Latent Tuberculosis Infection (LTBI) Questions and Answers for Health Care Providers

Who Should Be Screened for LTBI?

http://www.phac-aspc.gc.ca/tbpc-latb/pubs/tb-canada-7/tb-standards-tb-normes-ch4-eng.php#a4_0

Testing for LTBI is generally discouraged in people who are healthy and have no known risk factors for progression to active TB disease. The positive predictive value of the TST or IGRA is low and the risks of treatment will usually outweigh the potential benefits (unless required for school, volunteering, or employment).

LTBI screening is recommended for:

- Recent contacts of persons diagnosed with active infectious TB disease

- Persons with increased risk of progression to TB disease
    - High Risk
        - AIDS
        - HIV infection
        - Transplant recipient (r/t immune-suppressant therapy)
        - Silicosis
        - Chronic renal failure requiring hemodialysis
        - Carcinoma of head and neck
        - Recent TB infection (≤ 2 years)
        - Abnormal chest x-ray (fibronodular disease)
    - Moderate risk
        - Tumor necrosis factor alpha inhibitors
        - Diabetes mellitus (all types)
        - Treatment with glucocorticoids (≥ 15 mg/d prednisone)
        - Young age when infected (0-4 years)
    - Slightly increased risk
        - Alcohol consumption ≥ 3 drinks/day
        - Underweight (≤ 90% ideal body weight)
        - Cigarette smoker ≥ 1 pack/day
        - Abnormal chest x-ray (granuloma)

- Foreign-born persons from TB-endemic countries **c**onsidered to be at increased risk of progression to disease, and include:
    - Those with fibro-nodular changes on the chest x-ray
    - All children and adolescents < 20 years of age, as soon as possible after arrival
    - Refugees up to 50 years of age
    - Immigrants and refugees with underlying medical comorbidities

- Those with radiographic evidence of old, healed TB and no history of treatment

- Those from Aboriginal communities with high rates of TB

- Health care workers at risk for occupational exposure

- Travellers to countries with high TB incidence
    - ≥ 1 month travel with very high risk contact (e.g., direct patient contact, work/volunteer in prisons, homeless shelters, refugee camps or inner city slums)
    - ≥ 3 months travel in countries with TB incidence > 400/100,000 population
    - ≥ 6 months travel in countries with TB incidence 200-399/100,000 population
    - ≥ 12 months travel in countries with TB incidence 100-199/100,000 population

        Note: In those > 50 years of age with likelihood of prior TB exposure, conduct a 2-step TST. For all others, conduct a single test two months following return from travel.
- Staff and residents in communal settings including correctional facilities, long-term care**,** shelters/services for homeless or under-housed

What tests are used to screen for LTBI?

Both the TST and IGRA can be used with some preferences and exceptions.

- TB skin test (TST)
    - How to administer and read (http://peelregion.ca/health/professionals/com-tuberculosis.htm)
    - Contraindications
        - The following people can receive a TST:
            - History of receiving BCG vaccination(s)
            - Currently experiencing a common cold
            - Pregnant or breastfeeding
            - Immunized with any vaccine on the same day
            - Immunized within the previous four weeks with vaccines
            - History of a positive TST reaction (other than blistering) that is not documented
            - Currently taking low doses of systemic corticosteroids, <15 mg/d prednisone (or equivalent)

            Note: It generally takes a steroid dose equivalent to ≥15 mg/d prednisone for 2-4 weeks to suppress tuberculin reactivity.
        - People who should not receive a TST:
            - Experience of positive, severe blistering TST reactions in the past
            - Current burns or eczema present over TST testing sites due to greater likelihood of adverse or severe reaction
            - Documented active TB or a well-documented history of adequate treatment for TB infection or disease in the past. In such patients, the test is of no clinical utility
            - Experiencing major viral infections (e.g. measles, mumps, varicella)

• Those who have received measles or other live virus immunization within the past four weeks, as this has been shown to increase the likelihood of false-negative TST results.
Note: Only measles vaccination has been shown to cause false-negative TST results, but it would seem reasonable to follow the same 4-week guideline for other live virus immunizations (e.g., mumps, rubella, varicella (chickenpox) and yellow fever). However, if the opportunity to perform the TST might be missed, the TST should not be delayed in consideration of the receipt of live virus vaccines since these are theoretical considerations. A TST may be administered before or even on the same day as the immunizations but at a different site.

