Alberta Public Health Disease Management Guidelines

Tuberculosis

Alberta

This publication is available online at https://open.alberta.ca/publications/tuberculosis-tb

For further information on the use of this guideline contact:

Health.CD@gov.ab.ca

Health and Wellness Promotion Branch

Public Health and Compliance Division

Alberta Health

Tuberculosis | Alberta Health, Government of Alberta
© 2021 Government of Alberta | December 2021

Contents

Case Definition

Confirmed Case

A confirmed case can be either of the following.

Laboratory Confirmed Case

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

Clinically Confirmed Case

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

OR

- Clinical findings compatible with active TB in the absence of bacterial proof. Examples of clinical findings:
  - Chest radiograph changes compatible with active TB, including idiopathic pleurisy with effusion
  - Active non-respiratory TB (meningeal, bone, kidney, peripheral lymph nodes, etc.)
  - Pathologic or post-mortem evidence of active TB

Suspect (Probable) Case

High index of suspicion of TB in whom empiric treatment is being contemplated

Case Classification

New Case

No documented evidence or history of previously active TB

Re-treatment Case[A]

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

AND

- At least six months have passed since the last day of previous treatment[B]

AND

  - Diagnosed with a subsequent episode of TB that meets the confirmed TB 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[C] for six months or longer after the last day of previous treatment[B]

AND

- Diagnosed with a subsequent episode of TB which meets the active TB case definition

Outbreak Case Definition

This definition is provided for reporting purposes.

- Two or more active cases of TB are identified within less than one year of each other, with a known epidemiologic link (e.g., cases reside in same homeless shelter)

OR

- Two or more active cases of TB are identified within less than one year of each other, with a plausible epidemiologic link and with both cases having an isolate with identical genotype (e.g., one case resides in a homeless shelter and one case works in soup kitchen not known to be frequented by homeless shelter resident)

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

[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, do not report as a re-treatment case. Submit an additional *Treatment Outcome of New Active or Re-treatment Tuberculosis Case* form at the end of treatment.

[C] Inactivity for a respiratory TB case is defined as three negative TB smears and cultures with a three-month duration of stability in serial chest radiographs or in the event of overseas screening, the absence of mycobacteriology and a six-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.

Reporting Requirements

Physicians, Health Practitioners and Others

Physicians, health practitioners and others shall notify the Medical Officer of Health (MOH) (or designate by mail, fax or electronic transfer within 48 hours (two days) of identification of:

- any case confirmed by culture, TB Probe or PCR, and
- clinical and suspect cases in whom empiric treatment is being contemplated.

Laboratories

All specimens must be forwarded to the Public Health Laboratory (ProvLab) for smear and culture identification and susceptibility testing.

The ProvLab must report positive smear and culture results by Fastest Means Possible (FMP) (i.e., direct voice communication to the Medical Director of TB Services (geographically dependent)[(D)] and to the First Nations and Inuit Health Branch (FNIHB) MOH if the individual lives in a reserve community.

Lab reports are also to be sent to:

- Attending physician
- The Medical Director of the Edmonton TB Services (geographically dependent)[(D)]

Alberta Health Services

- Alberta Health TB Services is responsible for reporting and follow-up and shall conduct and direct public health staff in investigation activities.
  - Confirmed, clinical and suspect cases that may be cause for community concern (e.g., smear positive case with multiple contacts and high probability of transmission) shall be reported to the Chief Medical Officer of Health (CMOH) (or designate) by FMP.
  - Confirmed cases of multi-drug resistant (MDR) and extremely drug resistant (XDR) TB shall be reported to the CMOH by FMP.
- The MOH (or designate) shall notify the appropriate TB Specialist (AHS Provincial TB Consultant; or Medical Director, Edmonton or Calgary TB Clinics) by FMP of receiving case report for all remaining confirmed, clinical or suspect cases. Notification will include:
  - name of individual (full name and any aliases if known),
  - date of birth,
  - country of birth,
  - personal health number,
  - address of individual,
  - phone number of individual,
  - date of any tests (including tuberculin skin test [TST], AFB specimen collection, radiographic investigations, etc.),
  - any identified high risk medical conditions, and
  - signs and symptoms consistent with active TB.

[(D)] The Medical Director of the Edmonton TB Clinic (or designate) if the individual lives in the Edmonton Zone, or
The Medical Director of the Calgary TB Clinic (or designate) if the individual lives in the Calgary Zone, or
The Alberta Health Services (AHS) TB Medical Consultant (or designate) if the individual lives outside of Calgary/Edmonton Zones or if the individual lives on reserve.

