TUBURCULOSIS DISEASE (ACTIVE)

Disease Overview

Tuberculosis (TB) is an infection by one of the mycobacteria contained within the *Mycobacterium tuberculosis* Complex (MTBC), which include *M. tuberculosis*, *M. africanum*, *M. canetti*, *M. caprae*, *M. microti*, *M. pinnipedii* and *M. bovis* (excluding *M. bovis* BCG strain).

TB is an airborne disease and is typically transmitted from person to person via inhalation of the MTBC bacilli into the host's lungs where the bacilli bacteria replicates. TB usually infects the lungs; however, TB bacilli bacteria may spread from the initial infection in the lungs via the lymphatic and or circulatory system to other parts of the body such as kidneys and spine. Based on the location of infection, TB is classified as pulmonary (involving the lungs) or extra-pulmonary (outside of the lungs and respiratory tract).

TB exhibits a spectrum of infection, with a distinction between TB infection (TBI, previously known as latent TB infection) and TB disease. TB disease is notable for microbiologic and/or radiographic evidence of active disease and is typically symptomatic; TBI has no evidence of clinically active disease. TB disease can be a manifestation of primary TB disease, TB reinfection, or reactivation of a TBI. Less than 10% of infected individuals (i.e., with TBI) will develop active disease in their lifetime; half of those will develop TB disease within the first 2 years following infection.

If not treated properly, TB disease can be fatal.

For more information see the *Canadian Tuberculosis Standards, 8th Edition*.

Symptoms

The classic symptom of pulmonary TB disease is a chronic cough of at least 3 weeks' duration. This cough is initially dry but after several weeks to months it may become productive. Fever and night sweats are common but may be absent in the very young and the elderly. Hemoptysis, anorexia, weight loss, chest pain and other symptoms are generally manifestations of more advanced disease.

Reservoir

Primarily in humans, however, *M. bovis* is found in cattle and a variety of other mammals.

Mode of Transmission

Transmission of tuberculosis is mainly through exposure to airborne aerosolized droplet nuclei produced mostly during forceful expiratory efforts (e.g., coughing, singing, sneezing, playing wind instruments) but also to a lesser extent during speaking.

More rarely, TB can be transmitted through ingestion (e.g., bovine TB) or percutaneous inoculation (e.g., through laboratory or hospital accident).

Incubation Period

The risk of developing active TB disease is highest during the six months after infection and remains high for two years. HIV infection and other immunosuppressive conditions increase the subsequent

risk of progression to pulmonary or extra-pulmonary active TB and shorten the interval for the development of active TB disease following infection. TBI in an individual can persist a lifetime.

Period of Communicability

If viable tubercle bacilli are discharged in the sputum, the period of communicability could be many years. Effective antimicrobial chemotherapy usually eliminates communicability within 2-4 weeks. Children with pulmonary TB are generally not contagious; however, each case needs to be assessed individually.

For the purposes of contact tracing and management, a period of likely infectiousness can be determined based on case infectivity and symptom onset. See the *Canadian Tuberculosis Standards, 8th Edition, Chapter 3, section 3.2 for more information.*

Risk Factors

There are a variety of factors that influence the risk of transmission related to patients (both source and recipient), the infecting TB strain, as well as the environment in which exposure occurs. For a full list of factors, see the *Canadian Tuberculosis Standards* 8th Edition. *Chapter 2, section 1.2.*

As risk factors and exposure are not equally distributed in the population, the prevalence of active tuberculosis disease in Canada is increasingly concentrated in specific population subgroups such as:

- foreign-born people;
- Canadian-born Indigenous people;
- people with social or behavioral risks such as homelessness, or reside in correctional facilities;
- healthcare workers and
- people who use IV drugs.

Surveillance Case Definition

Laboratory confirmed case

Cases with Mycobacterium tuberculosis complex demonstrated on culture, specifically *M. tuberculosis*, *M. africanum*, *M. canetti*, *M. caprae*, *M. microti*, *M. pinnipedii* or *M. bovis* (excluding *M. bovis* BCG strain). OR

Clinically confirmed case

In the absence of culture proof, cases clinically compatible with active tuberculosis that have, for example: chest radiographic changes compatible with active tuberculosis; active non-respiratory tuberculosis (for example, meningeal, bone, kidney, and peripheral lymph nodes); pathologic or post-mortem evidence of active tuberculosis; favorable response to therapeutic trial of anti-tuberculosis drugs.

