Tuberculosis

<table>
<tr><td>Signs and Symptoms</td><td>TB infection to disease may be viewed on a continuum where someone may have several symptoms and others perceive none. Symptoms of active TB disease may include:
A cough that lasts three weeks or longer
Coughing up blood or sputum (phlegm from deep inside the lungs)
Chest pain
Weakness or fatigue
Weight loss
Loss of appetite
Chills
Fever
Night sweats
Symptoms can vary depending on the part of the body affected by TB and may be both pulmonary and extrapulmonary.
Extrapulmonary TB: TB disease that affects organs in addition to or instead of the lungs. Symptoms may include:
Blood in the urine if the TB affects the kidneys
Headache or confusion if the TB affects the brain (TB meningitis)
Back pain if the TB affects the spine
Hoarseness if the TB affects the larynx
Firm red or purple swelling under the skin if the TB affects the lymph nodes</td></tr>
<tr><td>Incubation</td><td>TB disease can develop very soon after infection or many years after infection. In the United States, unless treated, about 5% of the people who have recently been infected with MTB will develop TB disease in the first year or two after infection. Another 5% will develop TB disease later in their lives. The risk that active TB disease will develop is higher for some individuals than others. See complete document for common risk factors for exposure and progression to active TB disease.</td></tr>
<tr><td>Case classification</td><td>Clinical criteria for active TB disease: A case that meets all the following criteria:
A positive TST or positive IGRA for MTB
Other signs and symptoms compatible with TB disease (e.g., abnormal chest radiograph, abnormal chest computerized tomography scan or other chest imaging study, or clinical evidence of current disease. This may include symptoms for extrapulmonary TB which can occur anywhere in the body)
Treatment with two or more anti-TB medications
A completed diagnostic evaluation
Laboratory Criteria for Diagnosis
Isolation of MTB from a clinical specimen, * OR
Demonstration of MTB complex from a clinical specimen by nucleic acid amplification test (NAAT), ** OR
Demonstration of acid-fast bacilli (AFB) in a clinical specimen when a culture has not been or cannot be obtained or is falsely negative or contaminated.
**See complete document below for notes.</td></tr>
<tr><td></td><td>Confirmed:
A case that meets the clinical case definition or is lab confirmed.</td><td>Suspect / Probable:
A positive or negative TST or IGRA for MTB, + other signs and symptoms compatible with TB disease (e.g., abnormal chest radiograph, abnormal chest computerized tomography scan or other chest imaging study, or clinical evidence of current disease. This may include symptoms for extrapulmonary TB which can occur anywhere in the body.</td></tr>
</table>

Differential diagnosis	Pulmonary TB may look like any of the following: • Sarcoidosis: Mainly differentiated from tuberculosis by the presence of non-caseating granuloma. • Fungal infections: e.g. Coccidioidomycosis Histoplasmosis, Aspergillosis, Actinomycosis, Blastomycosis, and Nocardiosis. Epidemiological history aid in determining the risk of developing these infections. • Nontuberculous mycobacterial infections (NTM): such as *Mycobacterium kansasii*. • Lung malignancy and lymphoma: Tissue biopsy is needed to rule out this diagnosis if suspected • Lung abscess Extrapulmonary TB: depends on the part of the body affected. Pulmonary TB must be ruled-out when extrapulmonary TB is suspected or diagnosed. Diagnostic elements include: • Epidemiologic risk • Clinical syndrome • Physical exam findings • Imaging • Specimen collection • Accessory testing (HIV, TST/IGRA, CMP, CBC/DIFF) to aid with diagnosis and treatment. • Results of above + medical judgement
Treatment	Clinicians should not wait for bacteriologic culture results before starting therapy. **Therapy should be started when the potential risks of TB exceed the risk of therapy.** Consult the Official American Thoracic Society/Centers for Disease Control and Prevention/Infectious Diseases Society of America Clinical Practice Guidelines: Treatment of Drug-Susceptible Tuberculosis for evidence-based recommendations about TB treatment.
Duration	About 10% of people infected with TB will develop TB disease, especially in those with a weakened immune system like children under 5 and persons living with HIV. In most people, the TB bacteria remain inactive for a lifetime without causing disease. This latent state occurs when someone breaths in the bacteria, but their body can keep the bacteria from growing. People with latent TB infection: • Have no symptoms • Can't spread TB bacteria to others • May develop TB disease if they do not receive treatment for latent TB infection • Untreated active TB will eventually lead to death in up to 50% of cases
Exposure	TB spreads person to person through the air. When a person with infectious TB disease coughs, sneezes, speaks, or sings, tiny particles containing MTB may be expelled into the air. These particles, 1 to 5 microns diameter droplet nuclei can remain suspended in the air for several hours, depending on the environment. Persons who spend a lot of cumulative time in enclosed spaces with people who have infectious TB disease are the most likely to be infected with MTB.
Laboratory testing	Sputum and other body fluids/tissue testing is available through most commercial labs and includes: GeneXpert PCR or other MTB NAAT, AFB Smear, AFB/MTB Culture, Species Identification, and Drug Sensitivity Testing. Local Health Jurisdictions (LHJ) can arrange for testing through the Washington State Public Health Laboratory (PHL) to include most of the testing previously mentioned as well as Whole Genome Sequencing (WGS). The PHL can also arrange for specialized drug sensitivity testing by the CDC and other specialized laboratories at the request of LHJs. All laboratories that identify a positive MTB specimen from a Washington resident are required to submit a reference isolate to the WA PHL. The PHL Mycobacteriology Unit serves as a reference laboratory for the identification of mycobacterial strains as well as performing several

