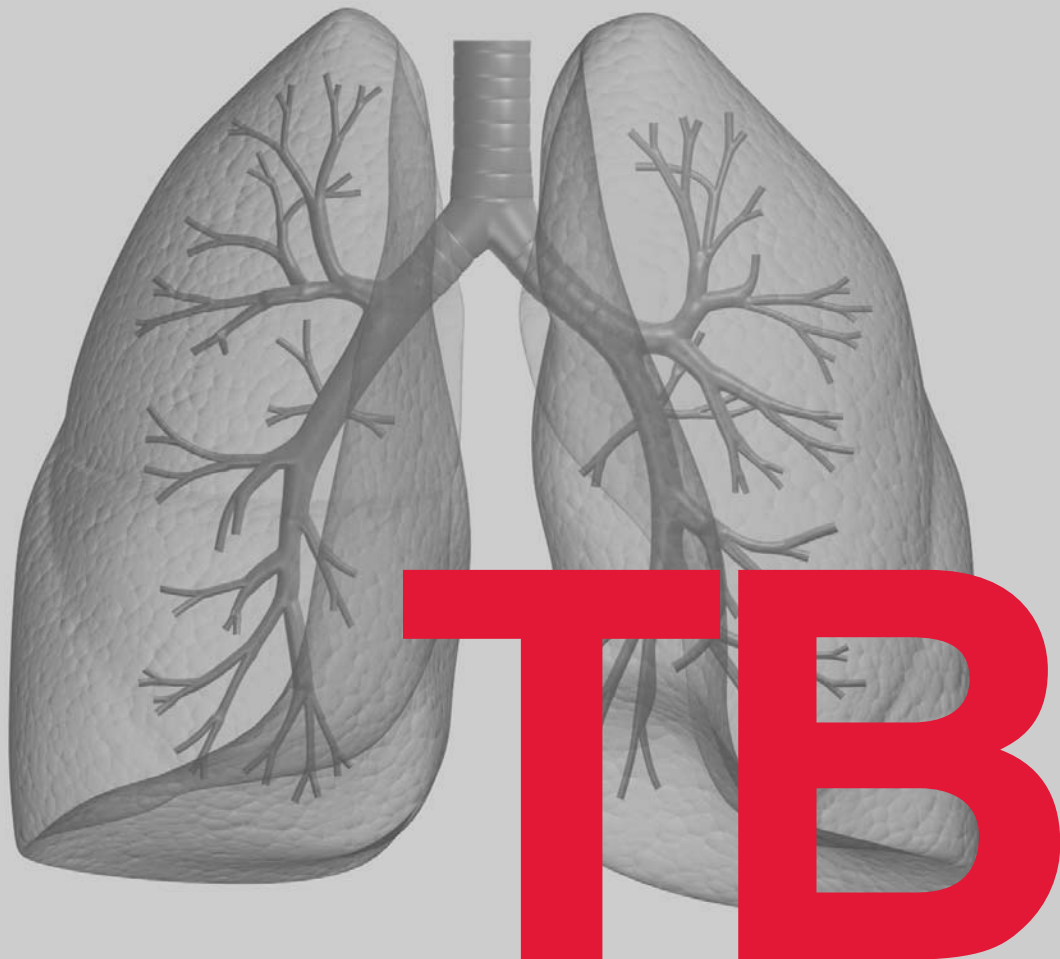


# TUBERCULOSIS

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Information for Health Care Providers

Fourth Edition



THE  LUNG ASSOCIATION™

When you can't breathe, nothing else matters.

# TUBERCULOSIS

## Information for Health Care Providers – 4th Edition

This booklet has been prepared by members of The Lung Association's Tuberculosis Committee and is published by the Ontario Lung Association (OLA). The project is supported by the OLA's medical and health professional societies, the Ontario Thoracic Society (OTS) and the Ontario Respiratory Care Society (ORCS).

The Lung Association is a registered charity that provides public information and lung health services across Ontario. One of Canada's oldest and most respected health promotion organizations, it began more than a century ago to prevent and stop the spread of tuberculosis. Today, it focuses primarily on the prevention and control of asthma and chronic obstructive pulmonary disease, tobacco cessation and prevention and the effects of air quality on lung health. Tuberculosis continues to be addressed provincially through the work of the TB Committee and OTS and ORCS professional education programs. Nationally, The Lung Association is involved in international TB programs and the work of StopTB Canada and the International Union Against Tuberculosis and Lung Disease (IUATLD).

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# 1. INTRODUCTION

Tuberculosis (TB) is not a disease of the past! TB remains a major cause of illness and death worldwide, especially in Asia and Africa. Globally, 9.2 million new cases and 1.7 million deaths occurred in 2006 (GTC 2008). Over the past two decades, the clinical presentation of TB cases has become increasingly complex. The spread of the human immunodeficiency virus (HIV) and the emergence of drug-resistant strains of TB have made some cases incurable (CTS, p. 2). New methods of diagnosis have been introduced and approaches to case management and public health practice have been revised.

In Canada, many physicians and other health care providers have little or no experience with TB. This has occurred because the Canadian incidence of TB has declined over the last 100 years due to improvements in the standard of living, and since the 1950s due to the availability of effective antibiotics and improved disease management. Although Canada is a low incidence country for TB, the disease continues to be a significant global problem. No doubt, the original declaration of the World Health Organization (WHO) in 1993 that TB is a “global emergency” remains true today. (CTS, p. 2)

The aim of this booklet is to:

- Increase health care provider awareness of TB as a possible diagnosis;
- Provide guidelines for case management and referral to specialists;
- Increase knowledge of the appropriate use and choice of preventative therapy for latent TB infection; and
- Increase understanding of the roles of family physicians, hospitals, TB clinics, public health, the Ministry of Health and Long-Term Care and public health labs in providing optimal TB care.

This booklet contains basic information about TB and is intended to be a reference for health care providers. It is not meant to provide detailed answers to all questions about TB. Further consultation with a TB specialist, infectious disease specialist or your local health unit is recommended.

## 2. EPIDEMIOLOGY

### 2.1 INCIDENCE

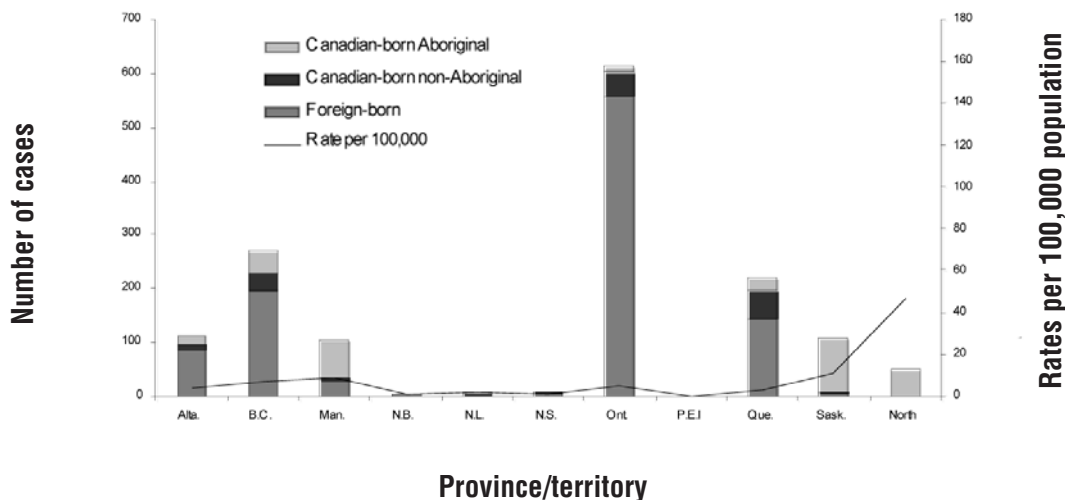
The World Health Organization (WHO) estimates that 1/3 of the world's population is infected with *Mycobacterium tuberculosis*. Rates of TB are highest in countries where poverty, crowding and lack of health care programs are characteristic. India, China, Indonesia, South Africa and Nigeria rank 1st to 5th respectively in terms of absolute number of cases. The African Region has the highest per capita incidence rate of 363 per 100,000 population. The WHO has identified 22 High Burden countries. These countries collectively account for 80% of the TB cases globally. (GTC 2008)

**FIGURE 1** 22 High Burden Countries

COUNTRY	INCIDENCE (all cases/100,000 population/year)
Afghanistan	161
Bangladesh	225
Brazil	50
Cambodia	500
China	99
Democratic Republic of Congo	392
Ethiopia	379
India	168
Indonesia	234
Kenya	384
Mozambique	443
Myanmar	171
Nigeria	311
Pakistan	181
Philippines	287
Russian Federation	107
South Africa	940
Thailand	142
Uganda	355
United Republic of Tanzania	312
Vietnam	173
Zimbabwe	557

Source: Adapted from *Global tuberculosis control – surveillance, planning, financing*, WHO Report 2008 [www.who.int/tb/publications/global\\_report/2008](http://www.who.int/tb/publications/global_report/2008)

**FIGURE 2** Distribution of tuberculosis cases by origin and incidence – Provinces/territories: 2007



Source: Tuberculosis in Canada 2007 – Pre-Release, Public Health Agency of Canada, 2008<sup>o</sup>, Ottawa (Canada).  
 Reproduced with the permission of the Minister of Public Works and Government Services Canada; 2009.

Data are provisional until the release of *Tuberculosis in Canada – 2007*.

By contrast, in 2007, Canada’s TB rate was 4.7 per 100,000 with a total of 1,547 new cases. The rate and number of new cases of TB continues to decrease. Foreign-born individuals accounted for 66% of all cases. Canadian-born Aboriginal individuals accounted for 20% of all cases and Canadian-born non-Aboriginal individuals accounted for 11% of all cases. In recent years, there have been several outbreaks of TB in homeless shelters and among other marginalized populations in Canada.

Ontario continues to have the most TB cases of any province: about 1/3 of Canadian TB cases live in the Greater Toronto Area (GTA). The majority of Ontario cases occur in foreign-born individuals. In 2007, Ontario reported 654 new cases for a rate of 5.1 per 100,000. (TB in Canada 2007 - Pre-release, PHAC).

## 2.2 DRUG RESISTANCE

Tuberculosis is an infectious disease that is preventable, treatable and curable. However, the emergence of drug-resistant strains of TB is a global threat to TB prevention and control efforts (CTS, p. 11). There are two types of resistance: primary (drug resistance among new cases) and acquired (drug resistance among previously treated cases). Primary resistance occurs in individuals who are infected with a strain of resistant tuberculosis. Acquired drug resistance occurs during treatment, because the drug regimen is inadequate, inappropriate or because the individual fails to take the drugs correctly (CTS, p. 156). Acquired drug resistance is rare in Canada.

The WHO and the International Union Against Tuberculosis and Lung Disease (IUATLD) have jointly sponsored a global surveillance project which monitors drug resistance. Of the 62 participating countries (1999-2002), the median prevalence of resistance to isoniazid (INH), rifampin (RMP), ethambutol, or streptomycin was 10.4%: 10.2 % in new cases and 18.4% in previously treated cases. The median prevalence of multidrug resistance (MDR), defined as resistance to at least INH and RMP, the two most important antituberculosis drugs, was 1.7%: 1.1% in new cases and 7.0% in previously treated cases. (CTS, p. 147)

In Canada, drug-resistant TB is most commonly reported in foreign-born persons with a past history of TB (relapsed cases, previously treated cases). Between 2000 and 2004, 5% of cases had an INH resistant strain and 0.7% had an MDR strain (CTS, p. 147). However, in Ontario and in particular the GTA, the rate of drug resistance tends to be much higher. One in every six TB patients in the GTA has a TB strain resistant to at least one first-line drug, most commonly INH.

Extensively drug-resistant (XDR) TB is defined as TB that is resistant to INH and RMP plus resistance to any fluoroquinolone and to at least one of the three injectable second-line drugs (capreomycin, kanamycin and amikacin) (CTS, pp. 12 & 166). The global scale of XDR-TB is unknown and requires urgent assessment. Drug-resistant TB is difficult and very expensive to treat. It requires an in-depth knowledge of appropriate and individualized treatment regimens. MDR and XDR treatment is often years in length with a higher associated relapse rate. To date, 5 cases of XDR-TB have been reported in Canada; 3 of these were in Ontario.

