>▪ <i>Mycobacterium tuberculosis</i> complex cultured (if this has been done)</li> <li>▪ Clinical, bacteriologic, or radiographic evidence of current disease</li> </ul>
4	<ul style="list-style-type: none"> <li>▪ TB disease</li> <li>▪ Not clinically active</li> </ul>	<ul style="list-style-type: none"> <li>▪ History of episode(s) of TB</li> <li style="text-align: center;"><b>Or</b></li> <li>▪ Abnormal but stable radiographic findings</li> <li>▪ Positive reaction to the TST or IGRA</li> <li>▪ Negative bacteriologic studies (if done)</li> <li style="text-align: center;"><b>And</b></li> <li>▪ No clinical or radiographic evidence of current disease</li> </ul>
5	<ul style="list-style-type: none"> <li>▪ TB suspect</li> </ul>	<ul style="list-style-type: none"> <li>▪ Diagnosis pending</li> </ul>

Source: Adapted from: CDC. Classification system. In: Chapter 2: transmission and pathogenesis. *Core Curriculum on Tuberculosis (2000)* [Division of Tuberculosis Elimination Web site]. Updated November 2001. Accessed July 3, 2006. Most recent version of this document available here.

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## High-Risk Groups

Certain factors identify persons at high risk for tuberculosis (TB) infection and/or for progression to TB disease. Persons in the high-risk groups listed in Table 2: **Persons at High Risk for Tuberculosis Infection and Progression to Tuberculosis Disease** are candidates for tuberculin skin testing in Montana.

Persons with risk factors from both columns may be at much higher risk than those with risk factors in only one column. For example, an individual born in a high-TB-prevalence country with HIV infection is at much higher risk of having active TB than a US-born individual with HIV infection.

TABLE 2: PERSONS AT HIGH RISK FOR TUBERCULOSIS INFECTION AND PROGRESSION TO TUBERCULOSIS DISEASE<sup>8</sup>

For Tuberculosis Infection	For Progression to Tuberculosis Disease <sup>9</sup>
<ul style="list-style-type: none"> <li>▪ High-priority contacts such as housemates or coworkers, or contacts of persons who have smear-positive pulmonary or laryngeal tuberculosis (TB)</li> <li>▪ Infants, children, and adolescents exposed to adults in high-risk categories</li> <li>▪ Recent immigrants (primarily &lt;5 years) from countries with high incidence of TB (Asian, African, Latin American, and Eastern European countries have TB rates 5–30 times higher than US rates, and an increasing percentage of TB cases in the United States are occurring among immigrants from those countries)</li> <li>▪ Residents and employees of high-risk congregate settings (e.g., correctional institutions, nursing homes and other long-term care facilities providing care to high-risk residents and clients, and homeless shelters)</li> <li>▪ Some healthcare workers who serve high-risk clients, especially emergency departments, staff involved in high-risk procedures, and laboratories manipulating TB cultures</li> <li>▪ Some high-risk racial or ethnic minority populations, defined locally as having an increased prevalence of TB</li> <li>▪ Some medically underserved, low-income populations as defined locally (e.g., homeless, transient populations)</li> <li>▪ Persons who inject illicit drugs; any other locally identified high-risk substance abuse users</li> </ul>	<ul style="list-style-type: none"> <li>▪ Persons with HIV infection</li> <li>▪ Infants and children aged &lt;5 years</li> <li>▪ Persons infected with <i>Mycobacterium tuberculosis</i> within the previous 2 years</li> <li>▪ Persons with a history of untreated or inadequately treated TB disease</li> <li>▪ Persons with radiographic findings consistent with previous TB disease</li> <li>▪ Persons who use alcohol or illegal drugs (such as injection drugs or crack cocaine)</li> <li>▪ Persons with any of the following clinical conditions or other immunocompromising conditions:               <ul style="list-style-type: none"> <li>• Silicosis</li> <li>• Diabetes mellitus</li> <li>• End-stage renal disease (ESRD)/chronic renal failure, hemodialysis</li> <li>• Some hematologic disorders (e.g., leukemias and lymphomas)</li> <li>• Other malignancies (e.g., carcinoma of head, neck, or lung)</li> <li>• Body weight <math>\geq 10\%</math> below ideal body weight</li> <li>• Prolonged corticosteroid use</li> <li>• Use of other immunosuppressive treatments (e.g., prednisone or tumor necrosis factor-alpha [TNF-<math>\alpha</math>] antagonists)</li> <li>• Organ transplantation</li> <li>• Gastrectomy</li> <li>• Chronic malabsorption syndromes</li> <li>• Jejunioileal bypass</li> </ul> </li> </ul>

