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Memorandum

To: Nurses and Physicians, Region 18 (Eeyou Istchee)

From: Dr. Kianoush Dehghani, CBHSSJB – Public Health Department (Region 18) In consultation with Dr. Dick Menzies, Respirology/TB, Montreal Chest Institute

Indications for latent tuberculosis infection (LTBI) screening in Eeyou Istchee

• What is LTBI?

Latent TB infection is a condition in which a person is infected with *Mycobacterium tuberculosis*, but does **NOT** have active tuberculosis disease. Individuals with LTBI are **NOT** contagious.

These individuals are often offered prophylactic treatment with one anti-TB agent, in order to reduce the probability of TB re-activation. Tuberculosis reactivation usually occurs when the individual's immune system becomes suppressed (i.e. due to aging, immune-compromising illnesses and/or immunosuppressive medications). For those individuals with LTBI who have been in recent contact with an active TB case, the probability of re-activation is the highest during the first 2 years after the last contagious contact. It is roughly estimated that for a healthy young adult with LTBI, the lifetime risk of TB re-activation is 10%: 5% during the first 2 years after latent TB infection, and 5% thereafter¹.

• What are the screening tests available for LTBI?

Both tuberculin skin test (TST²) and interferon gamma release assay (IGRA) are acceptable screening tests for LTBI.

Attention: Please note that TST and IGRA testing are **NOT** for active TB screening or diagnosis³.

→ What is the preferable LTBI screening test for Region 18?

Tuberculin skin test is the principle screening test for LTBI in Eeyou Istchee.

IGRA should **NOT** be routinely used as the basic screening test for LTBI in our region, due to the following:

- IGRA testing is **NOT** available in Eeyou Istchee (or its neighboring regions). It is important to note that the processing of a blood sample taken from a given patient in Eeyou Istchee, and the air transport of the sample to the McGill University Health Centre (where the IGRA testing is available) for analysis, are complex and not feasible in our setting at this time.
- IGRA is **NOT** recommended for repeat testing (e.g. in a contact investigation) or serial testing (e.g. of health care workers or other potentially at-risk populations).

Nevertheless, there are indications for using IGRA for LTBI screening among individuals in our region (e.g. individuals who had a BCG⁴ vaccine less than 10 years ago, or had multiple BCGs after 12 months of age). *Please note that routine dual testing with both TST and IGRA is NOT recommended.*

Attention: Please discuss all individual patients with a possible indication for IGRA or for dual screening tests with the designated coordinator of infectious diseases at the Public Health Department⁵.

¹Attention: For the assessment and management of adult patients (≥18 years old) with positive TST (and/or IGRA test), the on-line evidence-based calculator developed by the McGill TB group can be helpful. See: www.tstin3d.com

³ Symptoms screens and chest radiography are the primary screening tools for active pulmonary TB. Microbiological confirmation (i.e. diagnosis) with sputum smear and culture are required for those who screen positive for active pulmonary TB.

⁵ Presently, the coordinator of infectious diseases at the Public Health Department is **Dr. Kianoush Dehghani 514-861-2352** ext. **74237**, **kianoush.dehghani@mcgill.ca**)

² TST is the same as purified protein derivative or PPD test.

⁴ Bacillus Calmette-Guérin



→ What are the key points to remember about the TST?

