Diagnosis of Tuberculosis Disease

CONTENTS

Introduction

Purpose

Use this section to understand and follow national and Alaska 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 identifying and treating a TB case which, in turn, can lead to further transmission.

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 **11.1**. For information on treatment, refer to the Treatment of Tuberculosis Disease section **6.1**.

Improvement in the detection of TB cases is essential to progress toward elimination of TB in the United States.[1] Case detection includes the processes that lead to the evaluation, diagnosis, and reporting of persons with active TB.[2] Detecting and reporting suspected cases of TB are key steps in halting transmission of *Mycobacterium tuberculosis* because they lead to prompt initiation of effective treatment which rapidly reduces infectiousness.[3]

TB is commonly diagnosed when a person seeks medical attention for symptoms caused by the disease or another concomitant medical condition. Thus, healthcare providers, particularly those providing primary healthcare to populations at high risk, are key contributors to TB case detection.[4] 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.[5]

A diagnosis of TB disease is usually based on positive cultures or nucleic acid amplification (NAA) tests 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 Alaska:

- Persons who show or report signs and symptoms of TB should be; 1) evaluated for TB disease as described in the "Diagnosis of Tuberculosis Disease" topic in this section and 2) reported as suspected cases of TB as described in the "Reporting Tuberculosis" topic in the Surveillance section **2.6**.
- Contacts should be evaluated as described in the Contact Investigation section **11.1**.

For roles and responsibilities, refer to the "Roles, Responsibilities, and Contact Information" topic in the Introduction section **1.11**.

Reports of suspected or confirmed tuberculosis should be made as soon as possible and must be made within 2 working days after first diagnosing or suspecting the existence of the disease.

Forms

Reporting forms and information are available in the Forms section **(18.1)** or at http://dhss.alaska.gov/dph/Epi/Pages/pubs/conditions/default.aspx

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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**[6]

Class	Type	Description
0	▪ No tuberculosis (TB) exposure ▪ **Not** infected	▪ No history of TB exposure and no evidence of *M. tuberculosis* infection or disease ▪ Negative reaction to the tuberculin skin test (TST) or interferon gamma release assay (IGRA)
1	▪ TB exposure ▪ No evidence of infection	▪ History of exposure to *M. tuberculosis* ▪ Negative reaction to the TST or IGRA (given at least 8 to 10 weeks after exposure)
2	▪ TB infection ▪ No TB disease	▪ Positive reaction to TST or IGRA ▪ Negative bacteriologic studies (smear and cultures) ▪ No bacteriological or radiographic evidence of active TB disease
3	▪ TB clinically active	▪ Positive culture for *Mycobacterium tuberculosis* OR Positive reaction to TST or IGRA, plus clinical, bacteriological, or radiographic evidence of current active TB
4	▪ Previous TB disease (not clinically active)	May have past medical history of TB disease ▪ Abnormal but stable radiographic findings ▪ Positive reaction to the TST or IGRA ▪ Negative bacteriologic studies (smear and cultures) ▪ No clinical or radiographic evidence of current active TB disease
5	▪ TB suspected	▪ Signs and symptoms of active TB disease, but medical evaluation **not** complete

Source: Adapted from: CDC. Classification system. In: Chapter 2:Transmission and Pathogenesis of Tuberculosis. *Core Curriculum on Tuberculosis: What the Clinician Should Know (2016)* [Division of Tuberculosis Elimination Web site]. Updated May 2016. Available at: https://www.cdc.gov/tb/education/corecurr/pdf/chapter2.pdf . Accessed December 4, 2020.

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 should be targeted for tuberculosis testing in Alaska.

