November, 2015

Re: Tuberculosis Reporting and Case Investigation

Reporting of tuberculosis (Mycobacterium tuberculosis and other Mycobacterium species as defined in this protocol) is as follows:

**Laboratory:**
- All positive laboratory results for Mycobacterium species (identified in this protocol) are reportable to the Public Health Surveillance Unit by secure fax (204-948-3775).

**Health Care Professional:**
- Probable (clinical) cases of tuberculosis must be reported to the Public Health Surveillance Unit by secure fax (204-948-3775) within 5 business days of being identified. The Clinical Notification of Reportable Diseases and Conditions form (http://www.gov.mb.ca/health/publichealth/cdc/protocol/form13.pdf) should be used.
- Cooperation in Public Health investigation is appreciated.

**Regional Public Health or First Nations Inuit Health Branch (FNIHB):**
- Cases are referred for Public Health follow-up and responsibilities are described in this protocol.

Sincerely,

“Original Signed By”

Richard Baydack, PhD
Director, Communicable Disease Control
Public Health and Primary Health Care
Manitoba Health, Healthy Living and Seniors

“Original Signed By”

Carla Ens, PhD
Director, Epidemiology & Surveillance
Public Health and Primary Health Care
Manitoba Health, Healthy Living and Seniors
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1. **Tuberculosis in Manitoba**

Manitoba Health (MH) Public Health Branch (PHB), Health Canada (HC) First Nations and Inuit Health Branch (FNIIHB), Winnipeg Regional Health Authority (WRHA) and other regional health authorities (RHAs) work collaboratively to ensure that tuberculosis (TB) prevention and care are integrated, timely and comprehensive. A transition process was completed in April 2011 whereby all RHAs assumed responsibility for case and contact identification and management for their respective residents, and the WRHA provides consultation to all regions as requested. The WRHA has an agreement with FNIIHB whereby the WRHA coordinates case management and contact investigation for First Nations communities.

Manitoba’s TB prevention and management program operates within an overarching strategic approach of creating an enabling and supportive environment, establishing positive social norms and providing client-focused service.

The three major hierarchical goals of the TB program are:

1. Early diagnosis and effective treatment of persons with active TB disease.
2. Timely investigation and appropriate management of contacts of individuals with infectious TB.
3. Investigation of populations at risk of latent TB infection (LTBI) and progression to TB disease.

MH has established the Manitoba Tuberculosis Steering Committee (MBTBSC) to provide provincial leadership and strategic direction regarding TB prevention, diagnosis, and management strategies to RHAs and other relevant stakeholders and to address any emerging programmatic issues.

MH will continue to receive reports of laboratory-confirmed or clinical cases of TB; to manage and maintain the provincial TB registry including the provision of epidemiologic analyses using the data collected; and to maintain responsibility for protocol and policy development and updates.

Manitoba has a persistently higher disease burden of TB than that at the national level. From 2001 to 2011, the crude incidence rates of TB in Manitoba ranged from 8.5 per 100,000 to 12.8 per 100,000, whereas during the same period, the crude incidence rates of TB in Canada ranged from 4.7 to 5.7 per 100,000.[1]

In 2010 and 2011, 132 and 116 cases of active TB disease were reported among Manitobans, representing crude incidence rates of 10.7 and 9.3 per 100,000 persons, respectively.

The WRHA and Northern RHA reported 90% of the total number of cases of active TB disease in 2010–2011. The median age of reported cases of active TB disease was 39 years. The majority of those with active TB disease reported during these two years had respiratory TB.

In 2010 and 2011, 474 and 395 individuals, respectively, started treatment for LTBI in Manitoba.[2]

2. **Purpose of the Protocol**

This protocol has been developed by Manitoba Health, in consultation with various stakeholders, for physicians, nurses, and other health professionals working in public health, primary care, specialty care, community health and infection prevention and control. The protocol addresses case and contact identification and management and other related public health issues.

This protocol is meant to be used in conjunction with other resources available on the MH PHB website and the *Canadian Tuberculosis Standards (CTS)*, 7th edition.

3. **Etiology**

TB is caused by bacteria in the Mycobacterium tuberculosis complex (MTBC), including *M. tuberculosis*, *M. bovis*, *M. africanum*, *M. canetti*, *M. caprae*, *M. microti* and *M. pinnipedia*. M. *tuberculosis* causes the majority of human TB cases.[3]
4. Epidemiology

4.1 Reservoir
Humans (rarely other primates) are the main reservoir for MTBC with the exception of *M. bovis*, which is found in cattle and a variety of other animals.[3, 5]

4.2 Transmission
Transmission of *M. tuberculosis* is airborne, with infection following inhalation of droplet nuclei, usually produced by an adult or adolescent with respiratory (pulmonary or laryngeal) TB during forceful expiratory efforts (e.g., coughing, singing or sneezing).[6]

Health care workers are at risk of infection with *M. tuberculosis* when performing aerosolizing procedures (e.g., bronchoscopy, intubation, autopsy) if personal protective equipment is not used.[3] Airborne transmission is enhanced by crowded living or working conditions, poor ventilation in the shared environment and more frequent or prolonged exposure to an infectious host.[3, 5] Rarely, infection can occur when mucous membranes or breaks in the skin come into contact with *M. tuberculosis*.[3]