- False positives
    - Causes of False Positive TST results
        - BCG
        - Previous exposure to Nontuberculous mycobacteria (NTM)
- False negatives
    - Causes of False Negative TST Results
        - Using Tuberculin that is improperly stored or expired
        - Improper administration of Tuberculin
            - Using too little Tuberculin
            - Administering Tuberculin too deeply
            - Using Tuberculin that has been drawn up in the syringe longer than 20 minutes
        - Presence of Infections at time of Tuberculin administration:
            - Active TB (especially if advanced)
            - Other bacterial infection (typhoid fever, brucellosis, typhus, leprosy, pertussis)
            - HIV infection (especially if CD4 count <200)
            - Other viral infection (measles, mumps, varicella)
            - Fungal infection (South American blastomycosis)
        - Live virus vaccination, e.g. measles, mumps, polio
        - Immunosuppressive drugs:
            - corticosteroids, tumour necrosis factor (TNF) inhibitors, and others
        - Metabolic disease:
            - chronic renal failure, severe malnutrition, stress (surgery, burns)
        - Diseases of lymphoid organs:
            - lymphoma, chronic lymphocytic leukemia, sarcoidosis
        - Age: infants <6 months or those greater than 65 years of age

- When to do conduct two- step TSTs (http://www.peelregion.ca/health/professionals/pdfs/CDS-0219.pdf)

- Interferon gamma release assay (IGRA).

The test is available through Dynacare Lab. It is not covered by OHIP and costs approximately $90.00.

How are the TB skin test (TST) and Immuno Gamma Release Assay (IGRA) results interpreted?

The TST/IGRA should be interpreted in the context of patient's history:

- Size of the TST
- Positive predictive value of the test (i.e., the likelihood the test should be positive based on true exposure and elimination of false positives or false negatives)
- Risk of progression to active disease

Tools to guide the interpretation are the:

- Online TST/IGRA Interpreter helps to estimate the risk of active tuberculosis depending on the result and clinical profile.
- BCG World Atlas provides country specific information about practices of BCG administration

Preferences and exceptions to the use of TST and/or IGRA:

Neither TST nor IGRA should be used in the following situations:

- To test people who have a low risk of infection or low risk of progression to active TB disease even if they are infected
- To diagnose active TB diagnosis in adults
- For routine or mass screening for LTBI of all immigrants (adults and children)
- For monitoring anti-TB treatment response

IGRAs are preferred but TST is acceptable in the following situations:

- People who have received BCG as a vaccine after one year of age and/or have received BCG vaccination more than once.
- People from groups that historically have poor rates of return for TST reading (e.g., homeless or under-housed).

TST is preferred and an IGRA is NOT acceptable in the following situations:

- The TST is recommended whenever it is planned to repeat the test later to assess risk of new infection (i.e. conversions), such as repeat testing in a contact investigation or serial testing of health care workers or other populations (e.g. corrections staff or prison inmates) with potential for ongoing exposure.

Situations in which both tests can be used (sequentially, in any order) to enhance sensitivity

- When the risks of infection, progression to disease and poor outcomes are high
- In children (under age 18 years) with suspected TB disease, IGRAs may be used as a supplementary diagnostic aid in combination with the TST and other investigations to help support a diagnosis of TB. However, IGRA should not be a substitute for, or obviate the need for, appropriate specimen collection. A negative IGRA (or TST) does not rule out active TB at any age and especially not in young children.
- Repeating an IGRA or performing a TST might be useful when the initial IGRA result is indeterminate, borderline or invalid, and a reason for testing persists

Who should be prescribed LTBI treatment?

The decision to prescribe treatment in someone diagnosed with LTBI should be based on:

- The risk of progression to active disease
- The presence of medical contraindications
- The likelihood the patient will adhere to full treatment
- A risk/benefit analysis
- **Active TB disease has been ruled out by completing a medical assessment and history:**
    - TB symptom review (new or worsening cough that is not improving beyond three weeks, fever, weight loss,)
    - Risk factor assessment
    - History of previous TB or a contact of TB
    - Chest x-ray
    - Sputum collection (induced sputum in those with abnormal chest x-rays who cannot spontaneously expectorate regardless of symptomology)
    - Referral to a TB specialist for consultation as necessary.