Additional Reporting Requirements

Citizenship and Immigration Canada

- All immigration applicants, refugees or students who plan to remain in the country for more than six months, as well as certain visitors, are required to undergo an immigration medical at their point of application.
  - Those applying from outside of Canada, with evidence of active disease, are denied entry until treatment has been completed.
  - Individuals who do not have active disease but have a past history of TB and those who have evidence of past disease on their chest x-ray are reported to Alberta TB Program. As a condition of entry, these individuals are required to report to or be contacted by a public health authority within at least 30 days of their arrival in Canada.

Epidemiology

Etiology

Mycobacterium tuberculosis is the etiologic agent of TB in humans.[2] The organism is a slightly curved bacillus, 0.2–0.5 micrometres in diameter and approximately two to four micrometres in length.[3] Mycobacteria are aerobic, non-spore forming and non-motile.[2] Growth rates are very slow, with a doubling time of 15–20 hours.[2,4]

Other mycobacteria, including *M. bovis, M. africanum, M. microti, M canetti, M. caprae,* and *M. pinnipedii* are also capable of producing disease in humans,[4] but these organisms are very rare in Alberta and Canada. Generally, the many other environmental mycobacteria found in nature are infrequent causes of disease in humans.[5]

Clinical Presentation

While TB usually presents as respiratory disease,[4] *M. tuberculosis* can cause disease in almost any organ system.[4,6] Clinical presentation varies greatly depending on the site of disease. Symptoms usually begin insidiously and progress over a period of many weeks or months prior to diagnosis.

Systemic symptoms consistent with TB include:

- weight loss,
- fever,
- night sweats, and
- fatigue or weakness.[1]

Symptoms of respiratory TB include:

- persistent cough (of three weeks or more),
- sputum production, sometimes with hemoptysis,
- chest pain (TB pleurisy), and
- shortness of breath.[3]

Symptoms of non-respiratory TB are dependent on the site affected.

- TB of the spine might produce back pain.
- TB of the kidney may cause flank pain, frequency and dysuria.
- TB of the lymph nodes can result in lymphadenopathy (which may be painful if enlargement occurs rapidly).[7]

The majority of persons with extrapulmonary TB have concurrent pulmonary TB.[7]

Diagnosis

Definitive diagnosis of TB disease is made by isolation of the *M. tuberculosis* (MTB) in culture.

- Culture for MTB is considered the gold standard in diagnosis.[2,4,8] Because *M. tuberculosis* grows slowly, it may take up to seven weeks[1] to show definitive culture positive results.
- The use of the BACTEC system (i.e., a liquid culture system) allows for more rapid growth of bacteria of the *M. tuberculosis* complex.[4]
- DNA probes are used to differentiate *M. tuberculosis* complex from environmental mycobacteria. Results can be available within two hours, but the probe can only be used once positive cultures have been identified.[8]

Because it is not always possible to culture *M. tuberculosis,* a clinical diagnosis of TB is made in approximately 15–20% of cases on the basis of appropriate clinical and/or radiological and/or pathological presentation as well as treatment response.[8]

Treatment

Reference 11 applies to this section.

The goals for treatment of active TB disease benefit the individual with TB and the community in which they live by:

- relieving symptoms,
- preventing further transmission of TB,
- preventing development of drug resistance, and
- achieving lifetime cure of the disease for the treated individual.

Curing TB can be achieved in a variety of ways, all requiring the use of medications to which the organism is susceptible. Anti-TB drugs are always given in combination for a period of several months, and in general follow a two-phase regimen.

During the initial (intensive) phase (also called front-end-loading), four or five[1] anti-TB medications are used in combination to:

- relieve symptoms,
- rapidly reduce the number of MTB organisms present and interrupt transmission, and
- prevent the development of drug resistance.

The continuation phase is aimed at eliminating any remaining MTB organisms and ensuring lifetime cure (no relapse). This phase typically includes fewer medications than the initial phase, and is usually given on an intermittent (twice-weekly) basis for an additional four to seven months. Longer courses of treatment may be required for some forms of TB disease, such as those involving the central nervous system, miliary or disseminated TB, and bone and joint TB, or if standard first-line TB medication can not be used.

Patients receiving treatment should be monitored for drug side effects and response to treatment according to prescribed protocols.

