Prince Edward Island
Health and Wellness
CANADA

Prince Edward Island Tuberculosis Disease Guidelines

October 2025

Department of Health and Wellness
Chief Public Health Office

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Introduction

In 2022 the 8th version of the Canadian Tuberculosis Standards was published. This PEI Tuberculosis Disease (TBD) Guideline document is based on these updated standards.

Over the past 10 years we have seen an increase in the population of PEI. There are people coming to live on PEI from various countries across the globe. Some of these countries have a very high rate of TB disease in the general population and unknowingly people may have become infected. Prior to the 1960s, PEI had a high rate of TBD. As people born prior to 1960 increase in age, they are at higher risk of LTBI conversion that may result in an increase in active TBD incidence. Those who are infected with TB have a 5-10% risk of having active TBD in their lifetime. For more detailed information about LTBI please refer to the PEI latent TB infection guidelines.

This guideline outlines the processes and treatments for active TBD cases and their contacts. When a contact of a case is determined to be infected with LTBI during case follow up they will be treated per the process in this guideline. When a person is tested for LTBI for other reasons, the process outlined in the PEI LTBI guideline mentioned above will be followed.

In some cases, Primary Health Care providers may be asked to help with treatment of TB cases or contacts. In most situations specialists who are familiar with TB and LTBI treatment, such as infectious disease, respiratory or public health physicians will treat cases and their contacts.

Case Definition

Laboratory confirmed case

A person for whom laboratory testing has detected Mycobacterium TB complex (excluding M. *bovis* BCG strain) on culture; or

A person for whom laboratory testing has detected Mycobacterium TB complex (excluding M. *bovis* BCG strain) by nucleic acid amplification testing (NAAT) and with clinical findings consistent with TB disease.

Clinically diagnosed case

A person for whom microbiological confirmation of Active tuberculosis (TB) disease is absent and who meets one of more of the following[i]:

- Signs or symptoms clinically compatible with Active TB disease (respiratory or non-respiratory)
- Diagnostic imaging findings compatible with Active TB disease (respiratory or non-respiratory imaging)
- Pathologic evidence of Active TB disease (e.g. compatible histopathology, positive AFB staining)
- Post-mortem evidence of Active TB disease
- Favorable response to a therapeutic trial of antiTB drugs

New and re-treatment cases of TB

New case

No documented evidence or adequate history of previously Active TB disease

[i] To account for the variation across provinces/territories (P/Ts) in the definition of a clinically diagnosed case, national surveillance includes all clinically diagnosed cases that are accepted at the P/T public health authority level.

Re-treatment of case[ii]

Documented evidence or adequate history of previously Active TB disease that was declared cured or treatment completed by current standards

and

At least 6 months has passed since the last day of previous treatment[iii]

and

Diagnosed with a subsequent episode of TB that meets the Active TB disease case definition

and

Documented evidence or adequate history of previously Active TB disease that cannot be declared cured or treatment completed by current standards

and

Inactive[iv] for 6 months or longer after the last day of previous treatment[iii]

and

Diagnosed with a subsequent episode of TB that meets the Active TB disease case definition

Reporting Requirements

Laboratories

The Provincial Laboratory shall, in accordance with the Prince Edward Island *Public Health Act*[21], report all positive laboratory results by phone and mail, fax, or electronic transfer as soon as the result is known to the Chief Public Health Officer (CPHO) (or designate).

Ordering/Most Responsible Heath Care Provider

Any suspected Active TB disease case should be reported by the ordering/most responsible health care provider caring for the patient as soon as the diagnosis is suspected.

National Notification

All laboratory-confirmed and clinically diagnosed cases should be notified to the federal level. Whether treatment was started or not, there should be notification of all cases and TB diagnosed in Canada in the following groups:

- Canadian Citizens
- Permanent Residents
- Refugees
- Refugee Claimants

[ii] Prior to 2008 in Canada, re-treatment cases were known as relapsed cases.

[iii] If less than 6 months have passed since the last day of previous treatment and the case was not previously reported in Canada, report as a re-treatment case. If less than 6 months have passed since the last day of previous treatment and the case was previously reported in Canada, do not report as a re-treatment case. Submit an additional "Treatment Outcome of New Active ore Re-Treatment TB Case" form at the end treatment.

[iv] Inactivity for a repository TB case is defined as three negative TB smears and cultures with a three-month duration of stability in serial chest radiographs or a 6-month duration of stability in serial chest radiographs. Inactivity for a non-respiratory TB case is to be documented bacteriologically, radiologically and/or clinically as appropriate to the site of disease.

For temporary residents (visitors, students and people granted work permits) and foreign nationals who are in Canada illegally, notification is to be done only for cases for whom treatment was started in Canada. The province/territory where treatment starts is responsible for notification. This notification is done through the CPHO on PEI.

Etiology

TB properly refers only to disease caused by *Mycobacterium TB* (for which humans are the main reservoir). Similar disease occasionally results from the closely related mycobacteria, *M. bovis, M. africanum* and *M. microti.* These three bacteria, together with *M. TB* and other less common mycobacteria, are known as the *Mycobacterium TB* complex.

Clinical Presentation

TB infection can lead to TB disease (TBD). It is important to distinguish between infection and disease. This guideline deals with TB disease and latent TB Infection (LTBI) that results from being a close contact of a case of TBD. The LTBI Guideline deals specifically with LTBI testing done for other reasons.

While TB disease usually presents as pulmonary disease, *M. TB* can cause disease in almost any organ system. Clinical presentation varies depending on the site of disease. Symptoms usually begin insidiously and progress over a period of weeks or months prior to diagnosis.
Concurrent pulmonary TB disease must be ruled out in all cases of extrapulmonary TB . Extrapulmonary TB disease on its own is not considered infectious.

Systemic symptoms consistent with TB disease in any part of the body include:

- Weight loss
- Fever
- Night sweats
- Fatigue or weakness

Symptoms of pulmonary TB disease:

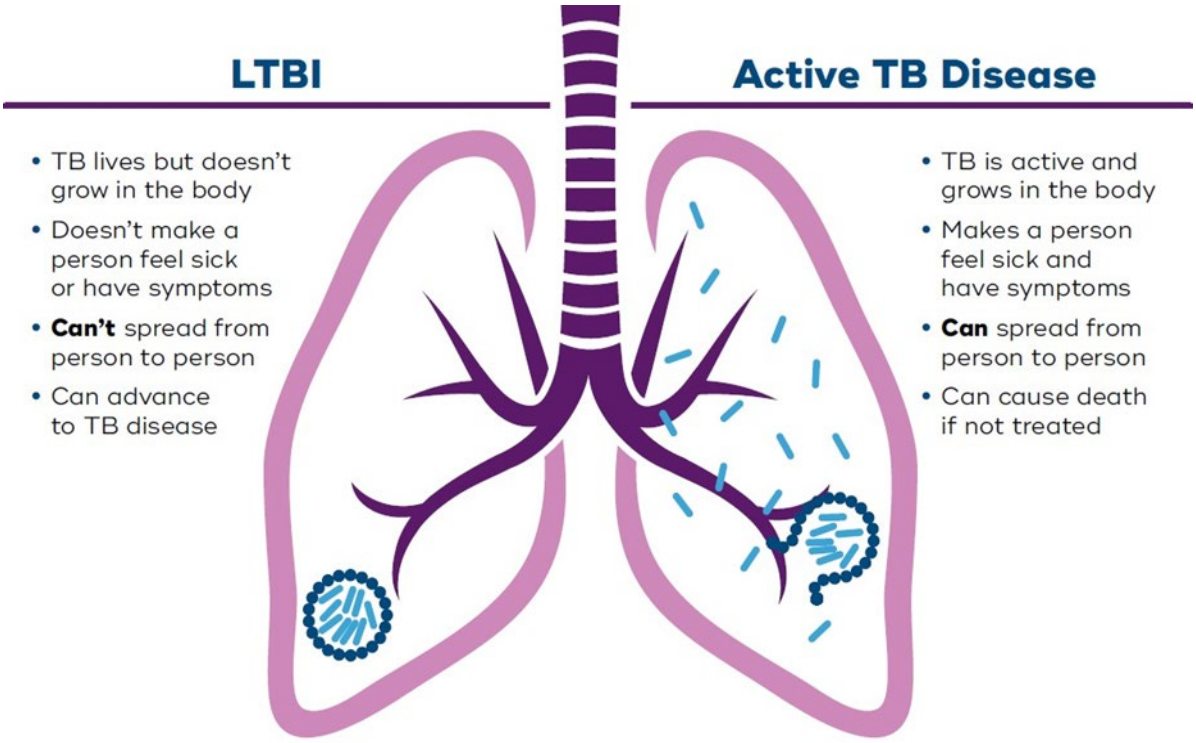
- Persistent cough (of 3 weeks or more)
- Sputum production, sometimes with hemoptysis
- Chest pain (TB pleurisy)
- Shortness of breath

Diagnosis

Radiology

- Posterior-anterior and lateral chest radiography should be an integral part of TB diagnoses but should be accompanied by confirmatory microbiological tests for TB disease because of the x-ray's low specificity. Chest radiography findings suggestive of pulmonary TB should be immediately reported to the ordering health care provider.
- In pregnant women suspected of having TB, a posterior-anterior chest radiograph should be performed, as the risk to the fetus of undiagnosed pulmonary TB disease far outweighs any risk from radiation exposure

Figure 1: LTBI vs. Active TB Disease Diagram



Source: [The time is now - Chief Public Health Officer spotlight on eliminating tuberculosis in Canada - Canada.ca] **(2018)**

In summary, chest radiograph is an imperfect tool. The sensitivity in people with symptoms is high, therefore a negative chest radiograph can be a helpful, albeit imperfect, rule-out test. However, it cannot be used as a stand-alone test to rule in TB disease.

Microscopy

All persons with suspected pulmonary TB disease, should collect at least three (either spontaneous or induced) sputum specimens and they should be tested with microscopy and culture. The three sputum specimens should be collected on the same day, at least 1 hour apart, with one being an early morning specimen. Sputum samples should be collected in sterile containers without any transport medium and transported to the laboratory within 1 day or stored at 2-8 °C until transport.

Every specimen of enough volume from patients with suspected TB shall undergo testing with both smear microscopy and culture. It is strongly recommended that in all new smear-positive patients, at least one acid-fast bacilli positive respiratory sample be tested with a Health Canada approved or validated laboratory-developed nucleic acid amplifications test.

In some circumstances with smear-negative patients suspected of having TB, a nucleic acid amplification test may be performed on one acid-fast bacilli negative sample upon request by the health care providers or public health.

Phenotypic drug susceptibility testing should be routinely performed for all first-positive-culture isolates obtained from each new TB case to determine the susceptibility of the isolate to TB medications.

Epidemiology

Reservoir

The reservoir for TB is humans. Bovine TB, which in the past was caused by ingestion of milk heavily infected my *Mycobacterium bovis* that then penetrated the mucosa of the oropharynx or the gastrointestinal tract, has been much reduced globally and almost eliminated in Canada as a result of the pasteurization of milk and tuberculin testing of cattle.

Transmission

With few exceptions, infection with TB is acquired by inhalation of small droplet nuclei (1-5 microns in diameter) that contain just a few mycobacteria that can reach the alveoli.

Through innate immune mechanisms, alveoli macrophages eradicate the bacteria in some individuals; in others, the bacteria can replicate and establish Primary TB infection.
Bacterial factors and host genetic factors that promote or limit acquisition of infection are not well understood.

The probability of transmission increases with the following:

- Bacterial burden (smear positivity) in the source patient
- Cavitary or upper long-zone disease on chest radiograph in the source patient
- Laryngeal disease in the source patient
- Amount of severity of cough in the source patients
- Duration of exposure of the contact
- Proximity of the contact to the source patient
- Crowding and poor room ventilation
- Delays in diagnosis and/or effective treatment of the source patient.

The most effective way to reduce transmission is to promptly diagnose and treat patients with active pulmonary TBD.

Incubation Period

After contact with TB nuclei, during a period lasting from 3 to 8 weeks, the host develops specific immunity (cell-mediated immunity and delayed-type hypersensitivity) to the bacilli. This is when individuals first show positive results on testing for LTBI such as the Tuberculin Skin Test (TST) or Interferon-gamma release assay (IGRA).

Local progression in the lung, or lymphohematogenous spread resulting in disseminated (military) disease and/or central nervous system disease, may occur as early as 2-to-6 months after infection in infants and severely immunocompromised hosts. Uncomplicated and asymptomatic lymph node disease (hilar or mediastinal lymphadenopathy without airway involvement) may also occur in the first 2-to-6 months of infection, although there is a debate about whether this should be called active disease.