TB disease in the elderly is generally due to reactivation of infection acquired in the remote past, whereas TB disease in young children indicates ongoing active transmission in the home or community.[5]

*M. bovis* is transmitted most often by the ingestion of unpasteurized dairy products, but airborne transmission from cattle to farmers and animal handlers can occur.[3, 6] Human-to-human transmission is rare unless the person infected is immunocompromised.[7, 8]

Extrapulmonary TB (other than laryngeal) is generally not transmissible, except in rare situations where there is aerosolization of secretions from a draining sinus.[3]

4.3 Occurrence
General: The global burden of TB remains substantial. In 2011, there were an estimated 8.7 million people newly diagnosed with TB disease (13% co-infected with human immunodeficiency virus [HIV]) and 1.4 million people died from TB disease, including almost one million deaths among HIV-negative individuals and 430,000 among people who were HIV positive. TB is one of the most important killers of women, with 300,000 deaths among HIV-negative women and 200,000 deaths among HIV-positive women in 2011. Geographically, the burden of TB is highest in Asia and Africa. About 60% of cases are in the South-East Asia and the Western Pacific regions. The African region has 24% of the world’s TB cases and the highest rates of cases and deaths per capita.[9]

Canada: There were 1,607 new active and retreatment cases of TB reported to the Canadian Tuberculosis Reporting System (CTBRS) in 2011, for a reported incidence rate of 4.7 per 100,000 population. This represents a national low since collection of TB data began in 1924. A disproportionately high number of cases was reported in Northern Canada (Northwest Territories, Nunavut and Yukon). All provinces and territories reported at least one case of active TB disease in 2011. For 2011, 34% of the cases were between the ages of 25 and 44, whereas the highest age-specific rate, at 8.5 per 100,000, occurred among those aged 75 years or older. Canadian-born Aboriginal peoples and foreign-born individuals are disproportionately affected.[1]

Overall, in 2011, 67% of all reported TB cases were among foreign-born individuals, 19% among the Canadian-born Aboriginal population and 12% of cases were among the Canadian-born non-Aboriginal population. The majority of reported TB cases in 2011 (67%) were diagnosed as pulmonary TB.[1]

Manitoba: Refer to Section 1, *Tuberculosis in Manitoba*.

4.4 Incubation Period
The incubation period from inhalation of *M. tuberculosis* to development of a positive tuberculin skin test (TST) or positive interferon gamma release assay (IGRA) is two to eight weeks. Positive TST and/or IGRA are evidence of TB infection.
The risk of developing TB disease is highest during the six months after infection and remains high for two years; however, many years can elapse between initial TB infection and the development of TB disease[6]; latent TB infection can persist for a lifetime[3].

4.5 Susceptibility and Resistance
The risk of infection with M. tuberculosis is most dependent on the degree of exposure and less on host factors. However, the risk of developing disease once infected is highest in children under three years of age, lowest in school-aged children and high again in adolescents and young adults, the very old and immunocompromised persons including persons with HIV infection.[3]

Among infected persons, susceptibility to reactivation and TB disease is increased by HIV infection and other immunocompromising conditions. People who are underweight or undernourished, have a debilitating disorder (e.g., diabetes, chronic renal failure, some forms of cancer, silicosis or gastrectomy) and substance users may also have a higher risk of developing TB disease.

4.6 Communicability
Theoretically, communicability persists for as long as viable organisms are discharged in sputum. Effective antimicrobial therapy usually eliminates communicability within a few weeks.[3] Individuals whose sputum is smear-positive for acid-fast bacilli (AFB) are the most infectious and the most likely to transmit the infection.[10] Individuals with respiratory TB who are smear-negative but culture-positive are capable of transmitting infection to others.[3] Children younger than 10 years of age with respiratory TB are rarely contagious because their respiratory lesions have few organisms (paucibacillary disease) and cough is non-productive so few or no bacilli are expelled.[6] In addition, environmental factors such as the air circulation/ventilation and proximity to the source case can influence communicability of the organism.

5. Case Definition
5.1 Confirmed Case
A case can be either laboratory or clinically confirmed.[4]

5.1.1 Laboratory-confirmed Case
M. tuberculosis detected by direct polymerase chain reaction (PCR) in a respiratory specimen; or MTBC (excluding M. bovis Bacillus Calmette-Guérin [BCG] strain, which has been largely eradicated) identified on culture from an appropriate clinical specimen (e.g., sputum, tissue biopsy, respiratory, gastric lavage).

5.1.2 Clinically-confirmed Case
In the absence of a positive culture or positive direct PCR, a TB expert has indicated TB disease is likely present, based on one or more of the following:

- Common signs and symptoms of respiratory TB, which include cough of at least three weeks’ duration. This cough is initially dry but after several weeks to months will become productive. Fever and night sweats are common but may be absent in the very young and elderly. Hemoptysis, anorexia, weight loss, chest pain (pleuritic pain) and other symptoms are generally manifestations of more advanced disease.
- Positive AFB smear.
- Chest radiographic changes compatible with active TB disease (e.g., pulmonary infiltrates, volume loss due to destruction of the lung tissue and cavitations in the upper segments of the lung lobes). These are the classic triad findings, mainly seen in non-immunocompromised adults.[3]
- Pathologic or post-mortem evidence of active TB disease.
- Favourable response to a therapeutic trial of anti-TB drugs.