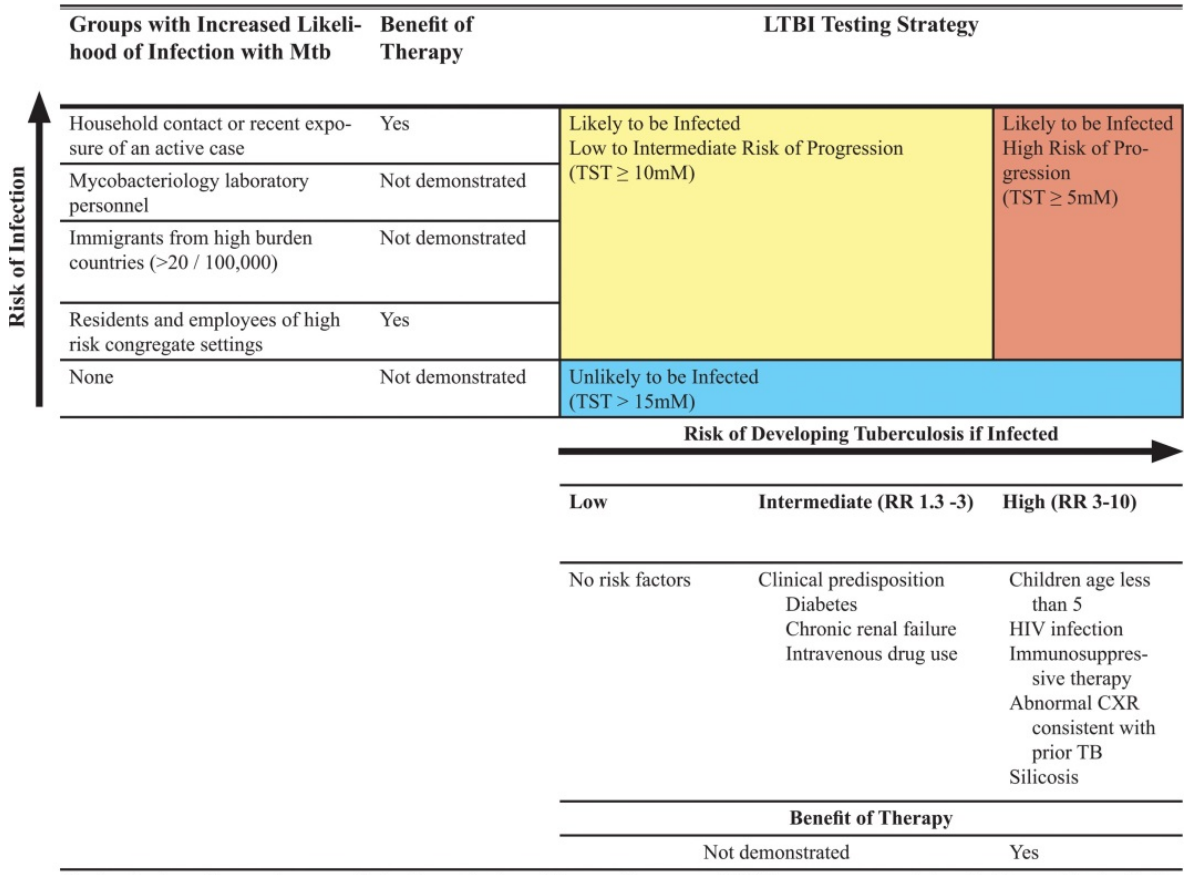
Persons with risk factors from both columns may be at much higher risk than those with risk factors in only one column. For example, an individual born in a high-TB-prevalence country with HIV infection is at much higher risk of having active TB than a US-born individual with HIV infection.

Table 2: **PERSONS AT HIGH RISK FOR TUBERCULOSIS INFECTION AND PROGRESSION TO TUBERCULOSIS DISEASE**[7]

For Tuberculosis Infection	For Progression to Tuberculosis Disease[8]
▪ High-priority contacts such as housemates or coworkers or contacts of persons who have smear-positive pulmonary or laryngeal TB ▪ Infants, children, and adolescents exposed to adults in high-risk categories ▪ Recent immigrants (<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 U.S. rates, and an increasing percentage of TB cases in Alaska are occurring among immigrants from those countries) ▪ Recent immigrants from Mexico ▪ Migrant workers ▪ Persons who have recently spent over 3 months in high-incidence countries (such as missionaries) ▪ Persons with high rates of TB transmission: • Persons experiencing homelessness • Persons who use substances • Persons with human immunodeficiency virus (HIV) infection • Persons living or working in institutions with individuals at risk for TB such as: ▪ Hospitals, especially staff in nursing, emergency departments, and laboratories ▪ Long-term care facilities ▪ Homeless shelters ▪ Residences for acquired immunodeficiency syndrome (AIDS) patients ▪ Correctional facilities ▪ Alaska-specific risk includes persons from the Southwest and Northern regions of the state and some Alaska Natives	▪ Persons with HIV infection ▪ Infants and children aged <5 years ▪ Persons infected with *Mycobacterium tuberculosis* within the previous 2 years ▪ Persons with a history of untreated or inadequately treated TB disease ▪ Persons with radiographic findings consistent with previous TB disease ▪ Persons who use alcohol or illegal drugs (such as injection drugs or crack cocaine) ▪ Persons who smoke cigarettes ▪ Persons with any of the following clinical conditions or other immunocompromising conditions: • Silicosis • Diabetes mellitus • End-stage renal disease (ESRD)/chronic renal failure, hemodialysis • Some hematologic disorders (e.g., leukemias and lymphomas) • Other malignancies (e.g., carcinoma of head, neck, or lung) • Body weight ≥10% below ideal body weight • Prolonged corticosteroid use • Use of other immunosuppressive treatments (e.g., prednisone or tumor necrosis factor-alpha [TNF- α] antagonists) • Organ transplantation • Gastrectomy • Chronic malabsorption syndromes • Jejunoileal bypass

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.