For purposes of disease reporting, most, but not all patients with a diagnosis of TB made within 18-24 months of infection should be considered to have “primary” disease. Those newly infected people in whom TB disease does not develop in this time period have three possible outcomes: they may remain

infected indefinitely and never develop disease, they may naturally clear their infection over time, or they may progress to Active TB disease at a later date, beyond the first 18-24 months.

Period of Communicability

There is no clear epidemiologic evidence on when infectiousness begins. Pulmonary TBD is generally considered to become infectious at the onset of cough (or worsening of a baseline cough), and this should be the priority timeframe for contact investigation.

If no cough or other respiratory symptoms are reported, the onset of other symptoms attributable to TB may be used to estimate the onset of infectiousness. In practice, it is often too difficult to know with certainty when symptoms began. The US Centers for Disease Control and Prevention recommend, based on expert opinion, that patients with *smear-positive* or *symptomatic disease* should be considered to have been infectious for *three months* before onset of respiratory symptoms or the first positive finding consistent with TB, whichever is longer. *Asymptomatic, non-cavitary* TB *with a negative smear* should be considered infectious *four weeks* before the first positive finding consistent with TB. For contact investigation, the period of infectiousness effectively ends when the index patient is placed in isolation from others (this may be before or after diagnosis; at home with no contacts, or on admission to formal airborne isolation in hospital) or is no longer infectious due to TB treatment, whichever comes first.

Host Susceptibility

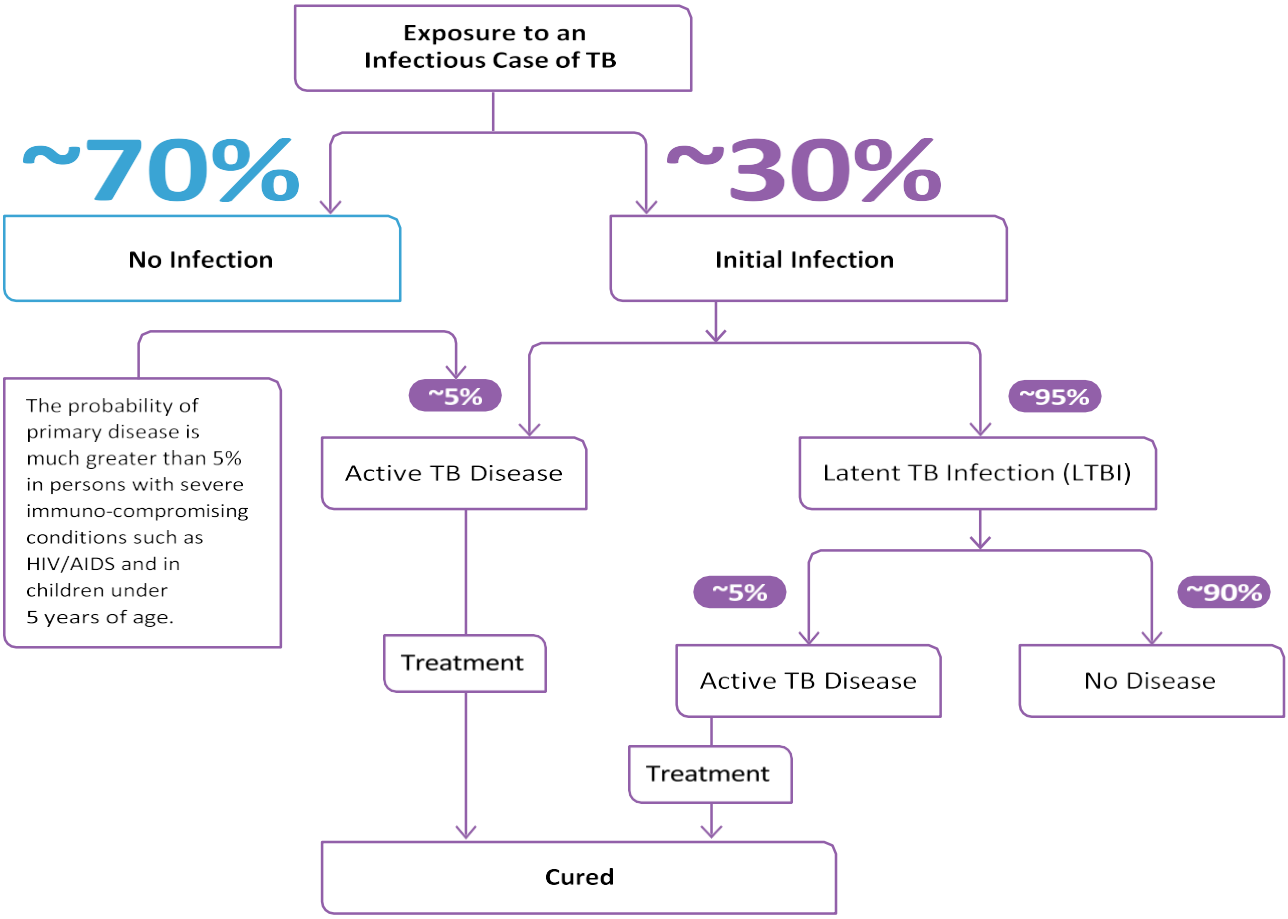
In most individuals, *Mycobacterium TB* (*M. TB*) infection is contained initially by host defenses, and infection remains silent (latent). However, TB infection has the potential to develop into TB disease at any time. Several risk factors, such as time since TB exposure, medical conditions, treatments or personal habits that affect host immunity, can affect an individual's risk for progression from TB infection to TB disease.

Occurrence

General

In 2022, The WHO estimated 10.6 million people fell ill with TB (TB worldwide, including 5.8 million men, 3.5 million women and 1.3 million children). TB occurs in every part of the world. In 2022, the largest number of new TB cases occurred in WHO's South-East Asian Region (46%), followed by the African Region (23%) and the Western Pacific (18%). Around 87% of new TB cases occurred in the 30 high TB burden countries, with more than two-thirds of the global total in Bangladesh, China, Democratic Republic of Congo, India, Indonesia, Nigeria, Pakistan and the Philippines. People living with HIV are 16 (uncertainty interval 14-18) times more likely to fall ill with TB disease than people without HIV. TB is the leading cause of death among people with HIV.

FIGURE 2:The Pathogenesis of TB in an Infected Host



Source: [The time is now - Chief Public Health Officer spotlight on eliminating tuberculosis in Canada - Canada.ca](#) **(2018)**

Canada

The rate of Active TB disease in Canada is among the lowest in the world. Canada experienced a steady decrease in the rate of TB between the 1940s and 1980s. Since then, the annual rates have remained about the same.

In 2022, the rate of Active TB disease in Canada was 5.1 per 100,000 population. The incidence of Active TB disease (per 100,000 population):

- Inuit = 136.7
- First Nations = 21.4
- People born outside of Canada = 14.4
- Metis = 2.0
- Non-Indigenous Canada-born = 0.3

Prince Edward Island

Since 2013 the rate of TB disease has been between 0/100,000 population and 2.7/100,000 population. As immigration from TB endemic countries increases, health care providers should have TB on their differential for those who demonstrate symptoms.

Management of a case

Process for initiating care for a new active TBD case in the community

As noted previously in the document, in most cases a specialist in TB care such as infectious disease, public health or respirology physicians will direct the treatment and care of active TB cases. Public Health Nursing along with the Chief Public Health Office, guide the investigation of the case for contact follow up. The following sections will outline the public health follow up and the treatment for a person who has TBD.

Public Health Investigation

Public Health Nursing can provide in-person, supportive care for people diagnosed with TBD as needed. Support will be tailored to individual needs and may include directly observed therapy. Meaningful and culturally appropriate patient engagement, education and support are critical for achieving successful TB treatment.

The following are steps to investigate a new TBD case. They may follow the order laid out or may happen in tandem. The work of case management and contact tracing is done in collaboration with the treating health care provider, Public Health Nursing and the Chief Public Health Office.

- Health care provider/lab reports TB positive results or clinically suspicious client to CPHO.
- CPHO obtains history from ordering health care provider.
- CPHO consults public health nursing (PHN) to initiate isolation (if case is in the community) and arrange initial interview. See Appendix 1 for more information about isolation and deisolation.
- PHN interviews the client to determine whereabouts during infectious period (**Appendix 2**). This information will inform contact identification. This is very important and should be done in person if possible.

The interview should focus on the following:

- Description of the household/congregate setting
- Number of household members living with the case
- Household contacts and their ages (including anyone who regularly sleeps in the home)
- Contact with children, if yes, obtain age
- Contact with people who are immunosuppressed e.g., HIV+, cancer, etc.
- Contacts who are ill with potential TBD symptoms or who have known TBD
- Close friends and relatives who are seen at least once per week - how often, for how long
- Work or school location and description of setting (type of work, size of room, ventilation)
- Transportation to work/school – bus, car-pool, etc.
- Place of worship, clubs, sports teams, recreation programs or hobbies
- Other places or groups the case has regularly been in while infectious
- Major events (e.g. weddings, funerals, parties) the case attended while infectious
- Recent travel or visitors staying at the home within the previous 2 years – if so, obtain details
- Visits to health care facilities prior to TB diagnosis- notify Employee Health Nurses who will arrange any follow-up with staff.
- Determine if directly observed therapy (DOT) is required

TB medical treatment and Care

- The ordering health care provider along with the CPHO will determine the appropriate referral for treatment and care of the patient.
- The treating physician should arrange for treatment and follow up bloodwork/sputum/vision testing.(see Table 1.)
- If isolating in the community, the initial bloodwork may need to be arranged through home care, until the client is no longer contagious and out of isolation
- A letter is sent to provincial pharmacy – signed by a CPHO physician to have the treatment medication covered by the Provincial TB program.
- If the client is not covered by PEI Pharmacare, the prescription is to be faxed to the case's local pharmacy and the pharmacy directed to invoice the CPHO for the cost.

For management of a case of TBD in hospital/health care facilities please refer to Appendix 4.

Treatment of a case

Regardless of insurance coverage or immigration documentation, people with active TB disease on PEI are provided with TB medications and appropriate treatment support free of charge.

- Treatment of drug-susceptible TB disease should always include 2 effective drugs, and at least 3 effective drugs in the intensive phase (i.e., first 2 months of therapy) see Table 2..
- Most patients with TB disease should be initiated on a regiment of isoniazid, rifampin, pyrazinamide and ethambutol until results of genotypic or phenotypic drug susceptibility are available (see Table 2.).
- While taking ethambutol monitoring of vision acuity and color vision should be completed monthly. See Appendix 5 for links to color vision testing plates.
- Therapy should be taken daily.

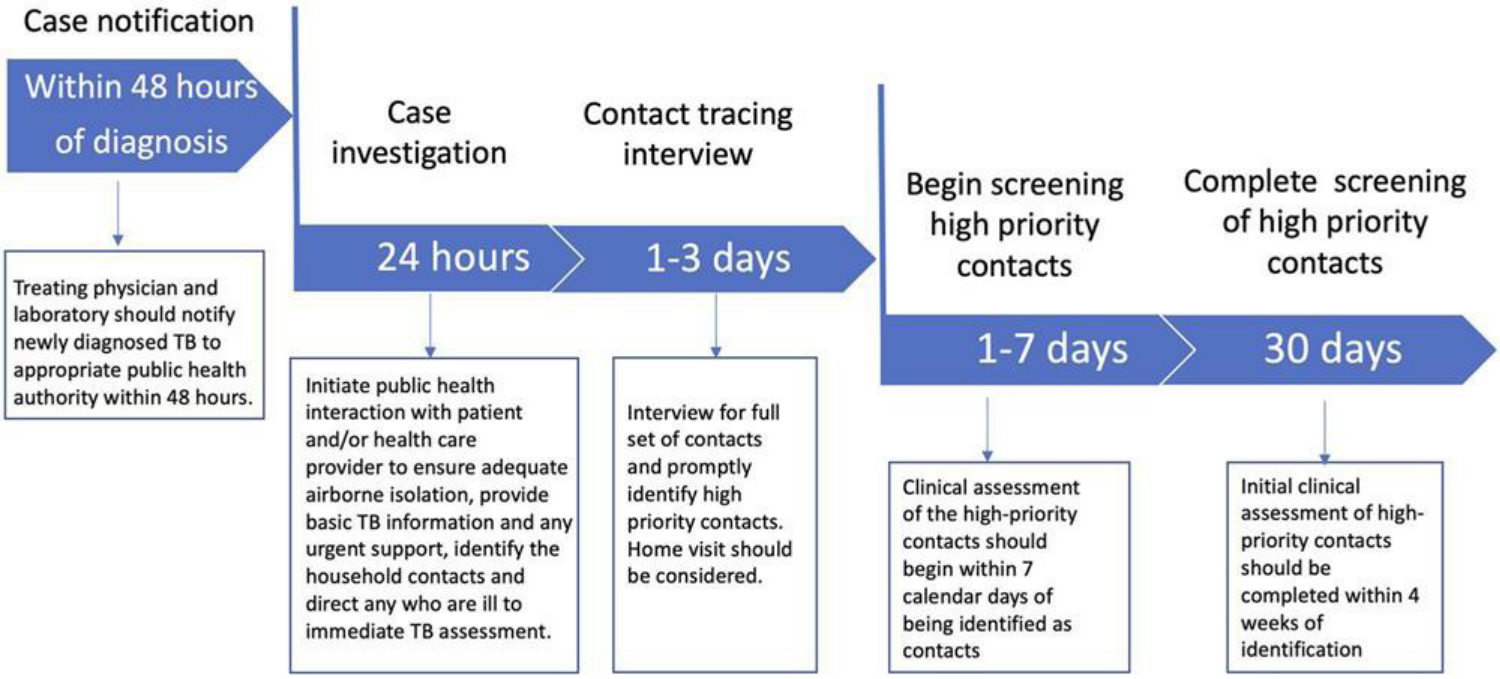
Directly Observed Therapy

The decision by a care provider to initiate treatment of Active TB disease implies a commitment to ensure that all the recommended doses are taken without interruption. The goal of Active TB disease treatment is to take 100% of the prescribed doses. This is best done by providing a comprehensive, patient-centered treatment program.