Confirmed cases can be further categorized into new or retreatment cases[4].
5.1.3 New Case
No documented evidence or adequate history of previous active TB disease.

5.1.4 Retreatment Case
A confirmed case with documented evidence or history of previously active TB disease that was declared cured or treatment completed by current standards\(^a\)

AND

At least six months have passed since the last day of previous treatment

AND

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

OR

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

AND

Inactive for six months or longer after the last day of previous treatment\(^b\)

AND

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

Note: A case should not be counted twice within any consecutive 12-month period, unless a second genotype is detected, then this would be considered a “new active case”.

6. Pathogenesis
Infection with \(M.\) \textit{tuberculosis} usually goes unnoticed by the host. However, a relatively small proportion (~5\%) of individuals with a newly-acquired infection will progress to active TB disease within two years of infection. TB disease that occurs soon after infection is acquired is referred to as “primary” disease (e.g., primary TB disease or primary progressive TB disease).

In the majority of infected individuals (~95\%), infection is followed by a period where the infection persists but causes no clinical signs or symptoms. This condition is referred to as Latent TB Infection (LTBI). Latency is believed to occur because the host’s immune system limits the organisms’ ability to replicate and disseminate within the host. TB organisms can remain dormant for years, sometimes for the lifetime of the host.

About 10\% of immunocompetent persons with LTBI will eventually go on to develop active TB disease (post-primary TB disease). This figure is higher if the host is under five years of age or immunocompromised.

7. Case and Contact Management

7.1 Management of Cases
Case management is a shared responsibility among the client, health care provider(s), Regional Health Authorities, FNIHB and MH. MH provides provincially-funded medications at no cost to individuals who are diagnosed with active TB disease or contacts with LTBI. Also, MH maintains a provincial registry of all individuals who have been diagnosed with active TB disease and those with LTBI who receive treatment.

\(^a\) Inactive tuberculosis

- Two chest radiographs with stable appearance documented over an interval of three months and three negative sputum smears and cultures; OR
- In the absence of cultures, chest radiographs are stable for a minimum of six months and the individual has been asymptomatic for six months after completion of treatment; OR
- Cultures for MTB complex are negative at the completion of treatment and for six months thereafter.

\(^b\) If less than six 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 six months have passed since the last day of previous treatment and the case was previously reported in Canada, don’t report as a re-treatment case. Submit an additional “Treatment Outcome of a New Active or Re-treatment Tuberculosis Case” form (\text{http://www.phac-aspc.gc.ca/tbpc-latb/pdf/torform-eng.pdf}) at the end of the treatment.
Among First Nations communities in Manitoba, the WRHA provides support for case and contact identification and management; FNIHB funds this service and is responsible for ensuring that TB case and contact management services are available within Health Canada’s jurisdiction.

Effective chemotherapy taken over an adequate period of time is the primary treatment of all forms of TB with goals to:

- cure the patient and restore quality of life and productivity.
- prevent death from active TB disease or its late effects.
- prevent relapse of TB.
- prevent transmission of TB to others.
- prevent the development and transmission of drug resistance.
- prevent LTBI from progressing to active disease.

Respiratory isolation procedures are important in the early phases of treatment when individuals may still be infectious. Some clients may require isolation in an airborne infection isolation room (AIIR) (also known as negative pressure isolation room). Ventilation in these rooms provides negative pressure so no air flows out into adjacent areas.[11]

These patients should be kept under airborne precautions until there is clinical evidence of improvement, evidence of adherence to at least two weeks of effective multi-drug therapy based on known antibiotic sensitivity of the patient’s organism and three consecutive negative AFB sputum smears on samples collected at least eight hours apart.[12]

If the patient is going to remain in hospital (for other underlying reasons), consideration should be given to keeping them on airborne precautions until such time as they can be discharged home.[13]

Multi-drug resistant TB cases and those with mono-resistance to rifampin (RMP) should have three consecutive negative sputum cultures after six weeks of incubation prior to discontinuing airborne precautions.[12]

Six months is the usual treatment duration for persons with newly diagnosed active TB disease in Manitoba. It is a two-phase regimen, with the majority of clients treated as follows:

**Initial or intensive phase**: This two-month phase consists of at least three anti-TB drugs, usually isoniazid (INH), rifampin (RMP) and pyrazinamide (PZA), administered preferably daily (or five days per week). The aim is to achieve rapid reduction in the number of tubercle bacilli in the body. Ethambutol (EMB) is added in the initial phase if there is any suspicion of initial drug resistance and while the results of drug susceptibility testing are pending.