New Case:

- No documented evidence or adequate history or previously active TB disease.

Re-treatment Case of active TB disease must meet the following criteria:

- Documented evidence or adequate history previously active TB disease that was declared cured, or treatment completed by current standards, and
- there is at least a 6-month interval since the last day of previous treatment and diagnosis of a subsequent episode of TB that meets the active TB disease case definition.

OR

- Documented evidence or adequate history of previously active TB that cannot be declared cured or treatment completed by current standards, and
- inactive for 6 months or longer after the last day of previous treatment, and
- diagnosed with a subsequent episode of TB that meets the active TB case definition.

Diagnosis and Laboratory Guidelines

Diagnostic tests can be classified into two categories, in relation to the type of TB disease that is/may be present:

TBI: Tuberculin skin testing (TST) testing and interferon gamma release assay (IGRA) are two diagnostic modalities that are predominantly used to assess suspect TBI cases. It is important to note that neither test can separate TBI from active TB disease. Therefore, neither the TST nor IGRA should be used in isolation for diagnosis of TB disease in adults and adolescents. TST/IGRA can be used as an adjunct diagnostic for diagnosis of TB disease in pediatric patients.

It may take from two to eight weeks from the time of infection to demonstrable primary lesions or significant tuberculin skin test (TST) reaction and positivity of the interferon gamma release assay (IGRA).

Active TB Disease: The main laboratory diagnosis test for tuberculosis is bacterial culture. However, the bacteria grow slowly, and the test can take up to 6-8 weeks before confirmation, especially for negative results. It is done usually on sputum, but many other specimens can be done. Sensitivity of the culture is not perfect and depends on the quality of the specimen. A negative culture result does not invalidate a diagnosis with clinical symptoms.

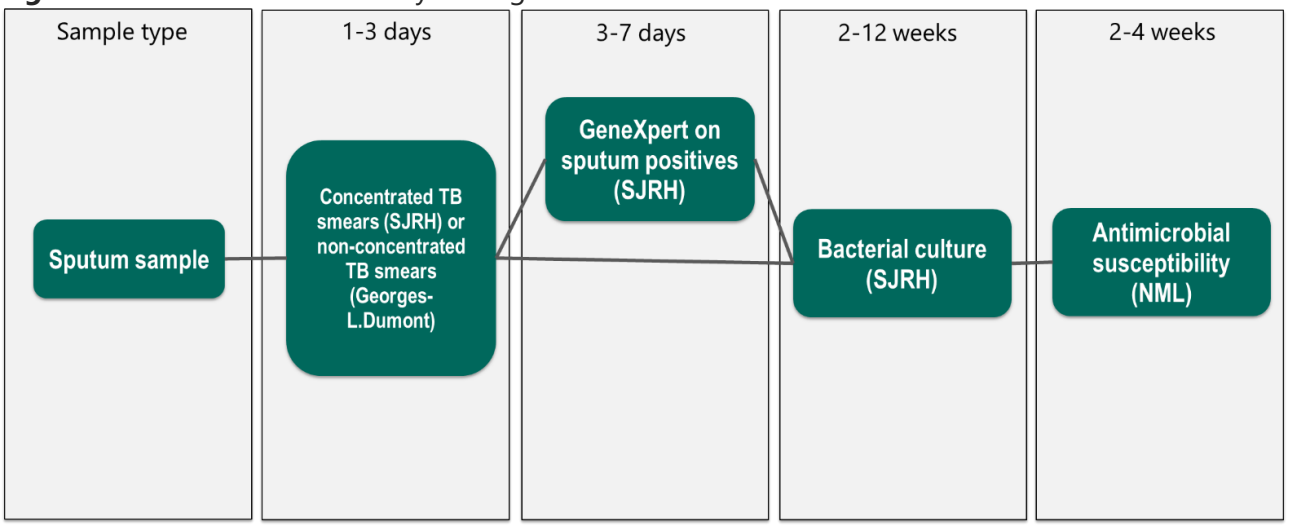
Acid fast smears can be done more quickly than bacterial culture. However, their detection limit is higher than the culture (i.e., reduced sensitivity). Acid fast smears result are considered presumptive and should be confirmed by bacterial culture as they cannot differentiate between the various types of mycobacterial TB complexes or otherwise. Concentrated auramine smears should be used as they have better sensitivity.

