Tuberculosis Prevention & Control in Long Term Care

Long Term Care Program Resource Guide
# LTC Tuberculosis Resource Guideline July 2018

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This resource guide replaces the following LTC IP&C manual documents:
Guidelines for Tuberculin Screening of Health Care Workers
Guidelines for Tuberculosis - Baseline Screening for Residents
Guideline for Tuberculosis - Management of Contacts

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To provide consistent guidance for the prevention and control of Tuberculosis in the Long Term Care Facilities (LTCFs)/Personal Care Homes (PCHs) within the Winnipeg Health Region.

Introduction
Tuberculosis (TB) is an infectious disease caused by the bacteria, *Mycobacterium tuberculosis* (MTB). In Manitoba, the disease burden is unequally distributed with disparities pronounced in certain population groups and geographic regions. Foreign-born individuals and Indigenous peoples (First Nation, Inuit, and Metis) in particular are disproportionately affected by TB. While the greatest number of cases in Canada are reported among foreign-born individuals, the reported incidence rate has consistently been highest among Canadian born Indigenous individuals over the past decade.

Definitions

**Acid-fast bacteria (bacilli):** Microorganisms that are distinguished by their retention of specific stains even after being rinsed with an acid solution. The majority of acid-fast bacteria (AFB) in patient specimens are mycobacteria, including species other than *Mycobacterium tuberculosis* complex. The relative concentration of AFB per unit area on a slide (the Smear grade) is associated with infectiousness. A positive culture or nucleic acid amplification test (NAAT) is required for laboratory confirmation of *M. tuberculosis* complex.

**Active tuberculosis disease:** Clinical disease that is usually symptomatic and for which microbiologic tests are usually positive and radiologic tests usually abnormal.

**Aerosol:** Small droplets that are exhaled or coughed up. In a patient with pulmonary tuberculosis these may contain *Mycobacterium tuberculosis* bacteria that are suspended in the air and lead to the spread of infection.

**Airborne infection isolation:** The conditions into which an individual with suspected or proven active tuberculosis may be placed for purposes of preventing transmission to other people (formerly termed airborne respiratory isolation)

**Airborne infection isolation room (AIIR):** Formerly, negative pressure isolation room. An AIIR is a single-occupancy patient care room used to isolate people with a suspected or confirmed airborne infectious disease. Environmental factors are controlled in an AIIR to minimize the transmission of infectious agents that are usually transmitted from person to person by droplet nuclei associated with coughing or aerosolization of contaminated fluids. An AIIR should provide negative pressure in the room so that no air flows out of the room into adjacent areas and should direct exhaust of air from the room to the outside of the building or recirculate the air through a HEPA filter before returning it to circulation.
**Bacille Calmette-Guérin (BCG):** A live attenuated vaccine derived from *Mycobacterium bovis*.

**Cavitary disease:** Evidence on chest x-ray or pathology tests of lung destruction resulting in cavities or cystic areas that communicate with a bronchus. Cavities generally harbor large numbers of bacteria and, as a result, patients with cavitary disease tend to be highly infectious.

**Conversion (tuberculin conversion):** An increase in the size of a tuberculin skin test (TST) reaction on repeated testing that may reflect new TB infection. Tuberculin conversion is defined as induration of 10 mm or greater when an earlier test resulted in a reaction of less than 5 mm. If the earlier result was between 5 and 9 mm, there are two criteria:

1) An increase of 6 mm or more - this is a more sensitive criterion, which is suggested for those who are immune compromised with increased risk of disease or for an outbreak;
2) An increase of 10 mm or more - this is a less sensitive but more specific criterion. In general, the larger the increase, the more likely that it is due to true conversion.

**Droplet nuclei:** Airborne particles resulting from a potentially infectious (microorganism-bearing) droplet from which most of the liquid has evaporated, allowing the particle to remain suspended in the air.

**Fit testing:** The use of a qualitative or quantitative method to evaluate the fit of a specific manufacturer, model and size of respirator on an individual.

**High-efficiency particulate air (HEPA) filter:** A filter that is certified to remove greater than 99.97% of particles 0.3 μm in size, including *M. tuberculosis*-containing droplet nuclei; the filter can be either portable or stationary.

**Immunocompromising condition:** A condition in which at least part of the immune system is functioning at less than normal capacity.

**Incidence:** The number of new occurrences of a given disease during a specified period of time.

**Induration:** The soft tissue swelling that is measured when determining the tuberculin skin test response to purified protein derivative (PPD) tuberculin. It is to be distinguished from erythema or redness, which should not be measured.

**Infectious:** The condition whereby the patient can transmit infection to others by virtue of the production of aerosols containing TB bacteria. Patients with smear-positive, cavitary and laryngeal disease are usually the most infectious.

**Interferon gamma release assay (IGRA):** In-vitro T-cell based assays that measure interferon-γ (IFN-γ) production and that have been developed as alternatives to TST for the diagnosis of latent TB infection. At the present time, two different types of IGRAs are registered for use in Canada. These are the
Quantiferon®-TB Gold In-Tube (Cellistis Limited, Carnegie, Victoria, Australia) and the T-SPOT.TB® (Oxford Immunotec, Oxford, UK) assays.

**Intradermal:** The method of injecting either PPD skin test antigen using the Mantoux technique or vaccinating with BCG vaccine.

**Latent tuberculosis infection (LTBI):** The presence of latent or dormant infection with *Mycobacterium tuberculosis*. Patients with LTBI have no evidence of clinically active disease, meaning that they have no symptoms, no evidence of radiographic changes that suggest active disease and negative microbiologic tests; they are non-infectious.

**Mantoux technique:** The recommended method of administering the TST – the intradermal injection of 5 tuberculin units of PPD into the forearm.

**Non-respiratory tuberculosis:** Refers to all other disease sites not part of respiratory TB. The definition overlaps with, but is slightly different from that of extra-pulmonary TB.

**Nucleic acid amplification tests (NAAT):** A process whereby genetic material is amplified and then subsequently evaluated for the presence of DNA material; useful to identify specific mycobacterial species. Polymerase chain reaction (PCR) is one example of a NAAT that can be performed to diagnose mycobacterial species.