**Continuation phase**: This is a four-month phase consisting of at least two anti TB medications, usually INH and RMP, administered either daily or, if using directly-observed therapy (DOT)’, at higher doses, three times per week.[12] The aim is to maintain treatment long enough to eliminate the small number of persisting organisms. Three times weekly therapy is preferred over twice weekly for programmatic reasons. If patients miss a single dose while receiving thrice weekly therapy, they effectively receive twice weekly therapy, which is still adequate.

c Although the 7th Edition of the Canadian TB Standards states that “three AFB negative sputum specimens either spontaneous or induced on the same day, a minimum of one hour apart are required to take TB patients off airborne precautions”, experts in Manitoba recommend that the three consecutive sputum samples should be collected at least eight hours apart and all of them should be AFB negative as mentioned above.

d TB patients who are AFB smear negative can still be infectious. However, they may not need to be isolated in their homes given that their household contacts have already been heavily exposed and are often receiving therapy for LTBI.

e DOT is the process whereby a health care worker watches the patient swallow each dose of medication, helping to ensure that higher treatment completion rates are achieved. It is an effective way to monitor adherence to therapy and is the standard of care for all individuals receiving treatment for active TB disease in Manitoba.
Therapy should be prolonged to nine months if there are risk factors for relapse. These include persistent cavity on the chest x-ray after two months or at the end of effective anti-TB therapy, persistent smear and/or culture positivity after two months of therapy, or HIV co-infection.

Although somewhat standardized, the drugs given along with the frequency is individualized.

Pyridoxine (vitamin B6) should routinely be added when prescribing INH to persons with diabetes, renal failure, malnutrition, HIV infection, substance abuse, seizure disorders or peripheral neuropathy or to women who are pregnant or breastfeeding, because of the increased risk of symptoms related to pyridoxine deficiency in these individuals.

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

The same drugs, dosing and duration as in the standard regimen are recommended for treatment of active TB disease in patients with renal insufficiency. However, prolonged dosing intervals are recommended for PZA and EMB from daily to three times weekly.

7.1.1 Fundamentals of TB in Children

- In Canada, pediatric TB is largely a disease of Canadian-born Aboriginal and foreign-born children.[12]
- Children under the age of five are at high risk of progression to severe forms of TB disease after acquiring infection.
- Every attempt should be made to collect specimens for culture before therapy, although yield is low.
- Induced sputum is a promising technique for diagnosis of TB disease in young children.
- TB often is diagnosed on the basis of a positive TST (or IGRA), abnormal chest x-ray, history of contact with a case of infectious TB, and compatible clinical signs or symptoms.
- BCG vaccine protects against serious forms of TB disease and in Manitoba is administered to infants who reside in most First Nations communities.

- BCG vaccination status should not be considered in the interpretation of a positive TST.
- A negative TST or IGRA does not exclude active TB.
- Parents of children for whom therapy of LTBI is recommended should be informed of the risk of side effects.
- INH remains the principal recommended regimen for LTBI.
- Directly-observed administration of medication (whether for latent infection or active disease) is recommended for all children.
- For treatment of active TB disease and LTBI, daily therapy, which can be given as five observed doses weekly, is preferred over intermittent regimens.
- Treatment regimens for children with drug-resistant LTBI must be individualized.[13] Twice weekly regimens should no longer be used because each missed dose represents a larger fraction of the total number of recommended treatment doses.
- EMB is now routinely used as part of initial empiric therapy of TB disease (pending sensitivities) in infants and children, unless contraindicated or if the source case’s organism known to be susceptible to INH, rifampin and PZA.
- PZA doses are higher than in the previous edition of the CTS.

7.1.2 Reporting Requirements

TB is a reportable disease under Schedule B of the Public Health Act (PHA) Reporting of Diseases and Conditions Regulation.

Confirmed cases (clinical and laboratory) are reportable the next business day following diagnosis by the physician/health care professional to the Public Health Surveillance Unit (see Sec. 10.1) using the clinical notification of Reportable Diseases or Conditions from:

The following are reportable by the laboratory to the Public Health Surveillance Unit (see Sec. 10.1):

- All clinical specimens culture-positive for *M. tuberculosis*
- All clinical specimens smear-positive for AFB
- All pathology sample findings suggestive of TB disease
- All respiratory specimens positive for *M. tuberculosis* by PCR molecular testing.

All active or suspected active respiratory TB cases with a history of airline travel that is eight hours or more in duration must be reported without delay. Reporting forms should be completed by the relevant regional health authority and sent through the provincial TB program to the Public Health Agency of Canada (PHAC), where a risk assessment will take place to determine the need for a contact investigation. Within the province of Manitoba where flights are generally only one to two hours in duration, neither PHAC nor MH notification specifically regarding the flight is required.

For further information on reporting criteria, contact investigation and reporting forms, please refer to the *Canadian Tuberculosis and Air Travel Guidelines* produced by PHAC:


### 7.1.3 Interruptions in Tuberculosis Treatment

Interruptions in TB treatment are most often attributed to circumstances that challenge the patient’s ability to follow the prescribed regimen of drugs.[14] The care delivery system that supports the patient to manage the identified challenges can reduce untimely or premature interruptions in TB treatment.