GeneXpert (NAAT testing) is performed locally on smear positive specimens for more timely results while the bacterial culture is incubating. The results need to be confirmed by culture. NAAT is not routinely performed on smear negative results given the low sensitivity.

Canada is a low prevalence area for TB, so it is recommended to take three sputum samples for smears and culture. They can be collected on the same day, but at least one hour apart. Genotyping

is not required for diagnosis or treatment, but it can be useful for epidemiological and surveillance reasons (i.e., linking two or more cases together).

Figure 1: Tuberculosis laboratory testing



Reporting

Per policy 2.2 Disease and Event Notification to the Office of the Chief Medical Officer of Health and Epidemiology (OCMOHE).

- Enhanced Surveillance:
  - For all confirmed cases, a Public Health Agency (PHAC) *Active Tuberculosis Case Report Form* should be completed and sent to OCMOHE within 5 days. In Canada, active TB disease is monitored at the national level by PHAC through the Canadian Tuberculosis Reporting System (CTBRS). The CTBRS is a case-based surveillance system that maintains selected non-nominal data on people diagnosed with active TB disease. The Epidemiology and Surveillance Unit communicate all reported TB cases to PHAC on a yearly basis or as requested by the Agency.
  - PHAC form for *Treatment Outcome of a New Active or Re-treatment Tuberculosis Case* for all cases reported in the previous year should be completed and sent to OCMOHE as soon as treatment outcome is completed.
  - All new and retreatment cases are to be reported to CTBRS with exception of temporary residents and foreign nationals who are in Canada illegally unless their treatment was initiated in Canada.
- Routine surveillance (RDSS) for all confirmed cases.

Case Management

Education

Education should include disease specific information, symptoms, period of communicability, risk factors for transmission and risk factors for susceptibility, as well as the importance of early diagnosis and treatment. Additional information to address includes methods of preventing transmission, including hand washing, cough etiquette, exposure prevention, environmental management, and any other educational points related to the specific case, in accordance with the *Canadian Tuberculosis Standards* and as outlined in the Respiratory section introduction of this manual.

Significant effort must be invested in exploring supports and barriers to implementation of the following:

- preventive measures to halt ongoing spread, which may include work absence and what types of supports and resources may be needed and available to ensure daily chores/needs are addressed (including financial impacts which may have a significant effect on adherence)
- proper adherence to prescribed treatment regimen.

Persons with active pulmonary or extra-pulmonary TB should be offered HIV testing.

Investigation

Patients who present with non-respiratory TB disease can also have concomitant respiratory involvement; thus, it is important for all TB patients to have the following (in accordance with *Canadian Tuberculosis Standards)* and in consultation with the RMOH:

- Chest radiography (and sputum testing if there are any respiratory symptoms or chest x-ray abnormalities) as part of their medical work-up.
- Follow-up of confirmed cases as authorized and guided by the Regional Medical Officer of Health (RMOH) in accordance with *Canadian Tuberculosis Standards*.
- Follow-up of suspect /possible cases as authorized and guided by the Regional Medical Officer of Health (RMOH) in accordance with *Canadian Tuberculosis Standards*.
- Consult with attending physician for any suspect or confirmed cases to discuss the case details and plans for follow-up. Inquire about currently available test results (i.e., x-ray, CT, sputum smears, cultures, PCR, bronchoscopy, bronchoalveolar lavage) or planned tests.
- Provide physician with the Public Health Agency of Canada form to complete or acquire necessary information to complete this form.
- Determine with the physician who may be potential contacts.
- Contact with the case on more than one occasion is usually required to get as accurate a picture as possible of symptom details, onset, contact and setting list etc.
- Discuss the collected details with the RMOH for further direction.

Other institutions with the appropriate investigation infrastructure may do the follow-up within that institution (e.g., Federal correctional facilities, regional health authorities). However, Public Health has the overall responsibility to ensure that contact tracing has been carried out.