## 2.3 TB & HIV CO-INFECTION

Globally, the HIV epidemic has had a dramatic impact on TB rates and control. TB is the most common cause of death in HIV-infected individuals. In Canada, there is limited data so far on the prevalence of TB-HIV coinfection at a national level. Coinfection is likely to become more important, particularly in immigrants and refugees from countries where both TB and HIV are endemic, as well as in Aboriginal Canadians. (CTS, p. 10, 11 & 201)

## 2.4 RISK FACTORS

### *Risk factors for Latent TB Infection (LTBI)*

- Close contacts of a recently diagnosed infectious case of TB
- Immigrants and visitors from countries of high TB incidence within 2 years of arrival in Canada
- Persons who are homeless or underhoused
- Elderly persons who lived through an era when TB was common
- Aboriginal communities with high rates of LTBI or TB disease
- Persons at risk due to occupational exposure (e.g., hospital, shelter, correctional, long-term care staff and volunteers)
- Residents of long-term care facilities and correctional facilities (CTS, pp. 55 & 277)

### *Risk factors for development of active TB among persons with Latent TB Infection*

#### HIGH RISK

- Acquired immunodeficiency syndrome (AIDS)
- HIV infection
- Transplantation (related to immunosuppressant therapy)
- Silicosis
- Chronic renal failure requiring hemodialysis
- Carcinoma of head and neck
- Recent TB infection ( $\leq 2$  years)
- Abnormal chest x-ray – fibronodular disease
- Children less than 12 months of age

#### INCREASED RISK

- Treatment with glucocorticoids
- Tumor necrosis factor (TNF) – alpha inhibitors
- Diabetes (all types)
- Underweight ( $< 90\%$  ideal body weight; for most persons this is a body mass index  $\leq 20$ )
- Young age when infected (0-4 years)
- Cigarette smoker (1 pack/day)
- Abnormal chest x-ray – granuloma

#### LOW RISK

- Infected persons, no known risk factor, normal chest x-ray (“low risk reactor”)  
(CTS, pp. 65, 183 & 184)

## 3. TRANSMISSION

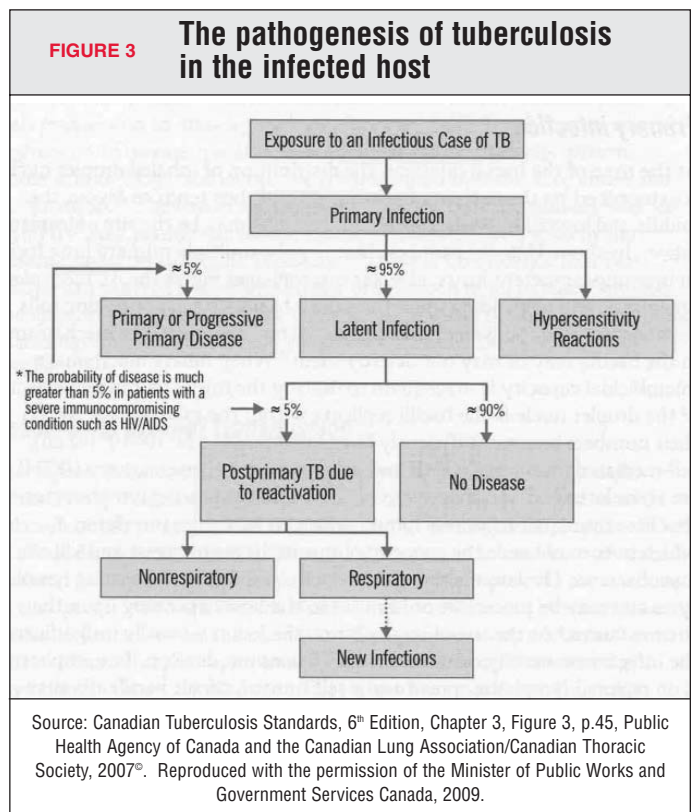
TB is not a highly infectious disease. Transmission usually requires close, frequent and prolonged exposure to a source case. Infection is almost exclusively transmitted by the airborne route from an individual with TB disease of the respiratory tract. However, transmission may also occur rarely from non-respiratory TB when infected fluid becomes aerosolized during a procedure (e.g., body fluid from a draining abscess during dressing changes).

A person with active respiratory TB can infect a large number of individuals, particularly if he or she has advanced symptomatic TB disease. The following factors must be present for the transmission of the disease to occur:

- Viable bacilli in the sputum or larynx of the source case;
- Aerosolization of sputum by cough or other mechanism (e.g., bronchoscopy, sputum induction);
- Adequate concentration of bacilli in the air;
- A susceptible host; and
- A sufficient length of time during which the host is breathing in bacillary-laden air.

(CTS, pp. 38-40)

## 4. PATHOGENESIS



Moist droplets containing the tubercle bacillus are transmitted from one person to another during coughing or sneezing. Larger particles fall to the ground, while the smaller ones rapidly evaporate, leaving droplet nuclei small enough to be inhaled. These nuclei are carried by air currents and are breathed into the lungs where they constitute an infection hazard. Viable bacilli must reach the lung tissue for infection to be established. This primary infection grows and spreads through the blood and lymphatic systems. It settles in secondary locations anywhere in the body (e.g., lymph nodes, bones, central nervous system, genitourinary tract).

The outcome of the primary infection depends on the body's immunity: the bacilli may be killed, may be sealed off (encapsulated), remaining dormant for years, or may progress to active disease. The development of the positive tuberculin reaction indicates the development of cell-mediated immunity to the tubercle bacillus and establishes the diagnosis of latent TB infection (LTBI). A weakened cellular immune system may allow multiplication of previously dormant bacilli and activation of the disease.

Tubercle bacilli can survive in the dormant stage (LTBI) for years. Approximately 5% of persons who have been infected with tuberculosis will progress to active disease within two years of exposure to the disease. Another 5% will go on to develop active disease sometime later in their lifetime. Persons with immunocompromising conditions will be much more likely to progress to active disease after being infected with TB. Their risk of progressing to active disease is 10% per year.

## 5. SCREENING FOR TB: DIAGNOSING TB INFECTION AND PREVENTING DISEASE

### TB IS PREVENTABLE

A significant number of new active tuberculosis cases come from the pool of people who have been infected with tubercle bacilli in the past. This is referred to as latent tuberculosis infection (LTBI). Treatment of LTBI is an important component in preventing tuberculosis disease and transmission. The following sections discuss indications for tests to diagnose TB, skin testing, and treatment of LTBI.

Please refer also to Figure 13, Assessment of Individuals for Tuberculosis on page 23.

## 5.1 TB SKIN TESTING

### GENERAL INFORMATION

TB skin testing (TST) is a useful tool for diagnosing tuberculosis infection. The test is NOT as helpful in the diagnosis of active tuberculosis and can produce a 'false negative' result in some patients with advanced disease and/or who are immunocompromised. In general, testing for latent TB infection is indicated when the risk of development of disease, if the patient is infected, is increased. There are three general situations when risk of disease is increased:

- Recent infection: contacts of persons with recent diagnosis of active, contagious respiratory TB or immigrants and visitors from countries of high TB incidence within 2 years of arrival in Canada;
- Increased risk of reactivation due to impaired immunity: HIV infection and other immunosuppressive conditions, diabetes, renal failure, immunosuppressive medication, and pulmonary silicosis;
- Untreated infection: when there is radiographic evidence of old, healed inactive TB but no prior treatment.

(CTS, p. 55)

### TARGETING GROUPS FOR SCREENING

High risk groups for screening change over time. Periodic reassessment of the level of risk in these groups is necessary. Systematic screening is usually conducted or directed by local public health authorities. These groups include:

- Close contacts of known or suspected cases of active TB;
- Persons with HIV infection (public health departments, primary care providers, and HIV treatment providers all share this responsibility);
- Persons with a history of active TB or chest x-ray evidence of past TB disease, who have not received adequate treatment;
- Foreign-born persons referred for medical surveillance by immigration authorities;
- Aboriginal communities with high rates of LTBI or TB disease;
- The poor, especially urban homeless or underhoused persons;
- Staff and residents of long-term care and correctional facilities;
- Those at risk for occupational exposure to TB, especially health care workers likely to be exposed to active cases of pulmonary TB.

Other groups should be considered for screening at the level of a primary care provider depending on local epidemiology and resources. These groups are:

- Persons of any age, particularly if foreign-born, with risk factors for development of active TB: HIV/AIDS, transplantation, silicosis, chronic renal failure, cancer of the head and neck, recent TB infection ( $\leq 2$  yrs), fibronodular disease on chest x-ray;
- Those persons, especially if foreign-born, who are receiving treatment with systemic glucocorticoids, tumor necrosis factor (TNF)-alpha inhibitors, people with diabetes, underweight people



## TB SKIN TESTING METHOD

**FIGURE 4 TB Skin Testing Method**

1. Cleanse the skin and allow it to air dry. With the bevel up, approach the skin at a 5-15° angle. The injection should be placed on the palm-side up surface of the forearm, about 5-10 cm below the elbow. Inject 0.1 mL of tuberculin using 5 tuberculin units (TU) of Purified Protein Derivative (PPD) intradermally. A wheal 6-10 mm in diameter should appear at the needle point. If no wheal appears or if the fluid substantially leaks out, inject again at another site at least 10 cm from the original site. This wheal will usually disappear in 10-15 minutes.
2. All TB skin tests should be measured and interpreted by a trained health care practitioner. Read the test at 48-72 hours. Find the border of transverse induration by moving a pen tip at a 45° angle towards the induration. The pen tip will stop at the edge of induration. Mark the border of induration on each side, using the pen. Measure the transverse diameter of the induration using a caliper ruler. If a caliper ruler is not available, a flexible ruler can be used. Document the induration size in millimeters (mm). **Only the indurated area should be measured, not erythema (redness).** Record the measurement. No induration or redness without induration is recorded as 0 mm.

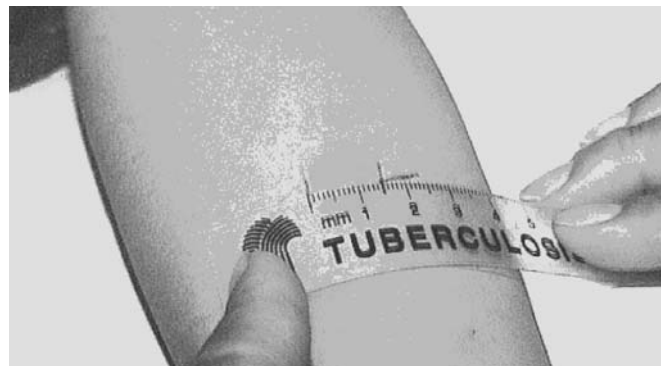
Note: A punctured vial of 5-TU PPD should be discarded after one month due to possible contamination and loss of potency (Date the vial when opened). Failure to store and handle the tuberculin preparation as recommended will result in loss of potency and inaccurate test results or false negative results.

(CTS, pp. 56-60)

(<90% ideal body weight; BMI  $\leq$  20), people infected at a young age (0-4 yrs), cigarette smokers (1 ppd), people with granuloma on chest x-ray;

- Children <15 years of age who have lived in a country with high TB incidence and have immigrated within the past 2 years (including adopted children);
- Persons  $\geq$ 15 years of age who have lived in a country with high TB incidence, have immigrated within the past 2 years and have either been living with or in known contact with a TB case in the past or are at high risk of developing active TB, if infected;
- Persons at risk of active TB who are employed in settings where they may infect infants or persons who are immunosuppressed;
- Persons with a history of substance abuse;
- Persons who are traveling or residing in an area with a high incidence of TB who have one or more of the following risks:
  - a high level of risk for development of active TB
  - plans to travel or reside for 3 months or longer
  - intention to participate in high-risk activities: health care, missionary work, or any activity that may involve exposure to the resident population. (CTS, pp. 65, 276-278)

**FIGURE 5 Technique of Administering and Reading Tuberculin Skin Tests**



## CONTRAINDICATIONS TO TUBERCULIN SKIN TESTING

### When to Avoid Skin Testing

Do not conduct skin testing for persons with:

- A previous severe reaction (e.g., blistering, necrosis or ulceration) to a TST;
- Known active TB or known treatment in the past (TST does not distinguish between prior and recent infection, and will not yield any useful information in this case);
- Extensive burns or eczema;
- Documented previous positive reaction read by a knowledgeable healthcare worker.

### When to Defer Skin Testing

Defer tuberculin skin testing in the following situations:

- Persons with viral infections (e.g., rubeola, mumps, influenza), which may temporarily depress the reactivity to TST. **Defer** skin testing for 4 weeks after infection;
- Recent immunization with measles vaccine has been shown to increase the likelihood of false negative TST results;
- Although no data are available regarding the effect on TST of other live virus immunizations (mumps, rubella, varicella and yellow fever vaccines), it would be prudent to follow the same 4 week guideline. However, if the opportunity to test may be missed, the TST should not be delayed for these vaccines (CTS, p. 56).

**Options:** either administer TST before or simultaneously with the live, viral vaccine (e.g., MMR) or defer skin testing for 4 weeks after immunization with a live, viral vaccine.

### When Not to Defer Skin Testing

The following persons can receive a TST:

- People who have been immunized with a non-live-virus vaccine (e.g., diphtheria, tetanus, polio, pertussis) which do not suppress the reaction;
- Pregnant women. Pregnancy is **NOT** a contraindication for TST;
- Anyone with a previous Bacille Calmette-Guérin (BCG) vaccination;
- Anyone who has a history of significant test reaction in the past (without a severe reaction, blistering, ulceration, or necrosis at the site) but the reaction was not documented in millimeters;
- Anyone with a common cold;
- Those taking low dose corticosteroids daily. It generally takes a steroid dose equivalent to  $\geq 15$  mg prednisone daily for 2-4 weeks to suppress tuberculin reactivity.

(CTS, p. 56)



## 5.2 INTERPRETATION OF SKIN TEST REACTIONS

### Positive Skin Test Reactions

A positive skin test reaction should be considered according to three dimensions – size, positive predictive value and risk of disease.

#### 1. SIZE

<b>FIGURE 6 The First Dimension of Interpretation of the TST – Size</b>	
<b>TST Reaction Size (mm induration)</b>	<b>Situation in Which Reaction is Considered Positive</b>
<b>0-4</b>	HIV infection with immune suppression AND the expected likelihood of TB infection is high (e.g. patient is from a population with a high prevalence of TB infection, is a close contact of an active contagious case, or has an abnormal x-ray)
<b>5-9</b>	HIV infection Close contact of active contagious case Children suspected of having tuberculosis disease Abnormal chest x-ray with fibronodular disease Other immune suppression: TNF-alpha inhibitors, chemotherapy
<b><math>\geq 10</math></b>	All others

Source: Canadian Tuberculosis Standards, 6<sup>th</sup> Edition, Chapter 4, Table 1, p. 63, Public Health Agency of Canada and the Canadian Lung Association/Canadian Thoracic Society, 2007<sup>o</sup>. Reproduced with the permission of the Minister of Public Works and Government Services Canada, 2009.

#### 2. POSITIVE PREDICTIVE VALUE

This number refers to the pre-TB skin test probability that a positive test represents the true presence of TB infection. This probability can be affected by issues such as the following:

##### ***Nontuberculous mycobacteria (NTM):***

Sensitivity to NTM is uncommon in Canada and is not an important cause of TST reactions of 10 mm or more. Some small positive TST reactions (5-9 mm) may be due to cross-reactivity with these antigens.