There are some instances where special considerations need to be taken into account for TB treatment. These include pregnancy, breastfeeding, pediatric individuals, people living with HIV, renal failure, concurrent hepatic disease/risk, nonrespiratory TB, and cases of drug resistant TB (DR-TB).

Directly observed therapy (DOT) is the most effective way to monitor treatment adherence.[7] A trained health care worker or other designated individual (excluding a family member) provides the prescribed anti-TB drugs and watches the individual swallow every dose. Studies show that 86–90% of TB cases receiving DOT complete therapy, compared to 61% for those on self-administered therapy.[17] In Alberta, all active TB cases receive DOT. This:

- encourages individuals to finish TB treatment as quickly as possible, without unnecessary interruptions,
- decreases in the risk of drug-resistance resulting from erratic or incomplete treatment,
- decreases the chances of treatment failure and relapse, and
- helps prevent TB from spreading to others.

Reservoir

The reservoir for *M. tuberculosis* is humans.[8] The reservoir for *M. bovis* is animals.[6]

Transmission

Infection is transmitted almost exclusively by inhalation of the tubercle bacillus in droplet form.[4] Droplet nuclei are created by individuals through coughing, sneezing, singing and other forceful expiratory efforts.[4] Duration of exposure needed for transmission is usually prolonged, but in highly infectious individuals, duration can be as short as a few seconds or a few minutes.[8] Person-to-person transmission of *M. tuberculosis* is determined by certain characteristics of the source-case and of the person exposed to the source-person, and by the environment in which the exposure takes place. The virulence of the infecting strain of *M. tuberculosis* might also be a determining factor for transmission.[9] The usual route of transmission of *M. bovis* is in unpasteurized milk from a diseased animal.[6]

Incubation Period

Reference 8 applies to this section.

Tuberculin skin test (TST) conversion occurs within eight weeks of exposure and infection. Infection may persist for a lifetime as latent infection. The risk of progression from infection to disease is greatest within two years after infection (5% in otherwise healthy individuals). There is a further 5% risk of progression to disease over an individual's lifetime. Age less than five years and certain medical conditions will increase this risk substantially (see Host Susceptibility).

Period of Communicability

As long as viable tubercle bacilli are being aerosolized, untreated or inadequately treated individuals with active respiratory disease are contagious. Adequate treatment with drugs renders most individuals non-infectious within a matter of weeks.

Young children with active pulmonary TB are often not infectious.[6]

Non-respiratory TB is not usually infectious.[6]

Host Susceptibility

Individuals are most susceptible if they have not had prior exposure to *M. tuberculosis*.[6]

Prior infection in immunocompetent individuals provides some protection against future infections, especially if prior infection gave rise to TB disease.[10]

Several medical conditions place individuals, once infected, at high risk of disease. These include:

- transplantation,
- silicosis,
- chronic renal failure requiring hemodialysis,
- carcinoma of the head and neck,
- abnormal chest radiograph – fibronodular disease,
- recent TB infection (≤ two years),[7]
- steroid use,
- hematological malignancies,[11] and
- HIV/AIDS – dual infection with HIV is the most important risk factor for the development of disease. The annual risk of active disease varies from 3–13%; risk increases as the CD4 count falls.

Incidence

General

Currently, TB is the second highest cause of death from an infectious disease worldwide,[12] after HIV/AIDS, and is the top killer of people infected with HIV.[4,8,12]

Globally, incidence rates of TB are increasing.[13] In 1993, the World Health Organization declared TB a global emergency.[14] In 2008, the global rate was estimated at 139 cases per 100,000 population, with 9.4 million new cases reported.[13]

Many developing countries experience great difficulty with treatment and control of the disease as a result of inadequate public health and TB control programs, widespread poverty and the spread of the HIV epidemic.[4]

The emergence of drug resistant strains is becoming an increasingly worrisome problem worldwide.[8,15,16] It represents a problem not only in treatment of the active case, but in their contacts as well.[16]

For more information see the World Health Organization website.

Canada

Canada continues to have one of the lowest reported rates of TB in the world.[13] Although TB is relatively uncommon among the general population, it continues to be a significant communicable disease of concern among certain higher-risk groups, including Aboriginal people, foreign-born residents from countries with a high prevalence of TB[8], disadvantaged inner-city populations, and those with HIV infection.[3] In 2008, the Canadian TB rate was 4.8 per 100,000.[17]

For more information see the Government of Canada website.