**Purified protein derivative (PPD) tuberculin:** A preparation of purified protein derived from culture filtrate of *Mycobacterium tuberculosis*. The tuberculin skin test uses 0.1 mL or 5 tuberculin units of PPD standardized to a common lot.

**Respiratory tuberculosis:** This consists of pulmonary tuberculosis, tuberculous pleurisy (non-primary) and tuberculosis of intrathoracic lymph nodes, mediastinum, nasopharynx, nose (septum) and sinus (any nasal) (ICD-9 codes 010-012; ICD-10 codes A15-16).

**Silicosis:** A condition associated with certain occupations (e.g., mining and construction) where respiratory inflammation is caused by inhalation of silica dust.

**Smear:** A laboratory technique for preparing a specimen so that bacteria can be visualized microscopically.

**Sputum smear positive:** Cases of pulmonary tuberculosis with positive smear results obtained from either spontaneously expectorated sputum, induced sputum, tracheal or bronchial washings/aspiration, or gastric wash.

**TNF alpha inhibitors:** Medications used to treat autoimmune and immune-mediated disorders (e.g., rheumatoid arthritis, inflammatory bowel disease etc.) Examples include: etanercept, infliximab, adalimumab, golimumab.
**Tuberculin skin test (TST):** Skin test to identify whether a person has delayed-type hypersensitivity reaction to tuberculin antigens.

**Tuberculosis case:** A reportable case of disease in Canada caused by *Mycobacterium tuberculosis* complex (e.g. *M. tuberculosis* [including subspecies *M. canetti*], *M. bovis* [excluding BCG strain], *M. africanum*, *M. caprae*, *M. microti* or *M. pinnipedi*).

**Transmission**

The reservoir for MTB is humans. Other animals, in particular primates, may be infected but are rarely a source of infection. MTB is communicable from one human to another mainly by the aerosol route and rarely through ingestion or percutaneous inoculation (e.g. through laboratory accident). Transmission from a case of infectious pulmonary TB is by the airborne route in minute droplets of moisture that become increasingly reduced by evaporation, creating “droplet nuclei”. Approximately forty droplet nuclei are created by forceful expiratory efforts, such as coughing, sneezing, singing, playing wind instruments and even speaking. In general, normal breathing produces few infectious particles, a bout of coughing or five minutes of speaking in a normal tone produce many more, and a sneeze produces the most. Before droplets dry out and become droplet nuclei, the large particles settle quickly and are either not inhaled by contacts or, if inhaled, are trapped in the mucus of the upper airway. Before these droplets reach the airspace of a room and have had an opportunity to evaporate down to a “droplet nucleus” their numbers can be reduced by having the symptomatic individual wear a simple gauze (surgical) mask or covering the mouth and nose during coughing. Certain procedures, for example, bronchoscopy, sputum induction, processing of specimens, autopsy and even irrigation or other manipulation of tuberculous abscesses, may also produce infectious aerosols. Droplet nuclei have an extremely slow settling rate (0.5 mm per second or less), which permits their transport by air currents, duct systems or elevator shafts for significant distances from the source case. Fomites (e.g. furniture, food utensils) do not constitute an infection risk.

**Infection versus Active Disease**

At the time of initial infection, inhaled droplet nuclei tend to follow the most direct path in the lung, favoring the middle and lower lung zones, which receive most of the ventilation. In immunocompetent hosts, it is theorized that cell mediated immunity may or may not destroy MTB when droplet nuclei are inhaled and it depends on the infected person’s immune response, genetic factors and resistance mechanisms of the MTB itself. A proportion of those who are infected are unable to successfully clear the MTB and there is progression to active pulmonary disease in a matter of months. This early disease progression is a function of age and immunologic response, disease being especially likely to occur in young children and the immunocompromised. Another proportion of people will have an initial infection followed by a variable period of latency; this is known as LTBI and is discussed in detail later in the document. Infection with MTB can also lead to extra-pulmonary infections (infections outside of the lung) and are generally not transmissible from person to person unless fluids from the site of infection become aerosolized (e.g., irrigation and/or manipulation of non-respiratory tuberculous abscesses).
The risk of transition from LTBI to active TB disease is largely dependent on the infected person’s immune response. Age and sex appear to directly affect this immune response and the risk of disease such that death occurs with greater frequency among young children (less than 3 years of age), especially infants, among young adults, especially females, and among older adults, especially males. Most important from a clinical perspective are the many medical conditions that are well known to affect immune response and increase the risk of progression from LTBI to active TB disease (see high risk factors for progression below). When TB progresses to active disease, it most commonly presents as a respiratory infection but it can also present in any system of the body. Signs and symptoms depend on the site of the disease. TB can also be multi-drug resistant (where there is resistance to at least isoniazid [INH] and rifampin), or extensive drug resistant (where there is resistance to INH, rifampin, and at least one of the three injectable second-line drugs [e.g., amikacin]).

**Active Respiratory TB**

In Canada, respiratory TB includes primary TB, pulmonary TB, tuberculous pleurisy (nonprimary) and TB of the intrathoracic lymph nodes, mediastinum, nasopharynx, nose (septum) and sinus (any nasal). Pulmonary TB refers to TB of the lungs and conducting airways, which includes tuberculous fibrosis of the lung, tuberculous bronchiectasis, tuberculous pneumonia, tuberculous pneumothorax, isolated tracheal or bronchial TB and tuberculous laryngitis.