Figure 1. **PARADIGM FOR EVALUATION OF THOSE WITH LATENT TUBERCULOSIS INFECTION (LTBI) BASED ON RISK OF INFECTION, RISK OF PROGRESSION TO TUBERCULOSIS, AND BENEFIT OF THERAPY**[9]



In developing a diagnostic approach for the evaluation of those with suspected LTBI, we recommend the clinician weigh the likelihood of infection, the likelihood of progression to TB if infected, and the benefit of therapy (Horsburgh, C.R., Jr., and E.J. Rubin. 2011. Clinical practice. Latent tuberculosis infection in the United States. The New England journal of medicine 364:1441-1448). Recommendations were formulated for each of the three groups illustrated above. These groups are concordant with current recommendations for the interpretation of the TST (2000. Targeted tuberculin testing and treatment of latent tuberculosis infection. American Thoracic Society. MMWR Recomm Rep 49:1-51).

Figure 1. In developing a diagnostic approach for the evaluation of those with suspected LTBI, we recommend the clinician weigh the likelihood of infection, the likelihood of progression to tuberculosis if infected, and the benefit of therapy (Horsburgh and Rubin, Clinical practice: latent tuberculosis infection in the United States. N Engl J Med 2011; 364:1441–8). Recommendations were formulated for each of the 3 groups illustrated above. These groups are concordant with current recommendations for the interpretation of the tuberculin skin test (American Thoracic Society, Targeted tuberculin testing and treatment of latent tuberculosis infection. MMWR Recomm Rep 2000; 49:1–51). Abbreviations: CXR, chest radiograph; HIV, human immunodeficiency virus; LTBI, latent tuberculosis infection; Mtb, Mycobacterium tuberculosis; RR, relative risk; TB, tuberculosis; TST, tuberculin skin test.

Case Finding

Identifying Suspected Tuberculosis Cases

Most 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.[10] Professionals in the primary healthcare sector, including hospital and emergency department clinicians, should be trained to recognize patients with symptoms consistent with TB.[11]

The clinical presentation of TB disease can vary considerably. However, 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 (Table 3).[12]

Note that these symptoms can suggest a diagnosis of TB disease but are not always present. TB disease should also be considered in asymptomatic patients with chest radiograph findings compatible with TB.

- Be alert for cases of TB disease among:
    - Persons who are contacts of patients with pulmonary TB
    - Persons with newly diagnosed infection with *Mycobacterium tuberculosis* (sometimes referred to as TB skin test converters).

- Evaluation for TB disease is especially important for:[13]
    - Immigrants and refugees with Class B1 or Class B2 TB notification status See B Notifications section **4.1**.
    - Persons involved in TB outbreaks.
    - Persons in jails, prisons, and other congregate facilities
    - Other persons at high risk for TB disease
    - Persons who work with populations with a known high incidence of TB (as appropriate)

Table 3: **WHEN TO SUSPECT PULMONARY TUBERCULOSIS IN ADULTS**[14]

Historic Features	▪ Exposure to a person with infectious tuberculosis (TB) ▪ Positive test result for *Mycobacterium tuberculosis* infection ▪ Presence of risk factors, such as immigration from a high-prevalence area, human immunodeficiency virus (HIV) infection, homelessness, or previous incarceration* ▪ Diagnosis of community-acquired pneumonia that has not improved after 7 days of treatment†,[15]
Signs and Symptoms Typical of TB	▪ Prolonged coughing (≥2–3 weeks) with or without production of sputum that might be bloody (hemoptysis)§,[16] ▪ Chest pain[17] ▪ Chills[18] ▪ Fever ▪ Night sweats ▪ Loss of appetite[19] ▪ Weight loss ▪ Weakness or easy fatigability[20] ▪ Malaise (a feeling of general discomfort or illness)[21]
Chest Radiograph: Immunocompetent patients	▪ Classic findings of TB are upper-lobe opacities, frequently with evidence of contraction fibrosis and cavitation¶
Chest Radiograph: Children and patients with advanced HIV infection	▪ Lower-lobe and multilobar opacities, hilar adenopathy, or interstitial opacities might indicate TB

* See Table 2: Persons at High Risk for Tuberculosis Infection and Progression to Tuberculosis Disease.

† Patients treated with levofloxacin or moxifloxacin may have a clinical response when TB is the cause of the pneumonia.

§ Do **not** wait until sputum is bloody to consider a productive cough a symptom of TB. Sputum produced by coughing does **not** need to be bloody to be a symptom of TB.

¶ 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.

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), may also consider evaluation for signs and symptoms of extrapulmonary TB (See Table 5). An individual can have pulmonary or extrapulmonary TB disease, or both.