- For **detailed** information on TST application and interpretation please refer to the *Canadian TB Standards* (7th edition)⁶: Chapter 4, p. 66-78.
- Training is essential for health care providers to gain proficiency in the administration, reading and interpretation of the TST.
- Generally speaking, a TST ≥10 mm is considered **positive**. For "certain" immuno-compromised individuals (e.g. people on immunosuppressive medications like anti-TNF alpha), and for close contacts of an active pulmonary TB case, a TST of ≥5 mm is considered **positive**.
 - Note: For people with diabetes, a TST of ≥10 mm is considered **positive**.
 - For more details on the interpretation of TST and cut-off points in various risk groups, please see Table 2 on p. 75 of Chapter 4, in *Canadian TB Standards* (7th edition).
- The TST should **NOT** be given to:
 - An individual with written documentation of a previous **positive** TST result.
 - Individuals with a history of a previous allergic reaction to TST.
 - Individuals with active respiratory TB or miliary TB, or individuals with a documented past history of treatment for TB.
- The TST should **NOT** be applied on non-intact skin (e.g. skin with burn, rash, ulcer or eczema).
- o The TST can be administered to persons who are pregnant or breastfeeding.
- The TST can also be administered to people with a common cold or influenza, but should **NOT** be administered within one month of the occurrence of mumps or measles disease **OR** live virus vaccinations.
- The effect of BCG vaccination in infancy (the first year of life) on TST reactions wanes over time, and has a negligible effect on TST in adolescents and adults. This negligible effect can be ignored when administrating and/or interpreting TST in these individuals⁷.
- Patients or family members should **never** measure TST results; this should only be done by a trained health care professional. A TST that is not measured and recorded by a health care professional after 72 hours is **NOT** valid (and should be repeated).
- The "two-step" TST should **NOT** be offered routinely as a screening test for LTBI. The indications for "two-step TST" are very limited (e.g. base exam for health care workers who may need serial testing in the future). These indications are summarized by the *Protocole d'immunisation du Québec* (2013 edition, p. 422). The "two-step" TST should **NOT** be offered more than **once** to any given individual in his/her lifetime. Please contact the coordinator of infectious diseases at the Public Health Department⁵, if you plan to apply the "two-step" TST on an individual beyond the limited recommendations in the PIQ.
- The most common prophylactic therapy for LTBI consists of daily isoniazid (INH) medication for 9 months⁸.
 INH medication (similar to alternative therapies for LTBI) has serious side effects including hepatotoxicity.
 The benefits of prophylaxis versus the risk of INH side effects have to be carefully assessed, preferably prior to administering LTBI screening.
- Prior to initiating antibiotic treatment in individuals with a **positive** TST:
 - They should receive a clinical assessment to rule out signs and symptoms of active TB.
 - They should also have a chest X-ray, to rule out evidence of active TB.
- "Immuno-compromised" individuals who have a history of "untreated" LTBI (i.e. positive TST or IGRA years ago) should be assessed by a physician for possible treatment with antibiotics⁸.

⁶ To download the "English" version of *Canadian TB Standards* (7th edition, 2013) see: <u>http://www.respiratoryguidelines.ca/sites/all/files/Canadian TB Standards 7th Edition ENG.pdf</u> The "English" version is purchased in the second s

The "French" version is available at: http://www.lignesdirectricesrespiratoires.ca/sites/all/files/NCLA_FR_7_edition.pdf

⁷ Studies in Canada and other countries show that if BCG was received in infancy, only 1% had a TST result ≥10 mm if tested >10 years later. Therefore, a history of BCG received in infancy can be **ignored** in all people age 10 years and older when interpreting an initial TST result of ≥10 mm.

⁸ For details of INH prophylactic treatment and other alternative prophylactic therapies for LTBI, please refer to the *Canadian TB Standards* (7th edition): Chapter 6, p. 125-152.



• What is the current epidemiology of tuberculosis (TB) in Region 18?

For several decades, Aboriginal communities in Canada have been considered particularly vulnerable to TB. In the 1960s and 70s, tuberculosis was an important cause of morbidity and mortality in Eeyou Istchee, as in many other Aboriginal communities in Canada. Fortunately, during the last three decades the reported incidence rate and number of cases of TB have continued to decline in our region (*see Appendix 1*). During the last 10 years, Eeyou Istchee has had one of the lowest rates of TB among many Aboriginal communities in Canada. **Eeyou Istchee is now considered a "low-incidence" region based on the World Health Organization's (WHO) criteria**⁹. Effective clinical and public health measures in controlling TB (in Eeyou Istchee and other parts of Quebec), lower incidence of TB in most neighboring regions (except for Nunavik), and the improved socioeconomic status of the Cree people, have likely contributed to the decline in the incidence of TB in Eeyou Istchee.

• Should we screen for LTBI in Region 18?

It is very important to note that "decision to screen for LTBI is decision to treat" with prophylactic antibiotics. The benefits of prophylaxis versus the risk of INH⁸ side effects have to carefully assessed, preferably prior to administering LTBI screening¹. As a general rule, the benefits of LTBI screening are significant in specific situations such as during an acute TB outbreak investigation, when the positive predictive value (PPV) of the TST is maximal and acute risk of TB re-activation is high¹. The risk of medication-induced hepatotoxicity increases with age¹⁰.