Directly observed therapy (DOT) is a method to monitor and enhance adherence to therapy. Clients with certain individual risk factors should be considered for DOT:

- Multidrug resistant disease
- Treatment failure or documented relapse
- Person who uses IV drugs or other substances
- Unhoused or precariously housed
- Suspected non-adherence or previous non-adherence
- Significant mental illness
- Child or adolescent

Figure 3: **Timeline for Case and Contact Follow Up**



People at high risk for TB recurrence should be monitored for signs/symptoms of TB recurrence during the first 12-24 months post-therapy.

Management of Contact Investigation

When a person is exposed to someone with active TBD, they can become infected with TB but not become sick right away. In order to prevent them from becoming an active case of TBD in the future, which is most likely to happen within the first 2 years of being infected, contact follow up is initiated as early as possible and testing for LTBI done. For those who are found to be positive, treatment is initiated as soon as possible.

Those who are tested for LTBI for reasons other than being a contact of an active TBD case (e.g. Health care providers, for entry into an educational program, or premedication) are addressed in the PEI LTBI guidelines

Objectives of contact investigation

Contact investigation has three main objectives. In order of priority these are:

- Identify and initiate treatment for secondary cases of Active TB disease.
- Identify and treat the infectious source patient if the index patient is less than 5 years old
- Identify contacts with LTBI to offer preventive treatment

Table 1. Monitoring during TB disease treatment

Initial	Baseline	1mo	2mo	3mo	4mo	5mo	6mo	7mo	8 mo	9mo
Clinical	Physical exam, weight, visual acuity, colour vision testing (Appendix 5)	weight, visual acuity, colour vision testing	weight, visual acuity, colour vision testing*							
Radiology	Chest x-ray		Chest x-ray							Chest x-ray
Lab	CBC with diff, ALT, bilirubin, creatinine, HIV serology, HBV and HCV serology, Hemoglobin A1C	CBC, Creatinine, ALT, bilirubin	CBC, Creatinine, ALT, bilirubin	CBC, Creatinine, ALT, bilirubin	CBC, Creatinine, ALT, bilirubin	CBC, Creatinine, ALT, bilirubin	CBC, Creatinine, ALT, bilirubin	CBC, Creatinine, ALT, bilirubin	CBC, Creatinine, ALT, bilirubin	CBC, Creatinine, ALT, bilirubin
Micro	Sputum twice monthly until smear negative		Sputum	If still smear positive repeat DST					Sputum	
Assessments	Daily if DOT May require weekly or more the first few weeks	In person	In person	Phone call or video	Phone call or video	In person	Phone call or video	Phone call or video	In person	Phone call or video

Table 2. Recommended doses for daily and Intermittent therapy for adolescents and adults

	Daily		Thrice weekly	
	By weight	Maximum[a]	By weight	Maximum[a]
Isoniazid	5mg/kg	300mg	15mg/kg	900mg
Rifampin	10mg/kg	no max[b]	10mg/kg	no max[b]
Pyrazinamide	25mg/kg	2000mg	30-40mg/kg	4000mg
Ethambutol	15mg/kg	1600mg	25-40mg/kg	2400mg

Abbreviations: TB, tuberculosis.

[a]Dosing based on body weight for people with body mass index (BMI) 18.5-30. In people with BMI >30 or <18.5 consider dosing based on ideal body weight and consider therapeutic drug monitoring if available.[1]

[b]This represents a change from previous Canadian TB Standard dosing recommendations, based on an evidence review performed by the WHO Pharmacokinetics and Pharmacodynamics Task Force.[2,27]

Prioritizing contacts

In PEI, prioritization of contacts is done in collaboration between PHN and the CPHO. When notification of a new TB diagnosis is received, the CPHO will review the case and determine the degree of infectiousness which will determine the timeline and aid in decision making regarding contact follow up. Once the contacts are identified for follow up, PHN conducts contact tracing activities involving tuberculin skin test, chest x-ray and IGRA.

Once pulmonary TB is confirmed, investigation of household and other high-priority contacts should begin promptly, especially for any children less than 5 years old and immunocompromised contacts.

Contact investigation should be prioritized according to the infectiousness of the source case and the extent of exposure and immunologic vulnerability of those exposed.

Factors in assessing infectiousness/contact risk

Risk of transmission

The transmission risk assessment focuses on how infectious the patient is, over what time-period, and the duration, proximity and characteristics of the space where exposure occurred.

Infectiousness of the index patient

With limited exceptions, only adolescents and adults with pulmonary and laryngeal TB are infectious and require contact investigation. Pleural TB should be assumed to include pulmonary involvement until ruled out by sputum results. Sputum-smear status is the most reliable indicator of infectiousness.

Likely period of infectiousness

- Pulmonary TB is generally considered to become infectious at the onset of cough (or worsening of a baseline cough), and this should be the priority timeframe for contact investigation.
- If no cough or other respiratory symptoms are reported, the onset of other symptoms attributable to TB may be used to estimate the onset of infectiousness.
- Patients with smear-positive or symptomatic disease can be considered to have been infectious for three months before onset of respiratory symptoms or the first positive finding consistent with TB, whichever is longer.
- Asymptomatic, non-cavitary TB with a negative smear can be considered infectious four weeks before the first positive finding consistent with TB.
- The period of infectiousness effectively ends when the index patient is placed in isolation from others (this may be before or after diagnosis; at home with no contacts, or on admission to formal airborne isolation in hospital) or is no longer infectious due to TB treatment, whichever comes first.

Degree of exposure to the index patient; duration, proximity

Household members are at highest risk of becoming infected, even if the case if smear-negative on sputum result, as they have very close contact over extended periods. Someone who shares a bedroom is at highest risk. In theory, there is no amount of exposure to infectious TB that is absolutely without risk; in practice, almost all transmission occurs with close, prolonged or repeated contact over days or months. It is not social closeness to the person with TB, but rather, the amount of time in a shared airspace that is the critical issue. For example, IT personnel may report working very closely with team members but spend little time together in shared air space if the work is mainly done electronically; someone who has minimal interaction with the TB patient but works in the neighboring cubicle is at much higher risk independent of other exposure factors.

Characteristics of the space where exposure occurred

The room size and ventilation where exposure occurred (e.g., large cafeterias or lecture halls vs small seminar rooms) may reduce or facilitate transmission: exposure in cramped, ill-ventilated spaces may lead to transmission in much shorter exposure times. Formal ventilation assessment is not generally

necessary. However, in hospitals, where ventilation rates can vary greatly, it may be possible to arrange for facility staff to measure air exchanged per hour in the exposure areas. Exposures in areas with lower ventilation can be prioritized, while those with very high ventilation pose much lower risk outside of unprotected aerosolizing procedures.

Smoking tobacco or other substances with others increases transmission risk, particularly in confined spaces. TB transmission is rarely thought to occur outdoors but has occasionally been documented in groups who smoke together regularly.

Prioritization of Contacts

High priority contacts are those with the most exposure, and those with the highest risk of progression to Active TB disease if infected. They may include:

- Household contacts, who regularly sleep in the same household as the infectious case on an ongoing basis (e.g., 3 or more times per week) and can include members of an extended family, roommates, boarders, couch-surfers, etc.
- Household-like contacts in congregate settings, such as homeless shelters, jails and long-term care facilities (generally, roommates or cellmates)
- Caregivers with extensive/daily exposure to the index patient
- Contact exposed (i.e., without an N95 mask) during bronchoscopy, sputum induction, autopsy or other aerosolizing medical procedures
- *Medium-priority contacts* who are at high risk of progression of LTBI to TB disease (e.g., ages less than 5 years, HIV, dialysis, transplant, silicosis).

Medium-priority contacts have regular contact with the index case and share air space at least several times weekly but do not sleep in the same household most of the time. Most social, school, workplace and close non-household contacts fall into this group. This group may include:

- Caregivers with less extensive exposure to the case
- Regular sexual partners
- Close friends
- Extended family
- Daycare and primary/secondary school classroom contacts
- Coworkers who work in close proximity, particularly in small rooms
- Homeless/underhoused individuals using the same drop-in program regularly
- Low-priority contacts who are at high risk of progression from LTBI to TBD, (e.g., aged less than 5 years, HIV, dialysis, transplant, silicosis).

Low-priority contacts are casual contacts who spend time together regularly but less frequently with the infectious case. Investigation should be expanded to this group only if there is significant evidence of transmission among closer contacts. This group may include:

- High school students who share only one course with the TB patient
- Classmates in very large college/university classes
- Less exposed colleagues at work
- Members of a club, team or other social/recreational/religious group
- Extended family members who are seen occasionally

When cases are **smear-positive** or have **cavitary disease,** the initial group of contacts to investigate should include both **high and medium-priority contacts.**

For **smear-negative** index patients**,** initial contact investigation should include **high-priority contacts only;** investigation should be expanded to medium-priority contact only if there is evidence of transmission among the closer contacts.

The specific circumstances should always be considered. For example, a choir group meeting once per week to sing close together indoors may pose significant risk, but a regular outdoor soccer game generally poses little risk.

Congregate settings and location-based screening

Screening of medium-priority contacts in schools, workplaces, hospitals, correctional facilities, shelters and other congregate settings is generally most efficiently and effectively carried out on site, especially if the number of identified contacts is large. However, it is critical to coordinate with site leadership and be very organized.

Anxiety may be minimized by limiting the delay between contacting the site and conducting testing, ensuring that key people at the site get the same information at the same time and holding general education sessions about TB and the investigation plan.

In many medium-priority exposure settings, it is more practical to do a single round of screening after 8 weeks from the last exposure. As more time elapses before the initial test, it is progressively less likely that conversions will be detectable since many infected contacts may have been already converted to a positive TST. Thus, if an additional screening cannot be organized 4 weeks before the last exposure, it is generally more efficient to do a single post-8-week screening.

In the rare situation where low-priority contacts are investigated, we suggest only a single test at least 8 weeks from the last day of exposure.

Contacts during air travel and other transport

The risk of TB transmission during commercial airplane travel is low, and the value of actively screening airplane contacts is limited. Nevertheless, the WHO has published guidelines outlining the procedures for notifying contacts exposed on international flights with a total duration of $\geq$ 8 hours within the previous three months. Notification of people with TB who report a history of air travel while infectious should be made to the Public Health Agency of Canada (PHAC) through the provincial/territorial TB program. The reporting form can be found online at this link.

Expanding contact investigation

Contact investigation is iterative; the results of each contact investigation should be reviewed by Public Health Nursing and the CPHO as they become available, to guide decisions about expansion and/or additional outreach interventions. Recent transmission is considered to have occurred if:

- A secondary case of Active TB disease is identified in any contact
- There are clear TST conversions among contacts
- The prevalence rate of TST $\geq$ 10mm among contacts is significantly higher than expected (for example, 60% among contacts when the expected prevalence rate is 40%). See Appendix 13for a table of LTBI prevalence in various Canadian population groups

- A contact who is less than 5 years of age is infected (without another probable source).