Source: Adapted from: CDC. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care settings, 2005. *MMWR* 2005;54(No. RR-17):4–5; CDC. Targeted tuberculin testing and treatment of latent tuberculosis infection. *MMWR* 2000;49(No. RR-6):7–9.



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# 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>10</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>11</sup>

Be alert for cases of TB among persons who have not sought medical care during evaluation of contacts of patients with pulmonary TB and of 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>12</sup>

Suspect pulmonary TB and initiate a diagnostic investigation when the historic features, signs, symptoms, and radiographic findings listed in Table 3 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 two to three weeks, or other compatible signs and symptoms.<sup>13</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 two to three weeks<sup>14</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 3: WHEN TO SUSPECT PULMONARY TUBERCULOSIS IN ADULTS<sup>15</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†.16</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)§.17</li> <li>▪ Chest pain18</li> <li>▪ Chills19</li> <li>▪ Fever</li> <li>▪ Night sweats</li> <li>▪ Loss of appetite20</li> <li>▪ Weight loss</li> <li>▪ Weakness or easy fatigability21</li> <li>▪ Malaise (a feeling of general discomfort or illness)22</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¶</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>* See Table 2: Persons at High Risk for Tuberculosis Infection and Progression to Tuberculosis Disease.</p> <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.

## Follow-up on Suspected Cases of Tuberculosis

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



When a suspected case of pulmonary TB is identified, refer to Table 4: **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>23</sup>



To formally report a suspected case of TB, see the “Reporting Tuberculosis” topic in the Surveillance section.



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 this manual. This section will be available in the Spring of 2007. Check the *Montana Tuberculosis Program Manual*.



Laboratories should report positive smears or positives cultures, and primary healthcare providers should report suspected or confirmed cases of TB to the health department, as specified in the “Reporting Tuberculosis” topic in the Surveillance section. Prompt reporting allows the health department to organize treatment and case management services and to initiate a contact investigation as quickly as possible.<sup>24</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. Evaluate the patient for TB disease as specified in the “Diagnosis of Tuberculosis Disease” topic in this section.

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# 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 or interferon gamma release assay
- Chest radiography
- Bacteriologic examination

When a suspected case of pulmonary TB is identified, refer to Table 4 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>25</sup>

TABLE 4: GUIDELINES FOR THE EVALUATION OF PULMONARY TUBERCULOSIS IN ADULTS IN FIVE CLINICAL SCENARIOS<sup>26</sup>

Patient and Setting	Recommended Evaluation
Any patient with a cough of $\geq 2$ –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), if available <sup>27</sup>
Any patient at high risk for TB with an unexplained illness, including respiratory symptoms of $\geq 2$ –3 weeks' duration <sup>†</sup>	Chest radiograph: If suggestive of TB, collect 3 sputum specimens for AFB smear microscopy, culture, and NAA, if available
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, if available
Any patient at high risk for TB with a diagnosis of community-acquired pneumonia who has not improved after 7 days of treatment <sup>†</sup>	Chest radiograph, and collect 3 sputum specimens for AFB smear microscopy, culture, and NAA, if available
Any patient at high risk for TB with incidental findings on chest radiograph suggestive of TB even if symptoms are minimal or absent <sup>†§</sup>	Review of previous chest radiographs, if available, 3 sputum specimens for AFB smear microscopy, NAA, and culture
<p>* Opacities with or without cavitation in the upper lobes or the superior segments of the lower lobes.<sup>28</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 3: **When to Suspect Pulmonary Tuberculosis in Adults**, Table 4: **Guidelines for the Evaluation of Pulmonary Tuberculosis in Adults in Five Clinical Scenarios**, and Table 5: **Symptoms of Tuberculosis Disease**)
- Previous TB infection or disease
- Risk factors (as listed in Table 2: **Persons at High Risk for Tuberculosis Infection and Progression to Tuberculosis Disease**)
- 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 5 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 3: **When to Suspect Pulmonary Tuberculosis in Adults.**