For clarity, we divide LTBI screening indications into "population" and "high-risk individuals" strategies:

I. Systematic population screening:

In accordance with the guidelines of Health Canada, Quebec's Ministry of Health (MSSS), and the WHO, we do **NOT** recommend routine LTBI screening in the general Cree population of Eeyou Istchee, as the region has a low incidence of tuberculosis.

→ Should the current systematic LTBI screening among Grade 6 students in the region continue?

Systematic screening of Secondary 1 and then of Grade 6 students in the region initially started in the 1980s, when the incidence of active TB in Eeyou Istchee was higher (*see Appendix 1*). It should be noted that as incidence of active TB falls, the prevalence of TB infection decreases and the positive predictive value of the TST also falls¹¹.

Therefore, at this time, considering the low incidence of active TB in the region and according to the available scientific evidence, we recommend STOPPING systematic LTBI screening of Grade 6 students in Eeyou Istchee.

II. Screening of high-risk individuals:

Three groups of individuals should be screened for LTBI: 1) Those who are at high risk of TB infection (e.g. close contacts of an active case of pulmonary TB); 2) Those who if infected, are at high risk of developing active TB infection (e.g. immuno-compromised patients); and 3) Those who if they developed active TB, would place vulnerable contacts at risk (e.g. health care workers).

i. Should we screen contacts of an active TB case?

YES. Immediately after an index case is diagnosed with active pulmonary TB, her/his close contacts should be medically assessed and receive their initial TST, if indicated. If the first TST is negative, a second TST has to be done 8 weeks after the contact person's last exposure to the infectious index case¹². As described above, the positive predictive value of the TST is high in recent contacts of an active TB case. The probability of re-activation is the highest during the first 2 years after the last contagious contact.

⁹ According to WHO criteria, a region with an active TB incidence of less than 25/100 000 population is considered "low incidence" for TB.
¹⁰ The risk becomes significant for patients ≥50 of age.

¹¹ A number of causes for false-positive TST results include: infection with non-tuberculous mycobacteria, previous BCG vaccination, incorrect administering of TST and incorrect interpretation of reaction.

¹² The time it usually takes for the tuberculin skin response to develop after infection with TB.

ii. Should we screen individuals travelling to TB endemic regions/countries?

DEPENDS. Individuals with planned "PROLONGED" travel of ≥ 6 months in endemic regions and countries (e.g. high TB-incident communities in Nunavik¹³, and countries¹⁴ in Asia or Africa) who have not had a previous positive TST, should have a baseline TST. The individual should then have a follow-up TST 8 weeks after his/her return to Eeyou Istchee, to rule out new latent TB infection (i.e. TST conversion) while staying in endemic areas.

iii. Should we screen incarcerated individuals who are going to prisons or jails?

YES. Prisons and jails are considered higher risk settings for active TB in Canada. Hence, LTBI screening is recommended for incarcerated individuals before entry (i.e. base TST) to the prison/jail¹⁵, and 8 weeks after release from the prison/jail.

iv. Should we screen immuno-compromised individuals?

YES. All of the following individuals should receive **at least one** TST since the onset of their immune-compromising condition^{16,17}:

- Individuals with human immuno-deficiency virus infection (HIV) or with acquired immune-deficiency syndrome (AIDS)
- Individuals who are candidates for organ transplantation and on the waiting list, and individuals who have received organ transplantation and are on immune-suppressant therapy
- Individuals with end-stage renal failure requiring hemodialysis
- Individuals with carcinoma of head and neck
- Individuals with diabetes mellitus (all types)
- Individuals on or about to start tumor necrosis factor alpha inhibitor medications
- Individuals on long-term glucocorticoids (i.e. at least one month at doses equivalent to ≥15 mg/day of prednisone)

Attention:

- → Especially for those individuals with above risk factors who are ≥50 years of age, benefit of LTBI prophylactic treatment has to be weighed against the hepatotoxic side effect of the treatment (see the TSTin3d on-line evidence-based calculator¹), and those that are treated have to be closely monitored¹⁸ for side effects.
- → In addition, individuals with the above immune-compromising risk factors who are **NOT** candidates for LTBI prophylactic therapy, have to be under **continuous clinical vigilance** to rule out TB re-activation.