A fundamental challenge is that transmission can be very difficult to evaluate when the background rate of positive of TST results is unknown or high. This is often the case in Canada, where the majority of patients with TB – and many of their close contacts – are foreign-born, originally from high-TB incidence countries; it is also the case in Indigenous communities with high rates of TB. Thus, Canadian-born contacts with no high-risk travel, particularly children, may have the clearest results for assessing transmission as they are less likely to have prior TB exposure.

Testing for identified contacts

To identify a true conversion (i.e., new infection):

- A single TST should be performed as soon as possible after an exposure to TB.
- If the first TST is negative and performed less than 8 weeks after contact with the index patient, then a second TST should be scheduled no sooner than 8 weeks after the contact was broken.
- Contacts that are identified more than 8 weeks after last contact with an index patient only require a single TST.

If the initial TST prior to 8 weeks post contact is positive, an IGRA will be performed in those who have had BCG vaccine or those in whom TB infection would not be expected (e.g. Canadian born non-indigenous). The result of the IGRA will be more specific for these clients. If positive, a chest x-ray should be ordered, and the contact should be assessed by a health care provider and TB preventative treatment (LTBI treatment) ordered.

For those who convert from an initial negative TST to a positive TST after 8 weeks post contact, they are considered a new infection. No IGRA is required. A chest x-ray should be ordered, and the contact should be assessed by a health care provider and LTBI treatment ordered.

Treatment of contacts

In most cases, contacts of cases are treated through the CPHO/LTBI treatment clinic, however, if there are many contacts related to a case who require treatment and some of those have primary care providers (PCP), the PCP may be asked by CPHO to assist in the treatment of their client and guidance will provide as required.

Pretreatment evaluation

It is critical to exclude Active TB disease prior to initiation of LTBI treatment to avoid undertreatment of TB disease, with subsequent development of drug resistance. The initial assessment should include:

- a clinical assessment
- chest x-ray
- baseline testing for all patients undergoing LTBI treatment, including:
    - complete blood count
    - alanine aminotransferase
    - bilirubin
    - hepatitis B and C serology
    - HIV serology
- medications evaluated for potential drug-drug interactions with proposed LTBI treatment regimens

- evaluation of potential risk factors and barriers for non-completion and patient understanding

Medications

In PEI, 4 months of rifampin is the treatment for LTBI that generally is prescribed due to availability of the medication and the shorter duration of treatment. However, the choice between regimens should be tailored to the patient's specific circumstances, considering factors such as patient preference, pill burden/number of doses and potential for adverse effects. Rifapentine and INH can be given as a once weekly regimen for 3 months as directly observed preventative treatment. Rifapentine is not approved for use in Canada and only available through the Special Access Program from the Federal Government.

Prior to starting LTBI treatment (all regimens), patients should be counseled regarding the following:

- 5-10% of those who are infected will develop TB during their lifetime and that half of those people will develop TB within the first two years of infection
- taking all doses of the LTBI treatment will reduce this risk significantly, thus preventing the development of Active TB disease
- possible adverse events associated with LTBI treatment that can occur but are rare
- contact the ordering health care provider should they develop possible adverse events
- if prompt evaluation of such events by a health care provider is not possible or if symptoms are severe then the patient should stop their treatment medication

Evaluation during LTBI treatment

Contacts should be evaluated at the end of the first month of treatment for medication tolerance and for a recheck of blood work including ALT, bilirubin and CBC.

- Monthly clinical assessments should be continued for the duration of treatment.
- In patients at low risk of adverse events and likely to complete treatment, the interval between visits may be extended.
- Patients taking 4 months of rifampin (4R) or 3 months of INH/Rifapentine (3HP) do not require further laboratory monitoring during treatment unless the patient has an abnormal test result, develops symptoms suggesting an adverse event or has risk factors for hepatotoxicity (history of previous drug-induced hepatitis, current cirrhosis or chronic active hepatitis of any cause, hepatitis C, hepatitis B with abnormal transaminases).
- For patients on regimens other than 3HP or 4 R, monthly monitoring of ALT and bilirubin should also be performed among patients with risk factors for hepatoxicity.

Table 3. Summary of recommended treatment regimens for LTBI

Regimen	Duration	Dose	Frequency	Common adverse effects
First-line regimens				
Rifapentine and isoniazid (3HP)	3 months (12 doses)	Isoniazid: 15 mg/kg Maximum: 900 mg Rifapentine: 10-14.0 kg: 300 mg 14.1-25.0 kg: 450 mg 25.1-32.0 kg: 600 mg 32.1-49.9 kg: 750 mg ≥50.0 kg: 900 mg Maximum: 900 mg	Once weekly	Flu-like reactions, drug interactions
Rifampin (4 R)	4 months (120 doses)	10mg/kg Maximum: 600 mg	Daily	Rash, drug interactions
Second-line regimen				
Isoniazid (9H)	9 months (270 doses)	5mg/kg Maximum: 300 mg	Daily	Hepatoxicity, peripheral neuropathy
Alternative regimens				
Isoniazid (6H)	6 months (180 doses)	5mg/kg Maximum: 300 mg	Daily	Hepatoxicity, peripheral neuropathy
Intermittent isoniazid for 9 months	9 months (78 doses)	15mg/kg Maximum: 900 mg	Twice weekly	Hepatoxicity, peripheral neuropathy
Isoniazid and rifampin (3HR)	3 months (90 doses)	Isoniazid: 5mg/kg Maximum: 300 mg Rifampin: 10mg/kg Maximum: 600 mg	Daily	Hepatoxicity, peripheral neuropathy, drug interactions

Outbreaks

Definition

An outbreak is the occurrence of more cases than expected over a given time period, with ongoing transmissions. Outbreaks may be suspected due to clustering of cases by location, time, behavioral factors or strain genotype.

Note that cases may increase *without* ongoing transmission, for example due to changes in migration patterns. The following is a working definition of outbreaks, intended to help identify and contain rapidly evolving clusters:

- During and because of contact investigation, 2 or more of the identified contacts are diagnosed as secondary cases of active TB disease (confirmed by genotyping/WGS if available); or
- Any 2 or more cases in TB patients occurring within 1 year of each other are discovered to be epidemiologically linked (and matched by genotyping/WGS if available), but the linkage is recognized outside of a direct contact investigation.

For more information regarding TB outbreak management refer to Chapter 11 of the Canadian TB contact investigation and outbreak management.

References

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2. Province of PEI Public Health Act R.S.P.E.I [Internet] 2023. Available from: Public Health Act

3. Menzie,D. (2022). *Canadian TB Standards -8th Edition.* Canadian Journal of Respiratory, Critical Care and Sleep Medicine, Volume 6, Issue sup1 DOI: 10.1080/24745332.2022.2033055

4. Public health Agency of Canada. 2018. CPHO Spotlight on TB elimination in Canada. Available from: https://www.canada.ca/content/dam/phac-aspc/documents/corporate/publications/chief-public-health-officer-reports-state-public-health-canada/eliminating-TB/PHAC_18-086_TB_Report_E_forwebcoding.pdf

Appendix 1

De-isolation

Treatment of TB disease reduces infectivity and is thus a fundamental component of TB public health management. Just how quickly people with TB become non-infectious after initiating effective therapy, and what biomarkers best predict this, remains controversial.

1) **De-isolation recommendations**

The following recommendations for discontinuation of isolation and airborne precautions (de-isolation[a]) are intended for patients in the community and in healthcare settings. The decision to de-isolate remains subject to expert clinical and public health judgement. TB treatment providers or infection control professionals may prolong isolation beyond the recommended minimal times; this is described further in the caveat section.

Smear-negative[b], rifampin-susceptible pulmonary TB[c]:-

- **It is recommended that airborne precautions can be discontinued (and person de-isolated) once there is clinical evidence of improvement and a minimum of 2 weeks of effective therapy[d,e] has been completed (poor evidence)**

Smear-positive, rifampin-susceptible pulmonary TB:

- **It is recommended that airborne precautions can be discontinued once there is clinical evidence of improvement[f], a minimum of 2 weeks of effective therapy has been completed and there are 3 consecutive negative acid-fast bacilli sputum smears[g]. Airborne precautions may be discontinued if there is clinical evidence of improvement after completing a minimum of 4 weeks[h] of effective therapy, even if the sputum smears are persistently positive (poor evidence).**

Confirmed or suspected rifampin-resistant pulmonary TB:

- **It is conditionally recommended that airborne precautions may be discontinued once there is clinical improvement, second-line drug susceptibility results are available, and a minimum of 4 weeks of effective therapy has been completed. In addition, for those initially smear positive, 3 consecutive sputum smears must be negative (poor evidence).**

Definitions/Footnotes

a. ***De-isolation: Airborne precautions can be discontinued and/or lifting of home-isolation restrictions. People de-isolated would be allowed to return to school and work and enter indoor public spaces without restriction unless otherwise stipulated by public health professionals.***
b. ***Smear-negativity can be re-confirmed at the time of treatment start, to exclude progression to smear-positive disease during the time from initial specimen collection to culture positivity. However, repeat sampling at the end of 2 weeks of therapy is not required.***
c. ***Rifampin susceptibility for the purpose of this protocol can be determined by genotypic or phenotypic methods.***
d. ***Two weeks refers to 14 doses of daily administered treatment or 2 calendar weeks of 5 days per week of directing-observed therapy.***
e. ***Effective treatment: for the purposes of de-isolation, effective therapy for rifampin-susceptible cases (based on genotypic and/or phenotypic testing) consists of at least 3 drugs, one of which is rifampin. For rifampin resistant***

TB, effective therapy consists of at least 3 drugs to which the isolate is confirmed susceptible or highly likely to be susceptible to.

f. ***Treatment Response: clinical evidence of improvement refers to a broad range of symptoms, including but not limited to improvement in cough, resolution of fevers, or decreased night-sweats.***
g. ***Sputum smear conversion: this is confirmed when at least 2 consecutive sputum samples (collected at least 1 hour apart) are smear-negative on fluorescent microscopy.***
h. ***Four weeks refers to 28 doses of daily administered therapy or 4 calendar weeks of 5 days pers week direct-observed therapy.***

Important Additional Costs

Before allowing de-isolation, ensure that the person is tolerating the treatment regimen and that an acceptable treatment plan with supported adherence is established.

The decision to deisolate remains subject to expert clinical and public health judgement. TB treatment providers or infection control professionals may prolong isolation or apply restrictions beyond the guidelines under certain circumstances. For example, longer de-isolation might be warranted for people with pulmonary TB who reside or work in congregate settings together with immunologically vulnerable individuals (such as day care facilities, neonatal or pediatric intensive care units, hospital wards and clinics for transplant recipients or those under treatment for hematological malignancies).

Sputum samples used to guide de-isolation should be of adequate volume and sputum induction may be required. Bronchoscopy should not be employed simply to obtain respiratory tract samples that are used to guide duration of isolation. In the event follow-up sputum samples cannot be obtained, de-isolation should be performed in consultation with Infectious Disease physician and/or CPHO.

Home Isolation:

For people with TB that are medically well enough, ambulatory treatment and home isolation is preferred over hospital isolation. Home isolation is acceptable when the following conditions are met:

- The person is tolerating the treatment regimen and an acceptable treatment plan with supposed adherence is established.
- The person does not share a common airspace with non-household members (e.g., rooming house) and the household air is not recirculated to other housing units (e.g., as seen in some apartment complexes).
- All household members have been previously exposed to the person. If any household members are TST negative, they should be informed and understand the potential risks of ongoing exposure.
- Children under the age of 5 or people with immunocompromising conditions present in the home are receiving treatment for Active TB disease or latent TB infection.

When on home isolation, no visitors should be allowed in the home except for health care workers wearing appropriate personal protective equipment. The person on home isolation should not go to work, school or any other public indoor environment and should not use any form of public transportation (if necessary, a taxi can be used to attend essential healthcare appointments provided the person is wearing a mask). **While in home isolation, the person can ambulate outdoors.**

Appendix 2

TB Case assessment guidance

First Name:
Last Name:
Sex:
Date of Birth:
Country of Birth:
Country of Origin:
Address and Phone:

Personal Information

- Who lives with them? Description of the household/congregate setting; household contacts and their ages (includes anyone who regularly sleeps in the home)
- Any contact with children? If yes, ages
- Contact with immunosuppressed people? Eg. HIV+, cancer, etc
- Close friends and relatives who are seen at least once per week – how often, for how long?
- Work or school location and description of setting (type of work, size of room, ventilation, etc)
- Transportation to work/school – bus, car-pool, etc
- Place of worship, clubs, sports teams, recreation programs of hobbies
- Any other places or groups the case has regularly been in or with while infectious
- Any contacts who are ill with potential TB symptoms or who have known TB
- Any major events (e.g. weddings, funerals, parties) the case attended while infectious
- Any recent travel or visitors staying at the home within the previous 2 years – if so, obtain details

Client should wear a surgical mask and the nurse and N95.

