

# Quick reference for Health Care Professionals

## Assessment and Treatment of Latent Tuberculosis Infection in Adults

### Indications for Tuberculin Skin Testing

To diagnose TB infection in persons at increased risk for progression to active disease

#### Who:

- Contacts of persons recently diagnosed with active pulmonary tuberculosis
- Foreign born persons from TB endemic country, especially if immigrated within the last five years
- Increased risk of progression to active TB disease due to impaired immunity

*Canadian Tuberculosis Standards, 2000, p. 45*

### Risk factors for development of active Tuberculosis in those infected with *Mycobacterium tuberculosis*:

#### High Risk

- Acquired immunodeficiency syndrome
- Human immunodeficiency virus infection
- Transplantation
- Silicosis
- Chronic renal failure/ hemodialysis
- Carcinoma of head and neck
- Recent infection ( $\leq 2$  years)
- Abnormal chest radiograph – fibronodular disease

#### Increased Risk

- Diabetes mellitus
- Underweight (<90% ideal body weight)
- Age when infected ( $\leq 5$  years)
- Abnormal chest radiograph – granuloma

#### Low Risk

Infected person, no known risk factor (“low risk reactor”)

*Canadian Tuberculosis Standards, 2000, p. 49*

### Other persons, particularly those who are at risk of exposure to TB

- Health care workers at risk for occupational exposure to TB
- Staff and residents in communal care including correctional facilities, long term care
- Persons from Aboriginal communities with high rates of TB
- *Tuberculin Screening is generally discouraged for those with no elevated risk for infection with TB and no known risk factors for progression to active TB disease.*

*Canadian Tuberculosis Standards, 2000, p. 45, 46, 207*

### Contraindications for Tuberculin Skin Testing

- Persons with a documented **positive skin test** in the past
- Persons with tuberculin reactions that have severely blistered in the past
- Persons with documented active tuberculosis in the past
- Persons with a clear past history of treatment for TB infection or disease
- Persons with extensive burns or eczema
- Persons with major viral infections or live-virus vaccinations in the past month for example MMR

### Note: These are NOT contraindications to Tuberculin Skin Testing:

- Recently vaccinated with non-live virus vaccines
- Pregnancy
- Received BCG vaccination in the past
- History of positive tuberculin skin test but this is not documented

*Canadian Tuberculosis Standards, 2000, p. 46*

### Technique for the Skin Test

- Administer 0.1 ml of purified protein derivative (PPD)
- Inject intradermally on volar aspect of the forearm
- Injection should raise a small weal 5 mm in diameter, which will disappear in 10-15 minutes.

*Canadian Tuberculosis Standards, 2000, p. 46*

### Reading:

- Must be read by a trained health professional. Self reading is inaccurate and strongly discouraged
- 48-72 hours after administration
- Induration of the transverse diameter to the long axis of the forearm should be measured and recorded in millimeters (mm) and not simply reported as negative or positive
- Erythema should **NOT** be read. Redness does not indicate TB infection

*Canadian Tuberculosis Standards, 2000, p. 47*

### Interpretation of Tuberculin Test

**Proper interpretation of the tuberculin skin test should take into account all three of the following:**

1. Size of the reaction (induration)
2. Predictive value of the test (considering potential causes of false-negative, false-positive reactions)
3. Risk of progression to active TB disease

Tuberculin reaction size, mm induration	Setting in which reaction considered significant (meaning probable TB infection)
0-4	HIV infection AND expected risk of tuberculosis infection is high (e.g. patient is an immigrant from a country where TB is endemic, is a household contact, or has an abnormal radiograph). This reaction size is not normally considered significant, but in the presence of immune suppression may be important.
5-9	HIV infection Close contact of active contagious case Abnormal chest radiograph with fibronodular disease
$\geq 10$	All Others

*Canadian Tuberculosis Standards, 2000, p. 50*

### Causes of False-Negative Tuberculin Skin Tests:

- **Severe illness, which can include tuberculosis**
- Poor injection technique
- Immune suppression due to advanced age, corticosteroids, cancer therapy agents, or HIV infection, especially if advanced (CD4 count < 500)
- Viral illness in the past 4 to 6 weeks such as measles, chicken pox, mononucleosis
- Live-virus vaccine in the past 4 weeks such as MMR
- Malnutrition, particularly when recent weight loss