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 **5.12**. This table presents guidelines for the initial steps of TB case detection in five clinical scenarios frequently encountered by providers of primary health care, including those serving in emergency departments.[22]

To report a suspected or confirmed case of TB, call the Alaska TB Program at 907-269-8000, or after hours, at 800-478-0084. Prompt reporting allows the health department to organize treatment and case management services and to initiate a contact investigation as quickly as possible.[23]

The patient should be masked and immediately excluded from workplace, school, and social activities and, if hospitalized, should be placed in airborne infection isolation (AII) until confirmed noninfectious. For more information, see the "Isolation" topic in the Infection Control section of this manual **17.15**.

Laboratories should report positive smear, NAA, or culture results, and primary healthcare providers should report suspected or confirmed cases of TB to the Alaska TB Program, as specified in the "Reporting Tuberculosis" topic in the Surveillance section **2.6**.

Within 48 hours of suspect identification, administer a tuberculin skin test (TST) or IGRA and obtain a chest radiograph. Evaluate the patient for TB disease as specified in the "Diagnosis of Tuberculosis Disease" topic in this section.

- In remote locations where radiographic services are not immediately available, consideration may be given to have the patient start empiric TB treatment based upon history, clinical findings, and smear results.
- Individuals who require commercial air transport to a medical facility for a chest radiograph should **not** travel until they are noninfectious. This generally requires completion of 14 days of TB medication, clinical improvement, and three (3) consecutive negative AFB smear results.

When managing TB suspects or cases in remote villages and communities, please consult the Alaska TB Program at 907-269-8000 for guidance.

Diagnosis of Tuberculosis Disease

TB disease is often overlooked because of the failure to consider it among other possible diagnoses. While a more definitive diagnosis may require supportive laboratory and radiographic findings, a high degree of suspicion can be based on epidemiology, medical history, and physical examination. It is also important to consider factors that may alter the typical presentation of TB, such as the patient's age, nutritional status, immunologic status, and other 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 for *Mycobacterium tuberculosis*

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 commonly encountered by primary care providers and emergency physicians.[24]

Table 4: **GUIDELINES FOR THE EVALUATION OF PULMONARY TUBERCULOSIS IN ADULTS IN FIVE CLINICAL SCENARIOS**[25]

Patient and Setting	Recommended Evaluation
Any patient with a cough of ≥2–3 weeks' duration	Chest radiograph and collect 3 sputum specimens for acid-fast bacilli (AFB) smear microscopy and culture[26] Note: Where chest radiography is not available, collect 3 sputum specimens for AFB smear microscopy and culture
Any patient at high risk for TB with an unexplained illness, including respiratory symptoms of ≥2–3 weeks' duration†	Chest radiograph and collect 3 sputum specimens for AFB smear microscopy, culture, and NAA. Note: Where chest radiography is not available, collect 3 sputum specimens for AFB smear microscopy, culture and NAA
Any patient with human immunodeficiency virus (HIV) infection and unexplained cough or fever	Chest radiograph, and collect 3 sputum specimens for AFB smear microscopy and culture
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
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 and culture
* Opacities with or without cavitation in the upper lobes or the superior segments of the lower lobes.[27] † See Table 2: Persons at High Risk for Tuberculosis Infection and Progression to Tuberculosis Disease (**5.6).** § Chest radiograph performed for any reason, including targeted testing for latent TB infection and screening for TB disease.	

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 the patient and document their medical history. A written record of a patient's medical history should include the following:

- History of exposure to infectious TB
- Symptoms of TB disease (as listed in Table 3: **When to Suspect Pulmonary Tuberculosis in Adults [5.8],** Table 4: **Guidelines for the Evaluation of Pulmonary Tuberculosis in Adults in Five Clinical Scenarios [5.12],** and Table 5: **Symptoms of Tuberculosis Disease [5.13]**).
- Previous TB infection or disease and any history of treatment with anti-TB medications
- Risk factors (as listed in Table 2: **Persons at High Risk for Tuberculosis Infection and Progression to Tuberculosis Disease [5.5])**
- Recent medical encounters (e.g., emergency department visits 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 any contact in the recent or distant past with persons diagnosed with pulmonary or laryngeal TB. Be aware that most persons become infected with *Mycobacterium tuberculosis* without knowing that they were exposed. It is important to note that patients may refer to latent TB infection (LTBI) as TB disease or fail to report a past history of latent TB infection. 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, residence in congregate settings (such as a jail, homeless shelter, or refugee camp), homelessness or Alaska-specific risk factors such as residing in the Southwest or Northern regions of the state or being of Alaska Native origin.

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 lead 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 or through a pre-operative chest radiograph.

The symptoms in Table 5 below may also 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 5.8**.