	other diagnostic tests. It also facilitates referral of all cultures for genotyping and specimens needing molecular detection of drug resistance. ***Specimen Collection and Shipping**:* Collect and ship specimens according to PHL requirements: https://doh.wa.gov/public-health-provider-resources/public-health-laboratories/lab-test-menu
Public health actions **URGENT**	**When to report:** See: WAC-246-101 and Notifiable Conditions Reporting Posters. • **Health care providers and Health care facilities**: TB disease (confirmed or highly suspicious, i.e., initiation of empiric treatment) notifiable to **local health jurisdiction** (LHJ) within 24 hours. • **Laboratories**: Positive results for *Mycobacterium tuberculosis* complex (MTBC) culture, nucleic acid amplification (NAT or NAAT), and drug susceptibilities (molecular and culture-based) are notifiable to the **Department of Health (DOH)** within 2 business days by secure electronic data transmission. Specimen submission is required for MTBC positive isolate (earliest available isolate for the patient) to the DOH Public Health Lab within 2 business days. • **Local health jurisdictions (LHJ)**: Notify **Department of Health** (DOH) using a secure electronic disease surveillance system within 3 business days of receiving a case report or laboratory report. • Persons with active TB who transfer from another jurisdiction must also be reported within timeframes above from time of arrival in the local jurisdiction. See: TB Manual Chapter 17: Statues & Regulations for all WACs and RCWs related to TB. **Infection Control:** The main goals of a TB infection-control program are to ensure early and prompt • detection of TB disease, • airborne precautions (e.g., isolation of people with confirmed or presumptive TB disease), and • treatment of people with confirmed or presumptive TB disease. Isolation of TB patients while infectious is critical in preventing the spread of TB. However, isolation should not be used any longer than is necessary to prevent the transmission of TB. See complete document below for information about Contact Identification, infection control in healthcare settings and special situations including home, congregate settings, airplanes and other modes of transportation.

Tuberculosis

1. DISEASE REPORTING

A. Purposes of Reporting and Surveillance

1. To identify and ensure the adequate evaluation, isolation, treatment, and continuity of care of persons with highly suspected and confirmed tuberculosis (TB) disease.
2. To identify and ensure the adequate evaluation and treatment of contacts to persons with infectious TB disease.
3. To assess trends in epidemic patterns, understand the impact of the burden of disease on populations and the health care infrastructure, and better target population-level disease prevention efforts.

B. Legal Reporting Requirements

1. **Health care providers and Health care facilities**: TB disease (confirmed or highly suspicious, i.e., initiation of empiric treatment) notifiable to **local health jurisdiction** (LHJ) within 24 hours.
2. **Laboratories**: Positive results for *Mycobacterium tuberculosis* complex (MTBC) culture, nucleic acid amplification (NAT or NAAT), and drug susceptibilities (molecular and culture based) are notifiable to the **Department of Health (DOH)** within 2 business days by secure electronic data transmission. Specimen submission is required for MTBC positive isolate (earliest available isolate for the patient) to the DOH Public Health Lab within 2 business days.
3. **Local health jurisdictions (LHJ)**: Notify **Department of Health** (DOH) using a secure electronic disease surveillance system within 3 business days of receiving a case report or laboratory report.
4. Persons with active TB that transfer from another jurisdiction must also be reported within timeframes above from time of arrival in the local jurisdiction.

See: WAC-246-101 and Notifiable Conditions Reporting Posters. and TB Manual Chapter 17: Statues & Regulations for all WACs and RCWs related to TB.

C. Local Health Jurisdiction Identification Responsibilities

1. Use every available means to ascertain the existence of, and immediately to investigate, all reported or suspected cases of TB in the infectious stages to ascertain the sources of such infection. (RCW 70.28) See: WAC 246-100-211 and WAC 246-170.
2. Coordinate all aspects of the prevention, treatment, and control of TB, including prevention and screening high-risk populations, diagnosis and monitoring, treatment planning, and case management. Assure provision of care including directly observed therapy and case management.
3. Conduct contact identification to identify person exposed to TB (see more in Routine Case and Contact Identification section).
4. Mandate isolation of a person with TB if infectious person does not observe precautions. Impose isolation of a person with tuberculosis in an infectious stage if that person does not observe precautions to prevent the spread of the infection.

5. Rule out infectious TB among all extrapulmonary TB through sputum collection and chest x-ray.
6. Report all confirmed case data (case definition below) to OCDE via the Washington Disease Reporting System (WDRS).

2. THE DISEASE AND ITS EPIDEMIOLOGY

A. Etiologic Agent

Mycobacteria are a group of bacteria that can cause a variety of diseases. Some mycobacteria are grouped as *Mycobacterium tuberculosis* (MTB) complex because they cause TB or diseases similar to TB. In the United States, most TB cases are caused by an organism called *Mycobacterium tuberculosis*, also sometimes called tubercle bacilli. Other mycobacteria that can cause human TB disease include *M. bovis*, *M. africanum*, *M. microti*, and *M. canetti*.

B. Description of Illness

Tuberculosis (TB), a disease also historically known as consumption, wasting disease, and the white plague, has affected humans for centuries. TB is caused by germs that are spread from person to person through the air. TB usually affects the lungs, but it can affect other parts of the body, such as the brain, lymph nodes, or bones. It is one of the most common infections in the world. Every year, about 10 million people develop TB disease, and 1.6 million people die of it. TB disease is the leading causes of death due to an infectious disease in the world.

To eliminate TB we must continue to find and treat people with active TB disease and test for and treat people with latent TB infection (LTBI) to prevent progression to disease. TB can be fatal if not treated in time, even in the United States and Washington State.

Infection with MTB may be viewed on a continuum from MTB infection to active infectious TB disease based on the bacillary burden of disease. For simplicity in clinical and public health settings patients are categorized as having either latent TB infection (LTBI) or active TB disease.