**Signs & Symptoms**

A cough of 2-3 weeks' duration with or without weight loss and fever in a person belonging to one of the at-risk groups below should prompt a thorough investigation to determine whether active respiratory TB is the cause:

- People with a history of active TB;
- Previously or currently incarcerated people;
- Injection drug users;
- Indigenous Canadians who resided in communities with high TB rates;
- People infected with human immunodeficiency virus (HIV);
- People born in Canada and other low TB incidence countries prior to 1966;
- People born or previously residing in countries with a high TB incidence in Asia, Eastern Europe, Africa and Latin America;
- People with the following high risk factors for progression from LTBI to active disease;
  - Acquired immunodeficiency syndrome (AIDS)
  - Human immunodeficiency virus infection (HIV)
  - Transplantation (related to immune-suppressant therapy)
  - Chronic renal failure requiring hemodialysis
  - Silicosis
  - Carcinoma of head and neck
  - Recent TB infection (within 2 years)
  - Abnormal chest x-ray - fibronodular disease
The classic symptom of pulmonary TB disease is a chronic cough of at least 2-3 weeks' duration. This cough is initially dry but after several weeks to months will become productive. Fever and night sweats are common but may be absent in the very young and the elderly. Hemoptysis (bloody sputum), unexplained loss of appetite, weight loss, chest pain and other symptoms are generally manifestations of more advanced disease. The most common physical finding in pulmonary TB is a totally normal examination, even in relatively advanced cases. Bronchial breathing, rales or crepitations will be found in more advanced cases. It is important to examine for signs of disease outside of the lung, such as lymphadenopathy, pleural effusion and abdominal or bone and joint involvement, as these may be present concomitantly, particularly when the person suspected to have TB is HIV infected. See the section on Implementation of Airborne Precautions for details of how to accommodate suspected or confirmed active respiratory TB disease cases.

**Diagnosis**

In Canada, standard testing for active TB includes a chest x-ray (posterior-anterior and lateral views) and collection of sputum for testing by the lab (sputum smear microscopy, mycobacterial culture and phenotypic drug susceptibility testing, and Nucleic Acid Amplification Tests (NAATs). **Tuberculin Skin Tests (TST) do not have any value in determining the presence of active disease.** See the section on LTBI for additional details regarding appropriate use of the TST.

**Chest X-ray (CXR)**

CXR has poor specificity for diagnosing TB disease and inter-reader variability can add to the difficulty of determining the presence of active disease. CXR is an integral part of diagnosing TB but it cannot provide a conclusive diagnosis on its own and must be followed by microbiological tests for TB disease.

Typical findings on CXR for immunocompetent adults with active pulmonary disease are:

- Position - infiltrates in the apical-posterior segments of upper lobes or superior segment of lower lobes in 90%.
- Volume loss - this is a hallmark of TB disease as a result of its destructive and fibrotic nature.
- Cavitation - this is seen at a later stage and depends upon a vigorous immune response. Therefore, it often is not seen in immunocompromised individuals.

Atypical CXR findings are seen in individuals with immunocompromising conditions (e.g. HIV infection, diabetes, renal failure, long-term corticosteroid and other immune suppressing agent use) and include:

- Hilar and mediastinal lymphadenopathy (particularly in HIV-infected individuals)
- Non-cavitary infiltrates and lower lobe involvement

Signs of complications on CXR can include endobronchial spread of disease where TB may spread via the airways to the ipsilateral and contralateral lower lobes. This results in irregular, poorly defined, small nodular shadows or acinar shadows that will slowly enlarge and coalesce to form TB pneumonia (formerly known as "galloping consumption"). Pleural effusion can also sometimes be seen with
pulmonary disease and may represent TB empyema. Pneumothorax can rarely occur as a result of erosion of a lesion into a bronchus and simultaneously into the pleural space, causing a bronchopleural fistula.

**Respiratory Specimens for Microbiology**

**Sputum**

At least three sputum specimens of 5-10 mL each should be collected at least one hour apart (under Airborne Precautions) and tested for AFB with microscopy as well as culture. While available evidence shows that the yield of the third sputum smear is only about 2-5%, the yield of the third culture may be as high as 5-10%, especially in HIV-infected people. Thus, it is important to collect at least three specimens for smears and cultures, especially in a low-incidence setting such as Canada, where smear-negative TB is the most common presentation.

Many residents in LTC are incapable of expectorating, making collection of a spontaneous sputum specimen impossible. These individuals will require transfer to an acute care facility equipped with the infrastructure to collect induced sputum or gastric aspirates (see below). Consideration should be given to transferring a resident to acute care when active disease is suspected as they will also require the implementation of Airborne Isolation Precautions which most LTC sites do not have the infrastructure to provide. Another advantage to transferring a resident to acute care is that induced sputum can be collected on the same day as long as the 3 required specimens are collected at least one hour apart. The LTC attending physician should contact Adult Chest Medicine Service at Health Sciences (page 204-787-2071, 24 hours a day, seven days a week; if non- urgent, fax 204-787-2420 or page 204-787-2071, Monday to Friday). Ensure the site Infection Control designate is made aware of the suspected case and the arrangements for diagnosis and implementation of precautions is reported to the WRHA LTC Program contact responsible for Infection Prevention and Control promptly. Both induced sputum and gastric washings are uncomfortable and invasive activities that should only be pursued after thorough assessment indicates there is a true suspicion of active TB disease.

**Bronchoscopy**

Bronchoscopy may be used to facilitate the diagnosis of TB when spontaneous sputum and induced sputum are unavailable, or all samples are smear-negative. Bronchoscopy must be done in an acute care facility with the appropriate infrastructure and can be very useful if other pulmonary diseases, such as lung cancer, are also suspected. However, for the diagnosis of active TB it entails risk and discomfort for the patient, is expensive and can contribute to nosocomial spread of TB if not performed in an appropriate environment with protection of staff. If bronchoscopy is done, post-bronchoscopy sputum should be sent for AFB testing, as this has a yield similar to that of bronchial washings and lavage.

**Gastric Aspirate**

When spontaneous or induced sputum cannot be obtained, a gastric washing can be performed by inserting a nasogastric tube in an attempt to retrieve swallowed MTB as soon as the resident awakens from a long sleep, at least six hours after ingestion of food or liquid, and before the stomach has emptied. Gastric aspirate should be performed in an acute care facility with the appropriate
infrastructure. Three early morning specimens on consecutive days are required and the specimen cannot wait for processing for more than four hours.

Waiting for results can be lengthy as gastric washings are a low yield test that is not specific for tuberculosis mycobacterium (e.g., other forms of acid-fast non tuberculosis mycobacterium can produce smear positive results), MTB is a slow growing organism, and the resident will likely require accommodation in an AIIR, which would also necessitate transfer to acute care.