Table 5: **SYMPTOMS OF TUBERCULOSIS DISEASE**[28]

Pulmonary	General: Pulmonary and Extrapulmonary	Extrapulmonary
▪ Coughing ▪ Coughing up sputum or blood ▪ Pain in the chest when breathing or coughing	▪ Chills[29] ▪ Fever ▪ Night sweats ▪ Loss of appetite[30] ▪ Weight loss ▪ Weakness or easy fatigability[31] ▪ Malaise (a feeling of general discomfort or illness)[32]	The symptoms depend on part of body affected by tuberculosis (TB) disease: ▪ TB of the spine may cause pain in the back. ▪ TB of the kidney may cause blood in the urine. ▪ Meningeal TB may cause headaches or psychiatric symptoms. ▪ Lymphatic TB may cause swollen and tender lymph nodes, often at the base of the neck.

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.

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, how the disease was treated, and how long they took medications. 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 (5.5)**.[33] 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 TB disease, see Table 2: **Persons at High Risk for Tuberculosis Infection and Progression to Tuberculosis Disease (5.5)**.

Human Immunodeficiency Virus Screening and Hepatitis Screening

Counseling and testing for human immunodeficiency virus (HIV) is recommended for all patients with TB. TB contacts at high risk for HIV infection should also be offered HIV counseling and testing.[34]

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, regardless of presence or absence of risk factors.
- Annual HIV screening of patients known to be at high risk[35]
- All patients in TB Clinics should be tested for HIV. This includes persons with TB disease or LTBI.[36]

For patients with a history of injection drug use, birth in Asia or Africa (or other hepatitis virus endemic regions), or who are HIV-positive, consider baseline testing for hepatitis B and C.[37,38]

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.[39]

Tuberculin Skin Test and Interferon Gamma Release Assays

Both the tuberculin skin test (TST) and interferon gamma release assay (IGRA) are acceptable tests for TB infection in most cases. Note that for patients with a previous documented positive TST reaction, a TST is not necessary. The IGRA currently approved by the Food and Drug Administration (FDA) and available on the market is QuantiFERON®-TB Gold (QFT-G), which can be used in all circumstances in which the TST is used. **At the present time, IGRA testing is only available through private laboratories in Alaska. The Alaska TB Program does not provide testing or routinely pay for IGRA testing without prior approval.**

The main advantage of the IGRA test is that results are more reliable in persons with a history of BCG vaccination (does not have false positive results related to this vaccine as TST can). Other advantages of IGRA testing include that results can be obtained after a single patient visit, and that the subjectivity associated with skin test reading can be eliminated. However, the IGRA test does require that blood collected is handled, incubated, and processed according to test-specific protocols.[40]

While a positive TST or IGRA result may indicate the presence of TB infection, additional tests, such as chest radiography and bacteriologic examination, are required to confirm TB disease.

Persons with a positive TST or IGRA 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.

A negative TST or IGRA does not rule out TB disease—as many as 20% of patients with TB disease have a negative TST reaction.[41] A negative TST or IGRA 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.[42]

For more information on the Mantoux TST, see the Diagnosis of Latent Tuberculosis Infection section **7.7**. For more information on IGRAs and the QuantiFERON®-TB Gold (QFT-G) Test, see the CDC's "Guidelines for Using the QuantiFERON®-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.

Chest Radiography

A posterior-anterior radiograph of the chest is the standard view used for the detection 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 undergo posterior-anterior and lateral radiographs. See Diagnosis and Treatment of Latent Tuberculosis Infection (LTBI) and Tuberculosis Disease in Children **9.1**

Certain abnormalities on chest radiographs are suggestive, but 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.

In HIV-infected and other immunosuppressed 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.[43]

For more information on chest radiography, see the Curry International Tuberculosis Center's *Radiographic Manifestations of Tuberculosis: A Primer for Clinicians* (2011) at

http://currytbcenter.ucsf.edu/products/product_details.cfm?productID=EDP-04

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**

Suspected Diagnosis	Specimen Needed
Pulmonary or laryngeal tuberculosis (TB)	Three morning sputum (phlegm from deep in the lungs) samples for TB 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.
Extrapulmonary TB	Depending on the anatomical site, other clinical specimens are necessary, such as: ▪ Urine ▪ Cerebrospinal fluid ▪ Pleural fluid ▪ Pus or other aspirated fluid ▪ Biopsy specimens ▪ Blood (heparinized)

CDC recommends the use of a rapid molecular test (NAA or GeneXpert) on at least one (1) specimen from each patient with signs and symptoms of pulmonary tuberculosis for whom a diagnosis of tuberculosis is being considered but has not been established, and for whom the test result would alter case management or tuberculosis control activities.[44]

Weblink:
https://www.cdc.gov/mmwr/preview/mmwrhtml/mm5801a3.htm?s_cid=mm5801a3

Contact the Alaska TB Program at 907-269-8000 to request molecular testing for patients meeting these criteria. Refer to Table 7 below for information on the bacteriology tests used to diagnose TB.