C. TB in Washington State

1. **TB Disease**

TB disease can be diagnosed in a myriad of ways primarily lead by epidemiologic evidence of exposure, immunologic evidence of infection, and bacteriologic and radiographic evidence of disease. TB disproportionately affects vulnerable populations in Washington. On average, almost four cases of TB disease are diagnosed in Washington each week or around 200 cases per year. Since 2011, incidence rates of TB in Washington have progressed downward overall, like the trend seen in the United States (U.S.) as a whole. The Washington TB incidence rate in 2021 was 2.6 cases per 100,000 population and is expected to increase over the next few years due to the syndemic impact of COVID-19. While the overall decline in TB incidence is encouraging, the current level of progress in the elimination of TB remains insufficient to eliminate TB in Washington in this century.

2. **Latent TB Infection (LTBI)**

LTBI is diagnosed by a positive interferon-gamma release assay (IGRA) or TB skin test after examinations (such a symptom review and chest radiograph with possible mycobacteriology) have ruled out TB disease. About 10% of people infected with TB will develop TB disease,

especially in those with a weakened immune system like children under 5 and persons living with HIV. In most people, the TB bacteria remain inactive for a lifetime without causing disease. This latent state occurs when someone breaths in the bacteria, but their body can keep the bacteria from growing. People with latent TB infection:

- Have no symptoms
- Can't spread TB bacteria to others
- May develop TB disease if they do not receive treatment for latent TB infection

An estimated 200,000 people in Washington are infected with TB. https://journals.plos.org/plosone/article/figure?id=10.1371/journal.pone.0249012.t003) Those at highest risk for progression to TB disease are outlined in the table below: ***Common Risk Factors for TB EXPOSURE and PROGRESSION to Disease***

D. Reservoir

MTB can infect and cause disease in several mammal species; humans are the overwhelming primary reservoir.

E. Modes of Transmission

TB spreads person to person through the air. When a person with infectious TB disease coughs, sneezes, speaks, or sings, tiny particles containing MTB may be expelled into the air. These particles, called droplet nuclei, are about 1 to 5 microns in diameter— less than 1/5000 of an inch. Droplet nuclei can remain suspended in the air for several hours, depending on the environment.

Persons who spend a lot of cumulative time in enclosed spaces with people who have infectious TB disease are the most likely to be infected with MTB. These persons, or contacts, may include family members, friends, roommates, coworkers, etc.

Transmission occurs when a person inhales air that contains droplet nuclei containing MTB, smaller droplet nuclei may reach the small air sacs of the lung (the alveoli), where infection may begin.

In the alveoli, some of the tubercle bacilli are killed, but a few multiply in the alveoli and enter the lymph nodes and bloodstream and spread throughout the body. Bacilli may reach any part of the body, including areas where TB disease is more likely to develop. These areas include the upper portions of the lungs, as well as the kidneys, the brain, and bone.

Within 2 to 8 weeks, however, the body's immune system usually intervenes, halting multiplication and preventing further spread. At this point, the person has latent TB infection (LTBI).

LTBI means that tubercle bacilli are in the body, and the body's immune system is keeping the bacilli suppressed and under control. The immune system does this by producing special immune cells that surround the tubercle bacilli. The cells form a shell that acts as a barrier and keeps the bacilli contained.

Not everyone who is exposed to a person with infectious TB disease becomes infected with MTB. The probability that TB will be transmitted depends on four factors:

- Infectiousness of the person with TB disease
- Environment in which the exposure occurred
- Frequency and duration of the exposure
- Susceptibility (immune status) of the exposed individual

LTBI is detected by the Mantoux tuberculin skin test (TST) or a blood test, an interferon-gamma release assay (IGRA). Most people with LTBI have a positive TST or IGRA result. From the time someone is infected to the time the test will show a positive result for infection can take up to ten weeks. The TST and IGRA are NOT appropriate tests to rule-out TB disease and can be falsely negative in those with active TB disease.

People who have LTBI, but not TB disease, are NOT contagious —they do not feel sick, and they cannot spread the infection to other people. Most of these people have a normal chest x-ray. It is important to remember that LTBI is not a "case" of TB.

Some people with LTBI develop TB disease later. TB disease develops when the immune system cannot keep the tubercle bacilli under control and the bacilli begin to multiply rapidly. The risk that TB disease will develop is higher for some people than for others.

Common Risk Factors for TB EXPOSURE and PROGRESSION to Disease

People at High Risk for **EXPOSURE** to or INFECTION with *M. tuberculosis*	People at High Risk for **PROGRESSING** to TB Disease after Infection with *M. tuberculosis*
• Contacts of people known or presumed to have infectious TB disease • People who were born in or who frequently travel to countries where TB disease is common, including Mexico, the Philippines, Vietnam, India, China, Haiti, Guatemala, or other countries with high rates of TB • People who currently live or used to live in large group settings where TB is more common, such as, homeless shelters, correctional facilities, or nursing homes • Employees of high-risk congregate settings • Health care workers who serve patients with TB disease • Populations defined locally as having an increased incidence of LTBI or TB disease, possibly including medically underserved populations, low-income populations, or persons who abuse drugs or alcohol • Infants, children, and adolescents exposed to adults who are at increased risk for LTBI or TB disease	• People living with HIV • Children younger than 5 years of age • People recently infected with M. tuberculosis (within the last 2 years) • People with a history of untreated or inadequately treated TB disease • Persons who are receiving immunosuppressive therapy such as tumor necrosis factor-alpha (TNF) antagonists, systemic corticosteroids equivalent to/greater than 15 mg of prednisone per day, or immunosuppressive drug therapy following organ transplantation • Persons with silicosis; chronic renal failure; leukemia; or cancer of the head, neck, or lung • Persons with diabetes mellitus • Persons who have had a gastrectomy or jejunoileal bypass • Persons with low body weight (<90% of ideal body weight) • People who use substances (such as injection drug use)

Core Curriculum on Tuberculosis: What the Clinician Should Know | Tuberculosis (TB) | CDC

F. Incubation Period

TB disease can develop very soon after infection or many years after infection. In the United States, unless treated, about 5% of the people who have recently been infected with MTB will develop TB disease in the first year or two after infection. Another 5% will develop TB disease later in their lives. In other words, about 10% of all people with normal immune systems who have LTBI will develop TB disease at some point in their lives. The remaining 90% will remain free of TB disease for the rest of their lives. However, some conditions can greatly increase the risk of developing TB disease.