Alberta

Since 1993, Alberta's annual rates for active disease have consistently been lower than the national rates. In 2007, the Alberta rate was 3.2 per 100,000; in 2008, the rate was 4.7 per 100,000.[17]

As immigration from TB endemic countries increases, the rate in Alberta can be expected to increase.

For more information see the Alberta Health Interactive Health Data Application.

Public Health Management

Key Investigation

Reference 11 applies to this section.

Assess risk of transmission to others by reviewing newly diagnosed cases, specifically for the following.

- Symptoms which may indicate pulmonary or laryngeal TB (with aerosolization) – specifically cough or hoarseness: pulmonary and laryngeal TB are infectious, but nonrespiratory TB is generally not.
- Duration of symptoms, especially cough – this will assist in determining how long the individual has been infectious.
- Places that the individual has been since the symptoms began, especially those places where they spent the most time, including information about the characteristics of each place such as size, ventilation, and length of time spent there.
- There is more risk in a small, enclosed, poorly ventilated room than a large, well-ventilated one.
- Contacts – names, approximate date of birth, addresses and telephone numbers of individuals they have spent time within each of the places identified, especially those they had daily contact with. Very high-risk contacts include children less than five years of age, those with immunocompromising conditions, and those with symptoms suggestive of active TB disease (potential source or secondary cases).
- Consultation with Alberta TB Program or the appropriate TB Clinic will give further information about the risk of transmission.
- Results of sputum smear and cultures for AFB – individuals whose sputum is smear-positive are more infectious than those whose sputum smears are negative.
- Chest radiograph findings – cavitary lesions suggest highly infectious disease.
- TB treatment – degree of infectiousness decreases rapidly once an appropriate treatment regime is started.
- The susceptibility of the contact – individuals who have had no prior exposure to TB are more susceptible to infection.

Management of a Case

Reference 11 applies to this section.

Management of active TB disease in Alberta involves a partnership between the patient, their physician, the zone MOH and/or FNIHB MOH and Alberta TB Program or Edmonton TB Clinic or Calgary TB Clinic.

- Alberta TB Program provides AH funded medications at no cost to all patients in the province; the program also monitors compliance with and response to treatment.
- Patients who are smear positive and/or culture positive respiratory TB cases are placed into respiratory isolation.
- All individuals with newly diagnosed TB should undergo HIV testing. Ideally, HIV testing should be performed at the time of diagnosis of TB or during the period of activity of TB.
- AHS maintains a registry of all individuals who have been diagnosed with active TB as well as those with latent TB infection (LTBI).
- In accordance with the *Public Health Act*, recalcitrant patients can be detained for treatment of active, infectious disease.

Management of Contacts

Reference 11 applies to this section.

- Whenever an individual is found to have active infectious TB, a contact investigation is initiated to determine whether others may have active disease or are infected without disease. Those who are infected without disease should be offered preventive therapy.

- Contact investigation begins with contacts found to be at high risk for infection (e.g., close household or close non-household contacts) and/or high risk for progression to disease (e.g., children less than five years of age, immune-suppressed contacts) and is expanded according to need (using concentric circle approach). The initial investigation consists of an interview with contacts to determine their risk of infection.
- At present the major tool for diagnosis of TB infection is the TST, consisting of the intradermal injection of a small amount of purified protein derived from *M. tuberculosis* bacilli. In most cases, infected individuals will show significant localized induration at the test site within 48–72 hours.
- TST is performed on contacts with no previous documentation of TB or significant reaction to TST in the past. It is performed as soon as possible after contact. Conversion of TST from negative to positive can take up to eight weeks after infection occurred; therefore, if initial test is done within eight weeks of last exposure to an infectious case and is not found to be positive, a second test should be performed at least eight weeks after the last exposure occurred.
- If the result of either test is significant, further investigation with chest radiographs and sputum investigation are necessary.
  - Young children (under five years of age) require clinical and radiographic investigation regardless of the TST results. Consultation with a TB specialist is critical.
  - Active TB in young children signals a recent infection and indicates the probability of an undiagnosed case amongst the child's close contacts. Therefore, when disease is diagnosed in children, contact investigation attempts to identify the source case.
- Ultimately, the TST may be replaced by or used in conjunction with an interferon gamma release assay (IGRA), a blood test assay that detects the presence of T-lymphocytes that have previously been exposed to *M. tuberculosis* antigens. These assays offer advantages over the TST; they appear to minimize false-positive test results due to vaccination with Bacille Calmette-Guérin (BCG), require only a single visit by the patient and pose no risk of serious skin or allergic reactions.[7]

Preventive Measures

Reference 11 applies to this section.