##### ***BCG Vaccination:***

Many populations in Canada will have had BCG vaccinations, i.e., immigrants from Europe and the developing world, Aboriginal Canadians, especially from northern communities (routine BCG at birth was discontinued in most of the southern reserves in the 1970s), and people born in Quebec or Newfoundland between the 1940s and 1970s. The prevailing opinion is that BCG does not prevent infection but does increase the resistance to uncontrolled multiplication and dissemination of *M. tuberculosis* throughout the body. The effectiveness in adulthood is likely lower than in children.

The interpretation of the TST result should ignore the history of vaccination with BCG (as a cause of a positive skin test reaction) when:

- BCG was given in infancy, and the person tested is now aged 10 years or older;
- There is a high probability of TB infection: close contacts of an infectious TB case, Aboriginal Canadians from high risk communities, or immigrants/visitors from countries with high TB incidence;
- There is a high risk of progression from TB infection to TB disease (HIV/AIDS, cancer, diabetes, etc.).

BCG should be considered the likely cause of a positive TST if:

- BCG vaccine was given after 12 months of age AND the person is either Canadian-born non-Aboriginal OR an immigrant/visitor from a low TB incidence country. (CTS, pp. 65, 349)

See also [www.bcgatlas.org/about.php](http://www.bcgatlas.org/about.php).

### 3. RISK OF DEVELOPMENT OF ACTIVE TB DISEASE

It is important to consider certain factors which increase the risk for developing active TB infection. These factors are summarized in section 2.

A web-based interactive algorithm is available to assist in TST interpretation ([www.meakins.mcgill.ca/respepi/homeE.htm](http://www.meakins.mcgill.ca/respepi/homeE.htm)). (CTS, p. 62)

#### False Negative Reactions

People who are immunosuppressed may have false negative skin tests associated with anergy. Other causes of false negative reactions are listed below:

- Poor injection technique;
- Expired or diluted tuberculosis purified protein derivative (PPD testing solution);
- Immune suppression
  - Advanced age
  - Treatment with systemic corticosteroids: at least 15 mg per day of prednisone for  $\geq$  one month
  - Cancer treatment
  - HIV infection ( $CD4 < 500 \times 10^6/L$ )
  - Tumor necrosis factor (TNF)-alpha inhibitors;
- Malnutrition (especially with recent weight loss);
- Severe illness which can include active TB;
- Major viral illnesses (mononucleosis, mumps or measles), or immunization with MMR, varicella or yellow fever vaccine within the last four weeks;
- Very young age (<6 months of age).

(CTS, pp. 61-62).

**Close household contacts who are under the age of five or are severely immunosuppressed (even if the initial tuberculin skin test is negative) should be investigated immediately for active disease.**

Treatment for LTBI should then be initiated until the second TST result is known. If the repeat TST (at least 8 weeks after the last contact) is negative, treatment for LTBI can be discontinued. If the repeat TST is positive, the course of treatment for LTBI should be completed. (CTS, pp. 191, 256).

#### Interpretation of TB Skin Tests: Contacts of Respiratory TB

Conversion of the skin test from negative to positive after exposure to tuberculosis may take at least 8 weeks. Therefore if skin testing is performed before 8 weeks from the last exposure and the result is negative, a second skin test must be done at least 8 weeks after a contact's last possible exposure to the active case. For guidelines for tuberculin skin testing in the context of a contact investigation, see Figure 7.

#### **FIGURE 7 Guidelines for Tuberculin Skin Testing in the Context of a Contact Investigation, According to Previous TST Results**

##### **No documented previous TST result**

In this case, a TST result of 5 mm or more on the first test or on the test at least 8 weeks after the last exposure is considered positive.

##### **Documented previous TST result less than 5 mm**

In this case, a TST result of 10 mm or more on the first test or on the test at least 8 weeks after the last exposure is usually considered positive. However the circumstances of the contact must be taken into account. For example, if the source case is highly infectious, if there was close or prolonged contact, if the contact is under age 5 or if the contact has impaired immunity, then an increase of 6 mm from the previous TST result may be considered a conversion. Decisions in this regard need to be individualized.

##### **Documented previous TST result between 5 and 9 mm, no history of treatment of TB disease or LTBI**

In this case, the TST should be repeated. An increase of at least 6 mm is considered a positive result, either on the initial TST or on the second test done at least 8 weeks after the last contact.

##### **Documented previous TST result of 10 mm or greater or history of treatment for TB disease or LTBI**

Contacts who have a documented prior positive TST or history of treatment for active TB disease or LTBI should not undergo post-exposure TST. Evaluation of these contacts should include assessment for signs/symptoms of active TB disease and additional investigations (e.g., chest radiography, sputum examination) as deemed necessary. Clinical history and results of clinical investigations should guide treatment decisions.

Very high-risk, severely immunocompromised persons (e.g., those who are HIV coinfecting) who are re-exposed to infectious TB after having already completed a satisfactory course of treatment for TB disease or LTBI in the past, should be considered for a repeat course of treatment for LTBI.

Source: Canadian Tuberculosis Standards, 6<sup>th</sup> Edition, Chapter 12, Table 2, p. 260, Public Health Agency of Canada and the Canadian Lung Association/Canadian Thoracic Society, 2007<sup>o</sup>. Reproduced with the permission of the Minister of Public Works and Government Services Canada, 2009.

### Interpretation of Two-Step Skin Tests

#### **The two-step TST is used to rule out the booster phenomenon.**

A positive tuberculin skin test may gradually wane over the years. The first skin test may be negative in persons whose exposure history is unknown or who may have been at risk for exposure to *M. tuberculosis* several years earlier. However, this initial test may stimulate the individual's immune response and a positive reaction may occur when the person is retested one or more weeks later. This delayed response is termed the "booster" phenomenon. The two-step TST provides an accurate "baseline" for individuals who will have future or serial testing. If a true baseline is not obtained with a two-step test and the individual is tested again at a future date, a positive result may be misinterpreted as a new infection or "conversion", when it may really represent a "booster" phenomenon.

The two-step TST requires the administration of two tuberculin (5TU PPD) skin tests. If the reaction to the first test is negative, a second test is given 1-4 weeks later. Repeated tuberculin testing does not sensitize the uninfected person.

The two-step TST needs to be done only once if properly performed and documented. Subsequent skin tests can be one-step regardless of how long it has been since the two-step test was done (CTS, pp. 67-68).

#### **Indications for the Two-Step Skin Test**

1. Perform two-step tuberculin skin testing if subsequent testing will be conducted at regular intervals, i.e., among health care workers;
2. Use the two-step test with residents of long-term care facilities who may be tested subsequently, if there is a suspected exposure, to ensure an accurate baseline result to guide post-exposure management;
3. Consider a two-step baseline test in other appropriate situations, i.e., staff in correctional facilities.

#### **Two-step testing is not appropriate in contact tracing.**

All positive skin tests must be reported to your local public health unit as required by the *Health Protection and Promotion Act of Ontario* whether or not you plan to prescribe TB prophylaxis for the patient.

## 6. DIAGNOSIS

Diagnosing active tuberculosis usually involves three aspects:

a) symptom presentation, b) radiographic presentation and, c) bacteriological evidence (i.e., specimen collection for Acid Fast Bacilli smear and culture).

A TB case is defined as an individual:

1. With positive culture of Mycobacterium tuberculosis complex (*M. tuberculosis*, *M. africanum*, *M. canetti*, *M. caprae*, *M. microti*, *M. pinnipedii* or *M. bovis* excluding BCG strain) from sputum, body fluids or tissues; **OR**
2. Without bacteriological evidence but with clinical signs or symptoms, radiological or pathological evidence of active pulmonary or non-pulmonary disease, preferably with:
  - a) A positive tuberculin skin test, AND/OR
  - b) Demonstration of AFB in smears from sputum or other body fluids or tissues, AND/OR
  - c) Response to anti-TB treatment.

(MOHLTC TB Best Practices 2006, p. 11)

A TB skin test is not recommended for diagnosing active tuberculosis because it is only partially sensitive. Some studies indicate that up to 20-30% of individuals with active tuberculosis will have a false negative reaction and not be able to mount a skin test response at the time of diagnosis (CTS, p. 74). Currently, in Canada, blood tests to detect tuberculosis infection or disease (i.e., Interferon-gamma release assays (IGRAs) - QuantiFERON-TB Gold or T-SPOT.TB) have been approved but have limited availability. The Canadian Tuberculosis Standards does not recommend that Interferon-gamma release assays replace the TB skin test in most circumstances (CTS, p. 391). (For the most recent Canadian Tuberculosis Committee advisory statement on IGRAs, refer to <http://www.phac-aspc.gc.ca/tbpc-latb/index-eng.php>).

### 6.1 SYMPTOMS

The presentation of tuberculosis can be highly variable depending on the duration and site of disease activation. Classic symptoms for respiratory tuberculosis include a chronic cough (productive or non-productive) for three or more weeks, fever, and night sweats are also common but may be absent in children or the elderly. Hemoptysis, anorexia, weight loss, and chest pain are generally associated with advanced disease. It is important to note that respiratory tuberculosis can occur without a cough and in some cases, individuals may present with no symptoms. Furthermore, the physical examination findings for active respiratory tuberculosis are usually within normal limits, even with advanced disease (CTS, p. 73).


Tuberculosis can also be non-respiratory. The presenting symptoms are often site specific such as lymph node swelling in

**FIGURE 8 Tuberculosis (TB) Infection or Disease?**

## Tuberculosis (TB) Infection or Disease?

<b>TB Infection</b>	<b>OR</b>	<b>TB Disease</b>
TB germ has entered the body but is not growing (dormant/inactive)	Status	TB germ has entered the body and is growing (replicating/active)
Positive Skin Test	Skin Test	May be positive or negative
No active TB disease	Chest x-ray (or e.g., CT scan, MRI)	Most show active TB on x-ray of chest OR on x-ray/ CT scan/ MRI of other parts of the body (e.g., lymph node, spine, kidney)
No TB germs in sputum	Sputum	May have TB germs in sputum
No symptoms	Symptoms	Symptoms which become worse over time (e.g., cough, chest pain, chills, weakness, weight loss, night sweats, coughing up blood, swollen lymph node)
<b>Not contagious</b> Cannot pass TB germ to anyone else	Infectiousness	<b>Contagious</b> If disease is in the lungs and not properly treated with medication
Person is at risk of developing disease in the future	Associated Risks	Person has disease and must be treated to prevent disease from getting worse or spreading to others
May be prescribed medication to prevent disease from developing	Treatment	Needs treatment with several medications for 6 months or longer to cure the disease

see Canadian Tuberculosis Standards for more detail

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lymphatic disease, neurological changes (i.e., headache or neck stiffness) in meningeal disease, bone pain/joint swelling in osteomyelitis, lower back pain in Potts disease (spinal compression or abscess), recurrent sterile pyuria (urinary tract infections) in renal disease, or abdominal pain or infertility in genitourinary disease.

Of note, respiratory and non-respiratory tuberculosis can occur concurrently. Hence, it is important to rule out evidence of respiratory tuberculosis when a diagnosis of non-respiratory tuberculosis is made. Although drug therapy does not change, airborne isolation precautions are necessary with respiratory disease.

### **HIV/AIDS**

The symptom presentation of tuberculosis in the HIV/AIDS individual is often dependent on their viral load and CD4 count. Individuals with higher CD4 counts and lower viral loads will tend to present with the typical tuberculosis symptoms as mentioned above. Those with lower CD4 counts and higher viral loads will have more atypical and systemic presentations. In some cases, symptoms may appear to be consistent with tuberculosis, but may be caused by other opportunistic infections like *Pneumocystis jirovecii* (previously known as *Pneumocystis carinii pneumonia*). This population is also at higher risk for non-respiratory tuberculosis, or multiple site involvement with lymph node, pleural, pericardial or meningeal TB (CTS, p. 206). Thus, the level of the immune function is a predictor of the degree to which symptoms will manifest and site involvement.

### **Pediatrics**

Most children who have TB disease in North America are asymptomatic and are discovered as part of the contact investigation of adult cases. Typically, these children appear entirely well without any clinical signs, but may have x-ray abnormalities.

In contrast, children in resource poor, high incidence countries where screening is not widely available are identified because of significant involvement of almost any organ system. This pattern is also seen in Canada, chiefly in immigrant children.

Older children and adolescents are more likely to experience reactivation disease, and similar to adults, often have the classic triad of symptoms of fever, weight loss, and night sweats. Signs are still unusual and may be quite subtle. These unusual presentations in adolescents may lead to a delay in the diagnosis and subsequent treatment of TB (Kam et al, 2007).

Miliary disease is much more common in young infants and in the immunocompromised. Miliary refers to diffuse tiny nodules similar in size to millet seeds, which are seen on x-ray. Hepatosplenomegaly and weight loss are frequent as is hemophagocytosis. The skin test is often negative.

Children co-infected with HIV and TB have an accelerated progression from infection to TB disease. Although co-infected adults often have atypical presentations with non-respiratory disease, children with HIV infection usually present with typical childhood disease. The skin test is often negative: a search for an infectious adult or adolescent is an important clue to the diagnosis.

## **6.2 RADIOGRAPHIC PRESENTATION**

Chest x-rays (both posterior-anterior [PA] and lateral views) are an effective tool towards diagnosing respiratory tuberculosis. Classic radiographic presentation of tuberculosis in an immunocompetent individual includes infiltrates, nodules, and/or cavities in the upper lobes of the lungs, or superior segments of the lower lobes. Tuberculosis can also have atypical radiographic presentations such as infiltrates in the lower lobes especially during primary infection in individuals who are immunocompromised, and/or hilar and mediastinal lymphadenopathy (CTS, p. 74).

Other abnormalities such as fibrosis, scarring, granulomas, or volume loss (this is a common tuberculosis finding as the tuberculosis bacillus destroys lung tissue and causes remaining tissue to be pulled or contracted) should be further investigated.

**Radiological presentation does not determine disease activity. Clinical and bacteriological correlation is also required to rule out active disease.**

### **HIV/AIDS and Immunocompromised Individuals**

Chest x-rays may have typical or atypical presentations in the immunocompromised individual. The greater the level of immunosuppression, the less likely these individuals will have upper lobe findings or cavitation, Hilar lymphadenopathy, pleural effusion, and disseminated disease are also apparent in this population. Individuals with HIV/AIDS can also have completely normal chest x-rays approximately 10% of the time (CTS, pp. 75 & 206).