Table 7: **BACTERIOLOGY TESTS USED IN DIAGNOSING TUBERCULOSIS DISEASE**[45]

Test	Description	Laboratory Turnaround Times
Acid-Fast Bacilli (AFB) Smear	▪ 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. ▪ 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).	▪ On-site test: within 24 hours from specimen collection. ▪ Off-site test: within 24 hours from laboratory receipt of specimen (time from specimen collection to laboratory receipt should be 24 hours or less).[46]
Nucleic Acid Amplification (NAA) Test [47]	▪ A test done on clinical specimens for the direct and rapid identification of the *Mycobacterium tuberculosis* complex. ▪ Allows for the amplification of specific target sequences of nucleic acids that will be detected by a nucleic acid probe. ▪ Does not replace the need for routine AFB smear and culture.[48]	GeneXpert® Xpert® MTB/RIF Assay: ▪ On-site test: within 24 hours from specimen collection Off-site test: within 24-48 hours from laboratory receipt of specimen [49,50] TB PCR ▪ Off-site test: within 24-48 hours from laboratory receipt of specimen
Culture	▪ Usually necessary for species identification of all clinical specimens suspected of containing mycobacteria. ▪ Is required for drug susceptibility testing and genotyping.	▪ Mycobacterial growth detection: within 14 days from specimen collection ▪ Identification of mycobacteria: within 21 days from specimen collection [51,52]
Drug Susceptibility Testing	▪ For first-line drugs: Is performed on initial isolates of all patients to identify an effective antituberculosis regimen. ▪ For both first-line and second-line drugs: Is repeated on interim isolates when a patient remains culture-positive after 3 months of treatment.[53,54]	▪ First-line drugs (ASPHL): within 15 days from identification ▪ Second-line drugs (Reference lab): 4 weeks from laboratory receipt of isolate

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, cultures, NAA or GeneXpert results, 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.[55]

For information on reporting, see the “Reporting Tuberculosis” topic in the Surveillance section **2.6**.

For a list of all of the laboratory services available and information on specimen collection and shipment, see the Laboratory Services section **(12.1)** or visit: http://dhss.alaska.gov/dph/Labs/Pages/publications/default.aspx

Resources and References

Resources

- ATS, CDC, IDSA. "Diagnosis of Tuberculosis in Adults and Children" (*Clinical Infectious Diseases 2017*;64[2]:1-33). Available at: https://www.cdc.gov/tb/publications/guidelines/pdf/cid_ciw694_full.pdf
- CDC. *Self-Study Modules 1 – 9 on Tuberculosis* (Division of Tuberculosis Elimination Web site; 2019). Available at: http://www.cdc.gov/tb/education/ssmodules/default.htm
- CDC. *Core Curriculum on Tuberculosis (2013)* (Division of Tuberculosis Elimination Web site; updated October 2013). Available at: https://www.cdc.gov/tb/education/corecurr/index.htm

References

[1] 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.
[2] 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.
[3] 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.
[4] 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.
[5] 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.
[6] Chapter 2:Transmission and Pathogenesis of Tuberculosis. *Core Curriculum on Tuberculosis: What the Clinician Should Know (2013)* [Division of Tuberculosis Elimination Web site]. Updated May 2016. Available at: https://www.cdc.gov/tb/education/corecurr/pdf/chapter2.pdf . Accessed December 23, 2020.
[7] 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.
[8] CDC. Targeted tuberculin testing and treatment of latent tuberculosis infection. *MMWR* 2000;49(No. RR-6):8–9.
[9] ATS, CDC, IDSA. Treatment of Drug-Susceptible Tuberculosis. *Clinical Infectious Diseases 2016*; 63(7):147-95.
[10] 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.
[11] 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.
[12] 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.
[13] 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.
[14] 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 4: diagnosis of TB. Core Curriculum on Tuberculosis (2013) [Division of Tuberculosis Elimination Web site]. Updated 2013. Available at: http://www.cdc.gov/tb/education/corecurr/pdf/chapter4.pdf. Accessed December 29, 2020. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care settings, 2005. *MMWR* 2005;54(No. RR-17):11; A ATS, CDC, IDSA. Diagnosis of Tuberculosis in Adults and Children. *Clinical Infectious Diseases 2017*; 64(2):1-33.; CDC. Module 3: Targeted Testing and the Diagnosis of Latent Tuberculosis Infection and Disease. *Self-Study Modules on Tuberculosis* [Division of Tuberculosis Elimination Web site]. 2019. Available at: Self-Study Modules On Tuberculosis Targeted Testing and the Diagnosis of Latent Tuberculosis Infection and Tuberculosis Disease (cdc.gov) Accessed December 29, 2020.