Because about half the risk of developing TB disease is concentrated in the first 2 years after infection, it is important to detect new infection early. People with LTBI should be offered treatment to prevent them from getting sick with TB disease. Thus, detecting new infection early helps prevent new cases of TB.

Children <5 years of age and some conditions increase the risk that LTBI will progress to disease. These conditions increase the risk by negatively impacting the ability of the body's immune system to control the spread of tubercle bacilli. The risk may be about 3 times higher (as with diabetes) to more than 100 times higher (as with human immunodeficiency virus [HIV] infection) for people who have these conditions than for those who do not.

G. Period of Communicability

The best way to stop transmission is to isolate infectious persons and to start giving them the standard TB treatment as soon as possible. The length of time required for a patient with TB to become noninfectious after starting TB therapy varies and cannot be determined with certainty. However, once the standard TB therapy is started, and the patient follows the prescribed treatment regimen, the infectiousness of the patient can rapidly decline.

H. Treatment for Drug Susceptible TB Disease

Clinicians should not wait for bacteriologic culture results before starting therapy. **Therapy should be started when the potential risks of TB exceed the risk of therapy.**

Consult the Official American Thoracic Society/Centers for Disease Control and Prevention/Infectious Diseases Society of America Clinical Practice Guidelines: Treatment of Drug-Susceptible Tuberculosis

There are several treatment regimens recommended in the United States for drug susceptible TB disease. TB treatment can take 4, 6, or 9 months depending on the regimen. TB treatment regimens for drug susceptible pulmonary TB include:

- **6- or 9-month RIPE TB Treatment Regimen** (RIPE = rifampin, isoniazid, pyrazinamide, ethambutol)
  Treatment of Drug-Susceptible Tuberculosis. *Clin Infect Dis*, 2016
- **4-month Rifapentine-moxifloxacin TB Treatment Regimen**
  Interim Guidance: 4-Month Rifapentine-Moxifloxacin Regimen for the Treatment of Drug-Susceptible Pulmonary Tuberculosis — United States, 2022. MMWR Morb Mortal Wkly Rep, 2022

Shorter regimens help patients' complete treatment faster. Healthcare providers can choose the appropriate TB treatment regimen based on drug-susceptibility results (when available),

coexisting medical conditions (e.g., HIV, diabetes), and potential for drug-drug interactions. The Washington State TB Program can provide additional assistance and support in treating people with TB disease.

Directly observed therapy (DOT) is standard of care for all infectious TB, drug-resistant TB and in many high-risk settings. It is recommended for all TB treatment, including extra-pulmonary TB.

Multidrug-resistant TB (i.e., TB resistant to both isoniazid and rifampin) presents difficult treatment problems and requires expert consultation. The consequences of treatment failure and further acquired drug resistance make DOT a high priority for cases of drug-resistant TB, regardless of site of disease.

3. CASE DEFINITIONS

A. Clinical Description

A chronic bacterial infection caused by MTB, usually characterized pathologically by the formation of granulomas. The most common site of infection is the lung, but other organs may be involved.

B. Clinical Criteria

A case that meets all the following criteria:

- A positive TST or positive IGRA for MTB
- Other signs and symptoms compatible with TB disease (e.g., abnormal chest radiograph, abnormal chest computerized tomography scan or other chest imaging study, or clinical evidence of current disease. This may include symptoms for extrapulmonary TB which can occur anywhere in the body)
- Treatment with two or more anti-TB medications
- A completed diagnostic evaluation

C. Laboratory Criteria For Diagnosis

- Isolation of MTB from a clinical specimen, * **OR**
- Demonstration of MTB complex from a clinical specimen by nucleic acid amplification test (NAA), ** **OR**
- Demonstration of acid-fast bacilli (AFB) in a clinical specimen when a culture has not been or cannot be obtained or is falsely negative or contaminated.

D. Case Classification

Confirmed

A case that meets the clinical case definition or is laboratory confirmed

Comments

A case should not be counted twice within any consecutive 12-month period. However, a case occurring in a patient who previously had verified TB disease should be reported and counted again if more than 12 months have elapsed since the patient completed therapy. A case should also be reported and counted again if the patient was lost to supervision for greater than 12

months and TB disease can be verified again. Mycobacterial diseases other than those caused by *M. tuberculosis* complex should not be counted in TB morbidity statistics unless there is concurrent tuberculosis.

*Use of rapid identification techniques for MTB (e.g., DNA probes and mycolic acid high-pressure liquid chromatography performed on a culture from a clinical specimen) are acceptable under this criterion.

** Nucleic acid amplification (NAA) tests must be accompanied by culture for mycobacteria species for clinical purposes. A culture isolate of MTB complex is required for complete drug susceptibility testing and also genotyping. However, for surveillance purposes, CDC will accept results obtained from NAA tests approved by the Food and Drug Administration (FDA) and used according to the approved product labeling on the package insert, or a test produced and validated in accordance with applicable FDA and Clinical Laboratory Improvement Amendments (CLIA) regulations.

4. DIAGNOSIS AND LABORATORY SERVICES

A. Diagnosis

Diagnostic Elements

- Epidemiologic risk
- Clinical syndrome
- Physical exam findings
- Imaging
- Specimen collection
- Accessory testing (HIV, TST/IGRA, CMP, CBC/DIFF) to aid with diagnosis and treatment.
- Results of above + medical judgement

Consult the Official American Thoracic Society/Infectious Diseases Society of America/Center for Disease Control and Prevention Clinical Practice Guidelines: Diagnosis of Tuberculosis in Adults and Children for evidence-based recommendations about diagnostic testing for latent TB infection, pulmonary TB, and extrapulmonary TB.

