Tuberculosis

Manitoba Health
Public Health

Communicable Disease Control Unit

Case Definition

Confirmed case: *Mycobacterium tuberculosis* complex [i.e., *M. tuberculosis, M. bovis* (excluding BCG strain) or *M. africanum*] demonstrated on culture.

Clinical case: Clinically compatible illness (see below), and a positive tuberculin reaction (see below), even though bacteriologic proof of infection has not been demonstrated. Relevant signs could include:

- chest x-ray change compatible with active tuberculosis, including idiopathic pleurisy with effusion;
- clinically active non-respiratory TB (meningeal, bone, kidney, etc.);
- pathologic or post-mortem evidence of active TB.

Both confirmed and clinical cases are counted for surveillance purposes.

Reporting Requirements

All positive cultures and all clinical and suspected cases of tuberculosis are reportable to the Central Tuberculosis Registry, Health Sciences Centre. The Registry reports all cases of positive *M. tuberculosis* complex cultures, as well as all clinical cases of tuberculosis, to Manitoba Health.

Clinical Presentation/Natural History

Primary Infection: More than 90% of cases are asymptomatic at the time of primary infection and can be identified only through conversion of the tuberculin skin test from negative to positive. The majority have normal chest x-rays, but fibrotic lesions may be visible radiographically. In the past, primary infection occurred almost entirely in childhood, but as the incidence of tuberculosis has declined, primary tuberculosis is also being seen in adults.

Pulmonary Tuberculosis (post-primary or adult-type): The symptoms usually begin insidiously and progress over a period of weeks or months. Constitutional symptoms such as anorexia, weight loss, night sweats and low-grade fever are often prominent. Most cases have a cough and produce sputum; hemoptysis is frequent. Chest x-rays frequently are highly suggestive of the diagnosis. The tuberculin skin test is positive in about 90% of cases with reactivation tuberculosis. Cases with advanced disease are often malnourished and may be anergic and test negative. Diagnosis of pulmonary tuberculosis can be confirmed in most cases by examination of sputum by microscopy and culture.

Miliary Tuberculosis (disseminated disease): Widespread dissemination of bacilli occurs when the bacilli enter the bloodstream during the initial stages of primary infection, before the host immune system has fully responded. Non-specific symptoms of fever, anorexia, weight loss and weakness are common, frequently leading to a delay or lack of diagnosis, with a high fatality rate. Diagnosis is difficult, and a high index of suspicion with institution of therapy before a firm diagnosis may be required to prevent morbidity and death.

Tuberculous meningitis: This is rare but extremely serious, associated with devastating complications and/or death. It is the most rapidly progressive form of tuberculosis. Fifty per cent of cases are ill for less than two weeks before diagnosis. The clinical course is characterized by headache, fever, meningismus, cranial nerve palsies, seizures, coma and death. Cerebrospinal fluid pressure is usually abnormal, with increased lymphocytes, high protein and low glucose. Direct microscopy is positive in 25% and cultures in 75% of cases. Therapy should be initiated on suspicion of the diagnosis.

Extra-pulmonary Tuberculosis: Almost all forms of tuberculosis involve regional lymphatics and nodes. Tuberculous lymphadenitis is the most common form of extra-pulmonary tuberculosis. Cervical nodes are the most commonly affected, but any node or group of nodes can be involved. Patients are usually afebrile, and show slowly enlarging, painless mass lesions. Tuberculous nodes can become fluctuant and drain through skin or to contiguous tissues. Other common extra-pulmonary sites are the genitourinary system, bones and joints.

Etiology

The bacterium *Mycobacterium tuberculosis*, or *M. tuberculosis* complex.

Epidemiology

Reservoir: Humans

Transmission: Transmission of pulmonary tuberculosis is person-to-person via inhalation of bacteria, and requires two essential elements:

- susceptible persons; and
- exposure to a case of tuberculosis whose sputum is positive on direct microscopy.

Characteristics that enhance transmission include:

- disease in the lungs, airways or larynx;
- presence of cough or other forceful expiratory measure;
- presence of acid-fast bacilli in the sputum;
- failure of the person to cover the mouth and nose when coughing;
- a procedure that can induce coughing or cause aerosolization of tubercle bacilli (e.g., sputum induction, bronchoscopy).

Environmental factors that enhance transmission include:

- exposure of susceptible persons to an infectious person in relatively small enclosed spaces;
- inadequate ventilation that results in insufficient dilution and/or removal of infectious droplet nuclei;
- recirculation of air containing infectious droplet nuclei.