**Treatment of Active Disease**

Residents with active TB disease should be transferred to acute care for diagnostics and to be accommodated under Airborne Precautions. In the unusual event that a resident cannot be transferred to acute care, treatment may be implemented while the resident resides in the PCH/LTCF. In this circumstance, the attending physician or prescriber shall not initiate treatment without consultation with either an Infectious Diseases Physician or Respiriologist with expertise in TB diagnosis.

**Infection Control Measures for Active TB**

*Anytime active pulmonary or laryngeal TB is suspected, the resident should be transferred to acute care for accommodation under Airborne Precautions unless the LTC facility is able to implement Airborne Precautions.*

Contact Adult Chest Medicine or Pediatric Respiratory Services, as appropriate, at Health Sciences Centre to discuss the need for transfer. While awaiting transfer, frontline staff should immediately implement Airborne Precautions. Due to the lack of AIIRs in the LTC setting, this usually means placing the resident in a private room with the door closed and having the resident wear a plain procedure mask when outside of the room (e.g., during transport). Staff entering the room to provide care shall wear a fit-tested N95 respirator. The LTC site Infection Control Professional or designate should be immediately informed of a suspected case however frontline staff should not wait for Infection Control to implement precautions. See the Airborne Precautions section of the LTC IP&C manual for additional details:

http://www.wrha.mb.ca/extranet/ipc/files/manuals/ltc/ManualPCH_Sec05.pdf#page=4

For residents who are contacts of an infectious case of TB, the most critical follow-up is assessment for active disease through careful symptom evaluation, and chest radiography. **Contact investigation in the LTC sector of the Winnipeg Health Region is conducted by Public Health.** Only respiratory tuberculosis (TB), with limited exceptions, is infectious; contact follow-up should be carried out for both sputum smear-negative and smear-positive cases. The objective of contact follow-up is to identify and treat any secondary cases, and to identify contacts with LTBI in order to offer preventive treatment. Source-case investigation is recommended for children under 5 years old with a diagnosis of active TB disease. TST is not recommended as a primary contact assessment tool for residents over 65 years. Interpretation of TST results in the elderly is often complicated by both immune suppression and the potential for boosting related to remote TB exposure or BCG. As well, for many elderly contacts the risks of LTBI treatment outweigh the potential benefits. However, contacts among staff and visitors less than 65 years old should receive a TST. In the absence of secondary cases, their results are likely to be a more reliable indicator of transmission in the facility.
Notify the site Infection Control designate and the WRHA LTC contact responsible for Infection Prevention and Control in the event that a resident is identified as a suspected active TB case or a contact of an active TB case to facilitate collaboration with the WRHA Tuberculosis Infection Control Professional and Public Health for the required follow up.

**TB Disease Prevention**

While the incidence of TB in Canada is generally low, exposure to people with unsuspected active respiratory TB disease followed by transmission of *M. tuberculosis* does occur in health care settings. Although the overall number of people admitted to Canadian health care facilities with active TB disease is low, both health care and community settings (e.g. homeless shelters and drop-in centers) serving at-risk populations continue to pose a hazard for the transmission of *M. tuberculosis*. Populations at risk of active TB disease include: people with a history of active TB disease; staff and residents of homeless shelters; urban poor; staff and inmates of correctional facilities, including previously incarcerated people; injection drug users; people born in Canada prior to 1966; Indigenous Canadians; people infected with human immunodeficiency virus (HIV); those born or previously residing in countries with a high TB incidence (in Asia, Eastern Europe, Africa and Latin America); and health care workers (HCWs) serving these at-risk groups.

Literature reviews show that the incidence of LTBI among HCWs increases with certain occupational risk factors, including: number of years working in health care settings where patients with active respiratory TB are cared for, providing direct care to those with respiratory TB disease, working in emergency departments or medical wards, providing services for patients infected with HIV, and participating in aerosol-generating medical procedures (e.g. sputum induction and bronchoscopy) on individuals with TB. The risk of health care associated transmission of MTB to HCWs, residents, and visitors varies with occupational group, effectiveness of TB prevention and control measures, and the resident population. Transmission risk is classified according to facility size and the number of active TB cases occurring in the facility annually.

LTC facilities are considered low risk when less than three active TB cases occur annually and are considered higher risk when three or more cases of active disease occur annually.

**Latent TB Infection (LTBI)**

A proportion of people who are infected with MTB will have a latency period before or if they progress to active disease. These individuals are considered to have LTBI, are asymptomatic, cannot spread TB to other people (i.e., are not infectious therefore do not require any Additional Precautions), usually have a normal chest x-ray, and may have a positive TST. Approximately 10% of non-immunocompromised individuals with LTBI will progress to active TB disease if untreated. As previously mentioned, MTB infection is contained initially by host defenses in most people where infection remains latent. However, latent infection can develop into active disease at any time.
Identification and treatment of LTBI can substantially reduce the risk of development of active disease and has the potential to protect the health of the individual as well as the public by reducing the number of possible sources of future transmission.

**Diagnosis**

There are two tests for identification of LTBI: the TST and the IGRA. Both tests evaluate cell-mediated immunity, and neither test can distinguish between LTBI and active TB disease. The TST consists of the intradermal injection of a small amount of purified protein derivative (PPD) from *M. tuberculosis* bacteria. In a person who has cell-mediated immunity to these tuberculin antigens, a reaction will occur within 48 to 72 hours. The reaction will cause localized swelling and will be manifest as induration of the skin at the injection site.

Due to the decreasing utility of TST to diagnose LTBI after age 65 and the increasing risk of adverse effects from LTBI treatment in this age group, screening with only a posterior-anterior and lateral chest x-ray for active TB is preferred upon admission for residents born in Canada prior to 1955, Indigenous persons, and people born in or previously residing in countries with high TB incidence. Baseline TST upon PCH/LTCF admission is not routinely required for residents according to the Manitoba Health Public Health Branch Tuberculosis Protocol and should be based on a facility risk assessment and local epidemiology.

IGRAs (Interferon- gamma Release Assays) are blood tests of cell-mediated immune response specific to *M. tuberculosis*. IGRAs are not generally used in the LTC sector.

**Tuberculin Skin Testing (TST)**

TST is recommended for those 65 years of age and under who also belong to an identified at-risk group and for those who are over 65 years of age at high-risk (see below).