Appendix 3

Management of a TB case in the hospital/health care setting

Admission to Hospital

- Airborne precautions should be instituted as soon as diagnoses suspected/confirmed

This includes:

- Negative air pressure room
- N95 mask for HCP and medical mask for case if leaving room
- Other PPE as determined by point of care risk assessment
- Treatment should be ordered by attending physician/respiratory specialist
- Employee Health/Infection Prevention and Control should be involved to determine follow up for staff/patients who may have been exposed prior to application of precautions
- Arrangements with the CPHO and provincial pharmacy must be made before the patient is discharged from the hospital and moves out into the community (see previous section)

Long Term Care Facilities

Residents of long-term care (LTC) homes are considered to be at the same risk for having latent TB infection as other populations in the community and have the same risk of developing Active TB disease as persons of the same age in the general population, with the exception of those belonging to identified at risk groups (See table 1). However, because of the concern for transmission of TB in LTC homes and the anticipated need for contact tracing should there be an exposure, many guidelines recommend screening newly admitted residents.

- A symptom screen to rule out Active TB disease should be done, preferably prior to, and on admission to a long-term care home
- A symptomatic resident should have a posteroanterior and lateral chest x-ray and should be referred for medical assessment if indicated
- Routine tuberculin skin testing on (or prior to) admission and periodic tuberculin skin tests (such as annually) are *not* recommended for residents
- If a resident has had an exposure to respiratory TB, the need for testing should be individualized as part of contact tracing

Ambulatory care/outpatient clinics

Ambulatory care settings include locations where health services are provided to patients who are not admitted to inpatient hospital units. This includes, but is not limited to, outpatient diagnostic and treatment facilities (e.g., diagnostic imaging, phlebotomy sites, pulmonary function laboratories, TB treatment facilities: community health centers or clinics, physician offices and offices of allied health professionals (e.g., physiotherapists).

- If possible, non-urgent assessments of people with, or being evaluated for, respiratory TB should be postponed until no longer infectious
- If a visit cannot be postponed, it should be scheduled at the end of the day to minimize exposure to others and, when possible, staff should be alerted of these visits to allow for prompt use of airborne precautions

- The patient should be provided with a medical mask before arrival or immediately upon arrival to be worn until an airborne infection isolation room becomes available
- If an airborne infection isolation room is unavailable, the patient should be temporarily assessed or treated in a single room with the door closed, away from vulnerable patients, and transferred as soon as medically feasible to a facility with airborne infection isolation rooms if admission is required

Home care settings

Home care is delivered to patients who reside in their home or a community care residence. M. TB transmission to HCWs who work in home-based healthcare settings has been documented, with recommendations developed to prevent transmission.

- Home care agencies, in consultation with CPHO, should develop a system for screening at risk clients for signs of respiratory TB before and during visits, (See appendix 5 for assessment) thus facilitating earlier diagnosis and use of appropriate infection prevention and control measures
- The room in the home where the health care worker sees the patient should be well ventilated
- Clients with Active TB disease should wear a medical mask and care providers wear an N95
- Health care workers should not perform aerosol-generating medical procedures in the home on clients with, or being evaluated for, respiratory TB.

Further information on TB in the health care setting can be found in Chapter 14 of the Tuberculosis Standards.

Appendix 4

Visual Acuity Testing Tools

Color blindness

Instructions:

https://web.stanford.edu/group/vista/wikiupload/0/0a/Ishihara.14.Plate.Instructions.pdf

https://pioneerstudent.com/amfile/file/download/file/81/product/61/

Plates

https://www.medical-world.co.uk/productfiles/pdfs/IshiharaTestPlates.pdf

Appendix 5

Tuberculosis

What are the symptoms of tuberculosis?

TB mainly causes symptoms in the lungs and airways. It can also affect other parts of your body, such as:

- bones
- kidneys
- lymph nodes (organs found throughout the body that help recognize and fight germs)

About 90% of people who become infected with TB do not develop the disease. This is called ***latent tuberculosis*** (LTBI). People with LTBI:

- do not feel sick
- have no symptoms
- cannot spread TB to others

Those who do get sick have ***active tuberculosis***. The symptoms of Active TB disease include:

- a bad cough that:
  - lasts longer than 2 weeks
  - makes you cough up blood sometimes
  - makes you cough up phlegm sometimes (thick liquid that comes up from your lungs or airways)
- chest pain
- weakness or tiredness
- weight loss
- a lack of appetite
- chills
- fever
- night sweats

In severe cases, the disease may lead to death if untreated.

What do you do if you become ill?

Call your health care provider if you:

- have any of the listed symptoms
- think you may have been exposed to TB

If you have TB, you may have spread it to other people without knowing it. Your health care provider will talk with you about the people you spend time with. This will ensure they also get tested. Treatment will help prevent the spread and/or worsening of the illness.

This information is adapted from the Government of Canada website. For more information please visit:
http://healthycanadians.gc.ca/diseases-conditions-maladies-affections/disease-maladie/tuberculosis-tuberculose/index-eng.php

Appendix 6

How to collect a sputum sample

Health PEI

Guide to Laboratory Services

How to Collect a Sputum Specimen

IMPORTANT: TO ENSURE ACCURATE TEST RESULTS, PLEASE FOLLOW THESE INSTRUCTIONS CAREFULLY.

Collection container:

- Sterile specimen container (C&S)

Collection instructions:

- The sputum specimen obtained should be the result of a deep cough, thick of nature and not saliva.
- Collect an early morning specimen BEFORE breakfast.
- DO NOT use mouthwash, brush teeth, or gargle before collecting the sputum specimen.
- The patient should cough the sputum directly into the sterile container provided.
- Replace the container lid and close securely.

After Collection:

- Clearly label the container and requisition with:
  - **NAME** and **Provincial Health Card Number** (as they appear on your Health Card)
  - the Date and Time of collection
  - specimen source
- Transport the specimen to the laboratory within two (2) hours of collection. If transport is delayed, refrigerate specimen.
- The specimen MUST be received in the laboratory within 24 hours of collection.

Apendix 7

Prince Edward Island CANADA
Health and Wellness

TB Contact Screening Tool

Case name/#: _____

This tool provides the **MINIMUM guidelines for initial follow-up** of contacts of infectious tuberculosis (TB) cases. Contact investigation outcomes must be analyzed for all settings to decide if contact follow-up should be expanded.

This tool is to be used with the *Prince Edward Island Tuberculosis Disease Guidelines* **This tool is adapted from Toronto Public Health.**

Definitions and Considerations	
Cumulative exposure	Total number of hours during the case's period of infectivity that contacts shared the same airspace with the case (and contact did not use an N95 mask). In facility settings, contacts may include direct care and support staff, volunteers, visitors, etc.
Period of infectivity (POI)	Calculate start of infectivity by counting back from TB symptom onset or date of first test indicating TB, whichever is first, as below: • *For smear negative and CXR normal/non-cavitary*: 4 weeks • *For smear positive and CXR cavitary*: 12 weeks POI normally ends on the date the case is placed in respiratory isolation. See break in contact.

Break in contact (BIC)	• Last date a contact was exposed to an active infectious TB case (e.g. last day at work/school, date placed in negative pressure respiratory isolation in hospital). Repeat TST is done at least 8 weeks after BIC.
	• BIC may vary in different settings – please note on the TPH Contact Investigation Line List (CILL) and on BIC column below.
	• For case in home isolation with fully sensitive TB (or INH resistant only), for household contacts 5+ years use BIC =
	  • *For smear negative*: 2 weeks on effective treatment
	  • *For smear positive*: 4 weeks on effective treatment OR date of smear conversion, whichever first
	• For household contacts <5 years old, when case is in home isolation BIC is the date case is no longer infectious.

Effective TB treatment (in relation to BIC)	On standard RIPE treatment, or as appropriate for known drug sensitivities (see Canadian TB Standards) AND clinical improvement AND tolerating medication with no breaks in treatment. For smear positive: AND repeat sputum smears declining.
Initial & repeat tuberculin skin test (TST)	All contacts should be assessed for TB signs and symptoms when doing a skin test. Initial tuberculin skin test means it should be done as soon as possible, then repeated ≥8 weeks after BIC date.
Ventilation	In poorly ventilated spaces, consider lowering threshold for exposure time. Example: a small room with radiator/baseboard heating, no forced air and no open windows. Consider the direction/path of air flow (e.g. fan blowing air from infectious patient towards others; basement apartment in a house with forced air furnace - air recirculates through entire house). If number of air changes per hour (ACH) is available, 6 or more ACH is considered good ventilation; below 2 ACH is considered poor ventilation.
Clinical pulmonary case	(a) Radiology suggestive of active pulmonary TB AND culture negative on respiratory sample (or no laboratory specimens available), OR (b) PCR positive on lung biopsy. If deceased and no specimens will be available, clinical consultation may be necessary to determine the working classification of the case.
Pleural TB	If sputum/BAL is culture positive, manage as pulmonary case. If radiology indicates pulmonary involvement (e.g. infiltrates, cavities) but sputum/BAL culture negative, manage as clinical pulmonary case. If radiology does not indicate pulmonary involvement and sputum/BAL culture negative, manage as extrapulmonary - no contact follow-up.
TB wounds (smear and culture positive tissue/fluid from surgical wounds, abscesses)	Diseased tissues are not typical sources of infection unless procedures create aerosols. Staff involved in high pressure irrigation of open TB wounds, orthopaedic procedures (i.e. cutting with power tools) or cauterization of TB infected tissue while not wearing a N95 mask should be screened. Dressing changes with or without packing but no irrigation do not need screening. Autopsy and embalming have also been associated with TB transmission; staff not using an N95 mask during these procedures on a deceased untreated TB case should be screened.
Cough inducing procedure	Refers to aerosol-generating procedures (e.g. bronchoscopy, sputum induction, suctioning if not a closed system, intubation/extubation, CPAP). Staff must be present during the procedure without an N95 mask to be at risk.
<1 year of age contacts	Start with minimum guideline for contacts <5 years old and consider lowering threshold based on closeness of exposure (e.g. index case held baby while infectious).
Elderly contacts	For community-living contacts 85 years or older: in addition to symptom screening, do a chest x-ray rather than a TST. For long-term care contacts, see section 3 below.
Immunosuppressed contacts	Examples of immunosuppressed contacts include HIV positive with low CD4 counts; dialysis, oncology, and transplant patients. Consider lowering threshold based on extent of immunosuppression and closeness of exposure (e.g. direct caregivers). Consider symptom assessment and chest x-ray with or without TST, and flag TB exposure in the client's hospital/physician chart.
Masks	Only N95 masks are considered adequate PPE for TB. Surgical masks are not considered sufficient PPE.

1. Assess Case Level of Infectivity (LOI)

- For **extrapulmonary cases,** no contact follow-up required so long as pulmonary involvement has been ruled out and no wound care.
- **Source case investigation** indicated for children less than 5 years of age only.
- **Child cases <10 years of age** are rarely infectious; no contact follow-up required unless cavitary disease or smear positive sputum / gastric lavage.
- For **clinical** pulmonary TB cases, only screen household contacts.
- For **laryngeal** TB, score as high risk regardless of smear/chest x-ray score. If also pulmonary involvement, lower exposure threshold.
- For all other pulmonary TB cases, score level of infectivity rating by adding highest smear count (from sputum, BAL, or gastric aspirate specimens) and chest x-ray results:

Check all that apply:

- ◯ Pulmonary - proceed to level of infectivity rating → → →
- ◯ Clinical pulmonary - proceed to section 3
- ◯ Extrapulmonary (wound care only) - proceed to bottom of page 2
- ◯ Extrapulmonary (no pulmonary involvement, no wound care) - stop here

Circle smear and chest x-ray score, add scores for level of infectivity rating:

HIGHEST SMEAR	Negative/Not applicable	0
	Scarce/Moderate (few, 1+, 2+)	1
	Numerous (3+, 4+)	2
plus		
CHEST X-RAY	Normal/Calcified granuloma	0
	Infiltrates/Opacities/Fibronodular densities	1
	Cavitation	2

LEVEL OF INFECTIVITY RATING =

Risk Level

0..... Low
1..... Low
2..... Low
3..... High
4.....High

To be used in section 3.