TABLE 5: SYMPTOMS OF TUBERCULOSIS DISEASE<sup>29</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>30</sup></li> <li>▪ Fever</li> <li>▪ Night sweats</li> <li>▪ Loss of appetite<sup>31</sup></li> <li>▪ Weight loss</li> <li>▪ Weakness or easy fatigability<sup>32</sup></li> <li>▪ Malaise (a feeling of general discomfort or illness)<sup>33</sup></li> </ul>	<p>The symptoms depend on part of body affected by tuberculosis (TB) disease</p> <ul style="list-style-type: none"> <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> </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** 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. (See Table 2: **Persons at High Risk for Tuberculosis Infection and Progression to Tuberculosis Disease.**)<sup>34</sup> For persons previously skin tested, an increase in induration of 10 mm within a two-year period is classified as a conversion to positive.

#### **4. Risk Factors for Developing TB Disease: Determine whether patients have any conditions or behaviors that are risk factors for developing TB disease.**

For a list of behaviors and conditions that appear to increase the risk that TB infection will progress to disease, see Table 2: **Persons at High Risk for Tuberculosis Infection and Progression to Tuberculosis 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>35</sup>

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

- Routine HIV screening for all patients ages 13–64 seeking health care for any reason, without regard to any patient’s known risks for HIV infection
- Annual HIV screening of patients known to be at high risk<sup>36</sup>

### 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>37</sup>

### Tuberculin Skin Test and Interferon Gamma Release Assays

Montana is still in the evaluation phase of implementation for interferon gamma release assays (IGRAs). IGRAs are not available in Montana at this time.

Use the Mantoux tuberculin skin test (TST) to test for *M. tuberculosis* infection. Note that for patients with a previous documented positive TST reaction, a TST is not necessary. Additional tests, such as chest radiography and bacteriologic examination, are required to confirm TB disease.<sup>38</sup>

Persons with a positive TST result, regardless of symptoms or signs, should be evaluated for TB disease before LTBI is diagnosed. At minimum, a chest radiograph should be examined for abnormalities consistent with TB disease.<sup>39</sup>

A negative TST does not rule out TB disease<sup>40</sup>—as many as 20% of patients with TB disease have a negative TST reaction.<sup>41</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>42</sup>



For more information on the Mantoux TST, see the Diagnosis of Latent Tuberculosis Infection section. 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]).

## 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>43</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>44</sup>



For more information on chest radiography, see the Francis J. Curry National Tuberculosis Center's *Radiographic Manifestations of Tuberculosis: A Primer for Clinicians* (2006).

## Bacteriologic Examination

Refer to Table 6 below to determine the types of specimens needed to assist in the diagnosis of TB.

TABLE 6: SPECIMENS FOR DIAGNOSING TUBERCULOSIS DISEASE

<b>Suspected Diagnosis</b>	<b>Specimen Needed</b>
<b>Pulmonary or laryngeal tuberculosis (TB)</b>	Sputum (phlegm from deep in the lungs) samples for smear and culture examination.  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.
<b>Extrapulmonary TB</b>	Depending on the anatomical site, other clinical specimens are necessary, such as: <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 (heparinized)</li></ul>

Refer to Table 7 below for information on the bacteriology tests used to diagnose TB.