The goal of testing for LTBI is to identify individuals who are at increased risk for the development of active TB and therefore would benefit from treatment of latent TB infection (formerly termed preventive therapy or prophylaxis). Only those who would benefit from treatment should receive a TST, so a decision to test presupposes a decision to treat if the test is positive. Only consider LTBI screening and treatment if treatment completion and adequate follow-up for hepatotoxicity can be achieved. In general, testing for LTBI is indicated when the risk of development of disease, if the individual is infected, is increased. In the LTC sector the following groups of people residing in the facility should be screened for LTBI with a two-step TST as they are at increased risk of progression to active TB:

- Any resident, regardless of age if they are a close contact of an active case of pulmonary TB
- Residents of any age with high risk for the development of active TB when their TST is positive which includes:
  - AIDS
  - HIV – discuss with their HIV physician
Transplantation on immunosuppressant therapy Examples include: cyclosporine (Neoral®), tacrolimus (Prograf®), mycophenolate mofetil (CellCept®), sirolimus (Rapamune®), azathioprine (Imuran®) - discuss with their transplant physician

- Chronic renal failure requiring hemodialysis – discuss with nephrologist
- Silicosis
- Carcinoma of the head and neck – discuss with their oncologist
- Recent TB Infection (within the last 2 years)
- Abnormal CXR showing fibronodular disease

- Residents up to 65 years of age with moderate risk of development of active TB when their TST is positive which includes residents:
  - Taking TNF alpha inhibitors
  - With diabetes mellitus (all types)
  - On treatment with glucocorticoids (greater than or equal to 15 mg/day prednisone)
  - Who were of a young age when infected (0-4 years)

- Residents up to age 50 with slightly increased risk of development of active TB when their TST is positive which includes residents:
  - With heavy alcohol consumption (greater than or equal to 3 drinks/day)
  - Who are underweight (less than 90% ideal body weight)
  - Cigarette smokers (1 pack/day)
  - With abnormal CXR showing granulomas

Purified protein derivative (PPD) tuberculin (Tubersol®) for TST testing for LTBI will be covered by the WRHA LTC Program when done for residents who meet the above criteria. For access to the tuberculin solution, complete the WRHA LTC Tuberculin (Tubersol®) Request Form and fax to the LTC Program as specified on the form. The PCH pharmacy provider shall only dispense the tuberculin solution upon confirmed approval by the WRHA LTC Program. If tuberculin is provided by the LTC Program, the Tuberculin Skin Test Results Form must be completed and submitted to the LTC Program.

The following people should not receive a TST:

- Those over 65 years old with low to moderate risk of past exposure to TB.
- Those with positive, severe blistering TST reactions in the past or with extensive burns or eczema present over TST testing sites, because of the greater likelihood of adverse reactions or severe reactions.
- Those with documented active TB or a well-documented history of adequate treatment for TB infection or disease in the past. In such patients, the TST is of no clinical utility.
- Those with current major viral infections (e.g. measles, mumps, varicella).
- Those who have received measles or other live virus immunization within the past 4 weeks, as this has been shown to increase the likelihood of false-negative TST results. Note that only measles vaccination has been shown to cause false-negative TST results, but it would seem prudent to follow the same 4-week guideline for other live virus immunizations e.g. herpes
zoster, mumps, rubella, varicella (chickenpox) and yellow fever. However, if the opportunity to perform the TST might be missed, the TST should not be delayed for live virus vaccines since these are theoretical considerations. (NOTE: a TST may be administered before or even on the same day as the immunizations but at a different site.)

The following people can receive a TST:

- Those with a history of receiving Bacille Calmette-Guérin (BCG) vaccination(s);
- Those with a common cold;
- Those who are pregnant or are breastfeeding;
- Those immunized with any vaccine on the same day;
- Those immunized within the previous 4 weeks with vaccines other than the ones listed earlier;
- Those who give a history of a positive TST reaction (other than blistering) that is not documented;
- Those taking low doses of systemic corticosteroids, less than 15 mg prednisone (or equivalent) daily. It generally takes a corticosteroid dose equivalent greater than or equal to 15 mg prednisone daily for 2-4 weeks to suppress tuberculin reactivity.

LTBI Screening for Health Care Workers
The importance of conducting proper baseline TST for all potentially exposed HCWs in all health care settings cannot be overemphasized. At the time of employment, many HCWs may already be TST positive because of prior exposure, particularly HCWs born or previously residing in countries with high TB incidence who may have been exposed and infected before moving to Canada. In addition, older Canadian-born HCWs in some provinces/territories may have received BCG vaccination, which can interfere with TST results. Prior exposure to M. tuberculosis, nontuberculous mycobacterial infection, or BCG vaccination can result in a boosting phenomenon that is misdiagnosed as a TST conversion. The occurrence of boosting phenomena has been documented in 3-10% of Canadian HCWs. Therefore, a baseline two-step TST is recommended. The Canadian Tuberculosis Standards, 7th Edition recommends baseline two-step TST for all HCWs upon hire unless there is documented evidence of any prior two-step TST when subsequent TSTs will be conducted after outbreak exposure to an infectious TB case. The two-step protocol needs to be performed once only if properly performed and documented. It never needs to be repeated as subsequent TST can be one step regardless of how long it has been since the last TST. Repeated TST testing (e.g., annually) for TB infection is not generally required in LTC settings in the Winnipeg Health Region where the vast majority of sites are considered low risk (e.g., less than 3 active TB cases per year) and high risk transmission activities do not occur (e.g., aerosol
generating procedures such as collecting induced sputum). Staff with a positive TST at baseline screening do not need to be re-tested but should be assessed by a physician knowledgeable in the treatment of LTBI. Such staff should also be instructed to promptly report any symptoms suggesting TB disease, such as cough of more than 2 weeks' duration with or without fever, night sweats or weight loss. PPD tuberculín (Tubersol®) for TST screening for HCWs on hire can be obtained from the pharmacy provider, but the cost of the tuberculín solution is the financial responsibility of the LTC site. The pharmacy provider will invoice the site directly. Most HCWs however will have had a two-step TST done as part of their education requirements. TST screening, when done as a part of a contact investigation, is covered by Manitoba Health. The same recommendations for those who can and cannot receive the TST listed above apply to HCWs.