2. Establish Case Period of Infectivity (POI)

Beginning of Infectiousness yyyy/mmm/dd:	**Date of Respiratory Isolation** yyyy/mmm/dd:	**Treatment Start Date** yyyy/mmm/dd:

3. Identify Contacts Requiring Follow-up and Establish Break in Contact

Assessment can be completed for each contact or group of contacts

Location of Exposure	Low Risk (0 – 2)	High Risk (3 – 4)	Contacts meeting criteria? (complete CILL for each "yes")		facility/household	BIC
Household	• Everyone in household – *initial & repeat TST* • For rooming houses/basement apartments, consider those on the same floor as "household"	• Everyone in household – *initial & repeat TST* • For rooming houses/basement apartments with forced air, consider all floors as "household"	No	Yes		
Close non-household (e.g. family, friends)	• Contacts ≥ 5 years old with **≥ 120 hours** cumulative exposure – *initial & repeat TST* • Contacts < 5 years old or immunosuppressed contacts with **≥ 60 hours** cumulative exposure – *initial & repeat TST*	• Contacts ≥ 5 years old with **≥ 96 hours** cumulative exposure – *initial & repeat TST* • Contacts < 5 years old or immunosuppressed contacts with **≥ 36 hours** cumulative exposure – *initial & repeat TST*	No	Yes		
Worksites / Universities / Colleges	• Smear negative index case – *no screening* • Smear positive index case – follow-up contacts with **≥ 120 hours** of cumulative exposure in a poorly ventilated or small space (e.g. approximately 150 square feet) – *TST > 8 weeks BIC*	• Contacts with **≥ 96 hours** of cumulative exposure in a medium space (e.g. classroom or smaller size space), or within 8 feet of index case in a large space (e.g. lecture hall, large open warehouse or open office floor) – *TST > 8 weeks BIC* • Lower threshold for poorly ventilated or small space (e.g. lunchroom, approximately 150 square feet)	No	Yes		
School Contacts ≥ 5 years of age (excludes universities/ colleges)	• Smear negative index case – *no screening* • Smear positive index case – follow-up contacts with **≥ 120 hours** of cumulative exposure in classroom and group activities – *initial & repeat TST or just 8 wk*	• Contacts with **≥ 96 hours** of cumulative exposure in classroom and group activities – *initial & repeat TST or just 8 wk*	No	Yes		
Daycare / School Contacts < 5 years of age	• Contacts < 5 years old with **≥ 60 hours** cumulative exposure – *initial & repeat TST* • Staff/volunteers with **≥ 120 hours** cumulative exposure – *initial & repeat TST*	• Contacts < 5 years old with **≥ 36 hours** cumulative exposure – *initial & repeat TST* • Staff/volunteers with **≥ 96 hours** cumulative exposure – *initial & repeat TST*	No	Yes		
Shelters / Group Homes / Drop-ins	• Contacts ≥ 5 years old who spent **≥ 5 nights** sleeping in the same room – *TST > 8 weeks BIC* • Staff and others with **≥ 120 hours** cumulative exposure – *TST > 8 weeks BIC* • Contacts < 5 years old or immunosuppressed contacts with **≥ 60 hours** cumulative exposure – *initial & repeat TST*	• Contacts ≥ 5 years old who spent **≥ 3 nights** sleeping in the same room – *TST > 8 weeks BIC* • Staff and others with **≥ 96 hours** cumulative exposure – *TST > 8 weeks BIC* (for staff, initial TST may also be feasible) • Contacts < 5 years old or immunosuppressed contacts with **≥ 36 hours** cumulative exposure – *initial & repeat TST* • If <u>infectious case</u> spent **≥ 60 hours** in facilities with drop-in services, consider holding site-based screening in addition to the above.	No	Yes		
Correctional Facilities	• Contacts who spent **≥ 5 nights** sleeping in the same cell – *initial & repeat TST* • Staff and others with **≥ 120 hours** cumulative exposure – *TST > 8 weeks BIC*	• Contacts who spent **≥ 3 nights** in same cell – *initial & repeat TST* • Staff and others with **≥ 96 hours** cumulative exposure – *initial & repeat TST*	No	Yes		
Long Term Care, Assisted Living and Retirement Facilities, Home Care	• Residents who spent **≥ 5 nights** sleeping in the same room or residents with **≥ 120 hours** cumulative exposure in a medium size space (e.g. classroom or smaller size space) – *initial symptom screen and CXR; if symptomatic, collect sputum as well. Consider TST if prophylaxis is an option. Recommend LTCF to flag TB exposure on resident chart and that they conduct enhanced TB symptom surveillance for 2 years.* • Staff with direct patient care and others with **≥ 120 hours** cumulative exposure in classroom size or smaller airspace – *TST > 8 weeks BIC*	• Residents who spent **≥ 3 nights** sleeping in the same room or residents with **≥ 96 hours** cumulative exposure in a medium size space (e.g. classroom or smaller size space) or within 8 feet in a larger size room (e.g. large dining hall) – *initial symptom screen and CXR; if symptomatic, collect sputum as well. Consider TST if prophylaxis is an option. Recommend LTCF to flag TB exposure on resident chart and that they conduct enhanced TB symptom surveillance for 2 years.* • Staff with direct patient care and others with **≥ 96 hours** cumulative exposure – *TST > 8 weeks BIC*	No	Yes		
Hospitals and Clinics	• Patients with **≥48 hours** cumulative exposure in the same room, or for larger bay areas the patients in adjacent beds, or participation in patient group activities (e.g. pediatric playroom, psychiatric group programs) – *TST > 8 weeks BIC, unless <5 years old, initial & repeat TST* • Staff with direct patient care for **≥60 hours** cumulative exposure; all staff involved during cough inducing/aerosolizing procedures if not wearing PPE – *TST > 8 weeks BIC*	• Patients with **≥ 24 hours** cumulative exposure in the same room, or participation in patient group activities (e.g. pediatric playroom, psychiatric group programs) – *TST > 8 weeks BIC, unless <5 years old, initial & repeat TST* • Staff with direct patient care **≥ 36 hours** cumulative exposure; all staff involved during cough inducing/aerosolizing procedures if not wearing PPE – *TST > 8 weeks BIC*	No	Yes		
Emergency Medical Services	Notify EMS of situation and recommend if any follow-up is needed (use above hospital staff parameters)	Notify EMS of situation and recommend if any follow-up is needed (use above hospital staff parameters)	No	Yes		
Public Travel	• For air travel, utilize Public Health Agency of Canada guidelines • For long distance (i.e.>8 hours) public bus and train travel, consider follow-up only if evidence of transmission among closer contacts. • No follow-up for local public transit.		No	Yes		
Wound Care	• Wound specimens smear negative – *no screening.* • Wound specimens smear <u>and</u> culture positive – staff involved in high pressure irrigation of open TB wounds, orthopaedic procedures (i.e. cutting with power tools) or cauterization of TB infected tissue while not wearing a N95 mask should be screened – *TST > 8 weeks BIC*		No	Yes		

Appendix 8

Interpretation of TST results

Table 1. Interpretation of TST results and cutoff thresholds in various populations.[7]

TST Result	Situation in which reaction is considered positive
<5 mm	In general, this is considered negative
≥5 mm	People living with HIV Known recent (<2 years) contact with a patient with infectious TB disease Fibronodular disease on chest x-ray (evidence of healed, untreated TB) Prior to organ transplantation and receipt of immunosuppressive therapy Prior to receipt of biologic drugs, such as tumor necrosis factor alpha inhibitors, or disease-modifying antirheumatic drugs Prior to receipt of other immunosuppressive drugs, such as corticosteroids (equivalent of ≥15 mg per day of prednisone for at least one month) Stage 4 or 5 chronic kidney disease (with or without dialysis)
≥10 mm	Recent (<2 years) conversion of TST from negative to positive Diabetes (controlled or uncontrolled) Malnutrition (<90% of ideal body weight) Current tobacco smoker (any amount) Daily consumption of >3 alcoholic drinks Silicosis Hematologic malignancies (lymphomas and leukemia) and certain carcinomas (such as cancers of head, neck, lung and/or gastrointestinal tract) Any population considered at low risk of disease.

Abbreviations: TST, tuberculin skin test; HIV, human immunodeficiency virus; TB, tuberculosis.

Table from Full article: Chapter 4: Diagnosis of tuberculosis infection

Appendix 9

Risk of TB disease and the incidence rate ratio of TB disease among different populations stratified by risk

Table 2. Risk of TB disease and the incidence rate ratio of TB disease among different populations stratified by risk.

Risk factor	Annual risk of TB disease for the first 2-3 years after testing positive (%)[a]	Reference
VERY HIGH RISK		
People living with HIV	1.7 to 2.7	2,56
Child or adolescent (<18 y) tuberculosis contact	2.9 to 14.6	56,57
Adult (≥18 y) tuberculosis contact	0.8 to 3.7	2,56
Silicosis	3.7	2
HIGH RISK		
Stage 4 or 5 chronic kidney disease with or without dialysis	0.3 to 1.2	2
Transplant recipients (solid organ or hematopoietic)	0.1 to 0.7	2
Fibronodular disease	0.2 to 0.6	Extrapolated from: 75–77
Receiving immunosuppressing drugs (eg, tumor necrosis factor α inhibitors or steroids)[b]	0.5	2
Cancer (lung, sarcoma, leukemia, lymphoma or gastrointestinal)	0.1 to 0.4	Extrapolated from: 70
MODERATE RISK		
Granuloma on chest x-ray	0.1	Extrapolated from: 77,78
Diabetes	0.1 to 0.2	Extrapolated from: 83
Heavy alcohol use (at least 3 drinks/day)	0.1 to 0.2	Extrapolated from: 79
Heavy tobacco cigarette smoker (at least 1 pack/day)	0.1	Extrapolated from: 80–82
LOW RISK		
General (adult) population with no known risk factor	0.03	2
Persons with a positive two-step TST booster and no known risk factor	0.02	Extrapolated from: 84,85

Abbreviations: TB, tuberculosis; HIV, human immunodeficiency virus; TST, tuberculin skin test.
[a]Risks are expected to halve after this period and continue to decrease subsequently.
[b]Risk does not appear significantly elevated with low-dose steroids (i.e., prednisone), but elevated with moderate or high dose (low dose, ≤9 mg/day; medium dose, 10–19 mg/day; and high dose, ≥20 mg/day).[86]

Table from Full article: Chapter 4: Diagnosis of tuberculosis infection

Appendix 10

Expected range of LTBI prevalence in various Canadian populations

	prevalence of LTBI (%)	type of test	publication year
Close contacts born in Canada/us[20]	31.0	TST (≥5 mm)	2020
Close contacts born outside Canada/us[20]	75.6	TST (≥5 mm)	2020
first nations schoolchildren on reserve, routine school screening (at low risk of TB exposure)[119]	BCG in infancy 5.7 no BCG 0.2	TST (≥10 mm)	2011
Kindergarten children, routine school screening, Iqaluit, Nunavut [120]	11.4	TST (≥10 mm)	2019
Government-assisted refugees[121]	36.0	TST (≥10 mm)	2016
refugees, medium-incidence origin (about 20/100,000)[122]	9.0	IGRA	2018
Migrant children, school-based screening[123]	22.8	TST (≥10 mm)	2010
refugees, very high-incidence origin (>300/100,000)[124]	51.0	IGRA	2016
federal inmates[125]	17.6	TST (≥10 mm)	2008
dialysis patients, routine screening[126]	11.5	IGRA	2020
Hematologic cancer patients, routine screening[127]	8.2	TST (≥10 mm)	2020

abbreviations: LTBI latent TB infection; TST, tuberculin skin tests; TB, TB; BCG, Bacille Calmette-Guerin; IGRA interferon-gamma release assay

Table from: https://www.tandfonline.com/toc/ucts20/6/sup1 Chapter 11

Appendix 11

Definitions

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

Aerosol-generating medical procedures: Medical procedures that may generate aerosols as a result of artificial manipulation of a person's airway.

Airborne infection isolation: The conditions into which a patient with suspected or proven Active TB disease 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 buildings or recirculate the air through a HEPA filter before returning it to circulation.

Bacille Calmette-Guerin (BCG): A live vaccine derived from attenuated Mycobacterium bovis

Break of contact (see also Contact): Moment when exposure to a person with active infectious TB ends. This can be when the active case is placed in airborne infection isolation or when he or she is deemed no longer infectious after a period of treatment.

Cavitary disease: Evidence on chest x-ray, CT scan, or pathology tests of lung destruction resulting in cavities or cystic areas that communicate with a bronchus. On chest imaging a cavity is defined as a gas filled space within pulmonary consolidation, a mass or a module. Cavities generally harbor large numbers of bacteria and, as a result, patients with cavitary disease tend to be highly infectious.

