OLMSTED COUNTY PUBLIC HEALTH TB CLINIC POLICY

Title: Treatment and Monitoring of Latent TB Infection (LTBI) September 2012

Purpose: LTBI treatment substantially reduces the risk of developing clinically active tuberculosis disease and is viewed as an integral component of the national TB control/elimination strategy as defined by the CDC. Targeted testing should guide the identification and screening of at risk individuals. (Note the terms client and patient are used interchangeably)

Candidates for LTBI Treatment:

1. A tuberculin reaction of <5 mm should be referred to TB Clinic for evaluation and possible LTBI treatment for the following:
   a. Child < 5 years of age and a recent close contact
   b. HIV-infected and recent close contact
   c. Immunosuppressed and recent close contact

2. The following risk groups should be considered candidates for LTBI treatment if they have a TST reaction ≥ 5 mm of induration or a positive interferon-gamma release assay (IGRA):
   a. Persons with HIV infection.
   b. Recent contacts of a potentially infectious TB case.
   c. Persons with fibrotic changes on chest x-ray consistent with prior TB.
   d. Persons with organ transplants and other immunosuppressed patients, including those receiving:
      1. The equivalent of ≥ 15 mg/day (or >/=2 mg/kg/day in children) of prednisone for 1 month or more.
      2. Tumor necrosis factor alpha (TNF alpha) antagonists or other immunomodulatory agents.

3. The following risk groups should be considered candidates for LTBI treatment if they have a TST reaction ≥ 10 mm of induration or a positive IGRA:
   a. Persons who have lived or traveled in high prevalence countries
   b. Injection drug users
   c. Residents and employees of the following high risk congregate settings: prisons and jails, nursing homes and other long-term facilities for the elderly, hospitals and other health care facilities, residential facilities for patients with AIDS and homeless shelters.
   d. Mycobacterial lab personnel
   e. Persons with the following clinical conditions that place them at high risk: silicosis, diabetes mellitus, chronic renal failure, some hematologic disorders (e.g. leukemias and lymphomas), other specific malignancies (e.g. carcinoma of the head, neck or lung), weight loss of ≥ 10% of ideal body weight, gastrectomy and jejunoileal bypass, and tobacco smoking.
   f. Children < 4 years of age or infants, children and adolescents exposed to adults at high risk.
4. Persons not in any of the high-risk groups who have a TST reaction ≥ 15 mm of induration or a positive IGRA should be considered candidates for LTBI treatment.

5. Children < 5 years of age who are contacts to potentially infectious TB cases should begin LTBI treatment regardless of initial TST results. The TST should be repeated 8 – 10 weeks after contact has ended or 8 – 10 weeks after last exposure to the case while still infectious, if the initial TST was negative. If the repeat TST is negative, treatment may be stopped. If the child is < 6 months of age and the repeat TST is negative, consideration should be given to continuation of LTBI treatment due to immaturity of the immune system of infants (and the possibility of false-negative TST result).

6. An immunosuppressed person (e.g. advanced HIV infection, patient receiving chemotherapy or other immunosuppression etc.) who are contacts to potentially infectious TB cases should be considered candidates for LTBI treatment, even if repeat TST or IGRA are negative.

7. LTBI treatment should generally be deferred until after pregnancy (3 – 6 months) for women who have a positive TST/IGRA during pregnancy, for women who become pregnant during LTBI treatment or for women who are TST/IGRA positive and are attempting to become pregnant.
   a. Exceptions to consider initiation of treatment with Isoniazid for LTBI would include women who are likely to have been recently infected (less than 2 years) or are recent contacts to a potentially infectious TB case and women who are immunosuppressed. LTBI should not be delayed in these pregnant women.

LTBI Treatment Regimens
1. One of three treatment regimens should be considered for LTBI treatment:
   a. Isoniazid (INH) daily for 9 months, self-administered
   b. Weekly Isoniazid and Rifapentine for a total of 12 weeks, given by directly observed therapy (DOT)
   c. Rifampin daily for 4 months, self-administered


2. Pyridoxine (Vitamin B6) 50 mg should also be given with Isoniazid when INH is used for those with known or suspected neuropathy, or those who are at risk for neuropathy including diabetes, thyroid disease, paraproteinemias, alcohol use, uremia, malnutrition, and HIV infection. Pregnant women, breast feeding women, and persons with seizure disorders should also take pyridoxine when taking INH. Infants being breast fed by mothers taking INH should receive Polyvisol 1 ml per day.

