Tuberculosis Program Manual

2017

Wyoming Department of Health
Communicable Disease Unit

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Abbreviations

AFB	acid-fast bacilli
BAL	bronchoalveolar lavage
BCG	bacille Calmette-Guérin vaccine
CDC	Centers for Disease Control and Prevention
CSF	cerebral spinal fluid
CXR	chest x-ray
DOT	directly observed therapy
EMB	ethambutol
HIPAA	Health Insurance Portability and Accountability Act of 1996
HIV	human immunodeficiency virus
IGRA	interferon-gamma release assay
INH	isoniazid
LTBI	latent tuberculosis infection
MDR-TB	multidrug-resistant tuberculosis
Mtb	*Mycobacterium tuberculosis*
NAAT	nucleic acid amplification testing
NTM	nontuberculous mycobacteria
PCR	polymerase chain reaction
PZA	pyrazinamide
PHI	protected health information
QFT	QuantiFERON®
RIF	rifampin
RPT	rifapentine
TB	tuberculosis
TNF-α	tumor necrosis factor alpha
TST	tuberculin skin test
U.S.	United States
WDH	Wyoming Department of Health
WGS	whole genome sequencing
WPHL	Wyoming Public Health Laboratory
XDR-TB	extensively drug-resistant tuberculosis

Glossary

acid-fast bacilli
Mycobacteria that when stained, retain color even after they have been washed in an acid solution and can be detected under a microscope.

active TB or TB disease
Condition in which M. tuberculosis has overwhelmed the defenses of the immune system, is actively replicating, and is causing disease.

airborne infection isolation room
Single occupancy patient care room in which ventilation, air pressure, and air filtration are controlled to minimize the transmission of infectious agents that are usually spread by droplet nuclei.

alveoli
The small air sacs at the end of airways in the lung.

anergy
Inability to react to skin test antigens because of a weakened immune system.

boosted reaction
An increased response of the immune system to a second or subsequent occasion on which it encounters a specific antigen.

cavity
A hollow space in the lung, visible on a chest x-ray, which may contain many tubercle bacilli; often occurs in people with severe pulmonary disease.

culture
Laboratory testing where organisms are grown on or in a nutritive media so they can be identified. A positive culture *grew* Mtb; a negative culture did not.

disseminated TB
TB disease that occurs when tubercle bacilli enter the bloodstream or lymph system and are carried to all parts of the body where they grow and cause disease in multiple sites, e.g., miliary TB.

droplet nuclei
Very small droplets, 1 to 5 microns in diameter. Expelled when a person coughs or sneezes; can remain suspended in the air for several hours depending on the environment.

extensively drug-resistant TB
TB that is resistant to isoniazid and rifampin, plus any fluoroquinolone and at least one of the injectable second-line drugs.

extrapulmonary TB
TB disease that occurs in places other than the lungs, such as the lymph nodes, pleura, brain, kidneys, or bones; most types of extrapulmonary TB are not infectious.

interferon-gamma release assay
Laboratory blood test that detects the presence of *M. tuberculosis* infection by measuring the immune response to Mtb in whole blood.

hemoptysis
Expectoration of blood or blood-stained sputum.

induration
A palpable, raised, hardened area.

latent TB infection or TB infection (LTBI)
Condition in which a person is infected with *M. tuberculosis* but does not have TB disease.

***Mycobacterium tuberculosis* complex**
A genetically related group of mycobacterium species that cause TB or diseases similar to TB. The organisms in the Mtb complex are *M. tuberculosis, M. bovis, M. africanum, M. microti, M. caprae, M. pinnipedii, M. canetti, and M. mungi.*

miliary TB
TB disease that occurs when bacilli enter the bloodstream and are carried to distant parts of the body; named because chest x-rays of patients with miliary TB often look like millet seeds scattered throughout the lung.

Multidrug-resistant TB
TB that is resistant to at least isoniazid and rifampin.

nontuberculous mycobacteria
Mycobacteria other than those comprising the *M. tuberculosis* complex, abundant in soil and water, rarely cause disease in humans.

paucibacillary
Having or made up of few bacilli.

peripheral neuropathy
Injury to nerves that provide sensation to the arms and legs, causing a tingling sensation or a weakened sense of touch in the hands or feet.

polymerase chain reaction
In vitro amplification of specific organism DNA.

primary TB
TB disease occurring soon after initial infection with Mtb. Occurs commonly in children or immunocompromised hosts. Primary TB is usually characterized by intrathoracic adenopathy, mid and lower lung zone infiltrates, and the absence of cavitation.

reactivation TB
TB disease occurring long after infection with Mtb. Usually occurs after a person has had latent TB infection for years and the immune system is compromised. May also be referred to as secondary TB.

silicosis
Form of lung disease resulting from occupational exposure to and inhalation of silica dust over a period of years, usually associated with concurrent tobacco use; characterized by a slowly progressing fibrosis of the lungs. It usually results in impairment of lung function.

skin test conversion
A tuberculin skin test reaction which increases in size by ≥10 mm within 2 years; indicative of recent infection with Mtb.

targeted testing
Recommendation of tuberculin skin testing for groups in which rates of TB are substantially higher than for the general population.

tubercle bacilli
Mycobacterium tuberculosis organisms.

Introduction

This manual was created to assist state and local health departments, private providers, and facilities in controlling, monitoring, testing, treating, and surveillance of TB infection and disease in the state of Wyoming. It is not possible for this guidance to address all situations or individuals; therefore, clinical judgement and common sense should always be exercised. Tuberculosis standards have been well established by nationally accepted scientific groups such as the American Thoracic Society, U.S. Centers for Disease Control, the National TB Controllers Association, and others. Although this manual is specific to the State of Wyoming, we follow those national standards and recommendations. As recommendations can change quickly, consulting with these organizations and using current best practices is suggested.

One of the goals of the Wyoming Communicable Disease Unit is to lower the burden of TB and ultimately help the U.S. obtain eradication of the disease. Reducing the incidence of TB will occur by reducing the risk of exposure and infection, reducing the risk of disease development once a person has been infected, and reducing the risk of transmission once a person develops disease. The fundamental strategies for reducing these risks are:

- Identification of high-risk persons with latent TB infection at risk for progression to TB disease and treatment with an effective drug regimen.
- Early and accurate detection, diagnosis, and reporting of TB disease, leading to initiation and completion of treatment.
- Identification of contacts to persons with infectious TB and treatment of those exposed with an effective drug regimen.
- Identification of settings in which a high risk exists for transmission of Mtb and application of effective infection control measures.

Authority

Medical care related to tuberculosis is provided on a cooperative basis by local public health offices, the private medical sector, and private and public employers throughout the state. Ultimately, the Wyoming Department of Health (WDH) is responsible for controlling transmission, preventing illness, and ensuring treatment of TB disease for any individuals within the state.

Wyoming laws and rules on TB are located within the Wyoming State Statutes. Please see http://legisweb.state.wy.us/LSOWeb/wyStatutes.aspx.

Roles and Responsibilities

Wyoming Department of Health

The state health department ensures compliance with applicable national and state public health laws and regulations related to TB reporting and control. The state consults with national organizations and authorities and communicates guidance to organizations in Wyoming. WDH conducts statewide TB surveillance, data evaluation, and development of policies and guidelines for the control and elimination of TB in the state. WDH is responsible for overseeing activities such as case management, contact and outbreak investigations, and source investigations.

WDH also provides training and education across the state, maintains patient drug assistance programs, and provides financial assistance for diagnostic testing for underserved or vulnerable individuals. WDH maintains records of all individuals diagnosed with active tuberculosis and is responsible for reporting to the CDC. WDH coordinates the state TB Advisory Committee and yearly cohort reviews.

The state epidemiologist provides consultation on issues related to disease transmission, isolation requirements, and infection control matters. State statute empowers the state health officer to direct and supervise prevention of communicable disease and maintain and enforce quarantine. The state health officer can delegate these powers to county health officers.

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Wyoming Department of Health
Communicable Disease Program
6101 Yellowstone Rd, Suite 510
Cheyenne, WY 82002

Program Manager (307) 777-3562
TB controller (307) 777-6563
State Epidemiologist (307) 777-7716
State Health Officer (307) 777-6340
Confidential fax (307) 777-5279
https://health.wyo.gov/publichealth/communicable-disease-unit/tuberculosis-2/

County Health Departments

Local public health departments cooperate with the state health department and healthcare facilities in their counties to ensure proper treatment and follow-up of individuals with TB and their contacts. County health officers may help ensure proper isolation and treatment of

individuals diagnosed with TB. Local health departments also perform many of the duties of contact and outbreak investigations, such as performing patient interviews and eliciting contacts. Local public health nursing routinely conducts targeted TB testing and case management of individuals with latent and active TB.

A list of local public health offices can be found at https://health.wyo.gov/publichealth/nursing/phn-co-offices/.

Wyoming Public Health Laboratory

The Wyoming Public Health Laboratory (WPHL) provides tuberculosis diagnostic services for any provider or facility in the state. This includes IGRA testing, AFB smears, culture identification and susceptibility testing, and nucleic acid amplification testing. WPHL also provides consultation, training, and referral services to other laboratories performing TB diagnostic services in the state.

Contact
Wyoming Public Health Laboratory
Combined Laboratories Facility
208 S College Dr.
Cheyenne, WY 82007
Phone (307) 777-7431
Fax (307) 777-6422
https://health.wyo.gov/publichealth/lab/

Private Providers

Medical providers and facilities in Wyoming are required to report individuals suspected or confirmed to have TB disease to the Wyoming Department of Health. Both the attending healthcare provider and laboratories performing diagnostic testing are required to report suspected or confirmed instances of TB disease within 24 hours of diagnosis. In addition, providers are encouraged to coordinate care and treatment of their patients with the state and local health departments. Together with the state and local health departments, the private provider assumes the responsibility for successful treatment of TB patients.

TB Advisory Committee

WDH coordinates a state TB Advisory Committee that is expected to meet annually to review TB program protocols and procedures and discuss and make recommendations in regard

to TB prevention and control in the state. The committee also functions as the cohort review team. The advisory committee is administered through the Communicable Disease Unit. Any person or entity within the state that has an interest in TB control is welcome to attend committee meetings.

Confidentiality

The U.S. Department of Health and Human Services created a privacy rule (colloquially referred to as HIPAA) in 1996 that ensures that individuals' health information is safeguarded while allowing high quality care and protection of the public's health and well-being. Protected health information (PHI) is any individually identifiable health information in any form, such as an individual's past, present, or future physical condition, health care provided to an individual, and information related to payment. The privacy rule permits the use and disclosure of PHI without an individual's authorization when required by law to public health agencies to prevent or control disease. The reporting of individuals with suspected or confirmed TB disease to WDH falls under this provision of the law.

TB disease often involves an extensive contact or outbreak investigation within communities, therefore, it is crucial to be conscious of individuals' privacy. PHI should be protected regardless of the situation and care should be taken when sharing information with the media, school systems, other healthcare workers, or other entities not directly involved with the medical care of persons diagnosed with TB. Health information can be "de-identified" by removing the specific identifiers of the individual (including name, birthdate, gender, age, residence) and relatives, household members, and employers and is adequately de-identified if it is reasonable to assume that the remaining information could not be used to identify the individual. In small communities where it may be harder to ensure that de-identified PHI will protect privacy, it is important to provide further safeguards to protect that PHI. Please see the Department of Health and Human Services website for more information.
http://www.hhs.gov/hipaa/for-professionals/privacy/laws-regulations/index.html

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Pathogenesis and Epidemiology

Pathogenesis

Mycobacteria are a group of bacteria that can cause a variety of diseases. The *Mycobacterium tuberculosis* complex is a genetically related group of Mycobacterium species that cause tuberculosis (TB) or diseases similar to TB. In the U.S., the vast majority of TB cases are caused by *Mycobacterium tuberculosis* (Mtb). Other organisms in the Mtb complex are *M. bovis, M. africanum, M. microti, M. canetti, M. caprae, M. pinnipedii, and M mungi.* Nontuberculous mycobacteria can also cause human disease, though they are not usually spread from person to person and are not a reportable disease. Some of the most common nontuberculous mycobacteria are the *M. avium* complex, *M. kansasii, M. abscessus, M. chelonae,* and *M. ulcerans.*

Mtb is carried on airborne particles, called droplet nuclei, of 1-5 microns in diameter. Infectious droplet nuclei are generated when persons who have pulmonary or laryngeal TB disease cough, sneeze, shout, or sing. Depending on the environment, normal indoor air currents can keep these droplet nuclei suspended for several hours. Mtb is transmitted through the air on droplet nuclei, not by surface contact. Transmission occurs when a person inhales droplet nuclei containing Mtb and the droplet nuclei travel though the upper respiratory tract and bronchi to reach the alveoli of the lungs.