[15] 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.

[16] 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.

[17] CDC. Chapter 4: diagnosis of TB. Core Curriculum on Tuberculosis (2004) [Division of Tuberculosis Elimination Web site]. Updated 2013. Available at: https://www.cdc.gov/tb/education/corecurr/pdf/chapter4.pdf. Accessed December 29, 2020.

[18] CDC. Classification system. In: Chapter 4: diagnosis of TB. Core Curriculum on Tuberculosis (2004) [Division of Tuberculosis Elimination Web site]. Updated 2013. Available at: https://www.cdc.gov/tb/education/corecurr/pdf/chapter4.pdf. Accessed December 29, 2020.

[19] 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. 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; Medical evaluation. In: CDC. Chapter 4: diagnosis of TB. Core Curriculum on Tuberculosis (2004) [Division of Tuberculosis Elimination Web site]. Updated 2013. Available at: https://www.cdc.gov/tb/education/corecurr/pdf/chapter4.pdf. Accessed J December 29, 2020.
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. Diagnosis of Tuberculosis in Adults and Children. *Clinical Infectious Diseases 2017*; 64(2):1-33.
CDC. Module 3: Targeted Testing and the Diagnosis of Latent Tuberculosis Infection and Disease. *Self-Study Modules on Tuberculosis* [Division of Tuberculosis Elimination Web site]. 2019. Available at: Self-Study Modules On Tuberculosis Targeted Testing and the Diagnosis of Latent Tuberculosis Infection and Tuberculosis Disease (cdc.gov) Accessed December 29, 2020; and CDC. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care settings, 2005. *MMWR* 2005;54(No. RR-17):11.

[22] 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.

[23] CDC. Diagnostic microbiology. In: Chapter 4: diagnosis of TB. Core Curriculum on Tuberculosis (2004) [Division of Tuberculosis Elimination Web site]. Updated 2013. Available at: https://www.cdc.gov/tb/education/corecurr/pdf/chapter4.pdf. Accessed December 29,2020.

[24] 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.

[25] 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.
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. The report includes the following references: (1) Gen-Probe Incorporated. Amplified *Mycobacterium Tuberculosis* Direct Test Package Insert. Gen-Probe Incorporated, San Diego, CA, 2001; (2) ATS, CDC, IDSA. Diagnosis of Tuberculosis in Adults and Children. *Clinical Infectious Diseases 2017*; 64(2):1-33. (3) Piersimoni, C. and Scarparo, C. Relevance of commercial amplification methods for direct detection of *Mycobacterium tuberculosis* Complex in clinical samples. *Journal of Clin. Micro.*, December, 2003: 5355-5365; (4) Centers for Disease Control and Prevention. Update: Nucleic acid amplification tests for tuberculosis. *MMWR*, 2000; 49:593-594; (5) Schluger, N.W. Changing approaches to the diagnosis of tuberculosis. *Am. J. of Resp. Crit. Care Med.*, 2001; 164:2020; (6) Catanzaro et al. The role of Clinical suspicion in evaluation as a new diagnostic test for active tuberculosis. *JAMA*, Feb. 2, 2000; Vol. 283 No. 5 P.639.

[27] Daley CL, Gotway MB, Jasmer RM. *Radiographic manifestations of tuberculosis: a primer for clinicians, second edition.* San Francisco, CA: Francis J. Curry National Tuberculosis Center; 2011:1–30.

[28] CDC. "The medical history." In: Module 3: Targeted Testing and the Diagnosis of Latent Tuberculosis Infection and Disease. *Self-Study Modules on Tuberculosis* [Division of Tuberculosis Elimination Web site]. 2019. Available at: Self-Study Modules On Tuberculosis Targeted Testing and the Diagnosis of Latent Tuberculosis Infection and Tuberculosis Disease (cdc.gov) Accessed December 29, 2020.

[29] CDC. Medical evaluation. : Chapter 4: diagnosis of TB. Core Curriculum on Tuberculosis (2004) [Division of Tuberculosis Elimination Web site]. Updated 2013. Available at: https://www.cdc.gov/tb/education/corecurr/pdf/chapter4.pdf. Accessed December 29, 2020.; and CDC. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care settings, 2005. *MMWR* 2005;54(No. RR-17):11.

[30] ATS, CDC, IDSA. Diagnosis of Tuberculosis in Adults and Children. *Clinical Infectious Diseases 2017*; 64(2):1-33; 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 4: diagnosis of TB. Core Curriculum on Tuberculosis (2004) [Division of Tuberculosis Elimination Web site]. Updated 2013. Available at: https://www.cdc.gov/tb/education/corecurr/pdf/chapter4.pdf. Accessed December 29, 2020.
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. Diagnosis of Tuberculosis in Adults and Children. *Clinical Infectious Diseases 2017*; 64(2):1-33.