**Mantoux Technique**

The only internationally recommended method of TST is the Mantoux technique, which consists of intradermal injection of tuberculín material into the inner surface of the forearm. See *Appendix A* for details on performing the Mantoux technique.

Acute allergic reactions, including anaphylaxis, angioedema, urticaria and/or dyspnea, have been very rarely reported following skin testing with PPD tuberculín (Tubersol®), refer to "Risk of Serious Allergic Reactions Following Tubersol® [Tuberculin Purified Protein Derivative (Mantoux)] Administration". These reactions may occur in people without a history of a TST. Health care providers should be familiar with the current *WRHA LTC Operational Guideline for Anaphylactic Shock* in preparation for a possible anaphylactic or other acute hypersensitivity reaction. Recommendations of the National Advisory Committee on Immunization on monitoring the patient for immediate reactions over a period of at least 15 minutes after inoculation and for the initial management of anaphylaxis in non-hospital settings (refer to *Canadian Immunization Guide*).

**TST Interpretation**

A TST is considered positive when the measurement of induration is a specific size for a specific situation (see Appendix B for instructions on how to read the TST).

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Situation result is considered positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-4 mm</td>
<td>In general this is considered negative, and no treatment is indicated unless the resident is a child under 5 years of age. In children under 5 years of age and at high risk of TB infection.</td>
</tr>
</tbody>
</table>
| Greater than or equal to 5 mm | HIV infection  
Contact with infectious TB case within the past 2 years  
Presence of fibronodular disease on CXR (healed TB which was not previously treated)  
Organ transplant recipient on immunosuppressant therapy  
TNF alpha inhibitors  
Other immunosuppressant medications, e.g., corticosteroids (equivalent of greater |
than or equal to 15 mg/day of prednisone for 1 month or more; risk of TB disease increases with higher dose and longer duration)

Tuberculosis Prevention & Control in LTC

<table>
<thead>
<tr>
<th>End-stage renal disease</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Greater than or equal to 10 mm</th>
<th>All others, including the following specific situations:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• TST conversion (within 2 years)</td>
</tr>
<tr>
<td></td>
<td>• Diabetes, malnutrition (less than 90% ideal body weight, cigarette smoking, daily alcohol consumption (greater than 3 drinks/day)</td>
</tr>
<tr>
<td></td>
<td>• Silicosis</td>
</tr>
<tr>
<td></td>
<td>• Hematologic malignancies (e.g. leukemia, lymphoma) and certain carcinomas (e.g., head and neck)</td>
</tr>
</tbody>
</table>

When interpreting a positive TST, it is important to consider much more than simply the size of the reaction. The TST should be considered according to three dimensions: size of induration, positive predictive value, and risk of disease if the person is truly infected. A web-based interactive algorithm, [The Online TST/IGRA Interpreter](Version 3.0), which incorporates all three dimensions, is available to assist in TST interpretation.

**FIRST DIMENSION - Size of induration**

The first dimension is the easiest to understand (but the least important). A criterion of 5 mm for a diagnosis of LTBI has a sensitivity of greater than 98%, but the specificity is lower. This criterion is used when maximum sensitivity is desirable because the risk of development of active disease is high. A criterion of 10 mm has a sensitivity of 90% and specificity of greater than 95%, and is recommended for most clinical situations. A criterion of 15 mm or more has sensitivity of only 60-70% but has high specificity (greater than 95%) in most parts of the world. However, this criterion is not appropriate for use in Canada, because specificity is not much higher than with 10+ mm, yet the sensitivity is reduced considerably.

**SECOND DIMENSION - Positive predictive value**

The positive predictive value of the TST is the probability that a positive test result represents the true presence of TB infection. This differs from the TST sensitivity, which reflects the probability of a positive TST result in the presence of known TB infection. Positive predictive value is primarily influenced by the pretest probability or prevalence of TB infection, as well as the specificity of the TST. Thus, the positive predictive value is low and the utility of the TST is limited in populations at low risk of TB infection, those with previous exposure to nontuberculous mycobacteria (NTM) or those with a previous BCG vaccination, each of which can reduce the specificity of the TST.

In parts of the world with tropical, subtropical or warm, temperate climates Nontuberculous Mycobacterium (NTM) are frequently found in soil and water, and most adults will have evidence of exposure and sensitization to some NTM antigens. Because the antigens of NTM are similar to
those of *M. tuberculosis*, there can be cross-reactivity with the TST causing small tuberculin reactions. In most of Canada, sensitivity to NTM antigens is uncommon and is not an important cause of TST reactions of 10 mm or greater.

Several population groups in Canada are likely to have received BCG vaccination. These include immigrants from many European countries and most developing countries. In Canada, many Indigenous Canadians have been vaccinated, as have people born in Quebec and Newfoundland and Labrador between the 1940s and the 1970s. BCG vaccination can be ignored as a cause of a positive TST under the following circumstances:

- BCG vaccination was given in infancy, and the person tested is now aged 10 years or older;
- There is a high probability of TB infection: close contacts of an infectious TB case, Indigenous Canadians from a high-risk community or immigrants/visitors from a country with high TB incidence;
- There is high risk of progression from TB infection to disease.

BCG should be considered the likely cause of a positive TST under the following circumstances:
- BCG vaccine was given after 12 months of age AND
- There has been no known exposure to active TB disease or other risk factors AND
  The person is either Canadian-born non-Indigenous OR an immigrant/visitor from a country with low TB incidence.

A PowerPoint presentation named "Recognition of BCG (versus smallpox) scars" offers some tips on identifying BCG scars may be viewed on the Public Health Agency of Canada website.

**THIRD DIMENSION - Risk of development of active TB disease**

After primary TB infection, the lifetime cumulative risk for the development of active TB is generally estimated to be 10%. Half of these cases will occur in the first 2 years after infection. Certain factors increase the risk of TB reactivation because of diminished local or systemic immunity.