After tubercle bacilli are ingested by alveolar macrophages, the majority of the bacilli are destroyed or inhibited. A small number may multiply intracellularly and are released when the macrophages die and can spread throughout the lungs or body. At this point, an individual may develop primary TB disease if the immune system is unable control the infection. In most immunocompetent individuals, the body's immune system usually intervenes within two to eight weeks, halting multiplication and preventing further spread.

The state in which Mtb bacteria are in the body, but the body's immune system is repressing multiplication and containing the bacilli is called TB infection (also known as latent TB infection or LTBI). The immune system does this by producing immune cells that surround the bacilli. People who have LTBI are not contagious and cannot spread the infection to other people. Individuals with LTBI do not feel sick, chest x-rays are usually normal, and sputum smears and cultures are negative.

Some people with TB infection will develop TB disease when the immune system can no longer contain the infection and bacilli begin to multiply rapidly. Often, reactivation or secondary TB disease develops many years after exposure when the immune system is compromised. In the U.S., about 10% of people with healthy immune systems who have TB infection will develop TB disease at some point in their lives. Some people are at higher risk of developing TB disease because of certain risk factors.

Conditions that increase risk of TB disease
Infection with HIV
History of inadequately treated TB disease
Recent TB infection (within 2 years)
Drug or alcohol abuse or smoking
Receiving immunosuppressive therapy
Silicosis
Diabetes mellitus
Chronic renal failure
Certain types of cancer
Certain intestinal conditions
Low body weight

TB disease can occur in many places in the body and in more than one place at the same time. TB disease most commonly affects the lungs; this is referred to as pulmonary TB. Most patients with pulmonary TB disease have respiratory and other symptoms and an abnormal chest x-ray. Extrapulmonary TB disease most commonly occurs in the larynx, lymph nodes, pleura, brain, kidneys, bones, and joints, but can occur anywhere. Extrapulmonary TB occurs more often in HIV-infected or other immunosuppressed people or in young children. Pulmonary and extrapulmonary TB can occur at the same time.

Disseminated TB disease occurs when Mtb enters the bloodstream and is carried throughout the body, causing disease at multiple sites. Miliary TB is a type of disseminated TB that appears on CXR as small (millet) seeds scattered throughout the lungs.

Persons with pulmonary TB disease are usually infectious and can spread the bacilli to other people. The infectiousness of a person with TB disease is directly related to the number of Mtb bacilli that he or she expels into the air. Persons who expel many bacilli into the air are more infectious that people who expel few or no bacilli.

The four factors that determine the probability of transmission of Mtb include the infectiousness of the individual with TB, the environment in which the exposure occurred, the frequency and duration of the exposure, and the susceptibility (immune status) of the exposed individual. The specifics of these factors will be addressed further in the Contact Investigation section of this manual.

The best way to stop transmission is to isolate infectious persons and to start standard TB antibiotics as soon as possible. The length of time required for a TB patient to become noninfectious after starting therapy depends on a number of factors. In general, once standard therapy is started and as long as the patient is compliant with the prescribed regimen, the infectiousness of the patient will decline quickly.

Epidemiology

It is estimated that one-third of the world's population, about 2 billion people, are infected with *M. tuberculosis*. Every year, about 9 million of those people develop TB disease and 1.5 million of those die from the disease. Among those over five years old, TB is still one of the leading causes of death due to infectious disease in the world. In 1953, when nationwide TB reporting first began, there were more than 84,000 people diagnosed with TB disease in the United States. Through 1984, the cases of TB disease decreased each year and reached a low of about 22,000 in 1985.

In 1986, there was in increase in the number of people diagnosed with TB disease, the first significant rise in case numbers since 1953. Between 1985 and 1993, there was a resurgence of TB disease, with an increase of about 20%. The resurgence of TB disease during those years can be attributed to a handful of factors, including:

-The HIV epidemic
-Increased immigration from countries where TB is common
-The spread of TB in congregate settings
-The development and spread of multidrug-resistant TB

This combination of factors occurred at time when funding cuts resulted in inadequate support and deterioration of TB control programs and other public health efforts. In the 1990s, after these increases in TB case rates, the U.S. recommitted resources to TB control efforts and the case rate again began decreasing in 1993. After two decades of progress in TB control, the incidence of TB disease in the U.S. during 2013-2017 remained steady at approximately 3.0 cases per 100,000 people. The incidence of TB disease among foreign-born persons in the U.S. is 15.1 cases per 100,000 people, which is thirteen times the incidence among U.S. born persons (1.2 cases per 100,000).

Barriers to TB elimination in the U.S.
TB cases continue to be reported in almost every state with increases in some areas.
More than half of all TB cases in the U.S. are among the foreign-born.
TB affects racial and ethnic minorities disproportionately. Hispanics, blacks, and Asians continue to have higher rates than white, non-Hispanics.
Drug-resistant TB remains a serious concern and incidence of drug-resistance is on the rise.

The CDC's Division of Tuberculosis Elimination establishes national objectives for TB incidence. National objectives for the year 2020 seek to reduce the incidence of TB disease to 1.4 cases per 100,000 people, 0.4 cases per 100,000 people among the U.S. born, and 11.1 cases per

100,000 among the foreign-born. Despite unprecedented low rates of TB disease, actual elimination of TB in the U.S. still faces several areas of ongoing concern.

Wyoming is a low-incidence state; from 2011-2015, there were 13 cases of TB disease reported in the state. 77% of those 13 cases were foreign-born in a country with a high prevalence of TB. In 2015, there were there were 0.7 cases per 100,000 people; in 2016 there were 0.2 cases per 100,000 people. Wyoming TB rates continue to remain lower than much of the U.S. and continue to meet the 2020 goal of maintaining a case rate below 1.0 per 100,000 people.

Because of the low population and number of cases of TB disease in Wyoming, it is difficult to interpret case data; generally the burden of TB disease in Wyoming follows the same trends as disease throughout the U.S. From 2011 to 2015, the top five countries of origin of foreign-born persons with TB disease were Mexico, the Philippines, India, Vietnam, and China. Among the foreign-born, Asians represented 47.8% of cases and Hispanics represented 32.0% of cases. Among the U.S. born, blacks represented 35.9% of cases and whites represented 31.1% of cases.

2015 Percentages by Ethnicity & Race. U.S.	
American Indian/Alaskan Native	1.5%
Asian	33.2%
Black/African American	20.9%
Native Hawaiian/Pacific Islander	1.1%
White	13.1%
Hispanic/Latino	28.2%
Multiple Race	1.7%

Several factors contribute to the disproportionate burden of TB disease in minorities, including: infection acquired in the country of origin, unequal distribution of risk factors contributing to greater exposure, increased risk of disease progression, lack of access to healthcare, lower socioeconomic status, and the effects of crowding.

People at High Risk for TB Infection and TB Disease

Years of statistics have demonstrated that rates of TB disease are higher in certain groups than in others. These high risk groups can be divided into two categories:

-People at high risk for **exposure** to or infection with *M. tuberculosis*

-People at high risk for **developing** TB disease after infection with *M. tuberculosis*

People with increased likelihood of exposure	People with clinical conditions that increase risk of developing TB disease
•Immigrants from TB endemic regions of the world (especially within the past 5 years) •Travelers to areas with high TB prevalence (especially if prolonged or frequent visits) •Close contacts of people with TB disease •Employees or residents of facilities or congregational settings who serve a high-risk population (hospitals, nursing homes, homeless shelters, correctional facilities, some residential facilities) •Infants, children, and adolescents exposed to adults who are at increased risk for LTBI or TB disease	•HIV infection •Children younger than 5 •People recently infected with Mtb (within past 2 years) •People with a history of inadequately or untreated TB infection or disease •People with other medical conditions, such as: diabetes, silicosis, chronic renal failure, gastric bypass surgery, organ transplant, head or neck cancer, prolonged use of immune suppressing medications, cigarette smokers, alcohol or drug abusers

Contacts

Contacts are persons who have spent time face-to-face with someone who has infectious TB disease. They are at high risk of being infected with Mtb. This group may include family members, co-workers, friends, classmates, roommates, and others who have had close contact with the infectious person.

Foreign-born persons

Most foreign-born people in the U.S. and Wyoming become exposed to and infected with Mtb in TB endemic areas of the world. TB endemic countries are those that have an annual TB incidence of greater than 20 cases per 100,000 people. Most countries in Asia, Africa, Eastern Europe, and Central/South America are considered endemic. The majority of foreign-born people who are diagnosed with TB disease in the U.S. are from seven countries—Mexico, Philippines, Vietnam, India, China, Haiti, and Guatemala. For the same reasons, visitors with extended visits to TB endemic countries, especially if those visits are frequent and visitors have extended contact with a high-risk population, are at a greater risk for TB exposure.

The World Health Organization (WHO) publishes a yearly Global TB Report where country specific information is available. It can be found on the WHO website at www.who.int/tb.

Congregate Settings

Congregate settings are facilities such as correctional facilities, homeless shelters, nursing homes, and some residential facilities (e.g. drug treatment centers) where the risk of being exposed to TB is higher than in other places. This is because many people in these facilities are

at risk for TB disease. The risk of transmission and exposure to TB is even higher if the facility is crowded. People who live or work in these settings are at higher risk of being exposed to TB.

Healthcare Workers

Healthcare workers who have face-to-face contact or potential to share air space with infectious patients are at a greater risk for TB exposure. The risk of exposure depends on the number of persons with TB in the facility, the employee's duties, and infection control procedures in the facility. Healthcare facility TB testing programs should include anyone working or volunteering in healthcare settings with the potential for exposure. Healthcare facilities should maintain infection control programs, including a facility risk assessment, within their facilities. See the *Infection Control* section of this manual for more information.

Children

Children younger than five years of age are at a particularly high risk for developing TB disease after Mtb infection. When a child has TB infection, it indicates that TB was transmitted relatively recently, the person with TB disease may still be infectious, and other adults and children in the household or community may have been exposed to TB.

Persons living with HIV

HIV infection is the strongest known risk factor for the development of TB disease. Worldwide, TB is responsible for the death of one-quarter of people living with HIV; it is the leading cause of death among the HIV positive. Because HIV weakens the immune system, the risk of developing TB disease is about 7% to 10% each year for people who are infected with Mtb and have untreated HIV.

Recent TB Infection or History of Untreated/Inadequately Treated TB Infection or Disease

TB disease is most likely to develop soon after infection. Approximately half the risk of developing TB disease is concentrated in the first two years after infection; about 5% of people who have recently been infected with Mtb (if left untreated) will develop TB disease in those first two years after infection. If left untreated, another 5% of people infected with TB will develop TB disease sometime later in life.

In total, roughly 10% of immunocompetent individuals who are infected with Mtb will develop TB disease at some point in their lives. Inadequately treated past TB disease can lead to treatment failure, relapse, ongoing transmission, and development of drug resistance. People with chest x-ray findings suggestive of previous TB disease should be evaluated to rule out previous inadequate treatment.

Other Medical Conditions

There are numerous other conditions that increase the risk of developing TB disease for a variety of reasons—usually related to a weakened immune system. These include persons who

are receiving immunosuppressive therapy such as TNF-α antagonists, corticosteroids, or immunosuppressive therapy following organ or tissue transplant. Persons with silicosis, diabetes mellitus (30% lifetime risk), chronic renal failure, leukemia, or cancer of the head, neck, or lung are also at higher risk for progression to TB disease. People who have had a gastrectomy or jejunoileal bypass or have low body weight (10% below ideal) are also at greater risk.