Clinicians should not wait for bacteriologic culture results before starting therapy. Therapy should be started when the potential risks of TB exceed the risk of therapy.

B. Tests Available at Washington State Public Health Laboratory (WA PHL)

Sputum and other body fluids/tissue testing is available through most commercial labs and includes: GeneXpert PCR or other MTB NAAT, AFB Smear, AFB/MTB Culture, Species Identification, and Drug Sensitivity Testing.
Local Health Jurisdictions (LHJ) can arrange for testing through the Washington State Public Health Laboratory (PHL) to include most of the testing previously mentioned as well as Whole Genome Sequencing (WGS).
The PHL can also arrange for specialized drug sensitivity testing by the CDC and other specialized laboratories at the request of LHJs.

All laboratories that identify a positive MTB specimen from a Washington resident are required to submit a reference isolate to the WA PHL. The PHL Mycobacteriology Unit serves as a reference laboratory for the identification of mycobacterial strains as well as performing several other diagnostic tests. It also facilitates referral of all cultures for genotyping and specimens needing molecular detection of drug resistance.

Specimen Collection and Shipping:
Collect and ship specimens according to PHL requirements: https://doh.wa.gov/public-health-provider-resources/public-health-laboratories/lab-test-menu

Bacteriologic Tests Performed at WA PHL

Tuberculosis Laboratory Diagnostics Summary	
AFB Smear	• Tests for the presence of any mycobacterium. • Results available within 24 hours. • Provides clue to potential infectivity. • Does not differentiate between live and dead mycobacterium. • Performed in most laboratories.
AFB Culture	• Gold standard for diagnosing TB. • Results typically available in 2-6 weeks. • Only detects live mycobacterium. • Performed at WAPHL, Harborview, SKC PHL, PAML, UW, and commercial labs.
Species Identification	• Performed automatically on positive cultures to determine the type of mycobacterium present. • WAPHL uses Nucleic Acid Amplification Test (NAAT) to identify MTBC or MAC.
GeneXpert PCR	• Detects MTBC and rpoB mutations. • Performed on decontaminated/concentrated samples (1x per new patient, second by request). Only sputum is validated for GeneXpert. • Performed after AFB smear, if ordered (more sensitive on smear positive specimens). • A positive GeneXpert is considered a diagnosed case of TB. • A negative GeneXpert does not rule out TB. • Results available in 24-48 hours. • Does not differentiate between live and dead mycobacterium. • Two methods for NAA testing include: ○ Real-Time Polymerase Chain Reaction (RT-PCR) performed at WAPHL. ○ Hsp65 Sequencing performed at UW for NTM.
Drug Sensitivity Testing	• First-line (SIRE) performed automatically, using MGIT instrument, on culture positive specimens. • Available within 30 days of culture positive result, or 17 days from receiving specimens for reference specimens. • Performed at Harborview, PAML, or WAPHL. • Second-line performed at WAPHL or CDC using plate or Agar Proportion Method, if first-line resistance detected (except PZA) or as requested.

Drug Resistance Mutation Detection	• Detects common mutations located within specific regions of TB DNA associated with drug resistance. • Performed when requested on NAAT or culture positive specimens. • Molecular Detection of Drug Resistance (MDDR) is performed at CDC for detecting mutations. • MDDR turnaround time is 5 weeks from date received at CDC (sequencing results usually within 1-2 weeks, and phenotypic DST up to 5 weeks). • Detected mutation does not always mean total resistance to the drug(s).
Genotyping	• Performed automatically on culture positive specimens. • Determines the strain of TB and whether it matches other strains of TB. • Performed by a CDC contracted lab in Michigan.
Acronyms: Washington State Public Health Lab (WAPHL), Seattle and King County Public Health Lab (SKC PHL), Pathology Associates Medical Laboratory (PAML), University of Washington (UW), Non-tuberculosis mycobacteria (NTM), Centers for Disease Control (CDC), Streptomycin, Isoniazid, Rifampin, Ethambutol (SIRE), Pyrazinamide (PZA)	

https://doh.wa.gov/public-health-healthcare-providers/public-health-laboratories/lab-test-menu

C. Specimen Collection

- Specimen Collection Instructions: https://doh.wa.gov/sites/default/files/legacy/Documents/5230/SputumCollectionInstructions2011.pdf?uid=635add0b1f984

- *Mycobacterium* Isolates Form: https://doh.wa.gov/sites/default/files/legacy/Documents/Pubs/302-014-MycobacteriumIsolates.pdf?uid=635add0b1f39f

- Specimen Kit Order Form: https://doh.wa.gov/sites/default/files/legacy/Documents/Pubs/308-003-LaboratorySupplyOrderForm.pdf?uid=635add0b1caca

- WA PHL information: https://doh.wa.gov/public-health-healthcare-providers/public-health-laboratories

- TB Program Sharepoint Site: Nebulizer Starter Kits for sputum induction

5. ROUTINE CASE AND CONTACT IDENTIFICATION

Consult the Guidelines for the Investigation of Contacts of Persons with Infectious Tuberculosis (CDC) for evidence-based recommendations about conducting contact identification to identify person exposed to TB. The WA DOH TB Program also has several resources available related to contact identification on the TB Partners SharePoint site.

A. What is a TB contact identification?

A TB Contact Identification is a TB elimination strategy used to identify, find, and assess TB contacts and if needed, provide appropriate treatment for latent TB infection (LTBI) or TB disease. Effective contact identification interrupts the spread of TB in communities and help prevent outbreaks of TB.

B. Who are TB Contacts?

Contacts are persons who have shared airspace with a person with infectious TB disease. These persons may include household members, friends, coworkers, classmates, and others. During contact identification, public health investigators identify contacts by interviewing the TB case and visiting places where the case spent time while infectious.