Occurrence:

General: Worldwide. Numerous industrialized countries, including Canada, have shown a decline in incidence of morbidity and mortality for many years. However, rates in many countries are now stabilizing or, in some cases, even rising again. The risk of active disease in recently infected persons is maximal (up to 5%) during the first years after infection. The risk of developing active tuberculosis is highest in children under age five, but a second peak occurs in early adulthood, and another in the elderly.

Manitoba: Approximately 100 new cases of tuberculosis are reported each year, although an increase in incidence has been observed recently. In 1999, 123 cases of tuberculosis were reported in Manitoba, a rate of 10.7 per 100,000. Most cases of newly active tuberculosis arise from defined risk groups, such as the following:

- aboriginal persons;
- persons living with individuals diagnosed with active tuberculosis;
- persons who previously have had active tuberculosis but received inadequate chemotherapy;
- persons with presumed inactive tuberculosis;
- immigrants from countries where tuberculosis is common;
- substance abusers;
- homeless people;
- residents of extended care homes;
- staff and inmates of correctional institutions;

- pre-school and school children in high-risk communities;
- health care workers, including those dealing with substance abusers;
- those with cellular immunosuppression: HIV infection, diabetes mellitus, certain malignancies, and those receiving immunosuppressive medications, glucocorticosteroids or radiotherapy.

Incubation Period: Four to 12 weeks. While the subsequent risk of progressive pulmonary or extra-pulmonary disease is greatest within the first year or two after infection, tuberculosis may persist for a lifetime as a latent infection.

Susceptibility and Resistance: The risk of infection with the tubercle bacillus is directly related to the degree of exposure and does not appear to be related to genetic or other host factors. The most hazardous period for development of clinical disease is six to 12 months after infection. The risk of developing disease is highest in children under three years old, lowest in later childhood, and high again among adolescents, young adults, the very old and the immunocompromised. Reactivation of long-latent infections accounts for a large proportion of cases of clinical disease in older people.

Period of Communicability: As long as infectious tubercle bacilli are being discharged in the sputum. Untreated or inadequately treated persons may be sputum-positive for years. Effective antimicrobial therapy reduces communicability promptly (within a few weeks). Extra-pulmonary tuberculosis is generally not communicable. Children with active pulmonary tuberculosis are often not contagious because their lesions are limited, output of bacilli is small and cough may be minimal or non-existent.

Diagnosis

The medical history may suggest tuberculosis but it leaves the specific diagnosis uncertain. A history of contact with a case of tuberculosis may also suggest the diagnosis. Diagnosis, however, must be based on the identification of *Mycobacterium tuberculosis* from the patient. The demonstration of caseating granulomata suggests, but does not establish, a diagnosis of tuberculosis. The presence of acid-fast organisms in stained tissue is an indicator but not a diagnostic certainty.

- **Absolute diagnosis:** Identification of *Mycobacterium tuberculosis* by culture or DNA probe. This constitutes a confirmed case.
- **Probable diagnosis:** Clinically compatible illness with acid-fast organisms seen on the stained smear of secretions or tissue (sputum, gastric aspirate or other). This constitutes a clinical case.
- **Possible diagnosis:** Positive tuberculin reaction, with clinically compatible illness, x-ray and other laboratory tests compatible with the diagnosis. This also constitutes a clinical case.

Tuberculin Testing: The tuberculin test (Mantoux) is an intradermal skin test, using PPD (bioequivalent to 5 TU PPD-S) and is the most accurate of all forms of tuberculin tests. A positive skin test is generally defined as an area of induration of 10 mm or more at 48 to 72 hours. Erythema is not considered as evidence of a positive skin test and should be ignored.

A positive tuberculin skin test does not necessarily indicate the presence of active tuberculosis at the time of the test, but it is evidence of invasion of body tissues by the tubercle bacillus. In addition, infection with certain non-tubercle bacilli (any mycabacterium) may cause a positive skin test.

- 1-4 mm induration is considered a negative reaction, reflecting lack of tuberculin sensitivity.
- 5 mm if induration or more is considered a positive reaction in an immunosuppressed person or in persons with HIV infection. It may also be considered positive in recent close contacts of someone with active pulmonary tuberculosis, or individuals with a chest X-ray with apical fibrotic lesions suggestive of old healed tuberculosis.
- 10 mm of induration or more is considered a positive reaction and is of particular significance in the following: immigrants from countries

where tuberculosis is prevalent; injection drug users; the homeless; residents of nursing homes and correctional institutions; and persons with other diseases that have been associated with a higher risk of tuberculosis.