Cigarette Smokers, Alcohol or Drug Abuse

Independent of alcohol use or other socioeconomic factors, smoking increases the risk of TB disease by more than two and half times. People who abuse drugs or alcohol are more likely to be in situations where they are exposed to Mtb and have other risks for exposure, such as correctional facilities or drug treatment centers. They may also have poor access to health care, are more likely to be HIV infected, and have other conditions that weaken the immune system.

Surveillance

Under Wyoming state statute (§35-4-107), TB disease caused by *Mycobacterium tuberculosis* complex is a reportable disease by both the attending healthcare provider/hospital and the laboratory performing diagnostic testing. Wyoming laboratories are responsible for reporting results when an out of state reference laboratory is used. Confirmed or suspected TB disease should be reported with 24 hours of diagnosis by either fax or telephone. Providers should report suspected and confirmed TB disease, laboratories should report positive AFB smears and positive *Mycobacterium tuberculosis* cultures, NAAT, or PCR testing.

Every year international, national, and state organizations publish TB statistics. International statistics can be found on the WHO website at www.who.int/tb. National data can be found on the CDC website at https://www.cdc.gov/tb/. Wyoming state data can be found at https://health.wyo.gov/publichealth/communicable-disease-unit/tuberculosis-2/.

Active TB Disease Case Definition

A case of active TB disease is an individual who meets the clinical case definition or is laboratory confirmed as described below. Individuals who meet this definition are counted as a case for statistical purposes.

Clinical criteria (all of the following):

-positive TB skin test or positive IGRA
-other signs and symptoms compatible with TB (clinical symptoms or an abnormal CXR or CT)
-treatment with two or more anti-TB medications
-completed diagnostic evaluation

Laboratory criteria:

-isolation of M. tuberculosis from a clinical specimen OR
-nucleic acid amplification testing (NAAT) positive for Mtb complex OR
-acid fast bacilli in a clinical specimen when a culture cannot be completed or is contaminated

For surveillance purposes, a recurrent diagnosis of TB is not counted twice in any 12 month period. Subsequent diagnoses should be counted again if more than 12 months have elapsed since the patient completed therapy. Mycobacterial diseases other than those caused by Mtb complex should not be counted for TB statistics unless there is proof of concurrent Mtb complex present.

Latent Tuberculosis Infection Case Definition

There is not such a rigidly defined case definition for latent tuberculosis infection. LTBI is described as a state of persistent immune response to stimulation by Mtb antigens without evidence of clinically manifested active TB. Generally, an individual with LTBI has an immune response indicated by a positive TST or IGRA, no symptoms of disease, no radiological evidence of disease (CXR or CT), and negative bacteriological tests. Currently, LTBI is not a reportable condition and accurate statistics for Mtb infection in humans is not available, though it is estimated that about one-third of the world's population is infected.

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Targeted TB Testing

Targeted testing is a basic TB prevention and control strategy used to identify, evaluate, and treat persons who are at high risk for LTBI or high risk for developing TB disease once infected with *M. tuberculosis*. Targeted screening should be focused on populations with the greatest risk for infection. The goal of targeted screening is to identify persons with LTBI, treatment of LTBI to prevent progression to disease, and prevent further spread of TB. All testing activities should be accompanied by a plan for appropriate follow-up, including medical evaluation and treatment. Necessary medical evaluation and treatment resources should be identified before testing activities begin. Healthcare agencies or other testing facilities can consult local health departments or WDH before starting a TB testing program to make sure that any person who tests positive will have access to follow-up care.

During routine patient evaluations, health care providers should identify persons who are at high risk for TB and test them for infection. People who are at low risk for TB generally should not be tested. Testing in low-risk populations can take resources away from other important screening activities and skin test reactions in low risk groups may sometimes be false positive.

Recent epidemiologic studies have defined those groups of people who have higher rates of TB transmission and an increased risk of TB disease. In the past, widespread testing of individuals or groups of low risk was done as part of administrative requirements. Testing of low risk persons for administrative purposes (school teachers, child care workers) should be replaced by targeted testing. Persons that were previously required to obtain TB testing for administrative purposes should only be tested if they fall into one of the high risk categories as defined below.

Targeted Screening Guidelines

Individuals in high-risk groups can be divided into two categories; those who are at high risk for exposure to or infection with Mtb and those who are at high risk for developing TB disease once infected with Mtb.

Epidemiology and the risk of LTBI or TB disease among groups may change over time. Groups currently considered high risk may lose vulnerability or likelihood of exposure over time, whereas other low risk populations may begin experiencing higher TB rates and be re-classified as high risk. Because of the flux in local demographics and TB epidemiology, the definition of high risk can be changed when necessary.

Current Wyoming targeted tuberculosis screening guidelines recommend that the following groups get tested for TB infection:

Those with increased likelihood of exposure, including;

- Persons who have immigrated from TB endemic regions of the world
- Close contacts of a person with infectious TB disease
- Persons who work or reside in facilities or congregational settings with people who are at high-risk for TB (hospitals, homeless shelters, correctional facilities, nursing homes, some residential facilities)

Those with clinical conditions that increase the risk of progression to active TB disease, including;

- HIV infection
- Injection drug use
- Radiographic evidence of prior healed TB
- Low body weight (10% below ideal)
- Other medical conditions, such as: diabetes, silicosis, chronic renal failure, gastric bypass surgery, organ transplant, head or neck cancer, prolonged use of immune suppressing medications (e.g. corticosteroids, TNF-α antagonists)
- Recent TST converters (persons with negative baseline results who have an increase of 10 mm or more in a 2 year period)
- Infants and children under 5 years who have a positive TB test

The decision to screen for TB infection and disease in each individual is influenced by numerous factors, including clinical circumstances. Clinical judgement by the healthcare provider is a critical component of the decision making process. Targeted screening guidelines should not be solely relied upon to direct clinical care and testing of individual patients for whom TB infection or disease is considered a genuine possibility by a healthcare provider.

Patient Risk Assessment

The WDH has developed a patient tuberculosis risk assessment that can be used for any individual requesting TB testing as a screening tool to document risk prior to testing and to determine whether testing is indicated. This patient risk assessment outlines a symptom assessment and a TB exposure risk assessment. Those risks should be reviewed before deciding to test an individual for TB. Persons with symptoms of TB, taken in context, or any of those risks factors are at a greater risk for TB infection or disease and should be tested. In individuals with a history of previous positive testing or previous TB treatment, this assessment can be used as a symptom and risk review. If no TB symptoms are present and no additional risks are identified, further diagnostic testing may not be necessary.

The patient risk assessment can be found on the tuberculosis page of the WDH website at https://health.wyo.gov/publichealth/communicable-disease-unit/tuberculosis-2/.

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Diagnosis

Since the 1950s, tuberculosis has become less common in the United States, therefore TB disease may not always be considered when a person has symptoms associated with tuberculosis. This can result in TB disease going undiagnosed for prolonged periods of time and allowing possible spread of the disease. Recognition of symptoms and early diagnosis of TB leads to prompt treatment and identification of contacts who may have been exposed. A complete medical evaluation for TB infection or disease should include all the components described in this section. The last part of this section describes the process of ruling out active disease.

Medical History

A medical history should include an evaluation of symptoms associated with TB, previous exposure to individuals with infectious TB, previous latent or active TB diagnoses, demographics (country of birth, age, ethnicity, occupation, travel history), nutritional status, and coexisting immunocompromising conditions or infections. If an individual does have a history of LTBI or TB disease treatment and received medications through the WDH patient assistance program, the program may be able to access specific information about the treatment.

Symptoms associated with TB

Symptoms of pulmonary TB disease (individuals with TB disease will usually experience one or more of these symptoms)	Symptoms of extrapulmonary TB disease (dependent on the part of the body affected by the disease)
• Cough (especially if lasting ≥ 3 weeks) with or without sputum production • Coughing up blood • Chest pain • Loss of appetite • Unexplained weight loss • Night sweats • Fever • Fatigue	• Blood in urine (TB of the kidney) • Headache or confusion (Mtb meningitis) • Back pain (TB of the spine) • Loss of appetite • Unexplained weight loss • Night sweats • Fever • Fatigue

Each individual should be evaluated in context. All of these symptoms may be caused by other diseases, but they should immediately prompt clinicians to suspect the possibility of TB disease.

Physical Examination

A physical examination cannot confirm or rule out TB disease, but can provide valuable information about the individual's overall health and condition. A physical exam can provide information that other diagnostic testing may not identify as well as reveal factors that may affect TB disease treatment.

Tests for M. tuberculosis Infection

Currently there are two available methods of testing for *M. tuberculosis* infection in the United States, the Mantoux tuberculin skin test (TST) and interferon-gamma release assays (IGRA), such as the QuantiFERON-TB Gold In-Tube test (QFT-GIT) or T-SPOT.TB test (T-spot). The selection of which test to use should be based on the reason for testing, testing availability, and overall effectiveness of testing.

While TST and IGRAs are useful diagnostic tools, some patients with TB disease may have a negative TST or IGRA. Patients with symptoms consistent with TB should always be evaluated for TB disease, regardless of the TST or IGRA result.

Mantoux Tuberculin Skin Test (TST)

Mantoux tuberculin skin tests are performed to determine if a person has been infected with M. tuberculosis. The test is done by injecting tuberculin, a protein derived from *M. tuberculosis* complex bacilli, between the layers of skin in an individual's forearm. Since tuberculin is similar to Mtb, the immune system of a person infected with tuberculosis will recognize the tuberculin and react at the site of injection. The immune response to the tuberculin antigen will become apparent and should be examined 48-72 hours after placement by a trained health care worker. If an area of induration (a palpable, raised, and hardened area) can be felt around the site of injection, the diameter of indurated area should be measured in millimeters transversely across the forearm. Areas of erythema (redness) at the injection site should not be measured and is not an indication of immune response.

Interpretation of TST reactions depends on the measurement of induration and the individual's risk of acquiring TB infection and risk of progression to TB disease as described below.

An induration of **5 or more millimeters** it is considered a positive reaction for the following people:

- Individuals living with HIV
- Recent contacts of people with infectious TB

- Individuals with chest x-ray findings suggestive of previous TB disease
- Individuals with organ transplants
- Other immunosuppressed patients (for example, patients on prolonged therapy with corticosteroids equivalent to/greater than 15mg per day of prednisone or those taking TNF-alpha antagonists)

An induration of **10 or more millimeters** is considered a positive reaction for the following people:

- Individuals who have recently come to the United States (within the last 5 years) from areas of the world where TB is common (for example, Asia, Africa, Russia, Eastern Europe, or Latin America)
- Individuals who abuse drugs
- Mycobacteriology laboratory workers
- Individuals who live or work in high-risk congregate settings (for example, nursing homes, homeless shelters, or correctional facilities)
- Individuals with certain medical conditions that place them at high risk for TB (for example, silicosis, diabetes mellitus, severe kidney disease, certain types of cancer, and certain intestinal conditions)
- Children younger than 5 years of age
- Infants, children, or adolescents exposed to adults in high-risk categories

An induration of **15 or more millimeters** is considered a positive reaction for people with no known risk factors for TB (although, in general, these individuals should not be tested in the first place—see *Targeted TB Testing* section of this manual).

It is important to note that individuals who have had a positive reaction to a TST in the past will usually have a positive reaction every time they are tested, regardless of whether they ever received treatment. If a person has a history of previous positive skin testing, repeat TSTs should not be placed on that individual. The immune response detected with a TST would be expected to remain active throughout life. Any future screening for those individuals should be based upon symptom and risk assessment, followed by chest x-ray if the individual reports signs or symptoms consistent with TB disease or if recommended by a clinician. Using IGRAs to further screen individuals with positive TSTs is not routinely recommended.

Vaccination with live viral vaccines can cause false negative skin testing. TSTs can be done concurrently (same day) or should be postponed until 4 to 6 weeks after administration of a live viral vaccine.

TSTs are entirely safe and reliable for pregnant women and pregnant women at high risk for TB should be tested, especially if they have been in contact with someone with infectious TB or if symptomatic.