C. Why is it Important to Identify and Assess TB Contacts?

It is important to quickly identify, find, and assess contacts for TB infection and disease. Approximately 1% of all TB contacts have TB disease at the time of the contact identification and need treatment for active TB disease. Additionally, about 20% to 30% of TB contacts are infected with MTB and are at risk for developing TB disease if not diagnosed and treated for LTBI.

Contacts who have either LTBI or TB disease should be offered the appropriate treatment. For contact identification to be considered successful, contacts should complete appropriate treatment if they have TB disease or LTBI.

Because of their age, young children with MTB infection are known to have been recently infected, and thus are at a high risk of progressing to life threatening forms of TB disease. Children younger than 5 years of age should be medically assessed, including a chest x-ray, regardless of a history of LTBI or TB disease treatment or an initial negative TST or IGRA result. Since TB disease may present differently in children than adults, clinicians with pediatric TB disease experience should be consulted, if available, during the assessment and medical evaluation process. Once TB disease has been ruled out, children younger than 5 years of age should receive LTBI treatment, even if their initial TST or IGRA result is negative, until TB infection has been completely ruled out 8-10 weeks post last exposure. This is called window period prophylaxis.

D. Who is responsible for conducting TB contact identification?

In Washington, local health jurisdictions (LHJs) are legally responsible for the prevention and control of TB in their communities. Thus, they are accountable for ensuring contact identification is performed for TB cases reported in their jurisdictions, even when patients are receiving care outside of the public health department.

Although LHJs are responsible for conducting contact identification, some steps of the process of contact identification and transmission of MTB occurs at a healthcare facility, contact identification may include hospital epidemiologists and infection control professionals. Whenever contact identification activities are delegated, the LHJ should work with those involved to ensure that the local policies and procedures are followed.

Contact identification is required for all confirmed cases that have infectious forms of TB disease (e.g., TB disease of the lungs, airways, or larynx).

The TB contact identification process should start as soon as a suspected or confirmed infectious TB case comes to the LHJs attention. This includes reviewing medical information and interviewing the case within one working day after the case is reported to the LHJ. It is important to respond promptly because

- some contacts may already have TB disease and need treatment.

- some contacts could be at risk for rapid development of TB disease.
- some contacts may become more difficult to locate as time goes by, such as persons experiencing homelessness.
- there could be ongoing transmission of MTB; and
- cases may have difficulty remembering all their contacts as time goes by.

Additional topics covered in CDC/WA guidance includes:

- Who should be prioritized in contact identification,
- Setting the infectious period, infectivity
- Expansion and using concentric circles
- When to test/how many rounds of testing
- Field visits
- LTBI treatment
- Congregate setting considerations
- Outbreaks
- Contacts to drug resistant cases
- Confidentiality
- Training
- Data management - WDRS

Notify the Washington State TB Program of contact identification that involves congregate settings or healthcare facilities and any that involve contacts to multi-drug-resistant cases.

6. CONTROLLING FURTHER SPREAD

Controlling the spread of TB is the responsibility of local and state public health.
Consult the CDC's Division of Tuberculosis Elimination resources for more comprehensive guidance and recommendations for controlling the spread of tuberculosis. Links to several of these resources can be found at the end of this section.

A. Infection Control Recommendations

The main goals of a TB infection-control program are to ensure early and prompt

- detection of TB disease,
- airborne precautions (e.g., isolation of people with confirmed or presumptive TB disease), and
- treatment of people with confirmed or presumptive TB disease.

Isolation of persons with TB while infectious is critical in preventing the spread of TB. However, isolation should not be used any longer than is necessary to prevent the transmission of TB.

B. Infection Control in the Home

Non-hospitalized patients with sputum smear positive TB should not attend school, go to work, fly on commercial airlines, etc. Patients with confirmed or presumptive TB disease are frequently sent home after starting treatment, even though they may still be infectious. Patients with TB disease can be sent home even if they are still considered infectious, if the following criteria are met:

- A follow-up plan has been made with the local TB program;

- The patient is on appropriate TB treatment and DOT has been arranged;
- No infants or children younger than 5 years of age or persons with immunocompromising conditions are present in the household (exception: such contacts who have been placed on window period prophylaxis can be present in the home);
- All household members, who are not immunocompromised, have been previously exposed to the person with TB; and
- The patient is willing to NOT travel outside his or her home until he or she has negative sputum smear results or has been deemed non-infectious by the local TB Control Officer.

If all the above criteria are met, patients with TB disease are allowed to isolate at home. Patients with infectious TB disease should not be allowed to return home where they may expose a person who is at high risk for progressing to TB disease if infected.

C. Infection Control in a Healthcare Facility

There are three types of infection control measures.

- The first are **administrative controls**, which are primarily aimed at early identification, isolation, and appropriate treatment of infectious patients.
- The second are **environmental controls**, which focus on preventing the spread and reducing the concentration of infectious droplet nuclei in the air. Examples include negative pressure air ventilation, HEPA filtration, ultraviolet germicidal irradiation (UVGI), etc.
- The third is **personal respiratory protection**, such as wearing fitted N95 respirators, which may provide additional protection for healthcare workers in high-risk settings such as isolation rooms and cough-inducing or aerosol-generating procedures.

D. Evaluating Exposure Settings

Field visits to sites of transmission are a key part of a comprehensive TB contact identification process. Physical conditions at each setting contribute to the likelihood of transmission. During field visits, the public health worker should observe environmental characteristics, such as room size, crowding, and ventilation systems and airflow patterns, to estimate the risk of TB transmission. Air volume, exhaust rate, and circulation assist in predicting the likelihood of transmission in an enclosed space. These factors should be considered in the context of how often and how long the index patient was in each setting.