In Manitoba, when a person with TB is unable to follow TB assessment, treatment and/or isolation recommendations, in order to prevent, reduce or eliminate the risk posed to public health, a Medical Officer of Health may issue a Communicable Disease (CD) Order by virtue of Sec. 43 of the PHA. If the person refuses to comply with the CD Order, the MOH may, by virtue of Sec. 47 of the PHA, apply to a Judicial Justice of the Peace (JJP) for an Order to Apprehend. If issued, the Order to Apprehend may be directed to any peace officer (typically the local police or the Royal Canadian Mounted Police), who must then locate and apprehend the person and bring him or her before a JJP. A JJP may then, by virtue of Sec. 49 of the PHA, issue an Order of Justice to Examine, Treat and Detain requiring a person to be detained for the purpose of examination, treatment, etc. and until such time that his or her release no longer presents a threat to public health. For more information, please see:


These legislated measures are only undertaken as a last resort when all reasonable, less intrusive supportive measures have failed. Public health interventions must balance the rights of the individual with the duty to protect the public.

### 7.2 Management of Contacts

TB is listed under Schedule A of the *PHA Reporting of Diseases and Conditions Regulation* as a disease requiring contact notification. Contacts are all persons with whom an infectious case (source case) has been in contact.[12] They may be close or casual contacts or contacts in the community. Assessment of close contacts, defined as those who regularly share breathing space with the source case and are therefore most likely to have acquired TB infection and sometimes active TB disease, is where contact management generally begins.

Contact investigation is a significant part of TB prevention and care programs in countries like Canada that have a low incidence of the disease. The following are the recommended contact investigation activities:

1. Assessment of information regarding the source case within reasonable time of receipt of notification of the case.
2. Initial interview of infectious source case to determine who the contacts are
   - Ideally begin within one business day of notification of the case, whenever possible
3. Assessment of close contacts:
   – Should begin within seven working days of their being identified (within three working days if known to be less than five years of age or to have high risk of disease progression if infected)
   – May be delayed where diagnosis of the source case is presumptive (i.e., not yet confirmed), except for contacts who are children or have high risk of disease progression if infected where active TB disease is strongly suspected in source case

4. Review of assessment of contacts to determine if contact investigation should be expanded to include lower-risk contacts
   – Within five working days, whenever possible, of completing assessment of previous cohort of contacts

5. Consideration of expansion of contact investigation if evidence of transmission has been identified among the previous cohort of contacts (see Sec 7.2.1), as resources permit

6. Consideration of repeating steps 4 and 5 for lower-risk contacts, as resources permit

7. Prevention of progression to active TB disease among contacts found to have LTBI
   – Achieved through the use of a single antibiotic medication, usually INH given for nine months or RMP for four months (adults) or six months (children)

All children exposed to a person with active TB should have a symptom enquiry and TST. Contacts less than five years of age should also have a physical examination and chest X-ray. Even if these younger children have a negative TST and no radiographic evidence of active TB, they should be offered “window period prophylaxis” to prevent the development of TB because it may take up to eight weeks after exposure for TST conversion, and TB infection can progress to disease during this time.

Preventive treatment of LTBI is generally self-administered. However, in some populations, for example, children, communities with a high prevalence of LTBI and/or high incidence of active TB disease, directly-observed preventive therapy (DOPT) may be considered.

7.2.1 Transmission Risk Assessment

Generally, there is no evidence to support contact tracing related to ground or air transportation except in circumstances involving a highly infectious case and specific environmental exposures (e.g., long, crowded school bus ride in winter or flights more than eight hours long).

The risk of transmission to others can be assessed by reviewing newly diagnosed cases for[12]:

- symptoms suggestive of infectious forms of the disease (e.g., pulmonary or laryngeal TB), specifically chronic cough, sore throat, and hoarseness
- duration of symptoms (e.g., cough) to estimate how long the individual may have been infectious
- information on where the individual has been since his or her symptoms began, especially places where the individual spent the most time
- result of sputum AFB smear and M. tuberculosis cultures; individuals who are smear positive generally are more infectious than those whose sputum smears are negative
- chest X-ray findings: cavitary lesions suggest infectious TB disease
- TB treatment, with degree of infectiousness decreasing rapidly once an appropriate treatment regimen is started.

Transmission is considered to have occurred if:

- a secondary case is identified in any contact
- there are TST converters among the contacts
- the positive TST prevalence rate among contacts is higher than the rate of a similar population without recent exposure
- a child contact less than five years of age is infected without another probable source.
7.2.2 Management of Cross-jurisdictional Contact Investigation

Contact investigations that involve multiple jurisdictional areas (regional health authorities [RHAs], provinces/territories, countries) require collaboration between jurisdictions to ensure contacts are located and evaluated and the outcomes of the evaluation, whenever possible, are reported back to the program that is responsible for overall management of the contact investigation. Typically, for cases within Manitoba, this responsibility will fall to the RHA that reports the index case. Manitoba Health is responsible for any required inter-provincial coordination.

7.3 Outbreak Management

The occurrence of more cases than expected in a given time period in a specific geographic area constitutes an outbreak. If data from a contact investigation or surveillance indicate a potential outbreak, an outbreak investigation should be conducted. In an outbreak investigation, greater emphasis is placed on active case finding, which may involve more contacts than usual requiring chest radiographs and sputum specimen collection for mycobacteriology as part of their assessment.