It can take between 2 to 8 weeks for the body to generate an immune response to tuberculosis. During this window period, a person may not produce a response to a skin test even though they have recently been infected. For this reason, contacts of someone with infectious TB disease who have negative initial testing should be retested 8 to 10 weeks after last contact.

False Negative Reaction	False Positive Reaction
• Anergy (inability to react to TST because of a weakened immune system) • Recent TB infection (within past 8-10 weeks) • Very young age (younger than 6 months) • Recent live-virus measles or smallpox vaccination • Incorrect method of giving the TST • Incorrect measuring or interpretation of TST reaction • Concurrent fungal infection, bacterial infection (e.g.; typhoid fever, brucellosis, typhus, leprosy, pertussis), or viral infection (e.g., measles, mumps, chicken pox, HIV) • Diseases affecting lymphoid organs (e.g., Hodgkin's disease, lymphoma, chronic leukemia, sarcoidosis)	• Infection with nontuberculous mycobacteria (NTM) • BCG vaccination • Administration of incorrect antigen • Incorrect measuring or interpretation of the TST reaction

Boosted reactions

The booster phenomenon occurs mainly in previously infected adults whose ability to react to tuberculin has waned over time. When these individuals are tested many years after they were infected with Mtb, the immune response may be too weak to produce a positive TST. If they are tested again soon thereafter (within a year), the immune system may have been triggered by the antigen, boosting its ability to react to the second TST. A second, positive TST within that time-frame is likely a boosted reaction indicating the individual was infected with TB in the past and not in the period between the first and second tests.

Two-step testing

Two-step testing is used to reduce the likelihood that a boosted reaction will be misinterpreted as a recent infection. Two-step testing should be used for the initial skin test of a

person who will be retested periodically, such as healthcare workers. If an individual does not have documentation of a negative TST in the prior 12 months and the first test of the two-step process is negative, a second test should be placed 1 to 3 weeks later. A positive second TST would not be considered a skin test conversion or recent TB infection, however it does indicate that the individual had been infected in the past.

Bacille Calmette-Guerin (BCG) Vaccine

BCG vaccines are live vaccines derived from *Mycobacterium bovis*. Their effectiveness in preventing infectious TB has never been validated in the U.S. and therefore they are not recommended as a TB control strategy. However, they are used commonly in other countries. A history of BCG vaccination is not a contraindication for TB skin testing, nor does it influence the indications for a TST. TSTs should be administered and measured in the same manner as those for individuals with no previous BCG vaccination.

Tuberculin reactivity caused by BCG vaccination wanes with time and a positive TST is most likely a result of Mtb infection if more than 5 years has elapsed since vaccine administration. Skin tests in persons with history of a BCG vaccine should be interpreted using the same criteria for those not vaccinated. A booster phenomenon may occur among persons who have had a prior BCG vaccine. In many situations, it may be worthwhile to use IGRA testing in place of a TST for those who were BCG vaccinated (see section below).

Interferon-Gamma Release Assays (IGRA)

IGRAs are laboratory blood tests that measure an individual's immune response to Mtb. The white blood cells of persons infected with TB will release interferon-gamma (a cytokine produced against infections) when mixed with antigens derived from Mtb. In the U.S. there are two approved IGRA tests, the QuantiFERON and the T-Spot and availability depends upon the laboratory. IGRAs require a blood sample to be mixed with antigens and controls and incubated; after incubation the level of interferon-gamma is measured. IGRAs must be processed within a certain time period after blood is drawn to ensure the test is accurate; this time differs between the QFT and T-Spot.

IGRAs were developed to improve specificity of diagnostic TB testing. IGRAs measure a response to specific Mtb proteins that are present on all M. tuberculosis species, but are absent from BCG vaccine strains and from most nontuberculous mycobacteria. Because these antigens are not found on BCG or most nontuberculous mycobacteria, IGRAs are more specific and yield fewer false-positive results.

If the results for an IGRA are positive, it is likely the individual has an Mtb infection or disease. If IGRA results are indeterminate or borderline, Mtb infection cannot be ruled out and

further testing should be performed. Negative IGRA results indicate that Mtb infection is unlikely but cannot be excluded, especially if the patient has symptoms or has a high risk for TB infection. If an individual has recently been in contact with someone diagnosed with infectious TB, they should be retested 8 to 10 weeks after the last contact.

IGRAs can be used in place of (but not in addition to) a TST in all situations in which a TST has historically been recommended as an aid in diagnosing Mtb infection. In particular, IGRAs may be preferred:

- for testing persons who may not return for a TST reading
- for testing person who have received BCG
- to test recent contacts of person with infectious TB disease, with an understanding that using the same test for repeat testing will minimize misclassification errors that occur due to test discordance.

IGRAs may be used in place of a TST for periodic screening that addresses occupational exposure to TB disease (e.g., surveillance programs for health-care workers). This may be advantageous because IGRAs do not boost subsequent test results and two-step testing is unnecessary when performing IGRAs.

Routine testing with both a TST and an IGRA is not recommended; however, results from both tests may be useful in the following situations when the initial test is negative:

- When the risk of infection, the risk of progression from infection to disease, and the risk of a poor outcome are high (e.g., HIV infection, children under 5 years of age who are exposed to person with infectious TB) and confirmation of negative testing is desired.
- When there is clinical suspicion for TB disease (e.g., signs, symptoms, and/or radiographic evidence suggestive of TB disease) and confirmation of M. tuberculosis infection is desired.

Results from a TST and IGRA may be useful in the following situations when the initial test is positive:

- Additional evidence of infection is required to encourage compliance (e.g., foreign-born health-care workers who believe their positive TST is due to BCG) with LTBI treatment.
- In healthy persons who have a low risk of both infection and progression from infection to TB disease and results of both tests can provide the best evidence of infection.

Repeating an IGRA or performing a TST may be useful when the initial IGRA result is indeterminate, borderline, or invalid, and a reason for testing persists.

Specific questions about IGRA collection, incubation, and testing can be answered by the Wyoming Public Health Lab at (307) 777-7431.

Chest Radiographs

Radiographs, or x-rays, of the chest are used to diagnose pulmonary TB, which is the most common form of the disease. A chest x-ray should be performed on any individual that has a positive TST or IGRA or symptoms consistent with TB. The purpose of radiographs is to help rule out pulmonary TB in an individual with a positive TST or IGRA and to check for lung abnormalities which are seen in individuals with TB disease.

Individuals with TB will likely have abnormal chest radiographs, which may have infiltrates (collections of fluid and cells in the tissues of the lungs) or cavities (hollow spaces within the lung that may contain tubercle bacilli). However, chest radiographs cannot confirm an individual has TB because a multitude of illnesses can resemble TB. Typically, TB is seen is the apical and posterior segments of the upper lobe or in the superior segments of the lower lobe. However, lesions can be anywhere in the lungs and appear as different sizes, shape, density and cavitation especially in HIV and immunosuppressed individuals. In patients with symptoms and signs of TB disease, a negative chest radiograph does not exclude the possibility of TB disease. A chest x-ray can help rule out the possibility of pulmonary TB in a person who has a positive TST or IGRA

Chest radiographs of individuals with HIV can appear atypical or normal with no lesions. Common chest radiographic findings in HIV positive individuals includes infiltrates in any aspect of the lung and mediastinal or hilar lymphadenopathy. Cavitary lesions are usually observed in patients with high CD4 counts and atypical patterns seen in patients with low CD4 counts.

Radiographs in children can be more difficult to interpret. Children have a greater likelihood of lymphadenopathy. TB may be easier to diagnose on a lateral radiogram.

Bacteriologic Examination of Clinical Specimens (sputum culture)

A critical test for diagnosis of TB is bacteriologic examination of clinical specimens; most commonly sputum, but also necessary for diagnosis of extrapulmonary TB. Laboratory testing for Mtb should include five components:

1. AFB smear to detect the presence of any acid-fast bacilli. The presence of AFB is not specific to Mtb, but is a good indicator of infectiousness. Negative smears do not exclude TB disease.
2. *M. tuberculosis* PCR or nucleic acid amplification testing (NAAT) are rapid methods of detecting Mtb complex in clinical specimens. NAAT or PCR should be performed at least once for any patient suspected of having active TB disease.

3. Specimen culturing and identification to classify the specific mycobacterium species. Mycobacterium species are extremely slow growing and final culture results are often not available for 2 to 3 weeks after collection.
4. Drug-susceptibility testing to determine proper drug regimen. PCR testing to detect molecular drug resistance is also available. Some laboratories perform molecular drug resistance testing anytime NAAT is ordered, in other cases, it would need to be ordered specifically.
5. Genotyping is performed nationwide on every TB positive specimen. Genotyping is used to track the epidemiology of disease and help associate patients diagnosed with TB. Whole genome sequencing (WGS) is available by request from the CDC. WGS provides information about a larger portion of the Mtb genome and can be useful when further discrimination is needed in epidemiologic investigations.

Sputum Specimen Collection

Any persons suspected of having TB disease **at any site** should have sputum collected for culture (even if respiratory symptoms are not noted). Patients who may have extrapulmonary TB should be examined for the possibility of pulmonary TB in addition to the disease elsewhere. In general, three consecutive sputum specimens are needed, collected in 8 to 24 hour intervals with at least one being an early morning specimen. All proper infection control measures should be observed when assisting in the collection of sputum samples.

Proper sputum samples should contain mucus coughed deep from the lungs not mucus from the nose or throat or saliva. Sputum samples that are mostly saliva will be rejected at the laboratory. 5mL (approximately 1 teaspoon) of sputum is required for all the laboratory testing needed. For patients who are unable to cough up sufficient sputum, sputum induction, bronchoscopy, and gastric aspiration (particularly for children) are all alternative collection methods.

TB disease can occur in almost any anatomical site and a variety of clinical specimens may be submitted for AFB smear and culture. Urine, CSF, pleural fluid, exudate, biopsy specimens, etc. should all be collected and handled as potentially infectious. Clinical specimens *should not* be placed in preservatives and transport to the laboratory should be prompt.

When collecting non-pulmonary specimens, please contact the Wyoming Public Health Laboratory before collection to receive specific collection instructions and shipment requirements. They are also able to answer questions about any other testing requirements, collection issues, and turn-around-time. The lab can be reached at (307) 777-7431.

Sputum Specimen Collection Instructions
Do not gargle or rinse your mouth with mouth wash or brush your teeth before collecting. Rinsing your mouth with saline or sterile water can help remove some normal oral bacteria, but is not necessary. The best time to collect sputum is first thing in the morning. Inhale and exhale deeply 3-4 times and then deeply exhale with an explosive cough. This should produce mucus from the lungs to be deposited into the container. The specimen must be from deep within the lungs. Spit or saliva from the mouth, nose, or throat is inadequate and will give incorrect results.

HIV Testing

HIV infection is the most significant known risk factor for progression from latent TB infection to TB disease. Progression to TB disease is often rapid among people infected with HIV and can be very deadly. HIV screening should be provided for all suspected or confirmed latent and active TB patients as well as contacts to infectious TB patients. Early diagnosis of HIV leads to improved health outcomes, including slower progression and reduced mortality. Identifying HIV allows for optimal treatment and the opportunity to prevent TB in those without disease. Rapid HIV tests (finger stick or oral) can be used to test TB patients.

Ruling out Active TB Disease

All persons with signs or symptoms of TB disease should be medically evaluated to exclude TB disease. All of the following are required for a complete medical evaluation of anyone suspected of pulmonary or extrapulmonary TB:

- TST or IGRA
- Chest x-ray
- 3 respiratory or sputum samples for AFB smear and culture. Specimens should be collected a minimum of 8 hours apart, with one of those specimens collected in the morning.
- NAAT or PCR for *M. tuberculosis* on at least one of the sputum specimens. The NAAT/PCR testing should be performed on an AFB positive smear, if available. If all AFB smears are negative, it is preferable to perform NAAT/PCR on the morning specimen.

In patients with signs of symptoms of TB disease, the table on the next page can be used to guide clinical management. All testing and imaging results should be interpreted in the context of the level of clinical suspicion for TB disease.