Congregate settings: Institutional settings where people reside in close proximity to each other, ranging from correctional facilities (prisons and jails) to homeless shelters, refugee camps, army barracks, hospices, dormitories, and nursing homes.

Contact: A person identified as having been exposed to a patient with infectious TB. The closeness and duration of exposure usually corresponds with the risk of becoming infected.

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

1. An increase of 6mm or more – this is 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 10mm or more – this is less sensitive but more specific criterion. In general, the larger the increase, the more likely that it is due to true conversion.

Culture-positive disease: The isolation of Mycobacterium TB complex (excluding BCG strain) from clinical specimens (sputum, body secretions or tissue).

Cure (active non MDR/XDR-TB) : Culture-negative at the completion of treatment.

Directly observed therapy (DOT): This term refers strictly to the direct observation of a person ingesting TB medications.

Disseminated TB: Active TB disease that affects three or more siters, or positive blood culture(s) for Mycobacterium TB. See also military TB

DNA probe: A molecular diagnostic technique whereby the organism grown on culture can be rapidly speciated within a matter or hours

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.

Drug resistance: In-vitro determination that growth of a strain of Mycobacterium TB is not inhibited by stander concentrations of an anti-TB drug.

Elimination: The elimination of TB as a global public health problem, meaning an incidence of TB disease of less than 1 per million population

Extensively drug-resistant TB (XDR-TB): MDR-TB with additional resistance to any fluoroquinolone (FQN) plus to bedaquiline (BDQ) or linezolid (LZD)

Extra-pulmonary TB: Site of TB that is outside the lings and respiratory tract. This includes TB pleurisy and TB of the intrathoracic lymph nodes, mediastinum, nasopharynx, nose (septum) or sinus (any nasal) and all non-respiratory sites.

First-line anti-TB drug: First-line antibiotics for the treatment of Active TB disease. These are isoniazid, rifampin, ethambutol and pyrazinamide, and are so considered the most effected and best tolerated. Streptomycin is no longer considered a first-line drug in Canada.

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

Healthcare-associated infection: Infections that are transmitted within a healthcare setting during the provision of healthcare (previously referred to as a nosocomial infection).

Healthcare facilities: Facilities where healthcare is delivered, including but not limited to acute-care hospitals, emergency departments, rehabilitation hospitals, mental health hospitals, outpatient clinics, and long-term care homes.

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

Immunocompromising condition: Abnormal chest x-ray with findings considered typical of previous TB infection or disease, plus at least three sputum cultures negative for TB or the chest x-ray abnormalities stable for at least 6 months.

Index patient: The initial patient identified with TB disease, from which the process of contact investigation begins.

Indigenous Peoples: The original inhabitants of North America, predating the arrival of Europeans. The Canadian Constitution Act of 1982 recognizes three major groups: Frist Nations, Inuit, and Metis.

Induration: The soft tissue swelling that is measured when determining the tuberculin skin test responded 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-y)IFN-y) production and that have been developed as alternatives to tuberculin skin testing (TST) for the diagnosis of TB infection. At the present time, two different types of IGRAs are registered for use in Canada. These are the Quantiferon ®-TB Gold Plus (Qiagen) and the T-SPOT.TB® (oxford Immunotec) assays.

Mantoux technique: The recommended method of administering the tuberculin skin test- the intradermal injection of 5 tuberculin units of PPD into the forearm.

Mono-resistant TB: Resistance to only one of the four first-line drugs.

Multi-drug resistant TB (MDR-TB): TB due to bacteria resistant to isoniazid and rifampin with or without resistance to other first line anti-TB drugs.

Mycobacterium TB complex (MTCB): M. TB (including subspecies M. canetti, M. bovis, M. bovis BCG, M. africanum, M. caprae, M. microti and M. pinnipedii. All of these species except M. bovis BCG are included in the Canadian case definition of TB.

Natural ventilation: Use of natural forces to introduce and distribute outdoor air into a building, to replace the indoor air. These natural forces can be wind pressure or pressure differences generated by temperature differences between indoor and outdoor air.

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.

Outbreak: The following working definition for an outbreak for planning investigations is based on that proposed by the U. S. Centers for Disease Control and Prevention:

- During a contact investigation, in two or more of the identified contacts a diagnosis is made of Active TB disease; or
- Any two or more cases occurring within 1 year or less of each other are discovered to be linked, but the linkage is recognized outside of a contact investigation.

For example, two patients who received a diagnosis of TB independently, out of a contact investigation are found to work in the same office, yet they were not previously identified as contacts of each other. The linkage between cases should be confirmed by genotyping results if cultures are available.

Pediatric TB: Active TB disease in a child or adolescent.

Pulmonary TB: In Canada, pulmonary TB includes TB of the lungs and conducting airways, and includes TB fibrosis of the lung, TB bronchiectasis, tuberculous pneumonia, tuberculous pneumothorax, isolated tracheal or bronchial TB and tuberculous laryngitis (ICD-9 codes 011-011.9, 012.2, 123.3; ICD-10 codes A15.0-A15.3, A15.5, A15.9, A16-0-A16-2, A16.4, A16.9).

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

Reactivation TB: The development of active disease after a period of TB infection.

Recurrence: Patient previously successfully treated (cure or completed) for Active TB disease in whom Active TB disease develops a second time, but without proof that this is the same organism.

Reinfection: Individual who previously infected with Mycobacterium TB as is exposed and infected a second time. This can be proven only if the individual had active disease once, then disease develops a second time, and the organism has a different "DNA fingerprint" from the original organism. Such cases are to be reported as a re-treatment case.

Relapsed: Patient with TB disease that was treated successfully (cure or completed), but it recurred. In the strictest sense the isolate should be the same (i.e. confirmed to have the same "DNA fingerprint" as the original organism), but relapse is commonly used interchangeably with recurrence. Such cases are to be reported as a re-treatment case.

Respiratory TB: Infectious TB of the larynx, pulmonary tree and parenchyma.

Second-line anti-TB drug: Anti-TB drugs reserved for use as alternative treatment to the first-line drugs. Second-line drugs consist of (1) bedaquiline, (2) linezolid, (3) fluoroquinolones, such as levofloxacin, and moxifloxacin (4) aminoglycosides, such as amikacin and streptomycin, (5) capreomycin, (6) cycloserine, (7) clofazimine, (8) ethionamide and protionamide, and (9) para-aminosalicylate (PAS).

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

Source patient: The person who was the original source of infection for secondary case(s) or contacts. The source patient can be, but is not necessarily, the index patient.

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

Subclinical TB: An intermediate state between TB infection and symptomatic pulmonary TB defined as a state of disease due to viable Mycobacterium TB that does not cause clinical TB-related symptoms but does cause other abnormalities that can be detected using existing radiologic and microbiologic assays.

Treatment completion (Active TB disease): Treatment completed without culture at the end of treatment and therefore the case does not meet criteria for cure or for treatment failure.

Treatment failure (active non-MDR/XDR-TB): Positive sputum cultures after 4 or more months of treatment or two positive sputum cultures in different months during the last 3 months of treatment, even if the final culture is negative and no further treatment is planned.

Treatment failure (Active MDR/XDR-TB): Two or more of five cultures recorded in the final 12 months are positive, or any one of the final three cultures is positive, or a clinical decision has been made to terminate treatment early because of poor response or adverse events.

Tuberculin skin test (TST): Skin test to identify whether a person has delayed-type hypersensitivity reaction to tuberculin antigens. TB infection (TBI): The presence of latent of dormant infection with Mycobacterium TB. Patients with TBI 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.

TB disease (TBD): Active clinical disease that is usually symptomatic and for which microbiologic tests are usually positive and radiologic tests are usually abnormal.

Appendix 12

How to perform a TST

Appendix 1

A.1. Tuberculin skin test (TST) administration and interpretation

A.1.1. Administration of TST

The only internationally recommended method of tuberculin skin testing is the Mantoux technique, which consists of intradermal injection of tuberculin material on the inner surface of the forearm. The instructions on how to perform this technique have been reproduced and adapted,[7,17] with supporting videos available.[18]

A.1.1.1. Handling the solution

- The purified protein derivative (PPD) should be stored between 2° and 8 °C and never frozen. Discard the solution if it freezes.
- Remove the tuberculin solution from the vial under aseptic conditions. A little more than 0.1 mL of PPD solution should be drawn into the TB 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, as the potency of the PPD 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 should be stored in the dark except when doses are actually being withdrawn from the vial.
- Use the solution within one month after opening, as the potency of the solution may be diminished. Label each bottle with the discard date when it is opened.

A.1.1.2. 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 record.
- Cleanse the area to be injected with an alcohol swab and let the area dry.
- Do not use EMLA® cream (or similar local anesthetic cream), as application of this cream has been reported to cause localized edema, which could easily be confused with a positive TST result.

A.1.1.3. 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 (see Appendix Figure A1).
- Administer the PPD by the slow intradermal injection of 0.1 mL (5 tuberculin units).
- 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 patient that they should not scratch the site but may perform all normal activities, including showering or bathing.
- Place uncapped disposable needles and syringes in appropriate puncture-resistant containers immediately after use.
- If the TST is accidentally given as a subcutaneous or an intramuscular injection, this should not pose a serious risk of harm. It is possible that tuberculin-sensitive persons may have localized inflammation, which should be self-limited. It would not be possible to take a measurement of, or clinically interpret, any such reaction, so the TST should be administered again immediately *using proper intradermal technique* on the volar surface of the forearm.
- After administration, record the following:
  - Date of injection
  - Dose of PPD (5 tuberculin units, 0.1 mL)
  - PPD manufacturer
  - PPD lot number
  - Expiration date of the PPD reagent
  - Site of injection
  - Person administering the TST.
- In settings where TST administration may be unsupervised or performed by persons with minimal experience, the quality of TST administration may be assessed by following mobile TST (mTST) protocols,[17,18] whereby photos of the wheal created after administration are taken and evaluated by an experienced reviewer.

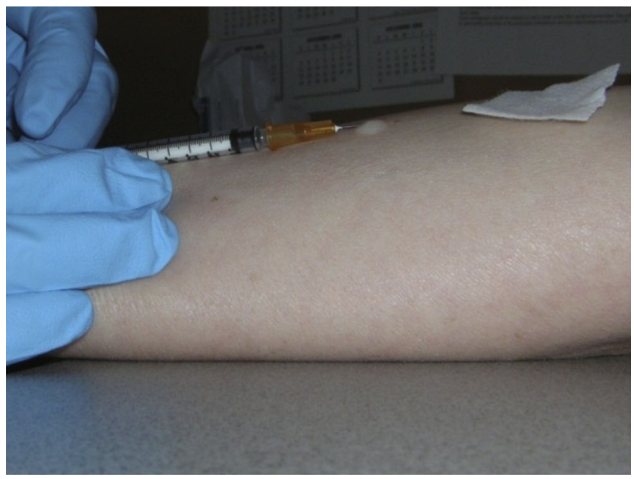

Figure A1. Technique of TST administration.

A.1.2. Precautions

- Acute allergic reactions, including anaphylaxis, angioedema, urticaria and/or dyspnea, have been rarely reported as temporally (not necessarily causally) associated with administration of Tubersol®.[108] The events have been reported in Canada at a rate of less than 1 per million doses; some were reported in persons without a prior history of TST.
- Epinephrine hydrochloride solution (1:1000) and other appropriate agents should be routinely available for immediate use in case an anaphylactic or other acute hypersensitivity reaction occurs. Health care providers should be familiar with the current recommendations of the National Advisory Committee on Immunization for monitoring of the patient for immediate reactions over a period of at least 15 minutes after inoculation and with the initial management of anaphylaxis in non-hospital settings.

The following persons can receive a TST:

- Those with a history of receiving BCG vaccination(s).
- Those with a common cold.
- Those who are pregnant or are breast-feeding.
- Those immunized within the previous four weeks with vaccines other than those listed below (live-virus vaccines).
- Those with a previous positive TST.
- Those taking low doses of systemic corticosteroids. A steroid dose equivalent to ≥15 mg prednisone daily for 2-4 weeks is required to suppress tuberculin reactivity.[109,110]

The following persons should **NOT** receive a TST:

- 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 or severe reactions.
- Those with documented TB disease or a well-documented history of adequate treatment for TB infection or disease in the past. In such patients, the test is of no clinical utility.
- Those with current major viral infections (eg, measles, mumps, varicella).
- Those who have received live virus immunization within the past 4 weeks, as this has been shown to increase the likelihood of false-negative TST results.[111] 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, including 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 on the same day as the immunizations but at a different site.