Drugs for the management of active TB or tuberculosis infection (TBI) are funded by Public Health for any patient (regardless of permanent residence) who presents a prescription on which "TB Plan" is written by the prescriber (no dispensing fee). The drugs covered by the TB Plan are listed in the NB Drug Plans Formulary.

Exclusion/Social Distancing

Respiratory isolation is important in the early phases of treatment when the person could still be contagious. Where available, adult patients with sputum smear-positive pulmonary TB who reside in congregate settings should be placed in an airborne infection isolation room with negative pressure ventilation.

See the *Canadian Tuberculosis Standards* for further information on criteria to consider for declaring a patient non-infectious, including criteria to consider for return to home prior to being declared non-contagious.

Treatment

Therapy is given in two phases: initial intensive, and continuation.

In the Initial intensive phase:

- Patients are usually treated with a regimen of isoniazid (INH), rifampin (RMP), Pyrazinamide (PZA) and ethambutol (EMB) initially.
- Drug sensitivity should be performed in all cases.
- If the isolate causing disease is fully susceptible to all first-line drugs, the EMB can be stopped and PZA is given for the first 2 months (end of the initial intensive phase).
- Tuberculosis medication should preferably be given daily during the initial intensive phase.

In the continuation phase:

- patients are usually treated with INH and RMP for an additional 4 months (6 months in total) and
- the length of this phase, and medication used, can be variable, depending on indicators of risk of relapse, on the drugs given in the initial phase, and on the results of pre-treatment drug susceptibility testing.

Treatment of active disease in pregnant or breastfeeding women should be the same as the standard regimen.

If health care providers are unsure regarding the client's ability to take medications as prescribed, directly observed treatment (DOT) may be used to monitor compliance (Appendix A). For further information on this issue, see the *Canadian Tuberculosis Standards*, *Chapter 5, section 3.2* and the following standard for New Brunswick (Directly Observed Therapy).

For specific treatment recommendations such as Treatment of drug-resistant, HIV-associated, extra-pulmonary and pediatric TB, see the Canadian Tuberculosis Standards.

Immunization

The Bacillus Calmette–Guérin (BCG) live attenuated vaccine is the only vaccine currently used against TB. However, BCG vaccine is not recommended for routine use in any Canadian population.

Contact Management

With limited exceptions, only TB in the respiratory tract is infectious and requires contact follow-up investigation for both sputum smear-negative and smear-positive cases. The objective of contact follow-up is to identify and treat any secondary cases, and to identify contacts with TB infection (TBI) to offer preventive treatment. Source-case investigation is recommended for children under 5 years old with a diagnosis of active TB. The *source* is a person with infectious TB disease who transmits *M. tuberculosis* to another person or persons. The patient is identified through a contact or source case investigation and may or may not be the index patient.

Contacts may be grouped as follows:

High priority contacts: most exposed and highest risk of progression to active TB if infected. Contacts include household contact in the same household for more than 3 times per week, household contacts in congregate settings, caregivers with extensive exposures, contact exposure without an N95 mask during aerosolizing medical procedures and medium priority contacts who are at an increased risk of a TB infection to TB disease progression (aged less than 5 years, HIV, dialysis, transplant, silicosis etc.). Note: High-priority contacts should have both an initial TST immediately and a second TST at least 8 weeks from the last day of exposure, to identify conversion. If TBI screening is done by IGRA, a single test at 8 weeks after exposure should be done.
Medium priority contacts are contacts who have regular contact with the active TB case and share air space several times weekly but are not part of the same household for most of the time. These contacts include caregivers with less extensive exposure, regular sexual partners, close friends, extended family, daycare/school classroom contacts, co-workers, and low priority contacts at risk for an TB infection to progress to an active TB disease (aged less than 5 years, HIV, dialysis, transplant, silicosis etc.).
Low-priority contacts are casual contacts who spend time 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. These contacts include high school students with one course with the active TB case, classmates in a large college, less exposed colleagues at work, members in social groups and extended family members who visit infrequently.

Recommended Steps in Contact Investigation and Follow-Up

1. TB programs should prioritize contacts by the infectiousness of the source case, the extent of the exposure and the risk of progression to active TB if infected.

2. Each contact should be interviewed regarding the circumstances and duration of exposure, presence of symptoms, previous history of tuberculosis, TB exposure, prior tuberculin skin test (TST) and previous BCG in country of origin.