Ruling out active TB disease

TST or IGRA	CXR	AFB smears	NAAT or PCR	Sputum culture**	Next step
Negative	Normal	All negative	Negative	Pending or Negative	Confirm negative final cultures; evaluate for non-TB cause; low suspicion
Negative	Abnormal	All negative	Negative	Pending or Negative	Confirm negative final cultures; evaluate for non-TB cause; low suspicion
Negative	Abnormal	One or more positive	Negative	Pending or Negative	Confirm negative final cultures; evaluate for non-TB cause; low suspicion
Positive	Normal	All negative	Negative	Pending or negative	Confirm negative final cultures; recommend LTBI treatment
Positive	Abnormal	All negative	Negative	Pending or Negative	Confirm negative final cultures; recommend LTBI treatment
Positive	Abnormal	One or more positive	Negative	Pending or Negative	Confirm negative final cultures; evaluate for non-TB cause; consider LTBI treatment
Positive or Negative	Normal or Abnormal	Negative or Positive	Positive for Mtb	Pending or Negative	Treat for TB disease; initiate/continue isolation if applicable (p. 39)
Positive or Negative	Normal or Abnormal	Negative or Positive	Positive for Mtb	Positive for Mtb	Treat for TB disease; initiate/continue isolation if applicable (p. 39)
Positive or Negative	Normal or Abnormal	Negative or Positive	Negative for Mtb	Positive for Mtb	Treat for TB disease; initiate/continue isolation if applicable (p. 39)

**Sputum cultures may take up to 6 weeks to finalize.

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Latent Tuberculosis Infection

The diagnosis of latent TB infection is based on the information gathered from the medical history, physical exam, x-rays, and laboratory testing. The presence of TB disease must be excluded before LTBI can be diagnosed and treated. Failure to properly diagnosis TB disease before treating LTBI can result in advanced disease, inadequate treatment, or development of drug resistance.

People with LTBI infections usually:

- Do not have symptoms or physical findings suggestive of TB
- Do not feel sick
- Have positive TST or IGRA testing
- Have a normal chest x-ray that is not suggestive of TB disease
- Have negative sputum smear and culture testing (if done)
- Cannot spread TB to others
- Have a 5 to 10% chance of developing TB disease in their lifetime

Anyone diagnosed with LTBI should be considered for treatment to prevent progression to active TB disease. There are several treatment regimens available for LTBI treatment. Currently, the most commonly prescribed drugs for LTBI treatment are isoniazid (INH), rifampin (RIF), or INH and rifapentine (RPT). Providers should choose the appropriate regimen based on coexisting medical conditions, potential for drug-drug interactions, likelihood of adherence, and drug-susceptibility results of the source case (if applicable). For persons who are at especially high risk for TB disease, nonadherent, or given an intermittent regimen, directly observed therapy should be considered. **The most up to date treatment regimens are available on the CDC website, www.cdc.gov/tb**.

High priority candidates for LTBI treatment:

People in these groups should be given high priority for LTBI treatment if they have a positive IGRA result or a TST reaction that is 5 or more millimeters
• Recent contact with people with infectious TB • People living with HIV • People with chest x-ray findings suggestive of previous TB disease • Patients with organ transplants • Immunosuppressed patients (e.g., prolonged therapy with corticosteroids or taking TNF-alpha antagonists)

People in these groups should be given high priority for LTBI treatment if they have a positive IGRA results or a TST reaction that is 10 or more millimeters
• People who have come to the U.S. within the last 5 years from areas of the world where TB is common (e.g., Asia, Africa, Eastern Europe, Russia, or Latin America) • People who abuse drugs • People who live or work in high-risk congregate settings (e.g., nursing homes, correctional facilities, homeless shelters, hospitals, or other health care facilities) • People who work in mycobacteriology laboratories • People with medical conditions that increase the risk for TB disease (e.g., silicosis, diabetes mellitus, severe kidney disease, certain types of cancer, and certain intestinal conditions) • Children younger than 5 years of age • Infants, children, and adolescents exposed to adults in high-risk groups

Special Considerations

- HIV-infected individuals are at an increased risk for developing TB disease and every effort should be made to treat LTBI in HIV positive individuals. Drug regimens vary depending on what other medications the individual is taking. See CDC website above for current recommendations. In HIV infected individuals who have had contact with a person who has infectious TB, but have negative TST or IGRA testing, LTBI treatment may still be indicated.
- In pregnant women, after TB disease has been excluded, consider LTBI treatment if the woman is HIV infected or has other risks and has recently been a contact to someone with infectious TB. In the absence of any risk factors, it may be best to avoid LTBI treatment until 2 to 3 months after delivery. Supplementation with 10-25 mg/day of Vitamin B6 is recommended.
- Breastfeeding is not contraindicated in women taking isoniazid (INH). Supplementation with 10-25 mg/day of pyridoxine (Vitamin B6) is recommended. The amount of INH in breast milk is inadequate for treatment of infants with LTBI.
- Infants and children under 5 years of age with LTBI have been recently infected and therefore are at high risk for progression to disease. Infants and children are also more likely to develop life threatening forms of TB disease (especially meningeal or disseminated disease) because they do not have fully developed immune systems. Children younger than 5 years who are close contacts to an adult with infectious TB may need *window prophylaxis* even if a TST or IGRA is negative. Infected infants may be anergic as long as 6 months of age. If a second TST or IGRA (8 to 10 weeks after last contact with infectious patient) is negative and the child is at least 6 months old, window prophylaxis could be discontinued after evaluating the risk of potential infection.

The potential for adverse effects of drugs used to treat LTBI is generally related to the length of treatment and the potential side effects of medications. As with any treatment, healthcare providers should weigh the risk and benefits of treatment for each individual to determine the most appropriate course of action. Current CDC guidelines and drug package inserts should be consulted when there is a question about side effects or drug-drug interactions.

All individuals treated for LTBI should receive monthly follow-up. A monthly assessment should include ensuring the individual is adhering to the prescription regimen, is not demonstrating symptoms of active TB disease, and is not experiencing adverse effects from the medications (e.g., jaundice, loss of appetite, fatigue, muscle or joint aches). Patients should be instructed to discontinue medications if they are experiencing potential severe adverse effects until evaluated by a healthcare provider. Routine laboratory monitoring should be done on all those with abnormal liver values or others who are known to have or are at risk of hepatic disease.

After LTBI treatment has been completed, patients should receive documentation that includes TST/IGRA and CXR results, medication regimen, and duration of treatment. TST and IGRA testing is expected to remain positive throughout life and treated individuals should be able to provide this documentation whenever TB testing may be required. Patients should be educated about the signs and symptoms of TB disease and advised that treatment greatly reduces the risk of progression to disease, but does not entirely eliminate it. Serial or repeat chest x-rays are not indicated unless the patient develops signs or symptoms suggestive of TB disease.

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TB Disease

TB disease (or active TB) is a condition seen when TB bacilli overwhelm the defenses of the immune system and begin to multiply and cause symptomatic illness. Some individuals develop TB disease soon after infection (primary disease) while others do not develop disease until years later when their immune system becomes weak (reactivation or secondary disease). General symptoms of TB disease include unexplained weight loss, loss of appetite, night sweats, fever, fatigue, malaise, and chills. Pulmonary TB may also cause prolonged cough (especially if lasting for 3 weeks or longer with or without sputum production), hemoptysis (coughing up blood), or chest pain. Other symptoms may vary depending on the location of infection.

A person with TB disease may

- have a positive TST or IGRA
- have an abnormal chest x-ray
- have AFB seen on smear, positive NAA or PCR testing, or a culture that grows Mtb
- have symptoms consistent with TB
- be able to spread TB to others

People with TB disease may or may not have symptoms, though most patients do have symptoms. Often, when patients do have symptoms, they have developed gradually and may have been present for weeks or even months. As soon as a person is suspected of having TB disease, clinical judgement and the index of suspicion for tuberculosis are critical in making a decision to initiate treatment. In children and adults who have a high likelihood of having tuberculosis or are seriously ill with a disorder suspicious for TB, empiric treatment with a 4-drug regimen should be initiated even before results of AFB smear, cultures, or NAAT are available.

Treatment of tuberculosis is focused on both curing the individual patient and minimizing the transmission of Mtb to other persons. TB treatment is intended to rapidly reduce the number of actively growing bacilli, eradicate populations of persisting bacteria to achieve durable cure and prevent relapse, and prevent the acquisition of drug resistance.

Many years of investigation, including many clinical trials, have consistently supported the necessity of treating with multiple drugs to achieve these treatment objectives. TB disease must be treated for at least 6 months, and in some cases even longer (depending on drug susceptibility results and patient response to medications). Most TB bacilli are killed during the first 8 weeks of treatment (initial phase), however, some bacilli will usually survive this initial phase and require longer treatment (continuation phase). If treatment is not continued for long enough, surviving bacilli may cause the patient to relapse, become ill and infectious again, and potentially develop drug resistance.

The standard of care for initiating treatment is the 4 drug therapy of isoniazid (INH), rifampin (RIF), ethambutol (EMB), and pyrazinamide (PZA) with a continuation phase of INH

and RIF (hinging on microbiological status). The CDC and organizations such as the American Thoracic Society publish current recommendations and those sources should be consulted for specifics of recommended treatments. There are several options for daily and intermittent therapy in the continuation phase. Currently accepted treatment standards for TB include the practice of observing the patient swallow their TB medications. This practice is called directly observed therapy or DOT and is required for patients with active TB in Wyoming (except under extenuating circumstances).

> *Warning--most pharmacies in Wyoming do not stock medications used to treat TB disease and patients may not be able to fill prescriptions for days after diagnosis. TB medications may also be very expensive, and some pharmacies may not be willing to order them until they have payment or proof of insurance.*

All TB patients should be assessed monthly during treatment by a healthcare professional for bacterial response and possible adverse reactions. Patients with pulmonary TB whose sputum cultures were positive before treatment should have sputum samples collected at least monthly until two consecutive specimens are negative on culture (sputum culture conversion). Patients with drug-resistant TB may need to have sputum samples collected monthly throughout the duration of treatment. If patients stop responding to TB treatment or experience adverse reactions, they should be immediately referred to their healthcare provider for a medical evaluation. As with treatment for LTBI, patients undergoing treatment for TB disease who may be experiencing severe adverse reactions should be instructed to discontinue taking medications until they can be evaluated by a healthcare provider.

Because of the complexity and length of TB treatment, adherence to a TB regimen can be difficult for patients. Ultimately, the responsibility for successful treatment falls on the healthcare providers, not the patient. Patients, providers, and local and state health departments should collaborate in ensuring a regimen can be completed. DOT can be offered in a clinic, at home, place of employment, or even electronically. Public health nurses are skilled at providing DOT to patients with active TB and should be utilized in treatment plans.

Isolation

In general, individuals with pulmonary TB should be isolated from first suspicion of TB disease until they are found to no longer be infectious. Infectiousness is directly related to the number of Mtb bacilli the patient expels into the air which is dependent on a number of factors. Requirements for patient isolation are under the direction of WDH and county health officers. Typically, patients can be considered noninfectious when they meet all of the following criteria:

- they have been receiving adequate anti-tuberculosis treatment for 2 weeks or longer

- their symptoms have improved
- they have had three consecutive negative sputum smears from sputum collected at 8 to 24 hour intervals

Decisions to remove TB patients from isolation should be based on all information available and in consultation with public health authorities. If sincere efforts to ensure proper TB treatment and isolation are not successful, public health authorities can require involuntary isolation of a patient. A patient may be involuntarily isolated, but a patient cannot be forced to swallow TB medications. Involuntary isolation should only be pursued as a last resort after all less-restrictive measures have failed.

Individuals with infectious TB may be isolated at home, in a healthcare facility, correctional facility, or other area where other people do not reside. If ideal conditions for isolation are absent, WDH and local public health nursing will work together to locate a place for isolation. If someone with TB disease is a hospital inpatient, WDH should be notified as early as possible before the patient is discharged to facilitate follow-up and continuation of DOT. If a patient will be discharged from an inpatient setting before they are considered no longer infectious, WDH must be involved with the discharge planning to ensure the patient can remain in isolation at home.