In large indoor settings, the degree of proximity between contacts and the index patient can influence the likelihood of transmission. The most practical system for grading exposure settings is to categorize them by size (e.g., “1” being the size of a vehicle or car, “2” the size of a bedroom, “3” the size of a house, and “4” a size larger than a house). The volume of air shared between an infectious TB patient and contacts dilutes the infectious particles. Local circulation and overall room ventilation also dilute infectious particles, but both factors have to be considered because they can redirect exposure into spaces that were not visited by the index patient.

Further information on this topic is available in the CDC/WA documents listed in Resources section below.

E. Guidance and Recommendations for Controlling the Spread of Tuberculosis

- Guidance for specific populations and settings is available from the CDC, e.g., Residents of Correctional Facilities, People Experiencing Homelessness, International Travelers, etc.; Health Disparities in Tuberculosis | Tuberculosis (TB) | CDC

- CDC. Healthcare setting guidance Guidelines for Preventing the Transmission of Mycobacterium tuberculosis in Health-Care Settings, 2005.

- CDC. Tuberculosis Screening, Testing, and Treatment of U.S. Health Care Personnel: Recommendations from the National Tuberculosis Controllers Association and CDC, 2019

- Maunank Shah, Zoe Dansky, Ruvandhi Nathavitharana, Heidi Behm, Shaka Brown, Lana Dov, Diana Fortune, Nicole Linda Gadon, Katelynne Gardner Toren, Susannah Graves, Connie A Haley, Olivia Kates, Nadya Sabuwala, Donna Wegener, Kathryn Yoo, Joseph Burzynski, on Behalf of the National TB Coalition of America, National Tuberculosis Coalition of America (NTCA) Guidelines for Respiratory Isolation and Restrictions to Reduce Transmission of Pulmonary Tuberculosis in Community Settings, *Clinical Infectious Diseases*, 2024.

- Washington State TB Program SharePoint Site: Interim Isolation Guidelines

7. MANAGING SPECIAL SITUATIONS

A. Multiple Drug Resistant (MDR) and Extensively Drug Resistant (XDR) TB:

Drug-resistant TB is caused by MTB organisms that are resistant to the drugs normally used to treat the disease. This means those drugs can no longer kill the bacteria. Drug-resistant TB can be mono-resistant if the tubercle bacilli are resistant to any one TB treatment drug, or poly-resistant if resistant to at least two TB drugs (but not both isoniazid and rifampin).

Multidrug-resistant TB (MDR TB) means that the tubercle bacilli are resistant to at least isoniazid and rifampin, the two best first-line TB treatment drugs.

Extensively drug-resistant TB. (XDR TB) is caused by MTB strains that are resistant to isoniazid, rifampin, any fluoroquinolone and at least one additional drug in this list (second-line injectable [e.g., amikacin], bedaquiline, or linezolid).

Drug-resistant TB is more difficult to treat because the bacilli can survive in a patient's body even after they start treatment with the first-line TB treatment drugs, and it usually takes longer to diagnose drug-resistant TB making these patients infectious for a longer period of time. This may result in more people being infected. Drug-resistant TB is transmitted in the same way as drug-susceptible TB.
Drug-resistant TB can be caused in two different ways: primary and secondary (acquired).

- Person-to-person transmission of drug-resistant organisms causes primary resistance.
- Secondary resistance develops during TB treatment, either because the patient was not treated with an appropriate regimen or because the patient did not follow the treatment regimen as prescribed. In other words, if patients do not take all of their pills, or if they do not take their pills as often as prescribed, they could develop secondary drug-resistant

TB. Patients with TB should be closely monitored to see if they are responding to treatment, and they should remain in isolation until it is shown that they are no longer infectious.

- **Treatment for contacts infected with drug resistant TB requires expert consultation.**

B. Extra-Pulmonary TB

TB disease can occur in different places in the body and in more than one place at the same time. Pulmonary TB is TB that occurs in the lungs. Most TB cases are pulmonary. Most patients with pulmonary TB have a cough and an abnormal chest x-ray, and they should be considered contagious until they meet certain criteria.

Extrapulmonary TB occurs in places other than the lungs, such as the larynx, the lymph nodes, the pleura (the membrane surrounding each lung), the brain, the kidneys, or the bones and joints. Some patients who have extrapulmonary TB also have pulmonary TB. Most types of extrapulmonary TB are not considered contagious. However, as extrapulmonary TB is often accompanied by pulmonary TB the individual may still be contagious and would require chest radiograph and sputum to rule out disease in the lungs.

Of note, extrapulmonary TB that occurs in the larynx and the pleura should also be considered contagious.

C. TB in Congregate Settings:

What is a Congregate Setting?

A congregate setting is a setting in which a group of persons reside in close physical proximity. Examples of congregate settings include:

- Schools
- Shelters
- Nursing homes
- Correctional facilities
- Workplaces
- Hospitals or other healthcare settings

D. How are Contact Identifications Conducted in Congregate Settings?

Contact identifications involving congregate settings should follow the systematic contact identification process. However, there may be some additional challenges to consider when conducting contact identification in a congregate setting, including:

- Large numbers of contacts
- Incomplete data for determining which contacts should be prioritized for assessment
- Difficulties related to maintaining confidentiality
- Incomplete information about contacts' names and locating information
- A need to collaborate with officials and administrators who are not familiar with TB
- Media interest, particularly for contact identification involving schools or worksites
- Political implications of negative publicity related to TB
- Legal implications for the facility

E. TB Outbreaks

What is a TB Outbreak?

Definitions for TB outbreaks are relative to the local context. However, a TB outbreak is generally defined as a situation where there are

- More TB cases than expected within a geographic area or population during a particular time period, AND
- Evidence of recent transmission of MTB among those cases

A TB outbreak indicates potential extensive transmission because

1. a TB patient was contagious, and
2. contacts were exposed for a substantial period, and
3. the interval since exposure has been sufficient for infection to progress to disease.