### **Pediatrics**

Chest x-rays are important in diagnosing pediatric tuberculosis, but can be difficult to interpret in a young child. Technique (inadequate inspiration or over-penetration) and the radiologist's experience in reading pediatric chest x-rays are variables that can influence the utility of the film. Therefore, before ordering a chest x-ray, the clinician should check that the facility has experience with pediatric patients. A lateral view is recommended as it is important to evaluate for hilar lymphadenopathy, a hallmark of primary tuberculosis. In primary disease, lung lesions can be found anywhere. However, abnormalities found in the lung apices tend to represent reactivation disease. Lastly, the age of the child must be considered when interpreting chest x-rays. Radiographic presentations in older children and adolescents can be similar to those of adults, with upper lobe involvement.

### 6.3 MYCOBACTERIOLOGICAL EVIDENCE: TESTING FOR ACID FAST BACILLI (AFB) SMEAR AND CULTURE

The causative agent of tuberculosis is *Mycobacterium tuberculosis* (MTB) which is a slow growing mycobacterium that can take up to seven weeks to grow in order to obtain a final culture result. MTB is the most significant human pathogen in the group of mycobacteria known as the *M. tuberculosis* complex (MTBC). The complex includes *Mycobacterium bovis*, *Mycobacterium bovis* BCG, *Mycobacterium africanum*, *Mycobacterium caprae*, *Mycobacterium microti* and *Mycobacterium pinnipedii* (CTS, p. 222).

#### The Microbiology of Acid Fast Bacilli Smears

The term “smear” refers to the laboratory technique for visualizing mycobacteria. The specimen is smeared onto a microscope slide, stained, and then examined.

Acid-fastness refers to mycobacteria’s resistance to decolourization in the staining process of the bacilli. Mycobacteria are rod-shaped organisms that have a cell wall largely composed of fatty acids. The cell wall prevents penetration by the stains used for other bacteria (e.g., Gram stain). The stain used to visualize mycobacteria is a highly concentrated phenolic dye. After the smear has been stained using this dye, the smear is then “decolourized” using acid-alcohol.

Mycobacteria will resist decolourization due to their complex cell wall and will retain the stain. Thus, the term “acid fast” refers to the mycobacterium’s ability to retain the stain in the presence of weak acids.

Both MTB and nontuberculous mycobacteria (NTM) will stain AFB smear positive, though only MTB is infectious. It is important to determine whether a positive AFB smear is due to MTB or NTM. This is usually determined by direct detection, using nucleic acid amplification such as the Amplified Mycobacterium Tuberculosis Direct (AMTD) test, or culture. However, until tuberculosis is ruled out, all positive smears should be considered to be tuberculosis and appropriate precautions taken. For further information on NTM, please refer to section 10. In Ontario, all fresh specimens sent for AFB smear are also cultured for mycobacteria.

#### AFB Smears in Clinical Practice

AFB smears are a rapid test used to examine specimens for possible tuberculosis. Each specimen sent for AFB is stained, and the number of AFB visualized is quantified using a numerical scale as shown by the Public Health Laboratory (Ontario Agency for Health Protection and Promotion) AFB Smear Report Interpretation Table.

**FIGURE 9 AFB Smear Report Interpretation Table**

Classification of Smear	Clinical Interpretation
No AFB	Negative
Few	Weakly positive
1+	Moderately positive
2+	Moderately positive
3+	Strongly positive
4+	Strongly positive

Source: Ontario Public Health Laboratories, *Labstract*, January 2007

Some laboratories perform a direct or unconcentrated AFB smear, for rapid results. An unconcentrated specimen smear lacks specimen processing steps that yield more sensitive smear results. Negative unconcentrated smears are considered to be preliminary until a concentrated AFB smear is performed (CTS, p. 21).

**Smear results are a rough indicator of the infectiousness of the active tuberculosis case.** Hence, they must be interpreted within the context of an individual’s symptoms and radiological presentation. Smear results are influenced by numerous factors including the quality of the specimen, the number of samples obtained, and the individual’s burden of disease.

A negative AFB smear result does not rule out the diagnosis of tuberculosis, as the culture can still be positive for MTB. Also of note, patients with negative AFB smears, but positive cultures, can still transmit tuberculosis (Behr MA et al, 1999).

If non-respiratory TB is suspected, specimens from non-respiratory sites should also be sampled for AFB and culture. The Public Health Laboratory (OAHPP) has specific requirements for the collection and transport of specimens. Please refer to Figure 10 for specimen collection guidelines from the Public Health Laboratory (OAHPP) for information and instructions on specimen submission.

**Sputa or other specimens that are submitted for AFB smear and culture must clearly specify testing for AFB on the microbiology requisition. Routine bacterial culture and sensitivity does not include AFB smear and culture.**

#### Amplified Mycobacterium Tuberculosis Direct (AMTD), (Gen-Probe, San Diego CA)

The AMTD test is a target-amplified nucleic probe test that detects *M. tuberculosis* complex (MTBC) rRNA directly from respiratory specimen concentrates. The AMTD differentiates between MTBC and NTM in an AFB smear positive specimen by detecting the presence or absence of MTBC ribosomal RNA (rRNA).

The test is performed at the TB and Mycobacteria Laboratory of the Public Health Laboratory (OAHPP) on all first specimens that are new to the laboratory, and are AFB smear positive. AMTDs are not performed on specimens from TB cases that are undergoing treatment.

The sensitivity and specificity of the AMTD for MTBC is greater than 97% in smear positive respiratory specimens, but is much less sensitive in smear negative respiratory specimens. The AMTD test is not FDA approved for non-respiratory specimens. However, testing will still be performed under “investigational/research use only” for smear positive non-respiratory specimens. Smear negative, non-respiratory specimens are not tested.

The following specimens cannot be tested by AMTD:

- Bloody specimens;
- Specimens from patients treated for TB within the previous 12 months;
- AFB smear negative specimens from non-respiratory sites.

A negative AMTD test does not exclude a positive MTBC culture. A negative AMTD may be the result of inhibitors in the specimen, blood in the specimen, low numbers of MTBC in the presence or absence of nontuberculous mycobacteria in the specimen, or if the patient is already on treatment for TB.

Smear positive specimens will automatically be tested by AMTD. For smear negative specimens, the treating physician must contact the Medical Microbiologist, TB Mycobacteriology, Public Health Laboratory (OAHPP) to request AMTD. Where possible, please call prior to specimen submission. Testing of smear negative specimens will only be performed where there is a high clinical suspicion of TB, and cannot be performed on multiple specimens.

### **Culture and Anti-Tuberculosis Drug Susceptibility Testing**

Culture is the gold standard for the laboratory diagnosis of TB. MTB is a slow growing organism, and cultures are held for seven weeks before a final report is issued. Species determination, including identification of *M. bovis* and *M. bovis* BCG is performed if susceptibility testing indicates pyrazinamide (PZA) resistance.

If a specimen results in a positive culture for MTBC, the first isolate from a patient will automatically be tested for susceptibility to the first-line tuberculosis drugs (i.e., isoniazid, rifampin, pyrazinamide, and ethambutol). Susceptibility testing results are usually available 7-10 days after the culture has grown. First-line antituberculous drug susceptibility results are automatically performed if a patient's cultures remain positive at three months or greater. Second-line drug sensitivity testing is automatically performed if resistance is detected to rifampin or to any two first-line drugs.

**If a specimen does not grow MTBC in culture, drug susceptibility testing cannot be done.**

### **Pathology**

Histopathological examination is often helpful for determining tuberculosis disease in tissue biopsies or specimens. AFB and/or caseating granulomata may be seen on microscopic examination, and should prompt further investigation, as these findings are highly suspicious for the diagnosis of tuberculosis. Fresh tissue specimens should be submitted to the laboratory for AFB smear, culture and susceptibility testing. Tissue and biopsy specimens must be placed in small amount of sterile saline and submitted in a sterile container to the laboratory. Do not submit on gauze. Frozen specimens are not optimal for culture.

Formalin-fixed paraffin-embedded specimens may be tested for the presence of MTB DNA by polymerase chain reaction (PCR) assay. The laboratory must be notified prior to submission for instructions.

Formalin-fixed tissue, or tissue from paraffin blocks (histopathology specimens) cannot be cultured, and anti-tuberculous drug susceptibility testing cannot be performed on these specimens.

## **6.4 SPECIMEN COLLECTION**

Specimens obtained by health care providers are usually sent to private or hospital laboratories, and from there are sent to the Public Health Laboratory (OAHPP) for processing. Specimens must be collected in a leak proof container, and appropriately labeled with the individual's:

- name
- date of birth
- address including postal code
- health information number (e.g., OHCN).
- submitting health care provider's name and address
- submitter's telephone and secure fax number
- type of specimen
- date of collection

Specimens should ideally be collected before starting drug therapy for tuberculosis. Please refer to Figure 10 for specimen collection guidelines and complete instructions on specimen submission. Specimens lacking required information or inappropriately collected will be rejected for processing.

### **Spontaneous and Induced Sputum**

Three spontaneous sputum specimens should be collected (5-10 mL each). Providing one specimen is an early morning specimen, they can be collected 8-24 hours apart (or longer if necessary). If an individual is unable to produce sputum spontaneously, induced sputum is also an effective way of obtaining a specimen as it has a



**FIGURE 10**

**Specimen Requirements for Mycobacterial Isolation and Acid-fast Stain**

SPECIMEN TYPE	SPECIMEN REQUIREMENTS	SPECIAL INSTRUCTIONS	UNACCEPTABLE SPECIMENS
Abscess contents, aspirated fluid	As much as possible in sterile plastic container.	Cleanse skin with alcohol before aspirating sample. Collect specimen on swab, and place in aerobic transport medium or saline, only if volume is insufficient for aspiration by needle and syringe.	Dry swab. Swab in anaerobic transport medium
Blood	10-mL SPS (yellow top) or 10-mL heparin (green top) blood collection tube.	Disinfect site as for routine blood culture. Mix tube contents immediately after collection.	Blood collected in EDTA, which greatly inhibits mycobacterial growth even in trace amounts (3). Coagulated blood. Serum. Plasma. Blood in bacterial blood culture medium.
Body fluids (pleural, pericardial, peritoneal, etc.)	As much as possible (10-15mL minimum) in sterile container.	Disinfect site with alcohol if collecting by needle and syringe.	Fluid in bacterial blood culture medium.
Bone	Bone in sterile container without fixative or preservative.		Specimen submitted in formalin.
Bone marrow	As much as possible in sterile collection tube or SPS or heparin tube.	Collect aseptically. Mix anti-coagulant tube contents immediately following collection.	
Bronchoalveolar lavage or bronchial washing	≥5 mL in sterile container.	Avoid contaminating bronchoscope with tap water. Saprophytic mycobacteria may produce false-positive culture or smear results (4).	
Bronchial brushing.	Sterile container. Add sterile saline if small amount.		
CSF	≥2 mL in sterile container.	Send maximum volume attainable. Transport immediately to the laboratory at room temperature.	Do not refrigerate
Gastric lavage fluid	≥ 5 mL in sterile gastric container. Collect in the morning soon after patient awakens in order to obtain sputum swallowed during sleep.	Collect fasting early-morning specimen on 3 consecutive days. Use sterile saline. Adjust to neutral pH with 100 mg of sodium carbonate immediately following collection. Laboratory provides gastric collection jars containing sodium carbonate.	Specimen that has not been neutralized.
Lymph node	Node or portion in sterile container without fixative or preservative. A small amount of sterile saline may be added.	Collect aseptically, and avoid indigenous microbiota. Select caseous portion if available. Do not wrap in gauze. Freezing decreases yield.	Specimen submitted in formalin.
Skin lesion material	Submit biopsy specimens in sterile containers without fixative or preservative. Submit aspirate in syringe with Luer lock cap, needle removed.	Swabs in transport medium (Amies or Stuarts) are acceptable only if biopsy sample or aspirate is not obtainable. For cutaneous ulcer, collect biopsy sample from periphery of lesion, or aspirate material from under margin of lesion. If infection was acquired in Africa, Australia, Mexico, South America, Indonesia, New Guinea, or Malaysia, note on request, because <i>Mycobacterium ulcerans</i> may require prolonged incubation for primary isolation (4).	Dry swab
Sputum	5-10 mL in sterile, wax-free, disposable container. Collect an early morning specimen from deep, productive cough on 3 consecutive days. Do not pool specimens (3). For follow-up of patients on therapy, submit 3 specimens after 2 months and again on completion of therapy.	For expectorated sputum, instruct patient on how to produce sputum specimen as distinct from saliva or nasopharyngeal discharge. Do not have patient rinse mouth with tap water which may contain environmental mycobacteria. For induced sputum, use sterile hypertonic saline. Avoid sputum contamination with nebulizer reservoir water. Saprophytic mycobacteria in tap water may produce false-positive culture or smear results (2). Indicate on request if specimen is induced sputum, as these watery specimens resemble saliva and risk rejection as inadequate.	24-h pooled specimens; saliva.
Stool	≥1 g in sterile, wax-free, disposable container.	Collect specimen directly into container, or transfer from bedpan or plastic wrap stretched over toilet bowl.	Frozen specimen. Specimen that has been in contact with water in toilet.
Tissue biopsy sample	1 g of tissue, if possible, in sterile container without fixative or preservative. A small volume of sterile saline may be added	Collect aseptically, and avoid indigenous microbiota. Select caseous portion if available. Do not wrap in gauze (3). Freezing decreases yield.	Specimen submitted in formalin.
Transtracheal aspirate	As much as possible in syringe with Luer lock cap, needle removed, or other sterile container (1, 3).		Do not submit specimens in endotracheal tubes.
Urine	As much as possible (minimum, 40 mL) of first morning specimen obtained by catheterization or of midstream clean catch in sterile container. For suprapubic tap, as much as possible in syringe with Luer cap or other sterile container.	Collect first morning specimen on 3 consecutive days. Accept only one specimen/day. Organisms accumulate in bladder overnight, so first morning void provides best yield. Specimens collected at other times are dilute and are not optimal.	24-h pooled specimens; urine from catheter bag; Specimens of <40 mL unless larger volume is not obtainable. Urine specimens should only be tested if renal TB is suspected, not as routine screening.
Wound material. See biopsy or aspirate.	Swabs are acceptable only if biopsy or aspirate is not obtainable. If used, they must be placed in aerobic transport medium. (Amies or Stuarts), or in saline. Negative results are not reliable.		Swabs in anaerobic transport medium. Dry swabs

sensitivity of 90%. Some studies indicate that a single sputum induction is equivalent to bronchoscopy. Sputum induction must be done in a negative pressure room. A sputum induction involves inhaling hypertonic saline mist which irritates the airways and causes the individual to cough up sputum. The mist is created by a nebulizer. It is normal for an induced sputum sample to look watery. Sputum samples must be refrigerated if not transported to the laboratory within one hour, in order to prevent overgrowth by other contaminating bacteria. Instruct the patient to not rinse his/her mouth with tap water prior to obtaining the specimen. (CTS, p. 76)

### **Bronchoscopy**

If the initial series of sputum smears are negative, and the clinical and/or radiological suspicion for tuberculosis remains high, then a bronchoscopy should also be considered in order to rule out tuberculosis. Bronchoscopy should also be done if the individual is unable to produce a specimen either spontaneously or via induction. Bronchoscopy is also helpful in determining other respiratory diseases such as malignancy or other infectious etiologies. When bronchoscopy specimens are submitted for tuberculosis testing, it is useful to also submit a post bronchoscopy aspirate lavage sputum specimen. It is always preferable to submit more than one specimen where possible.