*Canadian Tuberculosis Standards, 2000, p. 47, 48*

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## Assessment and Treatment of Latent Tuberculosis Infection in Adults

### Causes of False-Positive Tuberculin Skin Tests:

- Infection with nontuberculosis mycobacteria (i.e., environmental mycobacteria)
- Prior BCG vaccination

*Canadian Tuberculosis Standards, 2000, p. 48*

### BCG

May have been received by population groups including:

- Persons born in developing countries or TB-endemic countries and many European countries
- Aboriginal persons from communities with high rates of TB
- Persons born in Quebec and Newfoundland from 1940 to early 1980's

### History of BCG Vaccination and Relationship to Skin Test Results

Received in infancy	Unlikely to cause a tuberculin reaction of 10 mm or greater after 2 to 3 years. Therefore, history of BCG vaccination in infancy can be ignored when interpreting tuberculin reaction of 10 mm or more.
Received at 2 to 5 years of age	10-15% will have a positive skin test 20-25 years later.
Received at age 6 years or older	25% chance of having persistent positive skin test later in life.

*Canadian Tuberculosis Standards, 2000, p. 48*

### When prior history of BCG vaccination should be ignored:

- Close contacts of an active case
- Populations with high prevalence of TB infection
- Populations with high risk of developing active disease if infected
- Immigrants from TB endemic countries
- Persons from Aboriginal communities with high rates of TB
- Immunocompromised, including HIV
- Renal failure
- Diabetes
- Chest X-ray consistent with inactive TB

*Canadian Tuberculosis Standards, 2000, p. 49*

### Two-Step Tuberculin Skin Testing

- Reduces misinterpretation of subsequent positive tests by distinguishing a booster effect (i.e., due to past infection) from a conversion (i.e., due to recent infection)
- Should be performed if tuberculin testing will subsequently be conducted at regular intervals; this includes health care workers, prison workers
- Consider for travelers to high prevalence countries for prolonged visits
- **Do a second skin test** 1 week to 4 weeks later if the first test is negative
- **Both skin tests** should be read and recorded at 48-72 hours

*Canadian Tuberculosis Standards, 2000, p. 51*

### Management for Positive Skin Tests

- All persons with a positive skin test must be reported to Public Health
- Persons with a positive skin test should be further evaluated to rule out active TB disease

**This evaluation should include all three of the following:**

1. History and physical examination for signs and symptoms of active disease
2. Chest x-ray
3. In the presence of symptoms consistent with pulmonary TB a sputum for smear (acid fast bacilli) and culture

*Canadian Tuberculosis Standards, 2000, p. 52*

### 1. Clinical Picture

- The most common physical finding in a patient with pulmonary tuberculosis is a totally normal examination
- The classic symptom of pulmonary TB disease is a chronic cough of at least 3 weeks duration
- Cough is initially dry although after 2 to 3 months will become productive
- Fever and sweats are common but may be absent in the very young and elderly
- Hemoptysis, anorexia, weight loss, chest pain and other symptoms are generally manifestations of more advanced disease

**Note: TB can be in other parts of the body; symptoms will vary depending on location**

*Canadian Tuberculosis Standards, 2000, p. 53*

### 2. Interpretation of Radiographic Findings

- The chest x-ray is not considered the gold standard for the diagnosis of active TB disease
- The interpretation of chest x-rays is highly variable between readers
- About 10% of persons with HIV infection and active TB disease will have a normal chest x-ray

**The classic triad of chest x-ray findings of active TB disease**

1. Position: Apical posterior or superior segment in 90%
2. Volume Loss: Hallmark of TB disease because of its destructive and fibrotic nature
3. Cavitation: Seen at later stage of disease. Depends on a vigorous immune response. Not seen in immunocompromised individuals

**Note: Non cavity infiltrates and lower lobe involvement may be seen in the immunocompromised, such as patients with diabetes, renal failure or HIV infection**

*Canadian Tuberculosis Standards, 2000, p. 54*

### 3. Sputum Collection and Time Lines for Results

#### Sputum collection

- Series of three specimens is strongly recommended
- Collect 5 to 10 cc of sputum (early morning preferably)
- Specimens should be delivered to the laboratory within one hour of collection
- If transportation of specimens is delayed, specimens should be refrigerated at 4°C and protected from light