8. Diagnosis and Key Investigation Overview

8.1 Diagnosis of Active Tuberculosis Disease

- Testing for active TB is indicated in everyone with signs and symptoms of TB or considered to be at high risk of TB disease.
- Every effort should be made to obtain a microbiological diagnosis, which requires demonstration of acid-fast bacilli on smear microscopy and/or culture of \( \textit{M. tuberculosis} \), or requires amplification and detection of MTBC nucleic acid using nucleic acid amplification tests (NAATs).
- Chest radiography is an integral part of the TB diagnosis algorithm but is not specific for the diagnosis of pulmonary TB. Chest radiography cannot provide a conclusive diagnosis on its own and should be followed by microbiological tests for TB disease.
- At least three sputum specimens should be collected for microscopy as well as culture. Where feasible, three sputum specimens (either spontaneous or induced) can be collected on the same day, a minimum of one hour apart. If possible, one sample should be collected in the early morning.

Mycobacterial culture is the most sensitive and the current gold standard method for the detection of active TB disease. The use of culture remains necessary for the definitive diagnosis of smear-negative TB. The benefits of culture include identification, direct sensitivity testing and further use of culture isolates for molecular epidemiology using DNA fingerprinting. Culture can be performed on all specimen types, but typically sputum is used for the diagnosis of respiratory TB.

8.2 Diagnosis of Latent Tuberculosis Infection

The TST is a technique for diagnosing LTBI. A TST should not be used to diagnose active TB disease in adults. The Mantoux technique is the recommended method for administering the TST. This technique involves injecting intradermally a small amount of tuberculin purified protein derived (PPD) from the \( \textit{M. tuberculosis} \) bacteria, then measuring localized induration (not erythema) after 48 to 72 hours. A positive result is generally defined as an area of induration.

For the interpretation of TST results and cut-off points in various risk groups, please refer to the CTS, 7th edition (page 27-A).

The goal of testing for LTBI is to identify individuals who are at increased risk for the development of TB disease and therefore would benefit from treatment of LTBI. Only those who would benefit from treatment should be tested, so a decision to test presupposes a decision to treat if the test is positive.

\[ \text{There is a limited role for the TST as a supplementary test in the diagnosis of TB in children.} \]
In general, testing for LTBI is indicated when, if infected, the risk of development of disease in an individual is increased. For example:

- Possibility of recent infection, most commonly through contact with a patient with a recent diagnosis of infectious respiratory TB.
- Increased risk of reactivation due to impaired immunity. This includes HIV infection and other immunocompromising conditions, diabetes, renal failure, immunosuppressant medication and pulmonary silicosis.
- When there is radiographic evidence of old, healed inactive TB but no history of prior treatment.

A TST should not be done in the following situations:

- Where there have been severe TST reactions in the past, or extensive burns or eczema are present over all possible TST testing sites, greater likelihood of adverse or severe reactions.
- Where there is documented active TB disease or a well-documented history of adequate treatment for LTBI or TB disease in the past—no clinical utility.
- If the individual has a major viral infection.
- If the individual has received a live viral vaccination (e.g., measles, mumps, rubella, varicella, yellow fever) within the past four weeks—may increase the likelihood of false negative TST results.

Some persons may have a false-positive TST and react even though they are not infected with \textit{M. tuberculosis}. Others may not react to TST even though they are infected with the bacteria, exhibiting a false-negative reaction. A second TST, performed 7 to 21 days after the first one, will allow a screening program to determine more reliably whether someone is truly negative. This is called a two-step TST. The second test is only given if the result of the first one is negative.

For further indications for the two-step tuberculin testing, please refer to the CTS, 7th edition (page 28-A).

Special emphasis is given to assessment of those at high risk for progression to active TB disease, such as individuals with HIV, as recommended in Standard 16 of the International Standards for Tuberculosis Care (ISTC). Close contacts at high risk should be provided prompt radiologic and expert clinical assessment, regardless of TST results. Presumptive treatment for LTBI may be recommended for such contacts after active TB disease has been ruled out.

9. Public Health Preventive Measures/Issues

9.1 Key Public Health Messages

Public health has a responsibility to prevent, wherever possible, the cycle of TB transmission in order to protect the health of the public. This is accomplished in descending order of importance through the following key areas:

1. The rapid diagnosis, treatment and isolation of persons with active TB disease, particularly those who are infectious to others.
2. The identification of those who have recently become infected with LTBI through contact with an active TB case.
3. Screening individuals at increased risk for the presence of LTBI, outside of a TB contact investigation.

9.2 Vaccination

\textit{BCG} is a live attenuated vaccine derived from \textit{M. bovis}. It is the only vaccine currently in use against TB.

In Manitoba, routine vaccination of the general population with BCG is not recommended since the risk of exposure to infectious TB disease for this population is low. BCG vaccine administration for health care workers was discontinued in the 1970s. However, BCG vaccination continues to be offered to infants in most First Nations communities in Manitoba (62 out of 64 communities).

\textit{BCG} is also recommended for infants born in Canada who will be moving to and staying for extended periods of time in a country with a high TB incidence where BCG vaccination is still
standard practice, particularly when a program of TST and appropriate chemotherapy is not possible or where the prevalence of drug resistance, especially multi-drug-resistant TB, is high. It is often most practical to recommend vaccination soon after arrival in the high-incidence country.