[32] CDC."The medical history" In: Module 3: Targeted Testing and the Diagnosis of Latent Tuberculosis Infection and Disease. *Self-Study Modules on Tuberculosis* [Division of Tuberculosis Elimination Web site]. 2015. Available at: : Self-Study Modules On Tuberculosis Targeted Testing and the Diagnosis of Latent Tuberculosis Infection and

Tuberculosis Disease (cdc.gov) Accessed December 29, 2020.; and CDC. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care settings, 2005. *MMWR* 2005;54(No. RR-17):11.

[33] CDC."The medical history" In: Module 3: Targeted Testing and the Diagnosis of Latent Tuberculosis Infection and Disease. *Self-Study Modules on Tuberculosis* [Division of Tuberculosis Elimination Web site]. 2019. Available at: : Self-Study Modules On Tuberculosis Targeted Testing and the Diagnosis of Latent Tuberculosis Infection and Tuberculosis Disease (cdc.gov) Accessed December 29, 2020.

[34] 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.

[35] CDC. Revised Recommendations for HIV Testing of Adults, Adolescents, and Pregnant Women in Health-Care Settings. *MMWR* 2006;55(No. RR-14):1–17.

CDC. TB Elimination Recommendations for Human Immunodeficiency Virus (HIV) Screening in Tuberculosis (TB) Clinics. (2012) [Division of Tuberculosis Elimination Website]. Updated August 2012. Available at: https://www.cdc.gov/tb/publications/factsheets/testing/hivscreening.pdf

[37] CDC. Recommendations for Routine Testing and Follow-up for Chronic Hepatitis B Infection. Updated 2019. Available at: https://www.cdc.gov/hepatitis/hbv/HBV-RoutineTesting-Followup.htm

[38] CDC. Testing Recommendations for Hepatitis C Virus Infection. Updated 2020. Available at: https://www.cdc.gov/hepatitis/hcv/guidelinesc.htm

[39] CDC. Medical evaluation. In: Chapter 4: diagnosis of TB. Core Curriculum on Tuberculosis (2004) [Division of Tuberculosis Elimination Web site]. Updated 2013. Available at: https://www.cdc.gov/tb/education/corecurr/pdf/chapter4.pdf. Accessed December 29, 2020; and Colorado Department of Public Health and Environment. Tuberculosis Manual [Colorado Department of Public Health and Environment Web site]. (2017):3-1. Available at: Colorado TB Manual | Department of Public Health & Environment Accessed December 29, 2020.

[40] CDC. Guidelines for using the QuantiFERON®-TB Gold test for detecting *Mycobacterium tuberculosis* infection, United States. *MMWR* 2005;54(No. RR-15):52 and CDC. Updates Guidelines for Using Interferon Gamma Release Assays to detect *Mycobacterium tuberculosis* infection, United States 2010. *MMWR* 2010;59 (No. RR-5);1-25. Available at: http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5905a1.htm?s_cid=rr5905a1_e

[41] CDC. Targeted tuberculin testing and treatment of latent tuberculosis infection. MMWR 2000;49(No. RR-6):25.

[42]CDC. Medical evaluation. In: Chapter 4: diagnosis of TB. Core Curriculum on Tuberculosis (2004) [Division of Tuberculosis Elimination Web site]. Updated 2013. Available at: https://www.cdc.gov/tb/education/corecurr/pdf/chapter4.pdf. Accessed December 29, 2020.

[43]CDC. Medical evaluation. In: Chapter 4: diagnosis of TB. Core Curriculum on Tuberculosis (2004) [Division of Tuberculosis Elimination Web site]. Updated 2013. Available at: https://www.cdc.gov/tb/education/corecurr/pdf/chapter4.pdf. Accessed December 29, 2020.

[44] ATS, CDC, IDSA. Treatment of Drug-Susceptible Tuberculosis. *Clinical Infectious Diseases 2016*; 63(7):147-95.

[45] 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.

[46] 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.

[47] 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.

[48] ATS, CDC, IDSA. Diagnostic standards and classification of tuberculosis in adults and children. *Am J Respir Crit Care Med* 2000;161:1384.

[49] 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.

[50] 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.

[51] 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.

[52] 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.

[53] 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.

[54] ATS, CDC, IDSA. Treatment of tuberculosis. *MMWR* 2003;52(No. RR-11):12.

[55] CDC. Diagnostic microbiology. In: Chapter 4: diagnosis of TB. Core Curriculum on Tuberculosis (2004) [Division of Tuberculosis Elimination Web site]. Updated 2013. Available at: https://www.cdc.gov/tb/education/corecurr/pdf/chapter4.pdf. Accessed December 29, 2020.