**LTBI Treatment**

There is a well-recognized relationship between older age and greater risk of adverse events, particularly hepatotoxicity, during treatment with INH. In a recent study, patients over the age of 50 had increased rates of hospitalization attributable to liver toxicity from INH. In patients 65 and older, 2.6% were hospitalized for INH-associated hepatotoxicity. The greatest risk of hepatotoxicity was in the elderly with comorbidities; those without comorbidities under the age 65 had low rates of hepatotoxicity that were not age dependent. Rifampin monotherapy can be used as an alternative treatment for LTBI in older persons, if there are no contraindications.

**Patients who are under 65 years old and have no comorbidities should be offered LTBI treatment if they are at moderate or higher risk.** However, the risks and benefits should be considered very
carefully in people over the age of 65, although therapy may be reasonable in those at high risk of reactivation and without comorbidities. At any age, the risk of toxicity should be weighed against the benefit of therapy. In older people with greater risk of toxicity, therapy is indicated only if the risk of disease is high, meaning that they must have recent infection or medical risk factors for reactivation. As an example, a 25-year-old healthy individual with no risk factors for reactivation (detected through pre-employment screening) may be considered for LTBI treatment, but the risks might exceed the benefits if, instead, they were 45 years old. However, the benefits of INH therapy will exceed the risks of toxicity at almost any age in an HIV-infected individual. The online TST/IGRA algorithm will provide the annual risk of development of active tuberculosis disease, the cumulative risk of active tuberculosis disease up to the age of 80, the probability of clinically significant drug-induced hepatitis and the associated probability of hospitalization related to drug-induced hepatitis. In general, the risk of development of active disease should outweigh the probability of drug induced hepatitis and/or subsequent hospitalization arising from the drug-induced hepatitis before treatment is considered a viable option.

The attending physician or prescriber should consult with WRHA Specialist TB Clinicians for adult and pediatric cases of LTBI when the risk of progression to active disease/reactivation outweighs the risk of hepatotoxicity. Contact Adult Chest Medicine Service, the Health Sciences Centre: page 204-787-2071, 24 hours a day, seven days a week (if non-urgent, fax 204-787-2420 or page 204-787-2071, Monday to Friday).

**Nontuberculous Mycobacteria (NTM)**

Pulmonary nontuberculous mycobacterial disease is considered in the context of tuberculosis because it can initially be mistaken for TB. Lung disease associated with NTM is often characterized by cough, sputum, hemoptysis, a wasting illness, cavities on lung imaging, and AFB on sputum smear microscopy. Treatment for NTM disease is determined on a case by case basis and is generally not contagious. **Pulmonary NTM does not require any Airborne Precautions.** Certain NTM such as *M. gordonae* are rarely associated with clinical illness and it is generally accepted that when it is found in a sample, it does not require treatment. In juxtaposition, *M. kansasii* usually is associated with clinical illness. The severity of otherwise unexplained symptoms and CXR abnormalities should guide clinical decisions as to the relevance of the isolated NTM. Some individuals with NTM show no symptoms or CXR abnormalities and are colonized with NTM which does not warrant treatment. Others will demonstrate a spectrum of signs and symptoms and it can be difficult to judge whether the NTM is contributing to the findings or if other contributing factors such as chronic obstructive pulmonary disease (COPD) are the source. In the context of a NTM isolate form a normally sterile site (e.g. blood, pleural fluid, organ biopsy), NTM disease should be strongly considered. The NTM that are most closely linked to human disease inhabit moist environments, both natural and engineered. NTM have been recovered from all types of natural waters and soils from many parts of the world. There has been a relatively high rate of
NTM recovery from household water and plumbing fixture biofilms, but since NTM are common and NTM disease is rare, it is unclear whether environmental exposure in the home differs between people with and without NTM disease. A defect in pulmonary defenses is the most common risk factor for pulmonary NTM disease. COPD, bronchiectasis, and cystic fibrosis are risk factors for pulmonary NTM disease.

**Diagnosis**
The diagnosis of NTM includes clinical presentation, chest radiography and microbiological confirmation.

Clinical diagnosis includes pulmonary (e.g. cough, sputum production, hemoptysis, chest pain, dyspnea) and/or systemic (e.g. fatigue, weight loss, fever) symptoms where other potential causes of symptoms have been excluded. Progressive symptoms increase the likelihood of NTM disease, so that antimicrobial drug therapy may be necessary.

NTM on CXR can present as nodular or cavitary opacities. NTM on chest computed tomography (CT) can demonstrate as bronchiectasis with multiple small nodules or lung cavitation, or, in some cases, airspace disease (consolidation or ground glass opacification).

Positive culture results should be achieved from:

- At least two separate sputum samples OR
- Positive culture result from at least one bronchial wash or lavage OR
- Transbronchial or other lung biopsy with mycobacterial histopathologic features (granulomatous inflammation or AFB) AND
  - Positive culture for NTM or biopsy showing mycobacterial histopathologic features (granulomatous inflammation or AFB) AND
  - One or more sputum or bronchial washings that are culture positive for NTM.

**Treatment**
A key reason to make the clinical determination of whether there is NTM colonization or NTM disease is that the former is not likely to benefit from treatment, while the latter may benefit from targeted therapy. Furthermore, fulfilling the diagnostic criteria for NTM-associated lung disease does not necessarily imply the need for treatment. Initiating therapy is a decision that should be made carefully, considering individual patient characteristics, risk factors for treatment toxicities and the frustratingly low cure rates that are compounded by substantial recurrence rates after treatment completion. There is less urgency in deciding whether to treat NTM, as the clinical evolution of NTM is typically slower than that of TB, and the treatment is more complex (longer duration, greater toxicity). Where there is
doubt about whether to treat or defer, one should obtain more specimens and consider further investigations before formulating a treatment plan and defining the therapeutic goal(s). Chapter 11 of the Canadian Tuberculosis Standards 7th Edition provides further direction on treatment of NTM disease.

Evaluation

The Tuberculosis Prevention and Control in LTC Resource Guide will be re-evaluated as new evidence informed practice becomes available. Data collected from Tubersol requests, site Infection Control Professionals, and site outbreak debriefing reports will be reviewed and analyzed with each active TB case and lessons learned from these reports incorporated into the following update.