BCG is not recommended in the case of adults, such as health care workers, planning temporary travel to high-incidence countries due to the absence of evidence for the efficacy of BCG in such situations.[12]

9.3 Screening
Screening involves the application of tests and/or examinations on an apparently asymptomatic cohort of individuals to identify a previously unrecognized state such as disease and/or infection. When the goal of screening is the detection of LTBI, the TST, IGRA, or both may be used.

Populations that should be given a high priority for systematic screening for LTBI include[12]:

- Persons with impaired immunity. This includes HIV infection and other immunosuppressing conditions (e.g., diabetes types 1 and 2 and renal failure).
- Foreign-born persons referred for TB medical surveillance by immigration authorities.
- Foreign-born persons from countries of high TB incidence (>15 AFB smear-positive TB cases per 100,000 population) within two years of arrival in Canada.
- Communities with high rates of LTBI or of active TB disease.
- Homeless and under-housed persons.
- Those at risk of occupational exposure to TB, especially health care workers likely to be exposed to active cases of respiratory TB or who may be at risk of infecting patients.

Symptom review and, if necessary, chest radiography and sputum AFB are the primary tests used when the focus is the identification of undiagnosed respiratory TB disease (in order to treat and render the patient non-infectious). Chest x-rays suggestive of active TB disease should be confirmed with sputum AFB smear (if not already done) and TB culture.

Persons with a history of active TB disease and/or with chest radiographic findings suggestive of past TB who have not received adequate therapy should be given a high priority for systematic diagnostic assessment.

Contacts of individuals with known or presumptive active TB disease are assessed as part of a TB case investigation. Generally, such investigations are conducted by or in conjunction with local public health authorities or the occupational health unit within a facility and would include a symptom review, TST, chest X-ray, and/or sputum collection for AFB, as appropriate.

For most travellers judged to require screening for LTBI, a single post-trip TST or IGRA should be sufficient.[12]

9.3.1 Tuberculin Skin Test
MH provides tuberculin at no charge for contact tracing and case identification and management purposes through public health offices, as approved by regional Medical Officers of Health. It does not currently cover the cost of tuberculin for educational and occupational health purposes, nor for individuals being screened due to the presence of high-risk medical conditions.

Screening for LTBI in persons or groups who are healthy and are at low risk for the development of active TB disease is discouraged.

9.3.2 Interferon Gamma Release Assay
IGRA is an alternative test to the TST. It measures the interferon-gamma production of T-cells (lymphocytes) exposed to TB antigens through infection with MTB. A positive result suggests that latent infection with MTB is likely. IGRA has the advantage of having minimal false-positive results associated with prior BCG vaccination or sensitization by non-TB mycobacteria. In addition, IGRA requires only a single visit by the patient and poses no risk of serious skin reactions.

IGRA is currently not routinely offered in Manitoba. Cadham Provincial Laboratory has limited capacity to perform IGRA.
9.3.3 Baseline Tuberculin Skin Testing (Health Care Facilities)

- At the time of hiring, all prospective health employees without contraindications should have a two-step TST, with the following exceptions:
  - Known prior active TB disease does not require TST.
  - If first-step TST reaction is more than 10 mm, then further TST is not required.
  - Known and documented prior positive TST does not require any further TST.
- Persons found to have positive TST on pre-employment two-step TST (greater than or equal to 10 mm on first or second TST) require chest x-ray and medical evaluation.
- In the event an IGRA is performed as part of pre-employment screening and is positive, chest x-ray and medical evaluation are required.

In TST-positive persons, no further TSTs should be performed. Performing annual chest radiography of asymptomatic TST-positive staff is not recommended. No need to repeat an IGRA if it is done and is positive.

9.3.4 Screening in Long Term Care Facilities

Baseline posterior-anterior and lateral chest radiography is recommended on admission to a long-term care facility (LTCF) for the following populations:

- Persons born in Canada prior to 1955.
- Aboriginal persons.
- People born in or previously residing in countries with high TB incidence.

Baseline TST upon admission is not required for all residents. Facility risk assessment/local epidemiology should inform the decision. For example, were there any active TB cases in the facility within the past 10 years?

9.4 Tuberculosis and Human Immunodeficiency Virus

HIV-infected individuals have the highest estimated risk of development of active TB disease among persons with LTBI. TB is also often the first clinical indication that a person has underlying HIV infection.[10] Thus, all individuals newly diagnosed with active TB disease should be screened for co-infection with HIV. This is consistent with Standard 12 of the ISTC, which recommends that HIV counselling and testing should be considered in persons with TB infection or disease.[15]

A TST should be administered to all persons who are HIV-positive. As 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.

Active TB disease should also be ruled out at the time HIV infection is first diagnosed. For such individuals with LTBI, once active TB disease has been ruled out, INH prophylaxis is recommended for a minimum of nine months. Persons with TB and HIV co-infection respond well to standard anti-TB drugs.