In the event that a patient is treated for active TB in another state, WDH would be contacted to ensure continuity of DOT and need for isolation before the patient was discharged back to Wyoming. Through state TB control programs, WDH has a relationship with neighboring states and is able to share information necessary to protect patients and the public. If questions or concerns arise about isolation, WDH should be contacted for guidance.

Treatment interruption

When interruptions in TB treatment occur, it is the clinician's responsibility to decide whether to restart a complete course of treatment or simply continue as originally planned. In general, the earlier the break in therapy and the longer its duration, the more serious the effect and the greater need to restart treatment from the beginning. Continuous treatment is more important in the intensive part of therapy when the bacillary population is highest and the risk of developing resistance is greatest. It may be necessary to restart therapy and perform additional drug resistance testing on sputum cultures.

If a patient moves to a different county or state during treatment, WDH should be contacted to initiate a transfer notification. Preferably, a transfer notification should be initiated before a patient moves. If that is not possible, the notification should occur as soon as possible. The patient should be given copies of their medical records, labs, CXR, and prescriptions to provide to new providers and case managers.

Drug-resistant TB

Drug-resistant TB disease can occur in two different ways, called primary or secondary resistance. Primary resistance occurs when a person who is initially exposed to someone with drug-resistant TB and is infected with resistant organisms. Secondary resistance (or acquired resistance) develops during TB therapy, usually because the treatment regimen was improper or inadequate or the patient did not take the regimen appropriately. Much less frequently, acquired resistance can develop because of drug malabsorption or because of drug-drug interactions that lead to low serum levels.

INH resistant TB is resistant to only isoniazid. Multidrug-resistant (MDR) is TB that is resistant to at least isoniazid and rifampin. Extensively drug-resistant (XDR) TB is resistant to both isoniazid and rifampin plus a fluoroquinolone and a second-line injectable anti-TB drug. Patients with MDR or XDR-TB are at high risk for treatment failure, relapse, further acquired resistance, or death.

Drug resistance in newly diagnosed patients may be suspected on the basis of previous treatment, contact with known drug-resistant TB, or expected because of time spent in regions where drug resistance is common. Drug resistance can only be proven with drug-susceptibility testing, although there are some molecular tests available to detect genetic mutations typically associated with drug resistance. Alternative regimens should be used for treating drug-resistant TB and should be done with consultation from an expert in drug-resistant treatment.

It is possible that patients may not respond to treatment or that they may relapse with current therapy. Patients should be evaluated as soon as possible if symptoms do not improve after two months of therapy or worsen after improving initially, culture results have not become negative after two months of treatment or become positive after being negative, or CXR has worsened. These situations could be an indicator of drug resistance and drug susceptibility testing should be repeated. Depending on findings, a new treatment regimen may be required or extended treatment may be necessary; a TB expert should be consulted.

Re-Infection

TB infected individuals are typically cured with proper treatment, however up to 5-7% of individuals have recurrent disease within 1-2 years and will need retreatment. It has been shown these instances of recurrent disease are usually not caused by treatment failure but from re-infection with a different strain of TB. Those treated for TB disease are at increased risk of developing TB again. Individuals that have been treated for TB and re-exposed or develop new symptoms should be thoroughly evaluated for the possibility for re-infection.

Special Considerations

HIV Infection

The care of individuals co-infected with HIV and TB is complex and consultation should be made with an expert. Current treatment recommendations should be consulted. If there is evidence of slow or suboptimal response to therapy, the continuation phase should be prolonged. DOT is especially important for the treatment of HIV infected individuals.

Pregnant and breastfeeding women

Treatment should not be delayed for pregnant women who have TB disease. Clinicians should seek expert consultation in the treatment regimen for pregnant women. Streptomycin, a second-line drug, should not be used because it has been shown to be harmful to the fetus. Women being treated with first-line TB drugs should not be discouraged from breastfeeding. Only a small concentration of the drugs can be found in breast milk and is not harmful. The concentrations of drugs found in breast milk cannot be considered adequate treatment for infants. Vitamin B6 supplementation is recommended for all pregnant or nursing women taking INH.

Infants and children

TB treatments in infants and young children (<5 years) should be started as soon as a TB diagnosis is suspected. TB in children is a significant disease and an indicator of recent transmission. Young children may have difficulty coughing up sputum. Gastric aspiration, bronchoalveolar lavage, or tissue biopsy may be useful for collecting specimens on children. Because sputum culture yield is low in children (<10-15% of children with probable TB), a complete diagnostic evaluation and clinical judgement should guide treatment.

Pills given to children may be crushed or medications prescribed in liquid form. DOT by healthcare professional is especially important for young children; parents (or other family members) should not be asked to provide DOT.

Extrapulmonary TB

As a general rule, the principles for the treatment of extrapulmonary TB disease parallels treatment of pulmonary TB. A 6 month treatment regimen is recommended unless the isolated organisms are resistant to first-line drugs. Exception may be necessary in central nervous system TB; longer treatment may be crucial (9 to 12 months). Consultation with a TB expert should be sought when treating patients with extrapulmonary TB. In most cases, individuals with only extrapulmonary TB are not infectious to others, except through procedures that could aerosolize the Mtb.

Patient education

Educating patients about TB disease helps ensure successful completion of therapy. Individuals suspected of or confirmed to have TB should be instructed regarding TB transmission and pathogenesis, expected outcomes of treatment, potential adverse reactions of the prescribed treatment regimen, DOT requirements, infectiousness and isolation, and need for a contact testing.

Healthcare professionals should be conscious of using appropriate language levels for each patient. Using words that are familiar to the individual can make the information more relevant to them. A TB diagnosis can be overwhelming and care should be taken to cautiously limit the amount of information given at each visit to make certain the patient can process all of it. There are many written resources available for TB patients. WDH has various materials in English and Spanish at https://health.wyo.gov/publichealth/communicable-disease-unit/tuberculosis-2/. CDC resources in many languages can be found at https://www.cdc.gov/tb/education/patient_edmaterials.htm.

Clinical Consultation

The Mayo Clinic Center for Tuberculosis is designated as the medical consultation center for Wyoming. Mayo Clinic's doctors, pharmacists, and radiologists are available for any provider in Wyoming looking for expert advice in diagnosis, treatment, and prevention of TB. The consultation services can be accessed by phone at (855) 360-1466 or by email at tbcenter@mayo.edu.

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Case Management

Tuberculosis case management is a model that describes the activities undertaken by healthcare providers, the state and county public health departments, and other partners to ensure successful completion of TB treatment and the public health activities required to help halt the spread of disease in the community. Case management is a collaborative model of healthcare delivery that evaluates, provides, monitors, manages, and coordinates the healthcare services over an entire episode of disease. Establishments that are involved with managing the care of patients with TB may include local public health nursing offices, county health officers, healthcare providers, hospital infection control officers, state health department, and other local service organizations.

Ultimately, an individual's primary healthcare provider has the principle responsibility for the patient and their care. With the oversight of the healthcare provider and state and local public health authorities, case management services should include regular medication assessments, daily directly observed therapy, symptom evaluation, patient education, the use of incentives and/or enablers, contact investigation and testing, and addressing barriers to medication adherence. Local public health nurses are trained in performing DOT and are usually asked to perform it on a daily basis for the duration of TB treatment. They also may be asked to collect sputum specimens or other lab samples at patient homes, monitor for drug reactions, and counsel providers and the state health department in patient needs.

Depending on the capacity of the healthcare provider and their staff, some case management activities may be assigned to local public health agencies. If an individual with suspected or confirmed active TB does not have a primary healthcare provider, the local county health officer and public health nursing office may have to provide all case management services. In the end, it is essential that every client complete an effective course of anti-TB medication for the appropriate duration. Collaboration and communication between the patient, healthcare provider, and public health agencies is the only way to ensure proper treatment.

Incentives/Enablers

Patients who have difficulty adhering to their TB medication regimen or isolation requirements may be offered incentives and enablers to encourage adherence. An incentive (reward) encourages a patient to take his medication, keep clinic appointments, or stay isolated. Incentives can occur in many forms large or small, including food, goods, or services. An enabler is an item or service that empowers a patient to complete a behavior, which otherwise might be very hard to accomplish.

Healthcare providers and local public health nurses may be able to offer some incentives or enablers very easily, others may require more money and effort. All patients, regardless of their financial status are entitled to incentives or enablers if needed; the idea is to appeal to any

basic need of the patient that will encourage compliance. WDH is able to provide some funding for incentives or enablers and requests for that assistance should be discussed with the Communicable Disease Program Manager.

Examples of Incentives and Enablers	
Food, candy, drinks, gum	Oil change certificate
Clothing (esp. warm winter items)	Help obtaining insurance, birth certificate
Small birthday or Christmas present	Help obtaining driver's license, bicycle repair, bus fare (anything that would help a patient get to appointments)
Medication charts with stickers (esp. for children)	Personal care items
Books, crossword puzzles, magazines, newspapers	Energy or food assistance
Gas or food gift certificate	Other items related to client's hobbies

There are countless barriers to TB treatment and isolation requirements and healthcare professionals will likely need to be creative in helping achieve treatment goals. The use of incentives and enablers can be a very effective way to help and innovative strategies should be discussed with providers and the health department if they become necessary.

Patient Assistance

The Wyoming Department of Health maintains a patient assistance program to support TB screening and medication assistance for high risk and uninsured individuals within Wyoming. Any person living in Wyoming is eligible for this assistance. WDH is the payer of last resort and any private or employer provided insurance as well as government sponsored insurance must be billed prior to the program reimbursing for any services.

Currently financial assistance for IGRAs (highest risk individuals only), CXRs, liver function testing, and TB medications can be provided. Please see the patient assistance guidance at https://health.wyo.gov/wp-content/uploads/2016/12/TB-Program-Patient-Assistance-Guidance.pdf for more information and instructions for enrolling individuals in the patient assistance program.

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Contact Investigation

Transmission of tuberculosis occurs through close contact with a person who has infectious TB disease. An investigation must be conducted to identify, find, and assess individuals who had contact with an infectious person and provide appropriate treatment for LTBI or active TB if needed. The infectiousness of a patient with active TB is directly related to the number of droplet nuclei that are expelled into the air. Depending on the environment, these particles can remain suspended in the air for several hours. Infection occurs when another person inhales droplet nuclei that reach the alveoli of the lungs.

Infectiousness usually declines rapidly after adequate and appropriate treatment is started; however, the rate of decline varies from patient to patient. Persons with true extrapulmonary disease are usually non-infectious unless the disease occurs in the oral cavity or larynx or in open abscesses or lesions where the concentration of organisms is high.

The likelihood of transmission can generally be predicted depending on three factors: the extent of disease in the index patient, the duration and the proximity of contact between the source patient and the contact, and environmental conditions. After exposure, the risk of TB disease is influenced by any medical conditions of the infected patient that might impair the immune system. All of these factors are taken into account when deciding when and who to test in a contact investigation.

Infectiousness of Index Patient

In general, conditions associated with infectiousness of the source patient include:

- the presence of a cough and the amount of sputum production
- cavities in the lungs seen on CXR
- acid-fast bacilli seen on sputum smear (see chart below)
- TB disease of the lung, airway, or larynx
- cough or sputum inducing procedures
- sputum cultures positive for Mtb

Smear Classification	**Result**	**Associated infectiousness**
4+ (10x bacilli as 3+ smears)	Strongly positive	Probably very infectious
3+ (10x bacilli as 2+ smears)	Strongly positive	Probably very infectious
2+ (10x bacilli as 1+ smears)	Moderately positive	Probably infectious
1+	Moderately positive	Probably infectious
Numerical classification (e.g. *2 AFB seen*)	Weakly positive	Probably infectious
No AFB seen	Negative	Probably not infectious

In general, young children (<10 years old) with pulmonary TB disease are less likely than adults to be infectious, because they are more likely to have paucibacillary TB (smaller number of Mtb bacilli in general) and less likely to produce sputum. It is still possible for children to transmit Mtb to others if they have infectious characteristics such as positive AFB smears or cavities on chest x-ray.