References


Appendix A: Mantoux Technique

Handling the tuberculin solution

- Tubersol® 5 tuberculin units (5-TU) of PPD-S (purified protein derivative - standard) is recommended in Canada.
- Store at 2° to 8° C, but do not freeze. Discard the solution if frozen.
- Remove the tuberculin solution from the vial under aseptic conditions. A little more than 0.1 mL of PPD tuberculin solution should be drawn into a tuberculin syringe. Hold the syringe upright and lightly tap out the air, then expel one drop. Check that a full 0.1 mL remains in the syringe.
- Do not transfer the solution from one container to another (the potency of the PPD tuberculin solution may be diminished).
- Draw up the solution just before injecting it. Do not preload syringes for later use as the potency of the PPD may be diminished.
- The solution can be adversely affected by exposure to light. PPD tuberculin solution should be stored in the dark except when doses are actually being withdrawn from the vial.
- Discard the solution 28 days after the vial is punctured or for an undetermined amount of time (the potency of the solution may be diminished). Label each bottle with the discard date when it is opened.

Preparing the person to be tested

- Seat the person comfortably, and explain the procedure.
- Use the inner aspect of the forearm, preferably the nondominant arm (where administration and reading of the reaction is easiest), about 10 cm (4 inches) below the elbow; avoid areas with abrasions, swelling, visible veins or lesions. If there is a localized rash, a burn or localized eczema, avoid this area.
- If neither forearm is suitable, use the outside of the forearm or the upper arm. In this case mark the location clearly in the health record.
- Cleanse the area to be injected with an alcohol swab and let it air dry.
- Do not use local anesthetic cream (e.g. EMLA®), as application has been reported to cause localized edema, which could easily be confused with a positive TST result.

Injecting the PPD tuberculin solution

- Use a 0.6 to 1.3 cm (¼ to ½ inch), 26- or 27-gauge needle with a disposable plastic tuberculin syringe.
• Position the bevel of the needle so that it opens facing up.

• While holding the skin of the inner aspect of the forearm taut, insert the needle at a 5-15° angle to the skin without aspirating. The tip of the needle will be visible just below the surface of the skin. The needle is inserted until the entire bevel is covered (refer to Figure 1).

• Administer the PPD tuberculosis solution by the slow intradermal injection of 0.1 mL of 5-TU.

• A discrete, pale elevation of the skin (a wheal) 6-10 mm in diameter should appear. The wheal will typically disappear in 10-15 minutes. The size of the wheal is not completely reliable, but if a lot of liquid runs out at the time of injection and there is no wheal, then repeat the injection on the opposite forearm, or on the same forearm as before, but at least 5 cm from the previous injection site.

• A drop of blood may be seen - this is normal. The person tested should be offered gauze to remove the blood but should be advised not to massage the site in order to avoid squeezing out the PPD and disrupting the test.

• Do not cover the site with a bandage.

• Tell the person that he or she should not scratch the site but may perform all normal activities, including showering or bathing.

• Discard the uncapped disposable needles and syringes in the sharps waste container immediately after use.

• If the TST is accidentally given as a subcutaneous or an intramuscular injection, this should not pose a serious problem. It is possible that tuberculin-sensitive people will have localized inflammation, which should be self-limiting. It would not be possible to take a measurement of or clinically interpret any such reaction, so the TST should be administered again but using proper intradermal technique on the volar surface of the forearm. This should be done immediately (as soon as it is realized that the injection was too deep).

**Figure 1: Technique of administration of TST**

Document the following in the Integrated Progress Notes:
- date of injection;
- dose of PPD (5 TU, 0.1 mL);
- PPD manufacturer;
- PPD lot number;
- expiration date of the PPD reagent;
- site of injection;
- person administering the TST.
Appendix B: Measuring Induration

- The TST should be read by a trained health professional. Individuals without experience in reading a TST may not feel slight induration, and the TST would be mistakenly recorded as 0 mm.

- Reading should be performed 48 to 72 hours after administration, as maximum induration can take up to 48 hours to develop, but after 72 hours it is difficult to interpret a reaction. Reactions may persist for up to 1 week, but for as many as 21% of individuals with a positive reaction at 48 to 72 hours the reaction will be negative after 1 week. If the TST cannot be read within 72 hours because of unforeseen circumstances, it should be repeated at an injection site far enough from that of the previous test that the reactions do not overlap. No minimum wait is required before the repeat test.

- The forearm should be supported on a firm surface and slightly flexed at the elbow. Induration is not always visible. Palpate with fingertips to check whether induration is present. If there is induration, mark the border of induration by moving the tip of a pen at a 45° angle laterally toward the site of the injection (Figure 2). The tip will stop at the edge of the induration, if present. Repeat the process on the opposite side of the induration. This pen method has the advantages of being as reliable as the traditional palpation method (which relies entirely on fingertips) among experienced readers and of being easier for new readers to learn and use.

- Using a caliper, measure the distance between the pen marks, which reflects the diameter of the induration at its widest transverse diameter (at a right angle to the long axis of the forearm). A caliper is recommended because readings will be more precise and, most important, if the reader has to set the caliper and then read the diameter the rounding error is reduced. If a caliper cannot be found a flexible ruler could be used.

- **Disregard and do not record erythema** (redness). Approximately 2-3% of people tested will have localized redness or rash (without induration) that occurs within the first 12 hours. These are minor allergic reactions, are not serious and do not indicate TB infection. They are not a contraindication to future TSTs.

- Blistering, which can occur in 3-4% of subjects with positive tests, should be recorded.

- Record the result in millimetres (mm). Record no induration as "0 mm." Recordings of positive, negative, doubtful, significant and non-significant are not acceptable.

- Do not round off the diameter of the induration to the nearest mm as this can interfere with determining whether TST conversion has occurred in the event of a future TST. If the
measurement falls between demarcations on the ruler, the smaller of the two numbers should be recorded.

**Figure 2: Ball-point method for reading transverse diameter of TST induration**

Record the following in the Integrated Progress Notes:

- dates the induration was read;
- measurement of the induration, if any, in millimetres (mm);
- any adverse reactions, e.g. blistering;
- name of the individual reading the test.

Complete the Tuberculin Skin Test Result form and submit to the LTC Program