### **Gastric Aspirate**

Gastric aspirate is performed on individuals who cannot expectorate sputum, and is usually done on children or elderly patients with dementia in whom tuberculosis is suspected. A gastric aspirate consists of inserting a tube through an individual's nose through to the stomach. During sleep, the mucociliary mechanism in their respiratory tract sweeps mucus, which may contain tuberculosis bacilli, into the mouth. The material is swallowed and the gastric aspirate may be a source to obtain organisms, especially if the stomach has not emptied. Gastric aspirates are most commonly done in hospitals as it is an uncomfortable procedure, and must be done immediately after awakening. The Public Health Laboratory (OAHPP) will provide a kit upon request.

### **Tips for Obtaining Gastric Aspirates**

Aspirates are obtained after sleeping at least 6 hours. Individuals should not drink or eat anything for at least 6 hours before the test to prevent the stomach from emptying; avoid exposure to the smell or sight of food, which may encourage gastric emptying. When the individual first wakes, a nasogastric tube is introduced into the stomach, and the contents aspirated. If nothing is obtained, instill approximately 20-50 mL of sterile water, and aspirate. As soon as possible, place specimens in the container supplied with the gastric lavage for MTB specimen kit, as a special buffer is required (sodium carbonate). This is essential in order to neutralize the acidity of the specimen before submission to the lab.

## **7. REPORTING REQUIREMENTS**

Under the Health Protection and Promotion Act (HPPA) of Ontario, physicians and registered nurses extended class are required to report **all cases of active TB disease and latent TB infection** to the local Medical Officer of Health in the jurisdiction in which they practise. The HPPA also requires hospital administrators to report when an inpatient or outpatient has been diagnosed with TB infection or disease. Under the HPPA, superintendents of institutions, school principals, pharmacists and operators of laboratories are also required to report TB. Patient consent is **not** required for reporting this information. The Personal Health Information Protection Act (PHIPA) explicitly allows health care providers to disclose health information without consent where permitted or required by law.

### **Report all latent TB infection (LTBI) and TB disease to Public Health**

- **Report patients with clinical or lab confirmed TB disease (respiratory and non-respiratory) as soon as possible. Culture confirmation is not necessary for reporting of a TB case.**
- **Report patients with LTBI, indicated by a positive TB skin test (TST), regardless of plans for prophylaxis.**

It is important to report all cases of TB disease in a timely manner to ensure that the follow-up of contacts and public health supports such as Directly Observed Therapy (DOT) for TB patients can begin without delay. Physicians and other health care professionals who undertake the clinical management of TB patients must report any non-adherence to treatment and missed appointments. Under the Health Protection and Promotion Act, the Medical Officer of Health can order an individual with active infectious TB disease to comply with treatment. The health care professionals reporting must provide information requested by the Medical Officer of Health, including chest x-ray, CT scan, MRI findings, smear/culture results and demographic information such as date of birth, gender, address and telephone number. (See section 12 - The Role of Public Health in TB Control)



# 8. TREATMENT AND MANAGEMENT OF ACTIVE TUBERCULOSIS DISEASE

## 8.1 GENERAL INFORMATION AND PRINCIPLES

### TB IS TREATABLE AND CURABLE

Physicians with TB experience should treat all cases of active tuberculosis. In jurisdictions where this is not possible, the treating practitioner should consult with a TB clinic or TB specialist. Pregnant women, children <15 years<sup>1</sup>, drug-resistant cases, HIV co-infected cases and cases with known or suspected treatment failure, should ALWAYS be referred to a TB clinic or TB specialist.

The objectives of treatment and management of TB disease are to achieve a lifetime cure while preventing drug resistance, and limiting transmission. To accomplish these objectives, health care providers should:

- **ALWAYS** initiate treatment with four anti-tuberculosis medications, until sensitivity results are obtained (see specific treatment regimens below). The drug sensitivity reports follow the culture results within one to two weeks;
- **ALWAYS** consider the possibility of drug resistance, especially in patients with a previous history of tuberculosis or in foreign-born patients from countries with a high prevalence of drug-resistant strains (See Drug-Resistant Tuberculosis);
- **NEVER** add a single drug to a failing regimen. Referral to a TB specialist is essential with patients experiencing treatment failure;
- **ALWAYS** consider the need for airborne precautions; consult with Public Health;
- **ALWAYS** offer HIV testing to persons with TB infection/disease;
- **PROMPTLY** refer every TB patient to Public Health for TB education, contact tracing, and Directly Observed Therapy (DOT) to facilitate compliance, when available. The treating physician and public health authorities share responsibility for case management;
- At **EVERY** visit with the patient: review education about TB disease and how drug resistance occurs, emphasize the need for adherence to drug treatments and isolation requirements, and ensure that patients take their medication correctly;
- **PROMPTLY** notify Public Health if non-adherence with treatment or isolation is suspected. Refer to section 12, The Role of Public Health in TB Control, for more detail.

Drugs for the treatment of active tuberculosis disease and latent tuberculosis infection are publicly funded in Ontario. This includes first-line and second-line drugs and pyridoxine (Vitamin B6). Contact Public Health to order TB medications.

## 8.2 FULLY SENSITIVE ACTIVE TUBERCULOSIS

The treatment regimen for fully sensitive TB is shown in Table 1. Tuberculosis disease in children is treated the same as in adults (See Pediatric Tuberculosis section 8.5). Non-respiratory TB is treated with the same regimens as respiratory TB with a few exceptions (see Fully Sensitive Non-Respiratory TB in section 8.3).

- Ethambutol (EMB) is included in the initial phase until drug resistance is ruled out;
- Regimens with both Isoniazid (INH) and Rifampin (RMP) may be discontinued after 9 months;
- Regimens that include Pyrazinamide (PZA) for the first 2 months of treatment may be discontinued after 6 months;
- Extend 6 month treatment regimens to 9 months in patients with the combination of positive cultures after 2 months of treatment and cavitary lung disease;
- Patients with HIV infection should be managed by a specialist;
- Dosing interval options include daily administration for the entire treatment, daily administration initially followed by intermittent dosing twice or thrice weekly (using DOT) for the duration of treatment;
- Administration of therapy on an intermittent basis refers to an increased interval between doses, as opposed to daily dosing. Twice or thrice weekly doses have been shown to be as effective as daily dosing with no appreciable difference in relapse rate and no increase in toxicity and side effects. This regimen is effective because the beginning of re-growth of TB bacteria is inhibited for several days after ingestion of a dose of antituberculosis antibiotics. These regimens are usually more easily supervised as they require fewer doses and direct observation visits. **Intermittent dosing should only be initiated by physicians experienced with the treatment of TB and when DOT can be provided for the duration of therapy.**

(CTS, pp. 117-119; ATS pp. 34-35)

1 The World Health Organization (WHO) defines pediatric tuberculosis as TB in persons less than 15 years of age. (CTS, p. 183)

**FIGURE 11 TB Treatment Regimens**

**TABLE 1 TREATMENT REGIMENS FOR FULLY DRUG SENSITIVE TUBERCULOSIS**

Regimen	Intensive Phase (months)	Continuing Phase (months)	Total (months)
INH/RMP/PZA ± EMB <sup>1</sup>	2	4	6
INH/RMP ± EMB <sup>1</sup>	1 – 2	7 – 8	9

INH=Isoniazid, RMP=Rifampin, PZA=Pyrazinamide, EMB=Ethambutol

<sup>1</sup> See Table 2 re: Ethambutol use in children

**TABLE 2 DOSAGE RECOMMENDATIONS FOR THE TREATMENT OF TUBERCULOSIS IN ADULTS AND CHILDREN\***

	DAILY DOSE	TWICE-WEEKLY DOSE	THRICE-WEEKLY DOSE
DRUGS	Adult mg/kg [Children, maximum dose]	Adult [Children, maximum dose]	Adult
Isoniazid (INH)	5 mg/kg (300mg) [10-15 mg/kg, max. 300 mg]	900 mg [20-30 mg/kg to max. 900 mg]	600
Rifampin (RMP)	10 mg/kg (600 mg) [10-20 mg/kg, max. 600 mg]	600 mg [10-20 mg/kg, max. 600 mg]	600
Pyrazinamide (PZA)	18-26 mg/kg (1000-2000 mg) [15-30 mg/kg, max. 2 g]	2000-4000 mg [50 mg/kg, max. 4 g]	1500-3000
Ethambutol (EMB)	18-26 mg/kg (800-1600 mg) [15-20 mg/kg, max. 1 g]**	2000-4000 mg [50 mg/kg, max. 2.5 g]	1200-2400

\* Doses for children are based on weight. Once the dose maximum is reached adult doses apply, regardless of age.

\*\* “Ethambutol at 15 mg/kg daily presents a very low risk of optic neuritis but may sometimes result in sub-therapeutic serum drug levels in young children. When ethambutol is a very important part of therapy, 20 mg/kg can be considered after discussion of risks and benefits and with suitable monitoring. At this dose, ethambutol is bacteriostatic, but it will help prevent the development of resistance. High-dose ethambutol (25 mg/kg daily) is bactericidal and sometimes used to treat drug resistant TB but carries a higher risk of optic neuritis. Expert consultation is recommended in this situation.” (CTS, p.188).

Source: CTS, p.123 Table 5, and p.187 Table 3.

**Warning: Every effort has been made to ensure the accuracy of the dosages of drugs and the prescribing information included in this book. Nevertheless, those prescribing these drugs are urged to follow carefully the manufacturers’ printed instructions.**