TABLE 7: BACTERIOLOGY TESTS USED IN DIAGNOSING TUBERCULOSIS DISEASE<sup>45</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>▪ On-site test: within 24 hours from specimen collection.</li> <li>▪ Off-site test: within 24 hours from laboratory receipt of specimen (time from specimen collection to laboratory receipt should be 24 hours or less).<sup>46</sup></li> </ul>
<b>Nucleic Acid Amplification (NAA) Assay<sup>47</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>48</sup></li> </ul>	<ul style="list-style-type: none"> <li>▪ On-site test: within 48 hours from specimen collection.<sup>49, 50</sup></li> <li>▪ Off-site test: within 48 hours from laboratory receipt of specimen.</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>▪ Cultures are incubated for up to 6 weeks before reporting as negative. Time to detection of mycobacterial growth is dependent on growth rate. Ideally, growth of <i>M. tuberculosis</i> should be detected within 14 days of inoculation, although this is dependent on many factors.</li> <li>▪ Ideally, <i>M. tuberculosis</i> complex should be identified within 21 days of inoculation.<sup>51, 52</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>53, 54</sup></li> </ul>	<ul style="list-style-type: none"> <li>▪ Ideally, results of first-line drugs should be available within 30 days from specimen receipt in the laboratory, but this is dependent on many factors (for example, growth rate, presence of a pure culture).</li> <li>▪ Second-line drugs: within 4 weeks from date of request.</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 should report positive smears or positives cultures, and primary healthcare providers should report suspected or confirmed cases of TB to the health department, as specified in the “Reporting Tuberculosis” topic in the Surveillance section. Prompt reporting allows the health department to organize treatment and case management services and to initiate a contact investigation as quickly as possible.<sup>55</sup>



For information on reporting, see the “Reporting Tuberculosis” topic in the Surveillance section.



For a list of all of the laboratory services available, see the online version of the *Public Health Services Manual of Laboratory Services*.



For laboratory services available in Montana, contact Susanne Zanto, Laboratory Manager, Microbiology and Molecular Diagnostics, at the Montana Public Health Laboratory at 800-821-7284 or 406-444-3444.

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# 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]).
- CDC. *Self-Study Modules on Tuberculosis* (Division of Tuberculosis Elimination Web site; 1999). Document is no longer available online.
- CDC. *Core Curriculum on Tuberculosis (2000)* (Division of Tuberculosis Elimination Web site; updated November 2001).
- Department of Public Health and Human Services. *Public Health Services Manual of Laboratory Services* (Department of Public Health and Human Services Web site; March 1, 2006).
- Tenover, R., et al. “The Resurgence of Tuberculosis: Is Your Laboratory Ready?” (*Journal of Clinical Microbiology* 1993;767–770).