Prescribing Treatment Based on the TST result:

A TST result that is **0-4mm is generally considered negative** and no treatment is indicated. The **exception to this is children less than 5 years of age who are close contacts of someone with infectious TB** - these children should be treated pending results of repeat skin test 8 weeks following exposure.

Treatment is indicated for the following individuals with a TST result of ≥ 5 – 9 mm:

- HIV infection
- Contacts with infectious TB within past 2 years
- Fibronodular disease on CXR (untreated healed TB)
- Organ transplantation (related to immunosuppressive therapy)
- TNF alpha inhibitors
- Other immunosuppressive drugs e.g., corticosteroids
- End-stage renal disease

Treatment is indicated for the following individuals with a TST result of ≥ 10 mm:

- TST conversion (within 2 years)
- Diabetes
- Malnutrition (< 90% ideal body weight)
- Cigarette smoking
- Daily alcohol consumption (> 3 drinks/day)
- Silicosis
- Hematologic malignancies (leukemia, lymphoma)
- Certain carcinomas (e.g., head and neck)

Which antibiotics are used to treat LTBI?

The standard regimen of first choice is Isoniazid (5mg/kg to a maximum of 300mg/day) daily for nine (9) months. For children, the dose is 10-15mg/kg to a maximum of 300 mg/day.

Pyridoxine (Vitamin B6) 25 mg is prescribed in adults when there is:

- malnutrition, alcoholism, pregnancy, postpartum diabetes, uremia and/or other disorders that may predispose a patient to neuropathy
- Pyridoxine is not indicated in pediatric patients, except when breastfeeding or in malnourished children

If your patient prefers a shorter course of treatment (e.g., Rifampin x four months), please refer to a TB Specialist.

How should patients on LTBI treatment be monitored?

Patients on Isoniazid should be monitored monthly for treatment adherence and side effects, especially symptoms of hepatitis.

Symptoms of hepatitis include, fatigue, weakness, malaise, anorexia, nausea or vomiting, dark urine and/or yellowing of the skin.

Note: Should side effects occur, perform liver function tests immediately. Stop treatment if liver transaminases increase beyond 5 times the upper limit of normal (or 3 times in the presence of symptoms).

The frequency of liver function tests depends on the person's age:

- < 35 years of age - Baseline then as needed
- 35 - 50 - Baseline, month 1, 2, 3 then as needed
- > 50 years of age and other risk factors***** **-** Baseline and monthly throughout treatment

*****Risk factors include pregnancy or first 3 months postpartum, history of previous drug-induced hepatitis, current cirrhosis or chronic active hepatitis of any cause, hepatitis C, hepatitis B with abnormal transaminases, daily alcohol consumption or concomitant treatment with other hepatotoxic drugs (e.g., methotrexate). Infection with HIV is not an independent risk for drug-induced hepatitis.

When should patients be referred to a TB Specialist?

- Child (< 5 years)
- Pregnant
- Immunocompromised
- Suspect/Ruling Out Active TB
- Alternative LTBI treatment
- Contact of drug resistant TB
- Abnormal chest x-ray
- History of liver disease, alcohol/substance misuse
- Induced sputums required

What are the reporting requirements for LTBI to Peel Public Health?

Reportable disease elements are outlined in the Health Protection and Promotion Act. R. R. O. 1990 Regulation 569: Reports. Reporting requirements include but are not limited to:

- Positive TST and IGRA results
- Laboratory findings and investigative test results including but not limited to smear/culture and sensitivity, radiology, sputum, biopsy results
- Treatment initiation and completion dates
- Risk factors for the progression to TB disease including immigration status, country of birth and travel history
- Clinical history including past diagnosis/treatment of TB and/or medical surveillance
- Suspect or confirmed active TB disease

For more information on reporting requirements please visit
https://www.ontario.ca/laws/regulation/900569