Although the time period is not well defined, **recent transmission** generally refers to a situation where TB transmission occurred within the previous 2-year period. This implies that cases involved in an outbreak have been exposed and infected with MTB in the past 2 years, as opposed to having developed active TB disease from latent TB infection caused by exposure from a long time ago. Because an outbreak indicates that there is the potential for extensive transmission of MTB, a TB outbreak should always be considered a public health emergency.

Outbreak cases can be distinguished from other cases only when certain associations in time, location, patient characteristics, or MTB attributes (e.g., drug resistance patterns or genotype) become apparent. In low-incidence jurisdictions, any temporal cluster is suspicious for an outbreak. A working definition of a potential *TB outbreak* is helpful for planning and response, and may include any of the following six criteria (based on surveillance and epidemiology):

1. An increase in TB cases has occurred which is above the expected number of TB cases.
2. During and because of a contact identification, two or more contacts are identified as having TB disease, regardless of their assigned priority (i.e., high, medium, or low priority).
3. Any two or more cases occurring within one year of each other are discovered to be linked, and the linkage is established outside of a contact identification (e.g., two patients who received a diagnosis of TB disease outside a contact identification are found to work in the same office and only one or neither of the persons was listed as a contact to the other).
4. A genotype cluster leads to discovery of one or more verified transmission links that were missed during a contact identification within the prior two years.

Criteria based on program resources:

5. Transmission is continuing despite adequate control efforts by the TB control program.
6. Contact identification associated with increased cases requires additional outside help.

TB outbreak response is a process used by public health programs to investigate and intervene when a TB outbreak is suspected or confirmed. The ultimate goal of TB outbreak response is to interrupt ongoing transmission of MTB. An outbreak generally involves multiple TB cases with several overlapping contacts. Compared to TB contact identification, responding to TB outbreaks requires many more resources, a larger and more diverse group of partners and stakeholders, and more extensive collaboration and communication. More emphasis on active case finding is recommended, which can result in more contacts than usual having chest radiographs, specimen

collection for mycobacteriology testing, as well as the need for more resources for active and LTBI treatment. In an outbreak, contacts can be exposed to more than one case, and cases and contacts can be interrelated through multiple social connections which complicate efforts to set priorities. The risk factors contributing to a specific outbreak should be determined, because these findings will affect the contact identification process and inform the strategy.

F. Airplanes and Ships:

Transmissions of MTB have been confirmed on vessels at sea, commercial aircraft, passenger trains and buses. The WA State TB Program will notify Division of Global Migration Health (DGMH) regarding patients who are diagnosed after an international flight and who were potentially contagious during their flights. DGMH will work with the airlines and states to conduct a contact identification. Notification to DGMH is requested when the following parameters are met:

CDC criteria for initiating flight-related TB contact identification, June 2011

- Index case was diagnosed within 3 months of the flight **AND** the flight occurred within 3 months of notification to the DGMH.
- Flight lasted =8 hours gate-to-gate.*****
- Diagnosis of the index case was confirmed by sputum culture or nucleic acid amplification test for MTB **AND** is:
    1. Sputum smear-positive for acid-fast bacilli AND cavitation is present on a chest radiograph; **OR**
    2. Confirmed to have a multidrug-resistant isolate (regardless of the smear or chest radiograph results).

Note: A contact identification will be considered on a case-by-case basis for situations that are unusual or not clearly addressed by the criteria. Examples include, but are not limited to, situations in which an unusually high proportion of close contacts have positive TST or IGRA test screening results, an index case has laryngeal TB, or cavitation is detected on chest computed tomography scan but no chest radiograph was performed.
***** Gate-to-gate means all time spent on the aircraft, including boarding and deplaning time or delays on the tarmac.

8. ROUTINE PREVENTION

A. Vaccine Recommendations

None.

B. Prevention Recommendations

Prevention and control efforts should include three priority strategies:

1. Identifying and treating all persons who have TB disease.
2. Finding and evaluating persons who have been in contact with persons with TB to determine whether they have TB infection or disease and treating them appropriately.
3. Testing high-risk groups for TB infection to identify candidates for treatment of latent infection and to ensure the completion of treatment.

ACKNOWLEDGEMENTS

This document is a revision of the Washington State Guidelines for Notifiable Condition Reporting and Surveillance published in 2002 which were originally based on the Control of Communicable Diseases Manual (CCDM), 17th Edition; James Chin, Ed. APHA 2000. We would like to acknowledge the Oregon Department of Human Services for developing the format and select content of this document.

RESOURCES

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- Self-Study Modules on Tuberculosis Module 1: Transmission and Pathogenesis of Tuberculosis (cdc.gov)
- Self-Study Modules on Tuberculous. Module 5: Infectiousness and Infection Control (cdc.gov)
- Self-Study Modules on Tuberculosis Module 8: Contact Investigations for Tuberculosis (cdc.gov)
- Self-Study Modules on Tuberculosis Module 9 Tuberculosis Outbreak Detection and Response (cdc.gov)

Washington State Department of Health. Public Health Laboratory. Lab Test Menu | Washington State Department of Health

Washington State TB Program SharePoint Site:

- Washington State TB Services & Standards Manual (sharepoint.com)
- Case Management Tools (sharepoint.com)
- Other Program Resources (sharepoint.com)
- Laboratory Sciences
- Interim Isolation Guidelines

WHO. Departmental News. January 27, 2021. WHO announces updated definitions of extensively drug-resistant tuberculosis

UPDATES

December 2022: All sections of the TB Guidelines were reviewed and rewritten. For 2023 WAC revision combined provider and facility reporting requirement, updated laboratory submission (Section 1B).

December 2023: For 2024 WAC revision updated laboratory submission.

December 2024: TB cover pages were added to the TB Guidelines. All sections of the TB Guidelines were reviewed and updated including links to the TB Services and Standards Manual added, diagnostic elements expanded, WAPHL lab test and submission information updated, links added on guidance and recommendations for controlling spread of TB, resources were updated, and all hyperlinks were reviewed and updated.