3. 9 months of INH is the preferred treatment regimen for all LTBI patients although 3-months of INH-Rifapentine is an equal alternative to the 9-month INH regimen for otherwise healthy patients aged ≥ 12 years and who have LTBI and risk factors that are predictive of TB developing
(e.g. new conversion, recent contact to infectious TB, or healed TB on radiograph). Daily self-administered INH can also be given for 6 months but is generally felt to be less effective than a 9 month program. Rifampin daily for 4 months is also an approved treatment.

4. Feasibility of DOT, resources for drug procurement, program operations including patient monitoring, expectance of treatment completion as foreseen from medical and social circumstances of the patient, and preferences of the patient and the prescribing physician may play a role in the choice between INH and INH-Rifapentine regimens.

5. Weekly INH and Rifapentine should NOT be given to children less than two years of age, HIV-infected patients receiving antiretroviral therapy, pregnant women or women expecting to become pregnant during treatment, and patients who have LTBI with presumed INH or Rifampin resistance.

6. For those LTBI patients between age 2 and 11, the 9-month self-administered INH regimen is preferred. The 3-month, weekly DOT INH plus Rifapentine regimen should be considered if completion of 9-months of INH is unlikely and the likelihood of TB high.

7. Drug-resistant LTBI (e.g. exposure to known drug-resistant case contact) will require special consideration as outlined in above CDC documents.

8. Regimen completion is determined by number of doses given over a specified period of time per CDC guidelines. For example:

   - The 9-month daily self-administered INH regimen is a total of 270 doses given over a 12-month period.
   - 11 of 12 doses of weekly INH-Rifapentine need to be given over 16 weeks by DOT.
   - A total of 120 doses of Rifampin need to be given over a 6 month period.

9. Alternative intermittent regimens may be considered in highly select patients but DOT is required and specific regimens highlighted in the above references.

10. The previous 2-month Rifampin plus pyrazinamide regimen for LTBI is NOT recommended.

TB Clinic Process

1. LTBI treatment candidates will be evaluated by a Mayo Clinic physician in the Olmsted County TB Clinic to rule out active TB (pulmonary and extrapulmonary), and to determine if LTBI therapy is appropriate and whether the benefit of LTBI therapy outweighs its risks.

2. Clients must have documentation of a positive TST or IGRA to be considered for LTBI therapy or (as noted above) have an immunosuppressive medical condition and be considered a contact of a potentially infectious person with active TB.

   a. If clients are unable to produce documentation of a previous positive TST or IGRA, a repeat skin test or IGRA can be placed to confirm LTBI status after evaluation by the TB Clinic Public Health nurse (PHN) and/or clinician.
3. Prior to starting LTBI therapy, all patients should have a posterior-anterior (PA) and lateral (optional) chest x-ray done **within the last 3 months.** If it has been over three months since the last chest x-ray, another one should be performed to rule out active disease.

4. All clients considered to be at high risk for liver disease and/or hepatitis (e.g. history of alcohol or substance abuse, prior liver disease, etc.) and those born outside of the United States from endemic regions for chronic viral hepatitis) will have baseline liver function blood tests done prior to starting LTBI therapy.

   a. For adults (> 18 years of age) this will include an ALT and an alkaline phosphatase. For children under 18 years of age this will include an ALT only. All adult clients not already screened will have a serum glucose test. Patients to be started on Rifampin, Rifabutin or Rifapentine treatment should also have a CBC, Bilirubin and creatine levels in addition to ALT and alkaline phosphatase at baseline.