9.5 General Guidelines for Education of Persons with Tuberculosis Disease

1. If possible, find out what the persons with TB and their families know and believe about TB.
2. Reinforce and provide accurate TB information and correct any misconceptions.
3. Use language appropriate to the person’s level of understanding and cultural background. Assess for and use language services/interpreters as appropriate.
4. Go through all educational materials, including visual aids, to promote the messages and reinforce understanding.
5. Provide enough time, encourage participation in the discussion, and ask questions to reinforce key messages.
6. Be sensitive to individual abilities to understand instructions and any other barriers that can hinder the process of effective communication between you, as a service provider, and the person with TB.

7. Summarize the key messages at the end of the appointment.

9.5.1 Education Topics

Educate the persons with TB and their families, including providing any available educational materials, as needed, during the initial assessment, DOT appointments, and routine follow-up visits on the following topics[16]:

a. Medical Diagnosis

In the initial interviews, provide information about TB and the expected treatment plan. During DOT appointments and routine follow up visits, confirm and reinforce understanding of the following key topics/messages:

• The difference between active TB disease and LTBI.
• The signs and symptoms of TB, how TB is transmitted, prevention activities, and treatment.
• TB is both treatable and preventable.
• Importance of adherence to and completion of the prescribed management regimens (investigation, treatment and regular monitoring/ follow up) for complete recovery, cure and minimizing the risk of transmission to others.
• Discuss the different roles of the persons with TB, their families and communities, the public health staff and the prescribing physicians.
• Encourage the persons with TB to contact the health care professional responsible for their treatment and monitoring for issues and problems that arise during treatment and ensure they have the information necessary to do so (e.g., phone number, hours of availability, etc.).
• As treatment nears completion, explain the signs and symptoms of possible relapse or failure and provide encouragement to report them immediately to their primary care providers or health care professionals responsible for their treatment.
• Women of childbearing age should be advised of the importance of avoiding pregnancy during treatment for LTBI or active TB disease.

b. Contact Investigation

When a contact investigation is necessary, discuss with the persons with TB confidentiality and the contact investigation process.

• Stress the importance of providing the care provider with complete and accurate information about the duration of their symptoms (especially cough), the identities of their contacts, and locations where they spent time with other people so appropriate follow-up can be done.
• Reinforce with the client that during the investigation the client’s identity will be kept private by public health officials; however, on occasion it might be necessary to disclose information to a limited number of individuals for the purpose of following up with contacts (e.g., requesting class lists from staff during a school investigation). As well, clients should appreciate that for smaller investigations (e.g., household) it is possible that some contacts may deduce the identity of the case.

c. Isolation

If isolation is necessary, educate the persons with TB about how to take proper precautions.

• Discuss permitted and restricted activities, limiting and excluding visitors, covering the mouth and nose when coughing and sneezing, and using a mask.
• Explain how to dispose of items soiled with potentially infectious material.
• Discuss the requirements for discontinuation of isolation.
• Advise that discontinuation of isolation is contingent upon clinical condition and continued adherence to the treatment regimen.
d. Side Effects and Adverse Reactions
Educate all persons on TB medications about possible side effects and possible adverse reactions to the medications.

e. Adherence
Educate the persons with TB about the importance of treatment and regular monitoring visits, the respective responsibilities of health care providers and of those taking TB medications during treatment, and the potential consequences of not following treatment recommendations. As appropriate, discuss the role that alternative approaches (traditional healers, community elders, etc.) might be able to play in assisting persons with TB to follow treatment recommendations.

10. Contact Information

10.1 Manitoba Health
MH – PHB – Communicable Disease Control (CDC) will receive reports of laboratory-confirmed or clinical cases, be responsible for protocol and policy development, perform surveillance, maintain the TB Registry, and fund and provide overall direction for the provincial TB program. The contact numbers are as follows:

• For surveillance (reporting of cases and TB registry questions): Phone: 204-945-4816, Fax: 204-948-3775

• For CDC (for questions on provincial protocol/policies, funding and general questions about the TB program): Phone: 204-788-6737, Fax: 204-948-2040

You may also visit http://www.gov.mb.ca/health/publichealth/index.html.

10.2 Regional Health Authorities including the Winnipeg Regional Health Authority
Each regional health authority (RHA) is responsible for the provision of public health case and contact management for TB. The contact numbers can be found in http://www.gov.mb.ca/health/publichealth/offices.html.

10.3 Winnipeg Regional Health Authority
The WRHA will provide consultative service for case and contact identification and management to all RHAs as follows:

• Providing consultation for identification, medical management, by WRHA Specialist TB Clinicians for adult and pediatric cases of TB disease, LTBI or request for admission to a WRHA facility
  – For clients 17 years of age or older – Adult Chest Medicine Service, the Health Sciences Centre: page 204-787-2071, 24 hours a day, seven days a week (if non-urgent, fax 204-787-2420 or page 204-787-2071, Monday to Friday).
  – For clients younger than 17 years of age – Pediatric Respiratory Service, Health Sciences Centre: page 204-787-2071, 24 hours a day, seven days a week (if non-urgent, tel. 204-787-4697 or fax 204-787-4503).

• Providing consultation for population and public health case and contact management; TB case transfer (within Manitoba); TB issues involving correctional centres – RHA Population and Public Health: tel. 204-940-2274; fax 204-957-0884.

11. References