¹³ In Canada, certain communities in Nunavik and Nunavut have had increased numbers of active pulmonary TB cases during the past decade. Please note that "Great Whale" (which includes Cree and Inuit communities of Whapmagoostui and Kujjuarapik) is **NOT** considered a high TB-incident community in Nunavik at this time. If you have questions about the high-incident communities in Nunavik or Nunavut, please contact the infectious disease coordinator at the Public Health Department⁵.

¹⁴ To identify high-incidence countries for TB, refer to the WHO's tuberculosis data base at: http://www.who.int/tb/country/data/download/en/index.html

If you have questions, contact the coordinator of ID at the Cree Public Health Department⁵.

¹⁵ The TST testing for jail and prison inmates have to be coordinated with the medical staff in corresponding jails and prisons. Federal prisons (for criminal sentences of ≥2 years) already apply TST screening among inmates systematically (i.e. mandatory 2-step TST upon entry of a given inmate and voluntary yearly TSTs, thereafter). This is often **NOT** the case for Provincial jails (for criminal sentences of <2 years), for a number of reasons including, the high turnover of inmates and difficulty of follow-up of those who have a positive screening test for LTBI and need prophylactic treatment.

¹⁶ For interpretation of positive TST for individuals with these risk factors, please see *Canadian TB Standards* (7th edition): Chapter 4, p. 75, Table 2.

¹⁷ If they had a history of positive TST prior to the onset of their immuno-compromising condition, the TST should **NOT** be repeated. Individuals with a history of untreated positive TST and a newly-diagnosed immuno-compromising condition have to be assessed for LTBI prophylactic treatment.

¹⁸ For information on follow-up and monitoring during LTBI therapy, please see *Canadian TB Standards* (7th edition): Chapter 6, p. 142-3.



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III. Should we screen health care workers (HCWs) in Eeyou Istchee?

YES. All HCWs should have a **base-line test** for LTBI, preferably upon starting work in our region. The baseline testing for HCWs is preferably a two-step TST¹⁹. If the first TST proves negative, a second test has to be done in 1-4 weeks. Thereafter, due to the low incidence of TB in our region, regular (e.g. annual) LTBI screening of HCWs is **NOT** recommended.

Evidently, health care workers with a history of unprotected contact with an active case of respiratory TB, should be assessed by an appropriate clinician and receive a TST, per protocol. If the first TST proves negative, a second test should be done 8 weeks after the last infectious exposure.

IV. Others?

DEPENDS. There are other indications for LTBI screening including:

- Individuals with evidence of fibronodular disease on the chest X-ray (healed TB, and not previously treated)
- Individuals with pulmonary silicosis
- Injection drug users (IDU)
- Individuals with a history of homelessness²⁰ in an urban setting

However, we recognize that contrary to the available evidence-based guidelines, LTBI screening is often requested to meet administrative or legal requirements for individuals who are not considered to have an increased risk of TB infection. Please follow the LTBI screening principles summarized in this memo when caring for these patients, and contact the coordinator of ID at the Public Health Department for any questions⁵.

Attention: Please report ALL cases with positive LTBI screening test results from our region to the coordinator of infectious diseases at the Public Health Department⁵.

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¹⁹ This baseline testing for HCWs is preferably a two-step TST. A two-step baseline TST should only be done **ONCE** in a lifetime. Hence, if the HCW has a documented result of a prior two-step TST, a single-step TST should be given and prior TST results should be transcribed into the HCW's health record.

²⁰ Although the incidence of active TB and the prevalence of LTBI in the homeless population in Canada is known to be markedly higher than in the non-homeless population, given the potential risk of hepatotoxicity due to high rates of associated alcohol use and low rates of treatment completion, efforts to offer LTBI screening and treatment should be reserved for those with moderate or high risk of TB reactivation.







²¹ Based on available data, for all years (except for 1980-1983), average incidence for 3-year intervals have been used to plot this graph. For 1980-1983, average incidence for this 4-year interval was used.