- All individuals who are admitted to active treatment facilities (e.g., acute care hospitals) with suspected or confirmed infectious TB must be isolated until proven to be non-infectious.
- Prevention efforts are directed at ensuring that once an individual has been infected with the tubercle bacillus, the infection (LTBI) does not progress to disease. This is achieved through the use of TB medication.
- Without intervention, approximately 5% of newly infected individuals will develop active TB within two years. If the newly infected individual is a child or is immunocompromised, this percentage is much higher.
- Medications used to treat LTBI are the same as those used to treat TB disease, but the use of a single drug is acceptable practice, because the bacterial population is much lower in infection compared to disease. Treatment regimens may take anywhere from four to nine months to complete, depending on the drug chosen.
- The usage of BCG vaccine is limited to select population groups in only a few areas of Canada at this time. In many TB endemic countries it is still used extensively. It may interfere with the ability to interpret the TST.
- Individuals at higher risk for infection (i.e., health care workers or travellers with direct patient contact in high-risk facilities or performing high-risk procedures) receive routine serial tuberculin skin testing to ensure early diagnosis of latent infection and the provision of treatment.

Appendix 1: Revision History

Revision Date	Document Section	Description of Revision
November 2021	General	• Updated Template • Etiology, Clinical Presentation, Diagnosis and Treatment sections moved to Epidemiology • Key Investigation section moved to Public Health Management (formerly called Control) • Updated web links
	Reporting Requirements	• Updated to reflect current processes
	Incidence	• Surveillance weblinks added

References

(1) Dr.Richard Long, TB Medical Consultant. Personal Communication. 2010.

(2) Todar K. Mycobacterium tuberculosis and tuberculosis. Textbook of Bacteriology 2008

(3) Dyer CA. Tuberculosis. Santa Barbara, CA: Greenwood Press; 2010.

(4) Fitzgerald DW, Sterling TR, Haas DW. Mycobacterium tuberculosis. In: Mandell GL, Bennett JE, Dolin D, editors. Mandell, Douglas and Bennett's principles and practice of infectious diseases. 7th ed. Phildelphia, PA: Churchill Livingston; 2010. p. 3129-63.

(5) Tuberculosis. In: Pickering LK, Baker CJ, Kimberlin CW, Long SS, editors. 28th ed. ed. Elk Grove, IL: American Academy of Pediatrics; 2009. p. 680-701.

(6) Tuberculosis. In: Heymann DL, editor. 19th ed. Washington, DC: American Public Health Association; 2008.

(7) Tuberculosis Component of Techinical Instructions for the Medical Examination of Aliens in the United States. U S Department of Health & Human Services 2008 May;

(8) Public Health Agency of Canada. Canadian Tuberculosis Standards. 2007. 6-30-2010.

(9) Controlling Tuberculosis in the United States; Recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America. MMWR 2005 November 4. 54(RR12):1-81.

(10) Watt CJ, Hosseini SM, Lonnroth K, Williams BG, Dye C. The global epidemiology of tuberculosis. In: Schaaf HS, Zumla A, editors. Tuberculosis: a comprehensive clinical reference.Edinburgh, UK: Elsevier Sanders; 2009. p. 17-27.

(11) Alberta Health and Wellness. Tuberculosis Prevention and Control Guidelines for Alberta. Government of Alberta Website 2010 June;Available from:

(12) Young DB, Perkins MD, Duncan K, Barry CE I. Confronting the scientific obstacles to global control of tuberculosis. J Clin Invest 2008 Apr;118(4):1255-65.

(13) World Health Organization. Global Tuberculosis Control: A short Update to the 2009 Report. World Health Organization 2009;Available from:

(14) National Foundation for Infectious Diseases. Tuberculosis: A Global Emergency. National Foundation for Infectious Diseases 2006;

(15) Shah NS, Wright A, Bai GH, et al. Worldwide emergence of extensively drug-resistant tuberculosis. Emerg Infect Dis 2007 Mar;13(3):380-7.

(16) World Health Organization. Guidelines for the Programmatic Management of Drug-Resistant Tuberculosis. World Health Organization 2008;

(17) Public Health Agency of Canada. Tuberculosis in Canada: 2008 Pre-release. Public Health Agency of Canada website 2010;