A.1.3. 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.
- Self-reading is very inaccurate and is strongly discouraged.[112]
- 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 one 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.[113] If the TST cannot be read within 72 hours, it should be repeated at a location far enough from the previous test that the reactions do not overlap. There is no minimum wait time and the test can be readministered immediately.
- 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 if 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 (Appendix Figure A2). 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 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.[7]
- 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 setting the caliper may reduce rounding error. If a caliper cannot be found a flexible ruler could be used.
- Do not record erythema (redness). Approximately 2-3% of persons tested will have localized redness or rash (without induration) that occurs within the first 12 hours. These minor allergic reactions do not indicate TB infection and they are not a contraindication to future TSTs.[114]
- Blistering, which can occur in 3 to 4% of subjects with positive tests, should be recorded.
- Record the result in millimeters (mm). Record no induration as "0 mm." Recordings of positive, negative, doubtful, significant and non-significant are not recommended.
- Do not round off the diameter of the induration to the nearest 5 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.
- After measuring, record the following and provide a record of the result to the patient:
    - Date the induration was read
    - Measurement of the induration, if any, in mm
    - Any adverse reactions (eg, blistering)
    - Name of the individual reading the test

- In settings where TST measurement may be unsupervised or performed by persons with minimal experience, the quality of TST measurement may be assessed by following mTST protocols,[17,18] whereby photos of the induration are taken and evaluated by an experienced reviewer. This method is most accurate when applied to no or large indurations. In all settings, routine quality control and quality assessment measures of TST induration measurement should be employed to maximize accuracy.

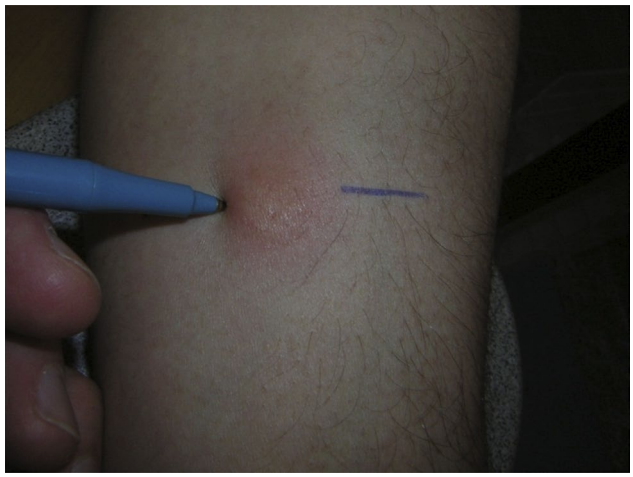

Figure A2. Ballpoint pen method for measuring the transverse diameter of the TST induration.

A.2. Reproducibility and causes of TST and IGRA variation

Table A1. Causes of variation with TST or IGRA.[88–90,92,115]

Common Causes of Variation	Causes of IGRA Variation	Causes of TST Variation
• **Pre-analytical errors**. For the TST, this includes possible issues with the PPD solution and administration (e.g., volume injected), while for IGRA these may include improper shaking of the tube after collection, delays in transport and/or incubation of samples, or errors in the actual time the sample is incubated. • **Within-person variations over time**. For the TST, responses may vary by up 5 mm in reaction size between tests. For the IGRA, a previous systematic review suggested there was a mean difference in two consecutive samples of 0.2 IU/mL between two QFT tests; similar data for T-SPOT.*TB* was not reported. • **Analytical errors**. For the TST, a mis-recording of TST measurements may lead to an incorrect conclusion of a change in induration on a second test. For the IGRA, if not recorded automatically, data-entry errors on quantitative values and interpretation may occur.	• **Test-retest variation**. While agreement is generally quite good when the same sample is tested in the same lab twice, there may be variation in the spots counted or IU/ml measured from the same sample. • **Inter-laboratory variation**. There may be different measurements when the same sample is tested in different labs. • **TST-induced variation**. A previous TST may "boost" a subsequent IGRA result. Conversions in a systematic review were uncommon but did occur with both T-SPOT.*TB* and QFT. Whether the risk of disease among persons with a boosted response is different than risk among those without a boosted response is unclear.	• **Variability associated with the reader** (eg, two different readers may measure the same induration differently).

A.3. Serial TST: Booster effect and conversions

A.3.1. TST booster effect

A single TST may elicit little response yet stimulate an anamnestic immune response, such that a second TST at any time from 1 week to one year later will elicit a much greater response.[89] This phenomenon is important to detect, as it represents a false positive, not a new TB infection. The booster effect was first described in older persons in whom it was felt to show TB infection acquired many years before (remotely) with subsequent waning of immunity.[95] It has also been described in persons with prior BCG vaccination or sensitivity to nontuberculous mycobacterial antigens.[94,116]

A two-step TST should be performed if subsequent TSTs will be conducted at regular intervals (eg, among health care or correctional workers).[89] This is to reduce the chance of a false-positive TST conversion when the TST is repeated. Please refer to Chapter 13: Tuberculosis Surveillance and Tuberculosis Infection Testing and Treatment in Migrants for recommendations on use of two-step TST in specific travelers.

The two-step protocol needs to be performed and documented ONCE. Any subsequent TST should be 1 step, regardless of how long it has been since the last TST.[7]

The same material and techniques of administration and reading should be used as with any other TST. The second test should be performed one to 4 weeks later. Less than one week does not allow enough time to elicit the booster phenomenon, while more than 4 weeks increases the possibility of a true TST conversion. Both tests should be read and recorded at 48 to 72 hours after administration. Expanding the interval to read the first TST after 1 week (and therefore immediately before a second TST) is less accurate and is not recommended.

Longitudinal studies of the risk of TB following a booster reaction defined the reaction simply as a second TST result of 10 mm or more induration.[85,117–119] Therefore, a second TST result of 10 mm or more should be considered significant and the patient referred for medical evaluation and chest radiography. [7,89]

All subjects with a reaction of 10 mm or more on the second TST of a two-step TST do not need a TST in the future. There is no clinical utility.[7] They should be referred for medical evaluation, as performed for those with a positive first TST. In longitudinal studies of the elderly, subjects with a second TST response of 10 mm or more had a risk of TB that was approximately half that of subjects whose first TST response was 10 mm or more. Similar findings were shown in a small cohort of hemodialysis patients. Since the risk of TB is about half that of patients from the same population group whose initial TST result is positive, the decision to provide TPT should be individualized.

A common question is how to manage a person whose first TST measured 5-9 mm and the second test measured 10 + mm but increased by less than 6 mm from the first test. As previously mentioned, this should be managed as a "positive TST," meaning referral for medical evaluation and no further TSTs. While appropriate epidemiologic data are lacking, it seems reasonable to suggest that the risk of TB disease would be lower than in persons whose second TST increased by at least 6 mm. The decision to provide TPT should be individualized.

A.3.2. TST conversions

If there has been recent exposure, such as close contact with a person with TB disease or occupational TB disease exposure, then TST conversion will be more likely than when there has been no exposure. Conversion is defined as a TST 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, the definition of conversion is more controversial. Increases of 6 or 10 mm have been proposed, but there is weak evidence supporting both.[89] In general, the larger the increase, the more likely it is due to a true conversion. However, like consideration of a "booster," any second TST result of 10 mm or greater should be considered a "positive" and the patient evaluated for possible TPT.

All available experimental and epidemiologic evidence consistently shows that TST conversion occurs within 3-8 weeks of exposure.[89] Therefore, to identify a true conversion (ie, new infection), a single TST should be performed as soon as possible after an exposure to tuberculosis is recognized and the contact is identified. If the first TST is negative and performed less than 8 weeks after contact with the index patient, then a second TST should be scheduled no sooner than 8 weeks after the contact was broken. This also means for contacts that are identified more than 8 weeks after contact with an index patient is broken (eg, casual contacts), a single TST can be performed, and the result acted upon.[7]

A.4. Dimensions to consider when interpreting TB infection diagnostic test results

A.4.1. Pretest probability of TB infection and predictive value

The pretest probability of TB infection refers to the probability a person truly has infection. The positive predictive value therefore reflects the likelihood that a positive result truly represents infection and the negative predictive value the likelihood a negative result truly represents absence of infection. The positive predictive value of the TST may be significantly reduced by BCG vaccination in populations with low pretest probability of infection; similarly, in populations with significant immune impairment, the negative predictive value of both TST and IGRA may be significantly impacted in populations with high pretest probability of infection.

A.4.2. Discriminatory ability of the test to identify individuals at increased risk of TB disease

The discriminatory ability of the test to identify individuals who will develop TB disease refers to the IRR, that is, the likelihood of developing disease among persons testing positive vs. negative. In populations where false negatives with a TST or IGRA are expected to be common (eg, due to immune impairment or other biologic reasons), the IRR of a test may fall substantially, even with very high specificity. Similarly, in populations where false positives are expected to be common, the IRR of a test may be substantially impacted, even if sensitivity is very high. Therefore, the discriminatory ability of a test is likely to be severely impacted in populations where sensitivity and/or specificity are expected to be reduced.

A.4.3. Risk of TB disease

The risk of TB disease is elevated among persons with medical conditions that affect immunity, recent infection or certain habits, and is described for various populations among persons with a positive test in Table 2 of the main text. Using estimates of IRR, risk of TB disease can be estimated among persons with a negative test. Risk of disease is the most paramount consideration when faced with a test result, as TB disease may result in long-term patient morbidity or even death. Risk of disease at the time the test is done should not be the only consideration; it is important to also consider future risk of disease. This is especially important among certain persons, such as those tested prior to initiating immunosuppressants, prior to transplantation, or early in chronic kidney disease, as risk of disease is likely to increase in the future.

Appendix 13

Process for initiating care for a new Active TB disease case at CPHO

For the case

1) The CD nurse, in coordination with ordering health care provider, determines if treatment has been ordered and if DOT is required.
2) CD nurse and HCP to determine where the treatment medication should be ordered from (Provincial pharmacy or community pharmacy).
3) CD nurse writes a letter for provincial pharmacy signed by CPHO physician for enrollments into the TB medication program as appropriate. If the medication is coming from the community pharmacy it should be indicated when ordering that the Rx should be provided at no cost to the client and to invoice CPHO by faxing the receipt with the patient's name, medication and cost to 902-620-3354.
4) CD nurse sends a letter/email/HCP note for PHN regarding the medication and dosages for them to review with client.
5) CD nurse/HCP to submit a home care referral for blood work until the client is no longer infectious, if the client is isolated at home. Once the client is not infectious, home care can be discontinued, and the client can go to the nearest hospital to have the blood work completed.
6) PHN/HCP to provide clients with requisitions for sputum samples. PHN/HCP to assess the client's vision during the first 2 months of treatment while the client is on ethambutol.

For Contacts

7) PHN to do
   a) Contact tracing
   b) TST's and reading
   c) Provide lab requisitions and x-ray requisitions to positive contacts
   d) Liaise between contacts/case and CPHO
   e) Create LTBI cases/forms for those who are positive for LTBI
8) CD nurse to provide IGRA recs as required for those with positive TSTs. If there is a large group of contacts requiring IGRA, CD nurse can make arrangements to do them together.
9) CD nurse to schedule those requiring LTBI treatment into the public health primary care clinic to start treatment.
10) CD nurse/CPHO physician follows blood work and reschedules contacts into the clinic as required.

Appendix 14

Process for contact testing, treatment and follow up

- Contacts are determined through information provided by the case during the initial and subsequent interviews
- Public Health Nursing provides contact follow up and ensure no contacts are symptomatic or are under the age of 5. For these contacts immediate treatment may be considered
- Tuberculin skin testing is completed as soon as possible after identification of the contacts
- A positive TST in a contact follow up setting is 5mm induration
- A contact tracing spread sheet will be shared with PHN and CPHO and kept up to date as new information arises
- All positive TSTs will have an LTBI case created in CD 2.0

If contact has a positive initial TST:

- PHN will provide a requisition for a chest x-ray
- They will be scheduled for IGRA testing
- If the initial TST is negative the contact will require another TST again 8 weeks post contact with the infectious case. If this person is still in contact with the case e.g. a household member, the 2nd TST will be scheduled for 8 weeks after the case is deemed non-infectious
- All those with positive IGRA test and chest x-rays that do not indicate TBD will be started on treatment for latent TB infection
- Treatment is generally rifampin and may be prescribed by the contact's Primary care provider or the Chief Public Health Officer through the public health primary care clinic
- Treatment is provided at no cost to the contact through the provincial pharmacy. If the contact is on a temporary visa and not covered by Pharmacare, the Rx can be sent to a community pharmacy and an invoice sent to the CPHO.
- Initial lab work including CBC and liver enzyme testing will be done prior to starting treatment.
- Lab work will be done again in 1 month while receiving treatment and further testing done only if required (e.g. abnormal results).