3. Public health authorities and the treating physician should collaborate to ensure that contacts with no previous history of TB or documented positive tests receive a TST and symptom assessment. Public health nurses within the regional health authority will provide Tuberculin Skin Testing (TST) through New Brunswick communicable disease follow up under the medical directive for TST and in

accordance with the policy and standards outlined in the New Brunswick Immunization Guide (policy 2.13, 2.14 & appendix 4.2.3).

4. In the context of contact investigation, a positive TST result is 5 mm or greater on initial or repeat testing, or an increase of at least 6 mm from a previous TST of 5-9 mm. Conversion can take up to eight weeks.

5. A medical evaluation to rule out active TB should be performed for all contacts who have symptoms compatible with TB; a positive TST result, whether before exposure or at initial or repeat testing; and (regardless of the results of the initial TST) all children under age 5, as well as contacts who are HIV seropositive or severely immunocompromised. This should include chest radiography, plus sputum collection as indicated.

6. Once active TB has been ruled out, treatment of the TBI should be offered according to the *Canadian Tuberculosis Standards* recommendations, *Chapter 6, section 3.*

7. Public health authorities should determine the need to extend the contact investigation based on the contagiousness of the index case, the results of the investigation of high priority contacts and the nature of the exposure of additional contacts.

8. Contact follow-up should be carried out for both sputum smear-negative and smear-positive cases in accordance with *Canadian Tuberculosis Standards* and as outlined in the Respiratory section introduction of this manual.

Education

Proper education on symptoms, methods of control and importance of early diagnosis and treatment should be conducted in accordance with the *Canadian Tuberculosis Standards* and as outlined in the Respiratory section introduction of this manual.

Investigation

Investigation of potential contacts is recommended using TST test for all household members and close contacts. Where a TST is contraindicated an IGRA can be used for testing of contacts.

Tuberculin Skin Test (TST) – Department of Health, through Serum Depot, provides tuberculin at no charge for contact tracing, case identification and management purposes.

Conduct contact investigation as per the *Canadian Tuberculosis Standards* and as outlined in the Respiratory section introduction of this manual.

Exclusion/Social Distancing

Immunization

Although not given in Canada it is common for other countries to give BCG, so it needs to be considered in contact tracing including foreign-born individuals.

Prophylaxis

Contacts with a positive TST should be sent for further assessment and need for TBI treatment. See treatment above as per the *Canadian Tuberculosis Standards*.

"Window prophylaxis" of TB preventive therapy is recommended for children identified as close contacts who are less than 5 years of age with an initial negative TST or IGRA and no evidence of TB

disease by examination or radiology. It may take up to 8 weeks after infection for the TST or IGRA to convert to positive, and during this time untreated infection may rapidly progress to severe disease. See *Canadian Tuberculosis Standards, Chapter 9, section 9.*

Management of Special Situations

Tuberculosis and Human Immunodeficiency Virus

HIV infected individuals have the highest estimated risk of developing active TB.

TB is often the first clinical indication that a person has underlying HIV infection. Therefore, all individuals newly diagnosed with active TB disease should be screened for coinfection with HIV.

A TST should be provided to all persons who are HIV-positive. False negative reactions may occur in immunocompromised individuals. A reaction of 5 mm or more induration is considered indicative of TB infection in a person with HIV infection.

For people living with HIV, the sensitivity of TST is significantly lower. High risk contacts who are HIV positive should receive treatment for presumed TBI regardless of the TST result.

Active TB disease should also be ruled out at the time HIV infection is first diagnosed. For such individuals with TBI, once active TB disease has been ruled out, INH prophylaxis is recommended for a minimum of nine months.

Immigration

Canada is a leading destination for migrants, both in numbers received and on a per-population basis. The proportion of immigrants originating from intermediate or high TB-incidence regions such as Asia, Africa and Latin America has increased. Most immigrant groups apply for permission to come to Canada while still living in their countries of origin, although asylum seeker claimants who apply upon or after arrival in Canada are an important exception.

Immigration, Refugees and Citizenship Canada requires all individuals applying for permanent residency and certain individuals applying for temporary residency to undergo an immigration medical exam. The objective of pre-entry TB screening is to detect prevalent active pulmonary TB in migrants prior to arrival to ensure that they are treated and no longer infectious when they enter Canada.