- If there is a history of BCG vaccination, the skin test reaction should generally be greater than 15 mm to be called positive. If there is a history of recent exposure, or if a person is immunosuppressed, a reaction less than 15 mm might also be considered positive.

Tuberculin sensitivity may vary from time-to-time, and from person-to-person. However, provided that proper testing material is used, and proper procedures are followed, a positive skin test can be elicited in the majority of patients with active tuberculosis. Negative or small reactions where anergy is suspected must be interpreted with caution.

Two-Step Tuberculin Testing: Over time, persons with a positive tuberculin skin test may lose the ability to develop a positive response because of memory loss in the immune system. Performing a two-step tuberculin test reduces the risk of falsely interpreting a positive response as a "new" positive response during subsequent skin testing. While skin testing does not "teach" the immune system to develop a positive response, it can cause the immune system to recover memory. This process is called boosting, and can generally be demonstrated seven days after the first skin test.

A second tuberculin skin test, performed seven to 21 days after the first skin test, will allow a screening program to determine more reliably whether someone is truly negative. If the second test is not administered until several months or years later and is positive, it is difficult to determine if the person has boosted, or has become infected during the intervening period. In the latter situation, such a person would probably be considered to have converted and would be offered preventive therapy. An investigation would also be initiated to identify the source of infection. These actions would not be necessary if the individual had received a two-step test.

Two-step tuberculin skin testing is therefore recommended, and should be offered in preference to a single skin testing, in the following situations (note that the second test is only given if the first one is negative):

- residents on admission to long-term care facilities;
- persons commencing serial skin testing programs, such as in occupational settings (hospitals, correctional services, etc.);
- where skin testing is clinically indicated, and the patient is over the age of 55 years, or is known or thought to have been previously vaccinated with BCG (for example, during an investigation of contacts of a tuberculosis case).

Laboratory Identification of *Mycobacterium tuberculosis*:

- Several laboratories in Manitoba are equipped to identify *Mycobacterium tuberculosis.* Positive results are reported to the Central Tuberculosis Registry.
- Persons should be asked to produce a morning sputum and to raise it from below the larynx. When satisfactory sputum is not available, gastric washing or tracheal secretions may be used. Gastric lavage must be carried out in the early-morning after an overnight fast. If genitourinary tuberculosis is suspected, early morning urine specimens should be examined.
- In the laboratory, direct smears are prepared and stained with Ziehl-Nielsen stains. Smears are positive when there are at least about 100,000 bacilli per ml of sputum. Cultures take two to eight weeks to grow. They are positive when there are a minimum of 100-500 mycobacteria per ml of sputum. In practice, 30-40% of smear-negative specimens may turn out to be culture-positive. Cultures also enable the laboratory to distinguish tuberculous from non-tuberculous mycobacteria and perform drug sensitivity studies.

- DNA fingerprinting is another molecular biology tool that can track persons who share a "common" strain of *M. tuberculosis*. One very sensitive molecular tool used for fingerprinting is RFLP (restriction fragment length polymorphism). DNA fingerprinting is very valuable in tracing down epidemics or outbreaks of particularly pathogenic organisms, such as multiple drug-resistant strains.

Key Investigations

- Appropriate specimen collection.
- Identification and screening of contacts.

Control

Management of Cases:

- Effective chemotherapy taken over an adequate period of time is the primary treatment of all forms of tuberculosis. The objective of tuberculosis therapy is to achieve lifetime control of the disease. Factors such as rest, diet and climate are relatively unimportant in determining the clinical outcome.
- Chemotherapy of tuberculosis is a two-phase process, the first aimed at rapid reduction in the number of tubercle bacilli in the body and the second at maintaining treatment long enough to eliminate the smaller number of persisting organisms. Treatment consists of a combination of three (sometimes four) drugs for the initial phase, and two drugs in the continuation phase, for a total of six months. Respiratory isolation procedures are important in the early phases of treatment.
- A major issue in tuberculosis treatment is failure to complete the prescribed regimen of drugs. A flexible system of delivery can reduce patient non-compliance. Directly observed therapy (DOT) on a daily or intermittent regimen is recommended for all patients being treated for tuberculosis. A detailed description of drug therapy, approved for use in Manitoba, can be found in *Tuberculosis – A Handbook for Public Health Nurses and Other Interested Health Care Workers*, available from Manitoba Health and the Manitoba Lung Association (see Additional Resources).
- Referral is made to the Tuberculosis Control Program, Health Sciences Centre, in Winnipeg, for tuberculosis assessment and management. Appropriate laboratory and radiologic investigations are available, as well as a patient and family educator.
- **Six-month regimen for active tuberculosis:** Six months of directly observed therapy is the treatment regimen used in Manitoba. The initial phase consists of four drugs provided daily for two weeks (INH, rifampin, pyrazinamide, and streptomycin or ethambutol). This is followed by six weeks of twice-weekly therapy with the same four drugs, and finally 18 weeks of twice-weekly therapy with two drugs (INH and rifampin).
- **Tuberculosis and HIV/AIDS:** A diagnosis of tuberculosis should be considered in persons with known or possible HIV infection. Conversely, a diagnosis of HIV infection should be considered in persons with tuberculosis infection or disease. A Mantoux skin test should be administered to all persons who are HIV positive. Immunosuppression may cause false negative reactions, so a reaction of 5 mm or more induration should be considered indicative of tuberculosis infection. Active disease should also be ruled out. For infection without active disease, INH prophylaxis is recommended for a minimum of 12 months. Persons with tuberculosis and HIV infection respond well to standard anti-tuberculosis drugs. However, treatment should be given for a minimum of nine months, and for at least six months beyond documented culture conversion, as evidenced by three negative sputum cultures.

Management of Contacts:

- All persons with whom the diagnosed client (index case) has been in contact, whether at

home, at work, or socially for a close and prolonged period of time since the index case first developed the symptoms of tuberculosis. Such symptoms include development of cough, loss of weight and hemoptysis.

- Issues to consider in prioritizing contacts include:
  - the young are at greatest risk of the infection and the development of disease, and should have high priority in contact investigation;
  - the risk of transmission of infection is greatest from cases with cavitary, sputum smear-positive pulmonary tuberculosis, who are coughing;
  - transmission of infection is most frequent in closed, warm, dry, non-ventilated environments;
  - brief or intermittent exposure is less risky, while prolonged continuous exposure carries greater risk.
- When a diagnosis of tuberculosis is made, the Tuberculosis Control Program works with the local public health jursidiction to prepare a list of contacts to be investigated. Public health staff should be alert to contacts found in the community who have not been previously considered.
- Procedures for dealing with contacts vary, depending upon the bacillary status of the patient's sputum, the site of disease and the perceived degree of risk of developing tuberculosis:

a) **Index case – pulmonary tuberculosis, active, bacilli on smear:** This person is potentially infectious, since the route of transmission is airborne. Family and work friends who have shared the patient's breathing space are at risk. The following procedures should be followed once contacts are identified and located:

  - Tuberculin skin test and chest x-ray. The tuberculin test results and chest x-rays should be sent to the Tuberculosis Control Program.
  - If the chest x-ray is positive for tuberculosis, standard treatment is provided (see above).
  - If the tuberculin test is positive and the chest x-ray negative, either INH chemoprophylaxis is given (six-month course), or the contact is followed and the chest x-ray repeated in three months time. Children under the age of 12 years may be treated for nine months with INH prophylaxis.
  - If the tuberculin test and chest x-ray are both negative, the skin test is repeated in three months.
  - Susceptible contacts are sometimes considered for INH chemoprophylaxis for three months even if their skin test is negative.

b) **Index case – pulmonary tuberculosis, active, smear negative, culture positive:** In this situation, a tuberculin skin test and chest x-ray are performed on close contacts. If cough is a predominant symptom, the circle is widened to more casual contacts.

c) **Index case – primary tuberculosis, pleural effusion, or tuberculous meningitis in children:** In this situation, a tuberculin skin test and chest x-ray are performed on all close contacts, since the objective is to find out how the case was infected.

d) **Index case – extra-pulmonary tuberculosis (lymph node, kidney, bone, etc.):** These forms of tuberculosis are not usually infectious and need not be investigated except in extraordinary circumstances.