**Public Health Laboratory-timelines and results for specimens received**

*Canadian Tuberculosis Standards, 2000, p. 56*

- Smear for Acid Fast Bacilli - result can be available in 24 hours
- AMTD – Amplified Mycobacterium Tuberculosis Direct tests for detection of Tuberculosis complex organisms are sent to Toronto Public Health Lab - done Monday, Wednesday, and Friday with results phoned on the same day (test is done on all new smear positive results for AFB)

**Note: Test can be done on smear negative results upon request**

- Culture for Mycobacterium Tuberculosis - results may be available anywhere from 4 days to 7 weeks
- Sensitivity testing for susceptibility to first line antituberculosis drugs - results available 4 to 7 days after organism has grown in culture

### Assessment of children with positive skin tests

- Consultation or referral to a paediatrician

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## Assessment and Treatment of Latent Tuberculosis Infection in Adults

### Treatment of Latent Tuberculosis Infection (LTBI)

In persons without risk factors for progression to active TB disease, approximately 10% of persons infected with TB will go on to develop active TB disease.

- 5% within 2 years of infection and
- 5% for the remainder of life

Treatment of latent tuberculosis infection reduces an individual's risk of developing active TB disease. It is very important to exclude active TB disease before treatment of LTBI is started to avoid the development of drug resistance.

### Indications for treatment of LTBI in High Risk Groups

Tuberculin Reaction Size, mm duration	Indication for Treatment of LTBI
≥ 5	<ul style="list-style-type: none"> <li>• Recent contact of infectious TB</li> <li>• Presence of lung scar (compatible with old healed TB but not previously treated)</li> <li>• HIV infection</li> </ul>
≥ 10	<ul style="list-style-type: none"> <li>• Recent skin test conversion (within last 2 years)</li> <li>• Immunosuppression:               <ul style="list-style-type: none"> <li>- Organ transplantation</li> <li>- Chronic renal failure</li> <li>- Prolonged corticosteroid or immune suppressive drug therapy</li> <li>- Hematologic malignancies eg. leukemia, lymphoma</li> <li>- Silicosis</li> <li>- Diabetes mellitus</li> <li>- &lt;90% of ideal body weight</li> </ul> </li> </ul> <p>Consider treatment of LTBI in other persons, particularly those &lt; 35 years of age who are in one of the following groups:</p> <ul style="list-style-type: none"> <li>- Foreign-born from TB endemic countries</li> <li>- Health care workers</li> <li>- Residents of communal care</li> <li>- Persons from Aboriginal communities with high rates of TB</li> </ul>

Canadian Tuberculosis Standards, 2000, p. 98

### Recommendations for treatment of LTBI in HIV Seronegative Persons\*

Drug	Interval & Duration	Dosage	Criteria for Completion	Comments
Isoniazid (INH)	Daily for 9 months  <b>OR</b> Daily for 6 months	Adult: 5 mg/kg Max: 300 mg/d  Children 10-15 mg/kg Max: 300 mg/d	Minimum 270 doses within 9-12 months  Minimum 180 doses within 6-9 months	<ul style="list-style-type: none"> <li>- Provides optimal protection</li> <li>- See effectiveness of INH</li> </ul> <p><b>For children: consult with a paediatrician</b></p> <p>See effectiveness of INH</p>
Vitamin B6 (Pyridoxine)	Daily with INH	25 mg		Vit.B6 indicated in HIV infection, poor nutrition, alcoholism, pregnancy, diabetes, uremia, neonatal period
Rifampin (RMP)	Daily for 4 months	Adult: 10 mg/kg Max: 600 mg/d	Minimum 120 doses within 4-6 months	<p>Alternate regimen for persons:</p> <ul style="list-style-type: none"> <li>- Who cannot tolerate INH</li> <li>- Who are contacts of INH-resistant TB</li> <li>- When INH x 9 months or 6 months is not feasible</li> </ul>

Canadian Tuberculosis Standard, 2000, p. 97, 98, 99

CDC Core Curriculum on TB, What Clinician Should Know, 2000, p. 112, 113

\*For treatment of LTBI in HIV positive persons refer to a medical specialist.