**TABLE 3 ANTI-TUBERCULOSIS DRUG INFORMATION <sup>1</sup>**

DRUG	MAJOR ADVERSE REACTIONS	MONITORING	REMARKS
Isoniazid (INH)	<ul style="list-style-type: none"> <li>Hepatotoxicity/ hepatitis</li> <li>Hypersensitivity reactions (e.g. rash, drug induced fever, thrombocytopenia)</li> <li>Peripheral neuritis (due to vitamin B6 deficiency)</li> <li>Drug interactions</li> </ul>	<ul style="list-style-type: none"> <li>Symptoms of hepatitis, hypersensitivity, or peripheral neuritis.</li> <li>Baseline CBC, and liver enzymes (ALT, AST, ALP) and bilirubin. Monitor monthly for patients with pre-existing liver disease, concurrent use of other hepatotoxic drugs, history of chronic or excessive alcohol use, prior drug induced hepatitis, age <math>\geq</math> 35 yrs, pregnant or within 3 months post-partum.</li> </ul>	<ul style="list-style-type: none"> <li>Never use INH alone in the presence of suspected/confirmed active TB disease as monotherapy may lead to the development of drug resistance.</li> <li>Never use INH where there is a high likelihood that patient has been exposed to an INH-resistant organism</li> <li>Asymptomatic minor elevations in AST level are common and not an indication for discontinuation of treatment.</li> <li>Withdraw hepatotoxic drugs and consult a TB specialist when AST or ALT exceeds five times the upper limit of normal without symptoms, or when AST or ALT exceeds three times upper limit of normal with symptoms or whenever clinical jaundice develops (CTS, p.136).</li> <li>Consult/refer to a TB specialist, and do not initiate INH, in patients with history of INH-induced hepatitis, severe adverse reactions, acute/active liver disease.</li> <li>Avoid alcohol consumption</li> <li>Best absorbed if taken on empty stomach (1 hour before meals or 2 hours after) but may be taken with food if stomach upset occurs</li> <li>Can increase the serum concentration of both drugs if given with Phenytoin (Dilantin) and some other anticonvulsant medications, and doses may have to be adjusted</li> <li>May lead to behaviour and coordination disturbances if given with Disulfiram (Antabuse).</li> <li>Administer INH at least one hour before antacids containing aluminum salts to avoid decreased gastro-intestinal absorption of INH.</li> <li>Pyridoxine (25-50 mg) may be given to prevent peripheral neuritis. It should routinely be prescribed with INH to adults/children with nutritional deficiencies, (including infants, children and adolescents on meat- and milk-deficient diets), alcoholism, diabetes, renal failure, HIV infection, seizure disorders, pregnant or breastfeeding women/teens,</li> <li>Advise patient to notify healthcare provider if any of the following symptoms appear: unexplained nausea, vomiting, anorexia, fatigue, weakness, fever lasting more than 3 days, persistent paraesthesia of hands and/or feet, rash, dark urine, jaundice, abdominal pain or tenderness especially in right upper quadrant, arthralgia.</li> </ul>
Rifampin (RMP)	<ul style="list-style-type: none"> <li>Hepatitis/ Hepatotoxicity</li> <li>Hypersensitivity reactions (e.g. rash, drug induced fever, thrombocytopenia)</li> <li>Drug interactions</li> <li>Flu-like illness</li> </ul>	<ul style="list-style-type: none"> <li>Same as for INH</li> </ul>	<ul style="list-style-type: none"> <li>Presents similar risks for hepatotoxicity as INH, therefore follow the same precautions. In Addition:</li> <li>Orange-red discolouration of body fluids e.g. urine, sweat, tears, saliva and feces is harmless, but permanently stain soft contact lenses.</li> <li>May accelerate clearance of many drugs metabolized by the liver, e.g. estrogens (i.e., oral contraceptives), coumadin, anticonvulsants, glucocorticoids, digoxin, antiarrhythmics, sulfonyleureas, theophylline, cyclosporine, methadone, ketoconazole and others; therefore: <ul style="list-style-type: none"> <li>Advise patients using oral contraceptive pill to use other methods of birth control</li> <li>Increases anti-coagulant drug requirement</li> <li>May precipitate Addisonian crisis in patients with marginal adrenal function.</li> </ul> </li> <li>Advise patient to notify healthcare provider if symptoms/adverse reactions appear.</li> <li>Memory impairment, thrombocytopenia, leukopenia and haemolytic anaemia have been observed.</li> </ul>
Pyrazinamide (PZA)	<ul style="list-style-type: none"> <li>Hepatotoxicity</li> <li>Hypersensitivity reactions</li> <li>Hyperuricemia</li> <li>Arthralgia (joint pain)</li> <li>Gastric irritation</li> <li>Drug interactions</li> </ul>	<ul style="list-style-type: none"> <li>Same as for INH</li> <li>In Addition:</li> <li>Uric Acid level if gout is suspected</li> </ul>	<ul style="list-style-type: none"> <li>Avoid alcohol consumption</li> <li>Discontinue for severe adverse reactions</li> <li>Absorption is not influenced by food intake</li> <li>Use with caution in patients with gout, renal failure, and diabetes mellitus; consult a TB specialist. <ul style="list-style-type: none"> <li>PZA may increase serum uric acid levels and decrease efficacy of gout therapy, requiring dosage adjustments of these medications.</li> <li>Dosing intervals may require adjustment in patients with impaired renal function and/or dialysis</li> </ul> </li> <li>Use with caution in pregnancy as the risk for teratogenicity has not been determined. Consult with a TB specialist.</li> <li>Withdraw hepatotoxic drugs and consult a TB specialist when AST or ALT exceeds five times the upper limit of normal without symptoms, or when AST or ALT exceeds three times upper limit of normal with symptoms or whenever clinical jaundice develops (CTS, p.136).</li> <li>Assess for interactions with other drugs, e.g. Allopurinol, sulfapyrazone, cyclosporine.</li> <li>Advise patient to notify healthcare provider if symptoms/adverse reactions appear.</li> </ul>
Ethambutol (EMB)	<ul style="list-style-type: none"> <li>Optic neuritis (most commonly seen in those receiving <math>\geq</math> 25 mg/kg but can occur with lesser dose, especially in patients with impaired renal function)</li> <li>Hypersensitivity reactions</li> </ul>	<ul style="list-style-type: none"> <li>Baseline and periodic assessment of visual acuity, visual field, and red-green colour perception.</li> <li>Monthly monitoring recommended for patients receiving <math>&gt;</math> 15 mg/kg.</li> </ul>	<ul style="list-style-type: none"> <li>Must be used in conjunction with at least one other antituberculosis drug</li> <li>Contraindicated in known hypersensitivity, and known optic neuritis</li> <li>Use with caution in patients with decreased renal function <ul style="list-style-type: none"> <li>Dosing intervals may require adjustments in patients with impaired renal function and/or dialysis</li> </ul> </li> <li>Use with caution in children, especially children too young for ophthalmologic monitoring – risk of optic neuritis is dose dependent. Consult with a TB specialist.</li> <li>EMB related visual changes usually reverse within weeks to months of stopping the drug. (CTS, p.125)</li> <li>Advise patient to notify healthcare provider if symptoms or adverse reactions appear, e.g. Patient should report any visual changes to physician immediately (usually occurs after taking drug for months)</li> </ul>

Source: CTS, p.123 Table 5, and p.187 Table 3.

<sup>1</sup> **Warning:** For complete information about the above drugs, their side effects, precautions and directions for use, the Health Care Professionals should always consult the manufacturers' printed materials or an equivalent pharmaceutical resource e.g., Compendium of Pharmaceuticals and Specialties (CPS)

## Monitoring and Follow-up

It is recommended that adult and child patients with active tuberculosis be seen monthly by the treating physician/clinic to evaluate symptoms of disease and/or drug toxicity, response to treatment and adherence to therapy.

See specific recommendations under each drug; and

- **Liver function testing:** all adults should receive baseline testing at the beginning of treatment, and follow-up, as necessary, to ensure hepatic stability on medications. Closely monitor liver enzymes of patients with underlying hepatic disease and the elderly. Routine liver function testing in children is not indicated but advise parents that the TB medication should be held and medical attention sought if anorexia, nausea, vomiting or jaundice occurs;
- **X-ray:** Obtain follow-up chest x-rays as required based on clinical assessment, for respiratory cases;
- **Sputum:** in respiratory disease, monitoring of sputum is recommended at 2 months and end of treatment to confirm smear conversion and diagnose cure. More frequent monitoring may be useful to help determine when a patient is no longer infectious and can be released from airborne precautions, or when clinical or radiographic response is unfavourable (CTS, p.128);
- **“Treatment Failure”** is defined as “positive sputum cultures after 4 or more months of treatment or two positive sputum cultures in different months during the last 3 months of treatment, even if the final culture is negative” (CTS, p.129). Drug sensitivities will be repeated to determine if there is drug resistance. Treatment failure requires more complex and longer treatment regimens;
- **Other monitoring:** for non-respiratory disease, monitor clinical outcome dependent on the site of disease;
- **Directly Observed Therapy (DOT):** All TB cases should be assessed for DOT by Public Health and the treating physician on an ongoing basis.

### 8.3 FULLY SENSITIVE NON-RESPIRATORY TUBERCULOSIS

Non-respiratory tuberculosis uses the same treatment regimen as respiratory tuberculosis. Longer courses of treatment are recommended for CNS TB, miliary/disseminated TB, and bone and joint TB (CTS, p. 119).

### 8.4 DRUG-RESISTANT TUBERCULOSIS (RESPIRATORY AND NON-RESPIRATORY)

Refer suspected or confirmed drug-resistant TB cases to a TB specialist/TB clinic because the management can be complex, lengthy and requires specific expertise.

All patients with MDR-TB or XDR-TB are hospitalized for the intensive phase of their treatment and **must** be treated with DOT upon discharge.

The possibility of drug resistance should **ALWAYS** be considered, especially in patients:

- with a previous history of tuberculosis - Patients previously treated for TB are at high risk for drug resistance and should be referred to a TB specialist prior to initiating treatment;
- who are from areas with a high prevalence of drug-resistant tuberculosis such as Eastern Europe and countries of the former Soviet Union, China, India, Korea, Philippines, Southeast Asia, and Africa (CTS, p. 147).

Treatment regimens for drug-resistant TB depend to which drug(s) the organism is resistant, and are the same, with few exceptions, for respiratory and non-respiratory disease (CTS, p. 161). The patient with drug-resistant respiratory disease may be infectious for longer periods than drug-susceptible cases. MDR-TB and XDR-TB cases will remain isolated on airborne precautions for the duration of hospital stay or until 3 sputum cultures, collected on consecutive days, are negative after 6 weeks of incubation (CTS, p. 331).

## 8.5 PEDIATRIC TUBERCULOSIS

Refer children promptly for assessment, diagnosis and treatment by a pediatric TB specialist. The diagnosis of TB disease in children can be difficult and is often based on a clinical presentation of a positive TB skin test, abnormal physical examination and/or chest x-ray, and a link to a suspect or known infectious TB case. Asymptomatic child cases are typically found when investigated as contacts of patients with infectious TB.

Children, especially those under 5 years of age, often present with non-specific or absent symptoms, they may have few bacilli present, and they may be unable to produce sputum. Gastric aspirates (see section 6) can be used in young children with suspected respiratory disease. Older children and adolescents are more likely to experience disease and symptoms similar to adults.

Tuberculosis disease in children is treated in the same manner as disease in adults. The child’s weight should be monitored monthly and anti-tuberculosis drug doses adjusted according to weight. Pyridoxine supplementation is given to selected children receiving INH. (CTS, pp. 183-186)

### 8.6 PREGNANCY AND BREASTFEEDING

Refer pregnant patients promptly for assessment and treatment by a TB specialist. “Untreated TB poses a far greater hazard to a pregnant woman and her fetus than does treatment of the disease” (CTS, p. 192). Isoniazid, rifampin and ethambutol are well studied and safe in pregnancy. The safety of PZA and second-line drugs in pregnancy has not been established so recommendations for their use cannot be made and advice from a TB expert should be

sought. The use of aminoglycosides (streptomycin, amikacin, kanamycin) and capreomycin are contraindicated because of effects on the fetus. The use of first-line drugs is not an indication for termination of pregnancy and is not a contraindication to breastfeeding. Pyridoxine is recommended for pregnant and breastfeeding women taking INH. The small concentration of TB medications found in the breast milk of mothers receiving treatment for TB or LTBI are ineffective as treatment or prophylaxis for the infant. Evaluate the newborn for congenital TB when the mother has been diagnosed with TB during the pregnancy or in the postpartum period. (CTS, pp. 127, 128 & 192).

## 8.7 HIV/AIDS

All persons with TB disease should have HIV testing. All persons with HIV should have TB testing.

Treatment of TB in HIV-infected patients should be guided by a physician with expertise in the management of both diseases (CTS, p. 210).

Pyridoxine (Vitamin B6) should be given to HIV-infected TB patients receiving INH. Use of antiretroviral therapy (ART) in combination with TB treatment is complicated by: 1) adherence problems with polypharmacy, 2) overlapping side effects, 3) drug interactions and, 4) the occurrence of immune reconstitution inflammatory syndromes (CTS, p. 127). Rifampin may interact with ART. Rifabutin, with appropriate dose adjustment, can be substituted for rifampin in TB treatment when required. (CTS, pp. 210- 211)

## 8.8 HOSPITALIZATION OF CASES OF ACTIVE TUBERCULOSIS

Hospitalization is not generally required for active tuberculosis patients except in circumstances as follows:

- For further investigation and/or treatment of symptoms;
- To establish acceptable therapeutic regimens and monitor patients closely with potential intolerance issues;
- To manage associated medical conditions, which may complicate diagnosis or treatment;
- Effective airborne precautions cannot be provided as an outpatient; and/or the patient has immunocompromised persons living in their home, e.g., young children/infants, persons infected with HIV;
- When MDR or XDR tuberculosis is suspected or confirmed;
- For socioeconomic reasons, e.g., homelessness;
- In congregate settings where airborne precautions are not available or possible, e.g., long-term care facility, group home, shelter.

(CTS, p. 126)

## 8.9 TRANSPORTATION OF PATIENTS WITH SUSPECTED OR CONFIRMED ACTIVE TUBERCULOSIS

When patients with suspected or confirmed infectious TB must attend an appointment, they should wear a surgical mask or N95 respirator. When transferring between health care facilities notify the transportation services and the receiving facility in advance. The infectious patient should be transported in well-ventilated vehicles (i.e., windows open) as much as possible and not use public transportation (CTS, p. 329). For community transfers consult with Public Health as needed.

(See section 11, In-Hospital Management of Tuberculosis)

# 9. TREATMENT AND MANAGEMENT OF LATENT TUBERCULOSIS INFECTION

**TB IS PREVENTABLE, TREATABLE AND CURABLE**

## 9.1 GENERAL INFORMATION

Treatment for latent tuberculosis infection is undertaken to prevent active disease in infected persons thereby preventing the potential transmission to others. Health care providers should consider treatment for persons with positive skin tests where the presence of active disease has been ruled out. The decision to offer treatment for LTBI should be made after weighing risk factors and benefits of treatment against the potential risks of treatment.

## 9.2 RECOMMENDED TREATMENT REGIMEN FOR LTBI

INH and Vitamin B6 (prophylaxis for peripheral neuritis) can be ordered free of charge through your local Public Health. Consider providing intermittent Directly Observed Prophylactic Therapy (DOPT) in situations where the patient may have potential problems with adherence, if staff resources are available. Intermittent dosing for the treatment of LTBI should be undertaken with the assistance of a TB specialist.

### PROVEN EFFECTIVENESS

INH has been used to treat LTBI since Ferebee et al first reported its effectiveness in 1957. While the drug has been shown to be safe, cheap, easy to take and well tolerated, its effectiveness is dependent on adherence to treatment and adequate duration. Patients who took at least 80% of the recommended doses of daily

INH for at least one year achieved a 93% protection rate against reactivation. Daily INH for 6 months provided 69% protection. The optimal protection is probably achieved by 9 months (CTS, p. 131).

Rifampin regimens have also been used to treat LTBI. It is recommended that a TB specialist be consulted if treatment of latent infection with rifampin is indicated.

<b>FIGURE 12 Dosage of Isoniazid for LTBI</b>	
<b>Adults:</b>	5 mg/kg/day (max. 300 mg daily)
<b>Children:</b>	10-15 mg/kg/day (max. 300 mg/day)

### 9.3 CONTRAINDICATIONS, SIDE EFFECTS, ADVERSE EVENTS AND CLINICAL MONITORING

Please refer to section 8 – Table 3 for a summary of adverse events, side effects and monitoring recommendations for INH and RMP.