- Results of contact follow-up testing should to be completed within thirty days following the initial diagnosis and sent to the Tuberculosis Control Program. Completed copies of contact lists will be returned to public health staff.
- **Field Admission to the Tuberculosis Control Program:** It is often possible for contacts to be placed on a nine-month regimen of INH chemoprophylaxis based upon tuberculin skin testing and chest x-rays performed in the community, without attending the out-patient clinic at the Tuberculosis Control Program. In this case, a supply of drugs will be sent to the local public health jurisdiction and monitored by the Tuberculosis Control Program. The local public health jurisdiction will develop a plan of treatment in consultation with the patient and his/her family. After three months of medication, the patient will be required to have a chest x-ray repeated, which should be submitted to the Tuberculosis Control Program. After treatment is completed, another chest x-ray is performed. If follow-up chest x-rays are negative, the patient will be required to have additional x-rays at twelve months and twenty-four months after completion of his/her nine-month drug program. Assuming that these chest x-rays are negative, the patient can be discharged from public health supervision.

Management of Outbreaks:

- See measures discussed above under **Management of Contacts**.

Preventive Measures:

- Improve socio-economic conditions, by such measures as reducing over-crowding and poverty.
- Prophylactic use of INH for persons at increased risk of disease, e.g., tuberculin converters.
- BCG Vaccination. The risk of infection in the general population is low and vaccination is generally not recommended. Vaccination in Manitoba is recommended by Medical Services Branch for aboriginal newborns in its jurisdiction.
- **Screening of health care workers in health facilities:** The following policy is adapted from Health Canada: Guidelines for Preventing the Transmission of Tuberculosis in Canadian Health Care Facilities and Other Institutional Settings, *Canadian Communicable Disease Report 1996*, Volume 22, Supplement 1.

  These recommendations for tuberculin screening of health care workers apply to health care workers in health facilities, and are dependent upon the nature of the facility in which they work (high or low risk) and their activity risk (high, intermediate or low). See the definitions provided below for high- and low-risk facilities, and for activity risk. It is recommended that health care workers without a previously documented tuberculin test result working in high-risk health care facilities be assessed for their tuberculosis (TB) infection status upon employment, using a two-step tuberculin test, if they are at high or intermediate activity risks. Health care workers working in high-risk facilities who are at low activity risk need not be screened upon employment, nor any health care workers working in low-risk facilities. For those employees who are screened upon employment, their test results should be on record; employees who should have been tested upon employment but were not, should be tested subsequently at the earliest convenient time. Documentation should indicate whether the health care worker is tuberculin test negative or positive (including the size of the reaction in millimetres), and whether the health care worker has received therapy for latent or inactive TB, or treatment for active TB.

Health care workers who are screened upon employment and have a negative tuberculin test should undergo subsequent screening as outlined below, using a one-step tuberculin test. Health care workers who have previously been treated for TB, given preventive therapy for TB, or have a documented positive tuberculin test should not undergo further tuberculin testing. They should be educated regarding the symptoms of active TB and instructed to seek medical evaluation as soon as possible if these symptoms develop.

Routine screening on employment is not recommended for health care workers who are not based in health care facilities, such as community health nurses. Post-exposure tuberculin testing may be indicated following significant exposures.

Frequency of ongoing health care worker tuberculin screening for TB

Activity risk	Health care facility risk	
	High*	**Low****
High[1]	Every six months	Post-exposure
Intermediate[2]	Annually	Post-exposure
Low[3]	Post-exposure	Post-exposure

* *High-risk facility:* Six or more individuals with TB seen annually, or any facility with a ratio of health care workers to TB cases of 100 or more.

** *Low-risk facility:* Less than six individuals seen annually, or any facility with a ratio of health care workers to TB cases of less than 100.

1 *High-risk activities*: Workers involved in cough-inducing procedures, autopsy, morbid anatomy and pathology examinations, bronchoscopy and TB-related laboratory procedures.

2 *Intermediate-risk activities:* Workers with direct patient contact on units which may have patients with active TB.

3 *Low-activities:* Workers with minimal patient contact (e.g., medical records, administration), or with direct patient contact on units which rarely have patients with TB (e.g., obstetrics, gynecology, neonatal intensive care)

Additional Resources

For Health Care Professionals:

- *Tuberculosis. A Handbook for Public Health Nurses and Other Interested Health Care Workers*, revised 1997. Available from Manitoba Health and from the Manitoba Lung Association.

For the Public:

- *What You Should Know About Tuberculosis (TB)*. Fact Sheet for the general public. Available from Audiovisual and Publications Department, Manitoba Health, telephone (204) 786-7112, fax (204) 772-7213.