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## Assessment and Treatment of Latent Tuberculosis Infection in Adults

Effectiveness of INH	Consultation or Referral to a TB Specialist is Recommended for Persons who are:
<p><b>Assuming sensitivity to INH and <math>\geq 80\%</math> compliance:</b></p> <ul style="list-style-type: none"> <li>• INH, when taken for 12 months, is 93% effective in preventing progression to active disease.</li> <li>• However, INH, when taken for 9 months, is almost as effective and is therefore the recommended duration of treatment</li> <li>• INH, when taken for 6 months is 69% effective in preventing progression to active disease</li> </ul>	<ul style="list-style-type: none"> <li>• HIV positive</li> <li>• Contacts of multidrug-resistant TB</li> <li>• Children</li> <li>• Pregnant women at high risk of TB</li> <li>• Abnormal CXR</li> <li>• When daily therapy is not feasible, intermittent therapy is needed</li> </ul>

Canadian Tuberculosis Standards, 2000, p. 97

Drug	Adverse Reactions	Monitoring	Comments										
INH	<ul style="list-style-type: none"> <li>Rash</li> <li>Hepatic enzyme elevation</li> <li>Hepatitis</li> <li>Peripheral neuropathy</li> <li>Mild CNS effects</li> <li>Drug interactions resulting in increased levels of                             <ul style="list-style-type: none"> <li>- phenytoin (Dilantin),</li> <li>- carbamazepine (Tegretol),</li> <li>- disulfiram (Antabuse)</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• For adults, baseline liver enzymes (AST, or ALT and bilirubin)</li> <li>• Clinical monitoring monthly</li> <li>• Regular ALT, AST for patients with                             <ul style="list-style-type: none"> <li>- Pre existing liver disease</li> <li>- Age <math>\geq 35</math></li> <li>- History of alcohol abuse</li> </ul> </li> <li>• If AST level <math>&gt;5</math> times baseline level, or when clinical jaundice develops, then INH should be stopped and a TB specialist consulted</li> <li>• Repeat monitoring of liver enzymes for patients with symptoms consistent with hepatic side effects</li> </ul>	<p>Hepatitis risk correlated with age</p> <table border="1"> <thead> <tr> <th>Age Group</th> <th>Risk</th> </tr> </thead> <tbody> <tr> <td>Under 20</td> <td>Rare</td> </tr> <tr> <td>20 to 34</td> <td>0.2%</td> </tr> <tr> <td>35 to 49</td> <td>1.5%</td> </tr> <tr> <td>over 50</td> <td>2.4%</td> </tr> </tbody> </table> <ul style="list-style-type: none"> <li>- Hepatitis risk increases with daily alcohol consumption or viral hepatitis</li> <li>- INH induced hepatitis is almost always reversible when INH is discontinued</li> <li>- INH given alone to persons with active TB disease can lead to INH resistant TB</li> </ul>	Age Group	Risk	Under 20	Rare	20 to 34	0.2%	35 to 49	1.5%	over 50	2.4%
Age Group	Risk												
Under 20	Rare												
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Rifampin	<ul style="list-style-type: none"> <li>G.I. upset</li> <li>Drug interactions</li> <li>Hepatitis</li> <li>Thrombocytopenia</li> <li>Flu-like symptoms</li> <li>Rash</li> <li>Renal failure</li> <li>Fever</li> </ul>	<p>Baseline CBC, platelets, and liver enzymes</p> <p>Repeat measurements if:</p> <ul style="list-style-type: none"> <li>- Baseline results are abnormal</li> <li>- Patient has symptoms of an adverse reaction</li> </ul>	<ul style="list-style-type: none"> <li>- Colors body fluid orange</li> <li>- May permanently discolor contact lens</li> <li>- May increase clearance of drugs metabolized by the liver: estrogen, coumadin, methadone, glucocorticoids, sulfonyleureas</li> <li>- By accelerating estrogen metabolism, RMP may interfere with effectiveness of birth control pills; alternative contraceptive method should be advised</li> <li>- Contraindicated in severe chronic liver disease</li> <li>- Contraindicated or used with precaution when administered with protease inhibitors, non-nucleoside reverse transcriptase inhibitors</li> </ul>										

Center for Disease Control, Core Curriculum on Tuberculosis, What the Clinician Should Know, 2000, p. 120, 121.  
Canadian Tuberculosis Standard, 2000, p. 90, 91, 101, 102

### References:

Canadian Lung Association. (2000) *Canadian Tuberculosis Standards. (5th ed.)*. Ottawa: Canadian Lung Association.

U.S. Department of Health and Human Services Centres for Disease Control and Prevention (2000). *Core Curriculum Tuberculosis; What the Clinician Should Know, Fourth Edition*, 2000, Atlanta, Georgia.

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