Most TB in the foreign-born population in Canada occurs as a result of reactivation of TB infection that was acquired in their country of origin.

Outbreak Management

Activate the local outbreak plan when an outbreak is declared.

Appendix A

Directly Observed Therapy (DOT)

Purpose

The purpose of this standard is to outline the requirements of the Regional Health Authorities- Public Health Service (RHA-PHS) on the provision of DOT in the treatment of active TB in New Brunswick.

Preamble

The goals of TB management are to treat the individual patient and minimize transmission of TB to other persons in the community. Treatment consists of taking a combination of medications for an extended period (6-12 months or more). Poor adherence to prescribed TB therapy is the most common cause of treatment failure. The consequences of poor adherence to TB therapy are relapses and risk of acquired drug resistance. The most effective strategy to ensure adherence to treatment is DOT.

With DOT, a patient meets with a health care worker every day or several times a week. The patient takes the TB medicines while the health care worker watches. The health care worker also asks the patient about any problems or side effects with the medication. DOT should be done at a time and place that is convenient for the patient.

Virtual DOT (VDOT) using video enabled communication devices, such as smartphones and computers may be considered an acceptable alternative to DOT in some settings. This should be in combination with in-person support and DOT within the context of jurisdictional policies regarding use of digital devices to deliver health care services.

According to the *Canadian TB Standards*, all jurisdictions should have the capacity to provide DOT. The evidence to support universal DOT use is considered weak. As such, the decision to initiate DOT should be made on a case-by-case basis, considering the benefits of direct observation on treatment adherence, the significant resource implications required, and the impacts to the patient's quality of life (Menzies, Dick et al. *Canadian Tuberculosis Standards, 8th Edition 2022*). The *Canadian TB Standards* does recommend DOT, at a minimum, for certain higher risk groups such as:

- Patients with individual risk factors for non-adherence;
- Population groups with historically increased rates of treatment failure or relapse or with inadequate rates of treatment completion; and
- Those for whom TB has major individual and/or public health implications if they fail treatment.

DOT Protocol Standards

The RHA-PHS will develop a protocol to guide in the implementation and evaluation of DOT services in their geographical areas. The RHA-PHS are responsible for ensuring that DOT services are available within their respective territory and that services are provided to clients for whom DOT is prescribed. They are not necessarily responsible for the direct provision of DOT to each client. They are, however, responsible for ensuring that DOT is properly provided when prescribed. The protocol will be included in the regional reportable disease and events investigation, prevention, and control plans.

Principles:

The following principles should guide the development of protocols for the delivery of DOT in NB:

1. The RHA-PHS protocol will include a clear process and procedures for when and how DOT is ordered, by whom, who needs to be notified, and within what timeframe.
2. The RHA-PHS protocol will identify potential agencies that may be involved in delivering DOT and the type of selection process that will be used to select a provider for each case.

3. The protocol will include information on training, equipment and procedures designed to address DOT worker safety issues.
4. The protocol shall include assessment of alternate means of DOT delivery (i.e., by video), their availability and selection, and specific procedures that guide the use of such options, including client eligibility, confidentiality, training, etc.
5. Alternate means of DOT delivery will incorporate the need for physical assessment and/or follow up testing.
6. The RHA-PHS protocol will clearly outline the role and tasks involved in DOT delivery by providers, including regular health-based assessments, considering a holistic and client-centered approach.
7. The protocol will clearly outline the process for reporting non-adherence (both business day and after hours), including triggers for when to report and to whom, as well as procedures for responding to non-adherence issues that arise.
8. The protocol will include procedures for routine reporting of adherence information. Routine adherence reporting will be required on a weekly basis.
9. The RHA-PHS must also ensure that processes are in place to respond to issues of non-compliance, should they occur.
10. At a minimum, non-adherence reporting, and routine reporting should be provided to the responsible clinician, the RMOH, and to a designated person in the RHA-PHS if they are not delivering the service directly.
11. The established protocol should involve and be communicated to all relevant partners who may be engaged in the delivery of TOD.
12. The protocol must be approved by the RMOH responsible for the geographical area served.