### 9.4 HIV OR OTHER IMMUNOCOMPROMISED CONDITIONS

HIV positive individuals or severely immunocompromised individuals, REGARDLESS OF TST STATUS, should be offered preventive treatment for LTBI. HIV positive persons should be prescribed the same dose and duration of INH as the HIV negative population (CTS, p. 127).

### 9.5 PREGNANCY/BREASTFEEDING

Although INH has not been shown to be teratogenic, it is not recommended during pregnancy except in recently infected women or women who have high risk medical conditions, such as HIV infection. Consider deferring treatment for LTBI at least until the second trimester in these high risk women and until the postpartum period for all others. The possibility of active disease must be ruled out. When treatment for LTBI is deferred, both the patient and physician should watch for any symptoms of active TB disease. Breastfeeding should not be discouraged during treatment for LTBI (CTS, pp. 127, 134).

### 9.6 PEDIATRICS

Treatment for LTBI should be initiated immediately once active disease has been ruled out. Children do not need baseline liver function tests unless they have a known or suspected underlying liver disease and are not taking any other hepatotoxic drugs. When children begin drug therapy, inform parents or guardians about symptoms associated with the most common adverse reactions and signs of hepatotoxicity (CTS, p. 192).

### 9.7 MANAGING CLOSE CONTACTS EXPOSED TO DRUG-RESISTANT ACTIVE CASES

When a source patient has a resistant tuberculosis organism, infected contacts should be managed with drugs to which the source case is sensitive and in consultation with an expert in TB.

### 9.8 MANAGING LTBI WHEN TREATMENT IS REFUSED, CONTRAINDICATED OR STOPPED BEFORE COMPLETION

- Regular follow-up for 2 years is recommended for those for whom the risk of TB is high (period of highest risk for development of active disease) (CTS, p. 136);
- Advise patient about the symptoms of active disease and the need to access health care in the event they experience any of these: weight loss, cough, hemoptysis, night sweats, fatigue, etc.

## 10. NONTUBERCULOUS MYCOBACTERIA (NTM)

Nontuberculous Mycobacteria (NTM) are species of mycobacteria sometimes called “mycobacteria other than tuberculosis” (MOTT), “atypical”, “environmental” or “opportunistic” mycobacteria. Common species include all mycobacterial species except those that cause tuberculosis (TB), e.g., *M. avium complex (MAC)*, *M. fortuitum-chelonae-abscessus family*, *M. goodii*, *M. kansasii*, *M. malmoense* and *M. xenopi*. These organisms may present with symptoms suggestive of pulmonary TB. They appear to be acquired from the environment and occur naturally in water, soil and food and also in association with animals. They are non-contagious and are not transmitted from person to person and contact follow-up is therefore not necessary (CTS, p. 222).

Nontuberculous mycobacteria present as opportunistic infection in the immunocompromised individual. The disease process may be self-limiting, chronic or life-threatening. Possible co-infection with *M. tuberculosis complex* should be considered. The common clinical syndromes associated with NTM are lymphadenopathy, chronic pulmonary disease and skin and soft tissue infections.

Acid-fast bacilli (AFB) in secretions or tissues should be interpreted to mean presence of *M. tuberculosis* until proven otherwise via polymerase chain reaction (PCR) assays and cultures. NTM are **not** reportable to Public Health, however, all AFB positive results should be reported.

Treatment of NTM disease is lengthy and complex and management by a specialist is recommended. NTM are resistant to a wide range of antimicrobial agents and the resistance develops rather readily, hence single drug therapy must be avoided (CTS, p. 225). Decisions



to treat NTM should be based on clinical presentations and demonstrating three consecutive sputum specimens that grow the organism.

Drugs for the treatment of NTM are **not supplied** through Public Health and are **not provided** free-of-charge.

# 11. IN-HOSPITAL AND INSTITUTIONAL MANAGEMENT OF TB

## 11.1 TRIAGE

The transmission of TB has been described in many institutional settings. Most nosocomial transmission from infectious cases occurs before diagnosis. People with undiagnosed TB disease often seek care in Emergency Departments. Early identification of patients with suspected TB and implementation of appropriate airborne precautions are important. This will reduce the risk of transmission of TB to health care workers, patients, visitors, volunteers and other people in the health care facility.

## 11.2 PREVENTING SPREAD OF TB

All health care facilities must assess for the TB risk classification of the facility, risk classification of TB exposure of the health care workers' activities and protocols in place to either admit TB patients or transfer out to an appropriate facility.

The current guidelines emphasize the importance of early diagnosis through worker and client education programs. It is essential that all facilities have a TB management program, supported at the highest administrative level.

The recommendations called for the hierarchical approach to controls are:

- *administrative controls*, such as more rapid isolation, diagnosis and treatment of patients with suspected or active TB;
- *engineering controls*, such as improved ventilation in patient care areas; and
- *personal controls*, such as tuberculin skin testing of workers and use of more efficient particulate respirators (i.e., masks).

In health care facilities where TB patients are rarely admitted and are transferred out, there should be at least one area where patients can be kept in airborne isolation until they are transferred.

### Risk classification: health care workers

#### *High-risk activities*

- cough-inducing procedures, autopsy, morbid anatomy and pathology examination, bronchoscopy and designated mycobacteriology laboratory procedures.

#### *Intermediate-risk activities*

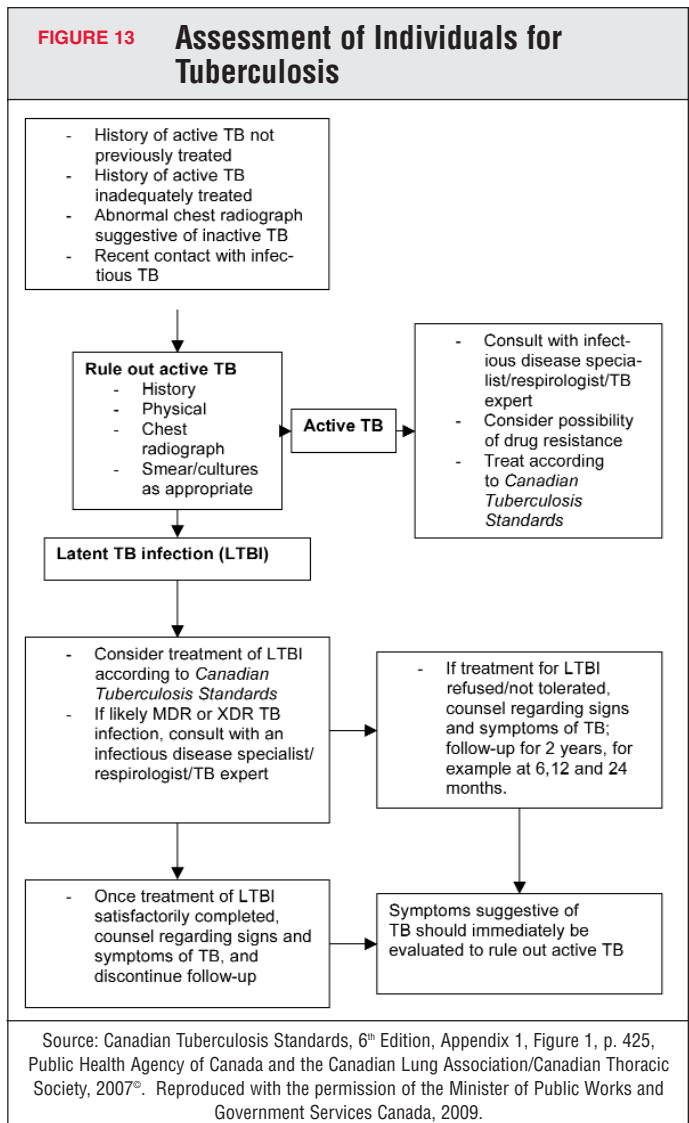
- regular direct contact on units with active TB patients (e.g., nurses, nursing aides, respiratory technologists, social workers, physiotherapists and housekeeping involved with cleaning their rooms.)

#### *Low-risk activities:*

- minimal direct patient contact on units with active TB patients (medical records, administration and maintenance). (GTS, p.326)

### **Early identification of patients with suspected TB**

The presence of cough of more than 3 weeks' duration with or without weight loss and fever in a person belonging to one of the risk groups should prompt a thorough investigation to rule out TB. Suspected or confirmed infectious TB patients should **immediately** be placed in appropriate airborne isolation precautions. For further assessment of individuals for TB see Figure 13.



## 11.3 AIRBORNE PRECAUTIONS

### 1 Airborne precautions:

Canadian Standards Association (CSA) and American Society of Heating Refrigeration and Air-conditioning Engineers (ASHRAE) recommend that airborne isolation precaution rooms in new buildings have a minimum of 12 air changes per hour (ACH). The Centers for Disease Control and Prevention (CDC) recommends that pre-existing rooms should have at least 6 ACH. Air from the room should be exhausted to the outdoors, ideally exiting from the roof. If the air will be re-circulated, or if the exhausted air could re-enter the building, it must be passed through a high efficiency particulate air (HEPA) filter before being exhausted. Air flow should be tested with smoke tubes at all 4 corners of the door daily when the room is occupied, unless the room is equipped with automatic pressure monitoring;

- 2 Notify infection prevention and control personnel;
- 3 Windows and doors should be kept closed at all times and the patient should have dedicated toileting;
- 4 All staff entering the room should wear an approved, fit-tested, particulate respirator (mask), e.g., N95; adult visitors should also wear an N95 respirator;
- 5 Visits by children should be discouraged because of their increased susceptibility;
- 6 Appropriate airborne isolation precaution signage should be posted in a visible location;
- 7 TB patients leaving the room should wear a surgical mask. Notify the receiving department;
- 8 Instruct patients to cover their mouth and nose with tissues when coughing or sneezing;
- 9 Limit the number of people that need to enter and leave the room;
- 10 Postpone elective procedures until the patient is non-infectious.

### **HEPA Filtration and UVGI**

Within existing facilities use of HEPA-filtered units (fixed or portable) may be used to recirculate air in a room to increase the germ-free ventilation without the need for an increase in the amount of outdoor air supplied. There have been very few studies to evaluate the efficacy of ultraviolet germicidal irradiation (UVGI) although this technology is being used with increasing frequency in some settings, such as homeless shelters, to improve germ-free ventilation without the cost of renovating the heating-ventilation-air conditioning (HVAC) system. Equipment must be maintained according to manufacturers' instructions.

For more details, refer to CTS, pp. 333-336.

Refer to CTS, p. 335 Table 3 to determine the time (number of air changes per hour) needed to remove airborne contaminants after generation of infectious droplet nuclei has ceased.

### **Personal Respiratory Protection**

Current recommendations call for respirators (masks) that filter 95% of particles of 1 micron or larger and have less than 10% leak to protect workers against airborne TB. In some Canadian provinces/territories, formal respirator fit testing is required.

## 11.4 DISCONTINUATION OF AIRBORNE PRECAUTIONS

Discontinuing airborne precautions can vary depending on if it is a suspect TB case, confirmed smear-negative and culture-positive TB case, confirmed smear-positive and culture-positive TB case, MDR-TB case or XDR-TB case.

Criteria for discontinuation of precautions should NEVER be based on a fixed interval of treatment (e.g., 2 weeks) but rather on evidence of clinical and bacteriological improvement and evidence of the adequacy of the treatment regimens. Airborne isolation precautions should be continued until patients are highly likely to be non-infectious.

### **Criteria for Discontinuing Airborne Isolation Precautions**

*Patients with smear positive TB can discontinue isolation after:*

- a) at least two weeks of effective multi-drug therapy based on the individual's drug sensitivity pattern; **AND**
- b) three spontaneous sputum samples over a 8-24 hour period are all negative AFB, with one sputum specimen being an early morning specimen; or bronchial washings or induced sputum, **AND**
- c) evidence of clinical improvement.

*Patients with smear negative TB can discontinue isolation after:*

- a) at least two weeks of effective multi-drug therapy based on the individual's drug sensitivity pattern,

**AND**

- b) there is clinical evidence of improvement.

(CTS, p. 330)

### **Key Principles in Discontinuing Airborne Isolation Precautions**

- An appropriate drug regimen must be established based on the individual's drug sensitivity pattern;
- The individual is tolerating tuberculosis medications;
- There are no medication adherence issues;
- There is evidence of clinical improvement, e.g., chest x-ray and symptom improvement;
- Individuals with multi-drug resistant tuberculosis (specifically, resistant to isoniazid and rifampin) should remain on airborne precautions for the duration of hospitalization or until 1 set of 3 consecutive sputum cultures (not AFB smears) are negative.

\*If there are any questions regarding discontinuing airborne isolation precautions, infection control practitioners or the local public health unit should always be consulted.

## 11.5 DISCHARGE PLANNING

Most individuals with active tuberculosis can be successfully treated as outpatients. If hospitalized, patients can be discharged into the community even when they are still infectious, with isolation at home until they meet criteria for release from isolation (see 11.4). However, this should occur only if there are no children under the age of 5 or persons with immunocompromising conditions (e.g., HIV) residing in the household, unless those people are already receiving treatment for TB disease or LTBI. (CTS, p. 331)

Discharge planning should begin as soon as the diagnosis is made.

**Collaboration with the local public health unit is essential for the patient to be successfully transitioned into the community.**

Prior to discharge, the following steps should be arranged for community transition:

- Confirm outpatient appointment with the provider who will manage the patient until cured;
- Provide individual with the clinician's phone number in case complications arise;
- Give sufficient TB medications until the next appointment;
- Notify Public Health of patient discharge in order to implement DOT and follow-up;
- Review isolation precautions with the infectious patient and provide masks for airborne isolation precautions;
- Assess if the patient requires absentee documentation for school/employer.

## 11.6 PERSONAL CONTROLS TUBERCULIN SKIN TESTING (TST)

The importance of proper baseline tuberculin skin testing for all potentially exposed health care workers in all health care settings cannot be overemphasized. Institutions should take steps to educate staff on the utility of annual testing. Facilities are strongly encouraged to meet the minimum standard of base-line two-step and post-exposure tuberculin skin testing. Workers who require further medical assessment should be seen by a physician experienced in the interpretation of TSTs and the treatment of LTBI. (See section 9)

### INTERFERON-GAMMA RELEASE ASSAYS

New interferon-gamma release assays have not been studied for use in serial testing. Therefore they are NOT recommended at this time for periodic or post-exposure testing of workers in health care facilities.