Environmental factors

There are several environmental factors that enhance the probability that Mtb will be transmitted. Those include:

- exposure in small, enclosed spaces
- inadequate local or general ventilation that results in insufficient dilution or removal of infectious droplet nuclei
- recirculation of air containing infectious droplet nuclei
- positive air pressure in patient rooms that result in Mtb flow to other areas

Duration and Proximity

Factors that should be taken into account when assessing duration and proximity of contact include size of rooms, frequency and length of contact, and the amount of close or direct contact.

Infectious Period

Determining the infectious period focuses the investigation on those contacts most likely to be at risk for infection and sets the timeframe for testing contacts. A practical estimation is necessary to determine the infectious period. If no other evidence exists, the infectious period can be presumed to have started 3 months before TB was diagnosed. If other evidence exists, an even earlier start should be used. Other evidence can include the approximate date when TB symptoms were noticed, mycobacterial results, and the extent of disease (especially the presence of large lung cavities which imply prolonged illness and infectiousness). See chart below for specific recommendations.

Respiratory TB Symptoms	Sputum Smear Positivity	Pulmonary Cavity on CXR	Recommended minimum beginning of infectious period
Yes	No	No	3 months before symptom onset or first finding consistent with TB disease, whichever is longer
Yes	Yes	Yes	3 months before symptom onset or first finding consistent with TB disease, whichever is longer
No	No	No	1 month (4 weeks) before date of suspected diagnosis
No	Yes	Yes	3 months before first finding consistent with TB disease

The infectious period ends when all of the following have occurred:
-the patient has been on effective anti-tuberculosis medications for at least 2 weeks
-symptoms have diminished
-mycobacterial response has been seen (decrease in grade of sputum smear positivity)
In the absence of any of those factors (e.g. unable to collect sputum samples for smears), other evidence, such as chest x-ray changes, can be used.

All contacts of a patient with infectious TB during their infectious period should have an exposure period estimated depending upon the amount and type of contact (based upon environmental and duration factors). After determining the exposure period of the contacts and the infectiousness of the index patient, the contacts should be grouped into three categories.

Priorities for contact investigation are determined on the characteristics of the index patient, susceptibility and vulnerability of the contact, and the circumstances of the exposure.

High priority contacts—those with the longest exposure period, closest contact, highest risks (e.g. roommates, family members, co-workers in same room, car-pool members, residents of homeless shelters)

Medium priority contact—those with shorter exposure periods, less close contact, lower risk, but still with considerable contact that puts them at risk (e.g. students in same classroom, co-workers in same suite, extended family members that visit weekly/monthly, members of youth group)

Low priority contact—those with brief exposure periods (minutes instead of hours), no really close face-to-face contact, no other risks (e.g. diners at a restaurant, classmates passed in the hall, large church congregation, well-ventilated grocery store)

An individual who may have only had brief contact but is high risk for TB (HIV positive, <5 yrs., immunocompromised) with the infectious TB patient may need to be categorized as higher priority. If any contacts are showing symptoms consistent with TB, they should also be

assigned a high priority. These categories are flexible; common sense and good judgement should be used when making assignments. Those assignments can be adjusted at any point in the contact investigation.

Contacts who are assigned high or medium priority require testing to rule out TB infection or disease according to the time frames below.

Type of contact	**1st test**	**2nd test (if 1st is negative)**
High priority	As soon as possible after diagnosis	8-10 weeks after last contact with infectious patient
Medium priority	Within 14 days of diagnosis	8-10 weeks after last contact with infectious patient
Low priority	Only after evidence exists to expand investigation	8-10 weeks after last contact with infectious patient

High and medium priority contacts to the index patient should be evaluated using the WDH patient risk assessment (found here https://health.wyo.gov/publichealth/communicable-disease-unit/tuberculosis-2/). In general, WDH recommends IGRA testing for most contacts; that testing can be pre-authorized and paid by the Communicable Disease Unit for individuals without insurance. Contacts with positive testing (either IGRA or TST ≥5mm) should be referred to a provider for further follow-up and evaluation for TB disease and offered a course of treatment for LTBI unless medically contraindicated.

Contacts who do not know their HIV status should be offered HIV counseling and testing. BCG vaccine status should not influence a contact evaluation. Positive testing in a foreign-born or BCG vaccinated person should be interpreted as evidence of recent *M. tuberculosis* infection. Diagnostic evaluation of any contact who has TB symptoms should be immediate regardless of testing results.

During the evaluation of high and medium priority contacts, it is important to be observant for the need to expand investigation efforts beyond the original priority contacts. Evidence of recent transmission and greater infectiousness includes:

-a greater than expected rate of TB disease (secondary case) or TB infection among priority contacts

-evidence of secondary transmission; or two degrees of transmission (TB infection in a contact to the contact)

-TB disease among contacts not initially considered priority

Generally, if any of the above evidence is found, expanding the contact investigation to include contacts at lower priority should be considered.

A contact investigation can be concluded if no further evidence of recent transmission is found, all high and medium priority contacts have been evaluated, all contacts with LTBI have started treatment, and no additional cases of secondary TB have been found.

The Communicable Disease Unit is ultimately responsible for ensuring that a contact investigation is conducted appropriately for every suspected and active case of TB. Many steps of a contact investigation can and should be performed by public health partners. County public health nurses often interview the index case, perform testing on contacts, and oversee LTBI treatment. County health officers may be asked to provide primary care services for contacts without health insurance or a primary care provider. Healthcare facility infection control officers will be asked to evaluate any healthcare workers who were contacts to someone with infectious TB. If an index patient or their contacts lives on a university/college campus, in a correctional facility, or on a tribal reservation, the governing bodies of those establishments may be asked to participate.

Special Considerations

- Airline passengers who are seated in the same or adjoining rows as a person with infectious TB for ≥8 hours are much more likely to be infected than other passengers and should be assigned a medium or high priority.
- A contact investigation should still be conducted for an index patient that has died before an interview could be conducted. Contact finding will have to be performed through family members, friends, social media, co-workers, healthcare workers, etc.
- Routine contact investigations with few contacts usually do not garner media attention but TB contact investigations have the potential for sensational coverage and attention from the media. If media attention is expected, issuing a press release in advance of other media coverage is recommended to provide clear, accurate messaging.
- A full course of treatment for presumptive TB infection may be necessary for HIV infected or other notably immune suppressed individuals, after TB disease has been excluded, even if testing results are negative.
- The decision to treat contacts who have documentation of previous positive testing results or previous treatment of LTBI or TB disease should be made by the provider on an individual basis. Those without documentation should undergo a standard evaluation.
- Although not normally required, directly observed therapy may be desirable for LTBI treatment in contacts < 5 years or others those who might not complete treatment because of social or behavioral impediments.

- If an index patient has contacts who reside in other states, interjurisdictional notifications should be sent to the health departments of those states, who are responsible for getting their residents tested.

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Immigration

Approximately 75,000 refugees and 450,000 legal permanent immigrants enter the United States annually. Those individuals are required to have a medical exam prior to immigration to determine whether the applicant has a condition of public health importance that requires treatment before entry into the U.S. Applicants are required to undergo TB screening depending on age and country of origin.

- Applicants ≥15 yrs. are required to undergo medical examination and chest x-ray (CXR). If an applicant has an abnormal CXR, signs/symptoms suggestive of TB, or has HIV, the applicant is required to provide three sputum samples for acid fast bacilli (AFB) smears and culture.
- Applicants 2-14 yrs. living in countries with a WHO estimated TB rate of ≥ 20 per 100,000 are required to be screened with either tuberculin skin test (TST) or interferon-gamma release assay (IGRA). If either of those tests is positive a CXR is then required. If an applicant has an abnormal CXR, signs/symptoms of TB, or is HIV positive, the applicant is required to provide three sputum samples for smears/culture.
- Applicants <2 yrs. living in countries with a WHO estimated TB rate of ≥20 per 100,000 must have a physical examination and history provided by parent or guardian. If signs/symptoms are suggestive of TB or applicant is HIV positive, applicant should then undergo TST or IGRA, CXR, and sputum smears/cultures.
- Applicants <15 yrs. living in countries with WHO estimated TB rate of <20 per 100,000 are required to have a physical exam and history provided by parent or guardian. If signs/symptoms are suggestive of TB or the applicant is HIV positive, applicant should then undergo TST or IGRA, CXR, and sputum smears/cultures.

All applicants are given a TB classification based on testing results:

No TB Classification—applicants with normal tuberculosis screening.

Class A TB—applicants who have tuberculosis disease.

Class B1 TB (pulmonary)—applicants who have medical history, physical exam, or CXR suggestive of pulmonary TB, but have negative AFB smears and cultures and can wait to have TB treatment started after immigration *or* applicants who were diagnosed with pulmonary TB and successfully completed treatment prior to immigration (in other words, are not infectious).

Class B1 TB (extrapulmonary)—applicants with evidence of extrapulmonary TB.

Class B2 TB (LTBI Evaluation)—applicants who have a positive TST or IGRA with an otherwise negative evaluation for TB.

Class B3 TB, Contact Evaluation—applicants who are a recent contact of someone with known TB disease.

Any applicant diagnosed with respiratory TB who needs treatment is not cleared for travel until completion of successful treatment. Immigrants who are classified as either B1 or B2 are allowed to travel to the US before any treatment begins. Class B1 immigrants are directed to seek medical evaluation for treatment within one week of arrival in the U.S. Class B2 immigrants are directed to seek medical evaluation for treatment within one month of arrival. Some of those individuals initiate that evaluation on their own, many do not; therefore state public health agencies are asked to follow-up with all B1 and B2 immigrants after their arrival in the U.S.

WDH receives notification through the CDC of immigrants who have arrived in the U.S. with an address documented in Wyoming. Those notifications include an Immigrant Data Summary that includes information from the pre-departure medical evaluation, which may include TST/IGRA, CXR, and/or sputum culture results, as well as documentation of previous treatment regimens. County public health nursing offices are asked to make contact with immigrants to initiate an evaluation as soon as possible.

Each immigrant will require different follow-up since every one of them underwent different testing and treatment before arriving. The end goal is to assess whether the immigrant needs treatment for either active or latent TB. This may require further testing or referral to a provider for assessment. As with any other patient, the state can pay for IGRA and liver function testing as well as chest x-rays for uninsured or underinsured patients. Pre-authorization forms can be found at https://health.wyo.gov/publichealth/communicable-disease-unit/tuberculosis-2/.

Considerations when conducting follow-up for immigrants include:

- Many countries with high TB incidence do not treat LTBI. That is not the case in the U.S. or Wyoming. The resources to treat LTBI are available and in most cases, LTBI treatment is recommended.
- The risk of recurrence in individuals from high-risk countries who have already been treated for TB disease is about 7% (either treatment failure or reinfection). Therefore, it may be necessary to re-evaluate someone even if they have been treated for TB previously.
- Pre-immigration medical exams are only required for refugees or individuals applying for immigration before presenting to the border authority. Foreigners coming to the U.S. on work, student, or travel visas are not required to complete medical exams before coming.

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Infection Control in Healthcare Settings

Mtb can be transmitted in virtually any setting, but is especially likely in healthcare settings where contact occurs with individuals who have unsuspected TB disease, who are not receiving adequate treatment, and have not been properly isolated. These healthcare settings may include hospitals, clinics, nursing homes, home-health care providers, emergency medical services, dental offices, dialysis centers, drug treatment centers, homeless shelters, and laboratories. Any settings where healthcare workers (paid or unpaid) have face-to-face contact with patients who may have suspected or confirmed TB disease should develop a TB infection control program. Residents of facilities where contact between residents can occur may need to be included in infection control programs.