## References

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- <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.
- <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> CDC. Classification system. In: Chapter 2: transmission and pathogenesis. *Core Curriculum on Tuberculosis (2000)* [Division of Tuberculosis Elimination Web site]. Updated November 2001. Available at: Accessed July 3, 2006.
- <sup>8</sup> CDC. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care settings, 2005. *MMWR* 2005;54(No. RR-17):4–5; CDC. Targeted tuberculin testing and treatment of latent tuberculosis infection. *MMWR* 2000;49(No. RR-6):7–9, 22.
- <sup>9</sup> CDC. Targeted tuberculin testing and treatment of latent tuberculosis infection. *MMWR* 2000;49(No. RR-6):8–9.
- <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):32.
- <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):32.
- <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):34.
- <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> 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. Accessed July 3, 2006; 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. Accessed July 3, 2006.
- <sup>16</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>17</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>18</sup> CDC. Medical evaluation. In: Chapter 5: diagnosis of TB. *Core Curriculum on Tuberculosis (2000)* [Division of Tuberculosis Elimination Web site]. Updated November 2001. Accessed July 3, 2006; and CDC. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care settings, 2005. *MMWR* 2005;54(No. RR-17):11.
- <sup>19</sup> CDC. Medical evaluation. In: Chapter 5: diagnosis of TB. *Core Curriculum on Tuberculosis (2000)* [Division of Tuberculosis Elimination Web site]. Updated November 2001. Accessed July 3, 2006; 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. 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. Accessed July 3, 2006.
- <sup>21</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>22</sup> CDC. Module 3: diagnosis of tuberculosis infection and disease. *Self-Study Modules on Tuberculosis* [Division of Tuberculosis Elimination Web site]. 1999:3. Accessed July 3, 2006; and CDC. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care settings, 2005. *MMWR* 2005;54(No. RR-17):11.
- <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> CDC. Diagnostic microbiology. In: Chapter 5: diagnosis of TB. *Core Curriculum on Tuberculosis (2000)* [Division of Tuberculosis Elimination Web site]. Updated November 2001. Accessed July 3, 2006.
- <sup>25</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>26</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>27</sup> Washington State Public Laboratory Tuberculosis Unit. Internal untitled report on the review, analysis, and recommendations on the Gen-Probe Amplified *Mycobacterium Tuberculosis* Direct Test (MTD). January 2004.
- <sup>28</sup> Daley CL, Gotway MB, Jasmer RM. *Radiographic manifestations of tuberculosis: a primer for clinicians*. San Francisco, CA: Francis J. Curry National Tuberculosis Center; 2003:1–30.
- <sup>29</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. Accessed July 3, 2006.
- <sup>30</sup> CDC. Medical evaluation. In: Chapter 5: diagnosis of TB. *Core Curriculum on Tuberculosis (2000)* [Division of Tuberculosis Elimination Web site]. Updated November 2001. Accessed July 3, 2006; and CDC. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care settings, 2005. *MMWR* 2005;54(No. RR-17):11.
- <sup>31</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. Accessed July 3, 2006.

- 
- <sup>32</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>33</sup> CDC. Module 3: diagnosis of TB infection and disease. *Self-Study Modules on Tuberculosis* [Division of Tuberculosis Elimination Web site]. 1999:3. Accessed July 3, 2006; and CDC. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care settings, 2005. *MMWR* 2005;54(No. RR-17):11.
- <sup>34</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. Accessed July 3, 2006.
- <sup>35</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>36</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>37</sup> CDC. Medical evaluation. In: Chapter 5: diagnosis of TB. *Core Curriculum on Tuberculosis (2000)* [Division of Tuberculosis Elimination Web site]. Updated November 2001. Accessed July 3, 2006; and Colorado Department of Public Health and Environment. *Tuberculosis Manual* [Colorado Department of Public Health and Environment Web site]. 2004:3-1. This document is no longer available online. Accessed November 1, 2006.
- <sup>38</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>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> ATS, CDC, IDSA. Treatment of tuberculosis. *MMWR* 2003;52(No. RR-11):3.
- <sup>41</sup> CDC. Module 3: diagnosis of TB infection and disease. *Self-Study Modules on Tuberculosis* [Division of Tuberculosis Elimination Web site]. 1999:13 This document is no longer available online. Accessed July 3, 2006.
- <sup>42</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>43</sup> CDC. Targeted tuberculin testing and treatment of latent tuberculosis infection. *MMWR* 2000;49(No. RR-6):25.
- <sup>44</sup> CDC. Medical evaluation. In: Chapter 5: diagnosis of TB. *Core Curriculum on Tuberculosis (2000)* [Division of Tuberculosis Elimination Web site]. Updated November 2001. Accessed July 3, 2006.
- <sup>45</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>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.
- <sup>48</sup> ATS, CDC, IDSA. Diagnostic standards and classification of tuberculosis in adults and children. *Am J Respir Crit Care Med* 2000;161:1384.
- <sup>49</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>50</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>51</sup> CDC. 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>52</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>53</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>54</sup> ATS, CDC, IDSA. Treatment of tuberculosis. *MMWR* 2003;52(No. RR-11):12.
- <sup>55</sup> CDC. Diagnostic microbiology. In: Chapter 5: diagnosis of TB. *Core Curriculum on Tuberculosis (2000)* [Division of Tuberculosis Elimination Web site]. Updated November 2001. Accessed July 3, 2006.