   If the liver function tests (LFT’s) reveal an elevated ALT, the following tests should be added to the blood work: AST, hepatitis B surface antigen, and hepatitis C antibody. If there is adequate supply of blood also add hepatitis core antibody and total bilirubin. If the LFT’s reveal an elevated alkaline phosphatase, an Alk Phos Isoenzyme test should be added to determine liver involvement.

   b. If the liver enzymes are less than twice normal levels and the hepatitis B and C tests are negative, do not initiate LTBI therapy and repeat LFT’s four weeks after the initial blood test. If the repeat tests remain less than twice normal levels, the client may begin LTBI therapy and client will be considered a “complex LTBI” case. A PHN will be assigned to case-manage the client to ensure monitoring of LFT’s and symptom evaluation during monthly medication refill appointments. If the repeat tests are normal, consult with the physician to determine if client will be considered routine or complex LTBI.

   c. If LFT’s are greater than twice normal levels or client is found to be hepatitis B or C positive, LTBI therapy will be deferred. Arrangements will then be made with one of the TB Clinic physicians to refer the client for a Gastroenterology/Hepatology (GI) evaluation at Mayo Clinic. Subsequent LTBI therapy will be determined based on outcome of the GI evaluation and their recommendations.

5. Clients to be started on LTBI therapy will meet with the TB clinic public health nurse (PHN) for a “med start” appointment. During this visit, the client will receive detailed instructions regarding the LTBI treatment, instructions on monthly refills or weekly DOT dependent on medication prescribed, the medication(s) ordered and side effects. The PHN will complete other case-opening procedures, and perform a baseline evaluation using the clinical assessment intervention on the PH- Doc computer system care plan for LTBI clients. The client will be given the first month supply of medicine if placed on INH or Rifampin or the PHN will set up a schedule for DOT (directly observed therapy) if client is placed on the 12-week regimen of INH and Rifapentine.

**Monitoring Patients Receiving Treatment for Latent TB Infection (LTBI)**

1. All clients receiving treatment for LTBI should be monitored for compliance and side effects.
a. Clients on INH or Rifampin will be seen monthly during routine Immunization Clinic hours by the immunization nurse on duty. Only one month supply of medications is to be given at a monthly monitoring visit. If a client is not able to return in one month for a refill, a maximum of two month supply can be given.

b. Clients on 12-week DOT with INH/Rifapentine will be seen monthly by the lead TB Clinic nurse for evaluation as designated by the TB Clinic physicians.

c. As part of the monthly assessment, review with the client the reasons for taking the medicine and the importance of taking it consistently in order to increase the likelihood of treatment success.

d. If the client is complaining of side effects consistent with liver toxicity, medication should be held and blood drawn for liver function tests. The TB program lead nurse should be consulted to determine if a physician evaluation in the TB Clinic should be arranged.

e. Monitoring visits are documented on the PH-Doc system under the LTBI Care Plan using the appropriate form for the specific therapy ordered. INH or Rifampin monitoring is recorded on the “LTBI Side Effects Refill Assessment” form. The 12-week INH/Rifapentine therapy monitoring is recorded on the “TB Monthly Nurse Clinical Assessment” form.

2. If the client reports symptoms consistent with active TB disease, the client should receive an expedited medical evaluation in TB Clinic. A repeat chest x-ray should be acquired as well as other appropriate evaluations based on presentation. Holding TB medication should be considered.

3. If there is reasonable suspicion that a client may be pregnant, a pregnancy test should be performed. If the client is found to be pregnant, medication should be stopped unless the following conditions apply:
   a. The client was a recent contact to an active pulmonary TB case.
   b. The client was a recent TST or Interferon Gamma Release Assay (IGRAS) converter.
   c. The client is immunocompromised

   If medication is stopped, the client should be encouraged to re-start LTBI therapy after giving birth. Client’s chart may be forwarded to the TB Program lead nurse for post-partum follow-up.

4. If the client is a child, ask the parent how the medication is given and whether the child is having any difficulty swallowing the medication. Suggestions may be offered regarding crushing the pills and mixing with a suitable medium (e.g. chocolate pudding, fruit jam, apple sauce, yogurt, etc).

5. If a family member comes in to pick up medication for the client, refills may be provided if they are able to answer the assessment questions or the patient can be called to answer the questions. However, the client should be seen in person by a clinic nurse at least every other month for an assessment. Clients on DOT for INH/RFT must present in person.

6. When clients are late in picking up refills, efforts will be made by the Immunization nurse or medical assistant to contact them by a minimum of 3 phone calls and one letter to encourage them to come in. Document all efforts to contact the client in the chart. Clients who do not respond will be documented as lost to follow-up.