The CDC's complete guidelines for preventing TB transmission in healthcare settings can be found at https://www.cdc.gov/mmwr/PDF/rr/rr5417.pdf. These guidelines state that a TB infection control program should be based on three levels of hierarchy:

1. Administrative measures (reduce risk of exposure)
2. Environmental controls (prevent spread and reduce concentration of droplet nuclei)
3. Respiratory protection controls (further reduce risk of exposure in special settings)

Current recommendations advise that healthcare facilities conduct a risk assessment for TB transmission every year. Performing a risk assessment determines the type of administrative, environmental, and respiratory protection controls that each setting would require. The risk of TB transmission is determined by examining the number of patients with TB disease in the setting; the promptness of detection, isolation, and evaluation of patients with suspected or confirmed TB disease; evidence of transmission of Mtb in the setting; and the community rate of TB disease. An in-depth framework for a risk assessment is available in the CDC's guidelines (link above).

Administrative controls are organizational policies and procedures that reduce the possibility of contact with persons who might have TB disease. These control measures involve:

-assigning someone the responsibility for TB infection control in a healthcare setting
-developing and implementing a TB control plan to ensure prompt detection and isolation
-conducting initial and yearly risk assessments
-implementing effective practices for managing patients with active TB
-ensuring proper cleaning and sterilization of instrumentation and equipment
-testing and evaluating healthcare workers or residents with potential exposure to TB disease or with possible TB disease or infection
-ensuring education and training for all healthcare workers.

Part of a yearly facility risk assessment is determining the setting's risk classification and requirements for the TB testing program and the frequency of testing for healthcare workers. Baseline TB testing should be conducted for healthcare workers upon hire; annual TB testing thereafter should be performed dependent upon the possibility for exposure as outlined below.

Low Risk

-For settings where exposure to Mtb is unlikely
-Baseline two-step TST or IGRA upon hire
-*No* annual testing (unless other risks occur)
-Standard contact investigation for unprotected exposure to Mtb

Medium Risk

-For settings where exposure to Mtb is expected
-Baseline two-step TST or IGRA upon hire
-Serial screening and testing (TST or IGRA every 12 months)
-Standard contact investigation for unprotected exposure to Mtb

Potential Ongoing Transmission

-For settings with evidence of person-to-person transmission of Mtb in past year
-Immediate investigation into cause of ongoing transmission
-Testing should be performed as often as necessary to verify that ongoing transmission has ended (perhaps every 6-8 weeks)
-After transmission has ended, facility must be reclassified as medium risk for at least one year.

A simple tool for determining a facility's annual risk classification was developed by WDH and can be found at https://health.wyo.gov/publichealth/communicable-disease-unit/tuberculosis-2/. A risk classification can be used for an entire facility, although in certain settings (e.g. healthcare organizations that encompass multiple sites or types of services), it may be practical to define risk classifications by geography, functional units, patient population, or job type. Examples of hypothetical risk classifications and recommendations for unusual settings are outlined in the CDC's guidance (link above).

Environmental controls are engineering technologies that are designed to prevent the spread and reduce the concentration of infectious TB droplet nuclei in the air. Primary environmental controls control the source of infection by diluting and removing droplet nuclei with natural or mechanical ventilation. In facilities where persons with infectious TB are expected to be encountered, there should be a negative pressure airborne infection isolation (AII) room available. Patients suspected of having TB disease should be placed into these rooms

immediately. Secondary environmental controls prevent contamination of areas adjacent to AII rooms and clean the air using filtration or irradiation.

Respiratory-protection controls further reduce the risk of contact in areas or circumstances where exposure cannot be avoided. Healthcare workers should be trained on the proper use of personal respiratory protective equipment and should use that protection in settings where contact is unavoidable, e.g. providing care in AII rooms, in rooms where cough or aerosol generating procedures occur, when transporting infectious patients, when performing field visits. Minimum respiratory protection standards are determined by the National Institute for Occupational Safety and Health (NIOSH) and more information can be found at https://www.cdc.gov/niosh/topics/respirators/. Any setting that uses respiratory protection controls is required by OSHA to develop, implement, and maintain a respiratory protection program.

Respirators are designed to protect healthcare workers and other uninfected individuals from inhaling droplet nuclei. Surgical masks are designed to reduce the number of droplets being exhaled into the air when infectious patients talk, cough, sneeze, etc. Persons with suspected or confirmed infectious TB disease should be given, and required to wear a surgical mask to minimize the amount of droplet nuclei expelled into the air. Respirators (e.g. N95 masks) should not be worn by patients and surgical masks should not be worn by healthcare workers.

Unprotected Exposure to Individuals with Active TB

Infection control plans are intended to reduce the possibility of unprotected contact with an infectious TB patient. If infection control procedures fail to accomplish this, healthcare workers may need to be tested for TB exposure as part of a contact investigation. The degree of infectiousness of the index patient and the environmental and duration limits of exposure are determined by WDH. Many factors are taken into account when determining the infectiousness of a TB patient (please see the *Contact Investigation* section of this manual). WDH will communicate the need for healthcare worker testing to infection control officers after someone has been diagnosed with active TB.

Usually, a TB test would be performed on exposed healthcare workers within 2 weeks of the unprotected exposure and again 8-10 weeks later. Healthcare workers who were using respiratory protection equipment properly are not at risk for exposure. Patients with LTBI are not infectious and do not require isolation or respiratory protection measures. Other patients may not be considered infectious (i.e. extra-pulmonary, smear negative TB, <10 years) and may not require a contact investigation. Infection control officers should be in contact with WDH when there is a patient with active TB in their facility.

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FAQ

1. *Does the Communicable Disease Program need to evaluate our TB infection control policy yearly?*
   No, the WDH Communicable Disease Program does not audit facilities or their policies and procedures. We make recommendations, provide guidance and consultation, and offer resources in relation to TB prevention and control. Compliance with proper infection control rules is under the jurisdiction of the WDH Office of Healthcare Licensing and Surveys. Other governmental agencies (e.g. OSHA) may also perform inspections if they have reason.

2. *A patient says they do not have TB infection and the test is a false positive. What do I do?*
   Any reaction to a skin test or a positive IGRA is an indication that a patient produces antibodies to Mtb. Those antibodies may have been produced because of exposure to someone with infectious TB, a BCG vaccine, or a non-tuberculous mycobacterial infection (this is explained briefly earlier in the manual). A reaction caused by a BCG vaccine or exposure to non-MTB may possibly be ruled out with an IGRA. If an individual is from any high risk group or has been recently exposed to someone with infectious TB, that reaction most likely represents a *true positive*. Anyone who has positive TB testing should be assessed to rule out the possibility of TB disease and considered for LTBI treatment if not medically contraindicated.

3. *How do I encourage patients to complete LTBI treatment?*
   By accurately communicating the value of LTBI treatment, e.g.:
   - As long as TB bacilli are present (as indicated through testing), they can begin to multiply and cause disease.
   - Certain individuals are at especially high risk for progression to disease, e.g. those with recent infection, certain medical conditions, or on certain medications.
   - Completing appropriate LTBI treatment regimens reduces the risk of TB disease by 90%.
   - Treatment recommendations are based on years of scientific research results.
   - By addressing barriers to adherence, which may include misinformation, financial burdens, side effects, language barriers, or stigma. Individuals who are at high risk for progression to disease or are a high risk contact to an infectious patient may need extra education that is appropriate to their literacy level, directly observed therapy, incentives, or reminders.

4. *Who needs to be tested for TB?*
   People who are at high risk for either exposure to TB or for progression to TB disease. See the *Targeted TB Testing* section of this manual or the Wyoming targeted screening guidelines

at https://health.wyo.gov/wp-content/uploads/2016/04/Targeted-recommendations-Nov-2016.pdf.

5. *Are people protected from TB if they have had the BCG vaccine?*
   BCG vaccine is routinely given to infants and small children in some countries. BCG vaccine protects against some severe, life-threatening forms of extra-pulmonary TB such as TB meningitis and miliary TB in childhood. However, it provides unreliable protection against pulmonary TB, the main form of tuberculosis.

6. *Once a person completes treatment for TB infection or disease, can s/he get TB again?*
   If a patient has taken the proper TB medications for the appropriate time-frame the chances of recurrent TB are low. However, previous TB infection or disease and treatment does not provide immunity or reduce the risk of new disease after subsequent exposure to other infectious individuals.

7. *What dose of medications should I use for my patient?*
   The most current medication and dosage recommendations are published by the CDC.
   - For LTBI treatment options and dosages, see https://www.cdc.gov/tb/publications/ltbi/ treatment.htm.
   - For TB disease treatment see https://www.cdc.gov/tb/publications/guidelines/pdf/clin-infect-dis.-2016-nahid-cid_ciw376.pdf.
   - For drug-resistant TB disease, a great resource is Curry International Tuberculosis Center's "Drug-Resistant Tuberculosis: A Survival Guide for Clinicians." Available here http://www.currytbcenter.ucsf.edu/products/view/drug-resistant-tuberculosis-survival-guide-clinicians-3rd-edition.

   The Mayo Center for Tuberculosis will provide consultation for any TB related treatment, see http://centerfortuberculosis.mayo.edu/consultation.html.

8. *Should I perform a TST on someone who had a BCG vaccine when they were a child?*
   A TST is not contraindicated in someone who has been BCG vaccinated. If used, a TST in someone with BCG vaccination history should be interpreted using the same criteria as any other TST.
   A booster phenomenon may occur among persons who have had a prior BCG vaccine. In many situations, it may be worthwhile to use IGRA testing in place of a TST for those who were BCG vaccinated.

9. *What should the county jail do about employee (or inmate) TB testing?*
   A disproportionately high percentage of TB cases occur among persons incarcerated in U.S. correctional facilities. The incarcerated population contains a high proportion of people at greater risk for TB than the overall population. Therefore, screening programs should be in

place for inmates and employees upon entry into the system. In facilities where there is minimal risk of TB, all new employees and inmates should be screened for TB symptoms or risk factors. Those with symptoms or risk factors require further testing with TST or IGRA. In facilities where there is risk for TB (this includes facilities that house inmates with risk factors or immigrants from endemic TB countries) all inmates and employees should be tested upon entry and perhaps tested or screened yearly.
Please see the CDC's guidance for correctional facilities at https://www.cdc.gov/mmwr/preview/mmwrhtml/rr5509a1.htm.

10. *Can our facility have TST testing supplies like we used to receive?*
WDH obtains TST testing supplies through the national 340B program. Requirements for that program only allow distribution to other 340B eligible and enrolled programs. All public health nursing offices in Wyoming are registered as 340B entities and can continue receiving those supplies. All other entities in the state would have to enroll in the 340B program themselves to get the discount on supplies. Please see the 340B website (https://www.hrsa.gov/opa/) for more information if you are interested in eligibility.

11. *We heard that an individual in our community had a positive TST. He has been an in-patient in our facility before so all of our nurses have been exposed to TB. What should we do?*
Only persons with active TB disease are infectious to others. A positive TB test alone is not definitive for active TB disease, that diagnosis comes after a provider takes multiple factors into account. Someone with active TB usually has a positive TB test, abnormal CXR, and symptoms consistent with TB.
After someone is diagnosed with active TB disease, WDH and the county public health nursing office will conduct a contact investigation. They will determine the infectiousness of the individual and the environmental and duration limits that necessitate testing. Specific guidance for testing individuals exposed to TB will come from WDH. Depending on the degree of exposure, that testing may need to occur immediately and/or may be performed 2-8 weeks after contact with an infectious patient.
Sometimes, active TB is not infectious. Patients with extra-pulmonary TB, smear negative TB, or younger than 10 years may be considered non-infectious. WDH and providers will make those determinations and communicate them to infection control officers. Latent tuberculosis infection is not infectious and contact with individuals with LTBI is not a public health concern.

Resources

WDH maintains a website with resources, statistics, and information specific to Wyoming https://health.wyo.gov/publichealth/communicable-disease-unit/tuberculosis-2/.

The CDC TB website has the most comprehensive information in regards to TB diagnosis, treatment, and prevention https://www.cdc.gov/tb/.

The National Tuberculosis Controllers Association provides contact information for every TB control program in the U.S. www.tbcontrollers.org.

The online TST/IGRA Interpreter is a calculator used to estimate the risk of active tuberculosis based on a patient's clinical profile http://tstin3d.com/.

The BCG World Atlas provides detailed information on current and past BCG policies and practices for over 180 countries http://www.bcgatlas.org/.