### TST FOLLOWING UNPROTECTED EXPOSURE

All health care facilities must have a process to contact and assess all workers, including contractors, volunteers and agency workers who had unprotected exposure to infectious TB. A single TST is performed soon after the contact is identified. If this TST is negative then a second TST is performed no sooner than 8 weeks after the contact was broken to detect TST conversion.

## 12. THE ROLE OF PUBLIC HEALTH IN TB CONTROL

Public Health has many roles to ensure TB standards are met and maintained in our communities:

- To ensure prompt and complete reporting of latent TB infection and active TB disease;
- To ensure effective case management and contact tracing for active TB cases;
- To ensure provision of publicly funded drugs at no charge to the patient for treatment of active or latent TB;
- To carry out post-landing medical surveillance for individuals identified by Citizenship and Immigration Canada (CIC) with inactive TB in recent immigrants, refugees and refugee claimants;
- To provide education and consultation as needed;
- To use local epidemiology to ensure needs are addressed and met at the regional level;
- To meet legislative requirements regarding the reporting of TB.

### 12.1 CASE MANAGEMENT

Public Health legislation provides local health units with the authority to ensure that suspected or confirmed cases of active TB receive timely diagnosis and treatment (CTS, p. 241). The fundamental purpose of case management is to render and maintain the TB case non-infectious through their course of treatment (MOHLTC TB Best Practices, p. 9).

A public health professional investigates suspected and confirmed cases of active TB and coordinates diagnostic services and treatment. The treating physician and case manager share responsibility for the case during the prolonged treatment period (CTS, p. 244).

An interview is conducted, ideally face to face, with each active case of TB to educate the client about TB treatment including the potential for side effects. Public Health monitors each case for side effects and adherence of medications, provides support and problem-solving for psychosocial issues related to TB, and can also supervise therapy with the use of Directly Observed Therapy. The case manager also follows up with potential close contacts of individuals with infectious TB to ensure they are assessed for active TB and offered TB prophylaxis if they are determined to have LTBI.

### 12.2 PROVISION OF MEDICATION

All TB medications are provided by the Ministry of Health and Long-Term Care at no cost for the treatment of both active and latent TB. Medication for non-mycobacterium TB is not covered. Each health unit has their own mechanism by which these medications are dispensed to the client. Contact Public Health to determine how your health unit distributes TB drugs.

### 12.3 DIRECTLY OBSERVED THERAPY (DOT)

In Ontario, this therapy is available through Public Health. Adherence to an effective treatment regimen is essential to cure tuberculosis, reduce the risk of transmission and prevent the development of drug-resistant strains. The best way to ensure adherence to treatment is for a health care provider to watch a person with tuberculosis take all of their prescribed medications. DOT is also invaluable for the early identification and close management of medication side-effects, in collaboration with the treating physician.

All persons with tuberculosis should be assessed for DOT therapy; persons on intermittent regimens must receive DOT. When resources are limited, individuals with respiratory tuberculosis who have the following risk factors should receive priority:

- Suspect or proven drug-resistant organisms;
- Sputum smear positive for acid fast bacilli;
- Treatment failure or relapsed/re-activated disease;
- Substance use (e.g., alcohol or drugs);
- Homeless or under housed individuals;
- Those with co-morbid conditions (e.g., HIV/AIDS, diabetes, end-stage renal disease);
- Suspected non-adherence or previous non-adherence;
- Children and adolescents;
- Those with mental health concerns/cognitive impairments.

(CTS, p. 121)

The DOT worker not only observes the person taking their medication but can also monitor for side effects of the drugs, watch for signs indicating relapse, ensure the person attends appointments, educate about tuberculosis and provide ongoing support and assistance for other issues (e.g., housing, welfare). In some jurisdictions, incentives and enablers (e.g., bus tickets, food supplements, and clothing) may be available for persons on DOT.

### 12.4 MANAGEMENT OF THERAPY NON-ADHERENCE

When individuals fail to take their medications as prescribed, they are at risk of infecting others, relapsing and/or developing drug-resistant tuberculosis.

As symptoms resolve, there may be less motivation to take all of these drugs as prescribed. Individuals may not appreciate the risks of not taking their medications as prescribed or may feel that these risks were exaggerated by the health care provider. DOT eliminates the risk of non-adherence. However, if the person is self-administering, then it is important for Public Health to maintain regular contact in order to ask key questions about adherence. These questions include:

- Are you taking your medication every day? If not, what days have you missed?
- Are you having any side effects from the drugs?
- When was your last medical appointment? When is your next appointment?
- Do you have any symptoms of illness?

Other methods that Public Health will use to monitor adherence include:

- Contacting the treating physician/clinic on a regular basis to ensure that the person has kept their follow-up appointments and that they are making appropriate clinical improvement (e.g., sputum conversion, x-ray has improved);
- Conducting a home visit to assess compliance and,
- Carrying out a pill count.

### 12.5 PUBLIC HEALTH ORDERS

If a health care professional has concerns of lack of adherence and cooperation from an active respiratory case, Public Health should be notified, who may then place the individual on DOT and notify the treating physician. Other scenarios include an infectious TB patient who is determined to travel by public transport, e.g., airplane, train. If measures to achieve compliance have failed and the public's health and safety are at risk, the Medical Officer of Health has the legal authority under the *Health Protection & Promotion Act* (HPPA) to act to prevent the spread of TB. As such, a person with TB can be ordered to comply with treatment and/or isolation. If necessary, the Medical Officer of Health can apply to provincial court for a detention order, whereby a TB patient may be detained in hospital for treatment in order to protect the public. (See Sections 22 and 35 of HPPA at: [http://www.e-laws.gov.on.ca/html/statutes/english/english/elaws\\_statutes\\_90h07\\_e.htm](http://www.e-laws.gov.on.ca/html/statutes/english/english/elaws_statutes_90h07_e.htm)). Public Health will collaborate with treating physicians to draft legal orders under the HPPA, e.g., requiring the client to remain in isolation, take medications or disclose contacts.

### 12.6 CONTACT FOLLOW-UP

Persons who have been in contact with an individual who has active, untreated respiratory, laryngeal, miliary or pleural tuberculosis (the index case) may be at risk of contracting the infection (CTS, p. 253). The more infectious the individual and the longer and closer the exposure, the more likely the contact is to become infected. Persons who have lower immunity such as children less than five years of age, persons who are HIV positive, persons who live in congregate settings such as homeless shelters and persons exposed during high risk medical procedures (e.g., bronchoscopy), are at higher risk of contracting tuberculosis infection/disease. Public Health will give priority to these groups during contact investigations.

**Contact follow-up is the responsibility of Public Health.** Under the HPPA of Ontario, all health units must have a program in place to trace and investigate contacts of tuberculosis cases. Public Health will identify, locate and notify contacts in order to recommend appropriate assessment, testing and treatment to prevent progression from latent infection to active disease. This includes referral of contacts who live outside Ontario or who have been exposed to infectious TB during long-distance travel to the Ministry of Health and Long-Term Care. Questions regarding contact investigation should be directed to Public Health (CTS, p. 244). The identity of the index case is not disclosed to contacts.

Guidelines for TST conversion in the context of contact investigation are dependent on a number of variables. True conversion is dependent upon: whether contacts have a previously documented skin test, level of infectivity of the source case, degree of exposure and history of previous treatment for TB disease or LTBI. Generally skin tests are repeated at least 8 weeks after the last exposure for all close contacts who had an initial negative result.

Contacts deemed to be at risk are most often referred for follow-up to their own health care provider. However, in group settings such as schools, shelters for the homeless, or workplaces, public health staff may hold screening clinics to facilitate the follow-up of large numbers of people. Individuals who test positive during these screening clinics are referred to their physician for further assessment and management. When the index case has drug-resistant tuberculosis, physicians and/or Public Health should refer contacts to or consult with a physician who has experience in dealing with drug-resistant TB.

## 12.7 INVESTIGATION AND MANAGEMENT OF TB OUTBREAKS

The goals of investigation and management include prompt identification of the source case(s), early identification of new cases and initiation of treatment, and identification of persons with recently acquired LTBI so preventative treatment can be provided. The end result will reduce the risk of ongoing transmission and prevent further development of active disease. Genotyping (DNA sequencing to identify matching strains) of TB specimens can be conducted by the Public Health Laboratory (OAHPP) to determine if there is evidence of transmission.

## 12.8 PATIENT, FAMILY AND COMMUNITY EDUCATION

Myths, misinformation and stigma about tuberculosis continue to present problems. It is thus very important for the individual with newly diagnosed infection or active disease to receive accurate and timely information. Education should begin at the time of diagnosis and continue until all of the patient's questions have been answered and he/she is knowledgeable about:

- The cause of tuberculosis;
- How to prevent transmission to others;
- Side effects to watch for with anti-tuberculosis medication;
- Why prolonged treatment is required and why it is important to take anti-tuberculosis medication as prescribed (adherence to therapy);
- The fact that people cannot be deported simply for having TB. TB status, disease or treatment has no impact on an individual's immigration status (the only exception being that immigrants on post-landing medical surveillance must have a medical assessment in Canada as a condition of landing).

Health promotion activities extend from the TB client and family to the community and can include provision of resources, presentations, acknowledgement of World TB Day (March 24) and collaboration with organizations to develop policies and initiatives for topics such as TB-HIV co-infection.

## 12.9 LIMITATIONS ON ACTIVITIES WHILE IN ISOLATION

The infectious patient should be counseled NOT to return to work, school, or usual social activities, nor to have visitors. The patient should also refrain from going into any other indoor environment or use public transportation where TB transmission could take place. The patient should be instructed to wear a mask when attending the Emergency Department or when seeing their doctor. These precautions must remain in place until consultation has occurred with Public Health (CTS, p. 331).

## 12.10 RESUMPTION OF NORMAL ACTIVITIES

The decision regarding when a person with active respiratory tuberculosis can resume normal activities, i.e., return to school or work, **must** be made in consultation with Public Health and the treating physician. The following characteristics must be considered:

- Characteristics of the individual;
  - Characteristics of the disease;
  - Characteristics of the work/school environment.
- (MOHLTC TB Best Practices 2006, p. 92)

## 12.11 MEDICAL SURVEILLANCE PROGRAM FOR INACTIVE TB

Over recent decades the epidemiologic and demographic nature of TB in developed countries such as Canada have been shown to be directly linked with international population movement. Thus, the Medical Surveillance Program has been established to help find and treat TB in a timely manner. The purpose of Medical

Surveillance is to provide new immigrants to Canada who have been referred by Citizenship and Immigration Canada (CIC) with appropriate medical follow-up to rule out active TB disease and to determine follow-up if either active or inactive TB is confirmed. By screening new arrivals for TB, persons can be offered treatment and therefore prevent the spread of TB in Canada.

All immigrant applicants to Canada must undergo an Immigration Medical Examination (IME). In most cases, the IME is carried out prior to arrival in Canada. It includes a comprehensive medical history, targeted physical examination guided by the history and available laboratory data, and other investigations considered relevant, including chest x-ray for all individuals 11 years and older. The IME does not include a TST, as the goal is only to detect active, infectious TB.

CIC refers new immigrants, refugees and refugee claimants who have been identified as high risk for pulmonary TB or LTBI progressing to active TB disease, for Medical Surveillance and follow-up. Individuals are most commonly put on Medical Surveillance because of abnormal chest x-ray findings or previous history of TB (CTS, p. 244). Once the local public health unit is notified that an individual is on Medical Surveillance for TB, the health unit will request a follow-up chest x-ray post-arrival as part of the program requirement.

CIC may also determine that a person is deemed an urgent referral (CTS, p. 422). Public Health will attempt to contact these persons as soon as possible and will arrange for medical assessment within a week of receipt of notification.

### 12.12 TB DIAGNOSTIC AND TREATMENT SERVICES FOR UNINSURED PERSONS (TB-UP) PROGRAM

TB-UP is a program funded by the MOHLTC and offered only in Ontario. It ensures that persons who are not covered by OHIP, Interim Federal Health (IFH) or any other provincial, territorial or private health insurance plan can be assessed and/or treated for suspect or active TB including their contacts. Persons must be enrolled in the TB-UP program before payment can be made by the MOHLTC. **Contact Public Health to enroll someone in TB-UP PRIOR to providing service.** The TB-UP program will not issue retroactive payments for persons who receive TB diagnostic and/or treatment services prior to registration in the program. TB-UP may cover some in-patient services directly related to the diagnosis and/or management of TB. Public Health should be contacted in this regard.

## 13. SUMMARY

### TB IS PREVENTABLE, TREATABLE AND CURABLE

Neither Health Care Providers nor Public Health Officials can achieve control of tuberculosis without each other. It is important that we work together.

#### ADDITIONAL TB RESOURCES

The Lung Association (Ontario) - order by calling 1-888-344-5864

- Facts about Your Lungs: Tuberculosis – Preventable, Treatable, Curable (pamphlet)
- TB Infection vs. Disease (poster - see page 11)
- Think TB if you work or volunteer in... (poster)
- Website: [www.on.lung.ca](http://www.on.lung.ca)

Canadian Lung Association website (includes pamphlet in English and 20 other languages and information on the history of TB in Canada): [www.lung.ca](http://www.lung.ca)

Public Health Agency of Canada website: [www.phac-aspc.ca/tbpc-latb/index-eng.php](http://www.phac-aspc.ca/tbpc-latb/index-eng.php)

StopTB Canada website: [www.stoptb.ca](http://www.stoptb.ca)

Contact your local health unit for additional TB resources.

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Figure 10: Specimen requirements for mycobacterial isolation and acid-fast stain and Labstracts: [http://www.health.gov.on.ca/english/providers/pub/pub\\_menus/pub\\_labs.html](http://www.health.gov.on.ca/english/providers/pub/pub_menus/pub_labs.html)

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