Diagnosis and Management of Latent TB Infection

Tuberculosis Overview
Nearly one-third of the world’s population has been infected with M. Tuberculosis, with 8.6 million new cases and over 1.3 million deaths from tuberculosis in 2012 alone. Second only to HIV/AIDS, tuberculosis (TB) remains one of the leading causes of infectious disease deaths in the world. Fortunately, the overall incidence and prevalence of tuberculosis has been steadily declining for the past decade. This has left the majority of cases localized to the developing world and those emigrating from endemic areas. With only an estimated 1-5% of U.S. cases due to primary infection, the majority of cases of active TB in the United States are due to reactivation rather than primary infection. Thus, the key to disease control and prevention in our country is successful diagnosis and management of latent tuberculosis.

Defining Latent TB Infection (LTBI)
A patient with latent TB must first demonstrate a positive TB test (either PPD or an interferon gamma release assay (IGRA) such as the Quantiferon Gold (QFT-gold)). However, the patient should display no signs or symptoms of active TB. For example, a patient with LTBI would lack symptoms such as cough, fever, night sweats, weight loss, lymphadenopathy or abnormalities suggesting tuberculosis on chest x-ray. Thus, the patient would indeed be infected, but does not have active disease. A helpful analogy to explain this sometimes confusing situation is to tell patients the type of TB they have is “asleep.” Thus it must be treated so the bacteria does not “wake up” and become active or make them sick. It is important to inform patients with latent disease that they pose no public health risk, and they are not contagious.

Who and When to Screen
The purpose of testing for LTBI is to identify patients who are at risk for developing active tuberculosis (TB) and would therefore benefit from treatment. This provides benefit to the individual and also decreases the burden of future active disease in this country. The Center for Disease Control (CDC) recommends screening for tuberculosis in all individuals at high risk for exposure to tuberculosis. This includes all foreign-born patients from high-incidence countries. In fact foreign-born patients make up the majority of cases of LTBI in Minnesota, with nearly 81% of cases reported coming from foreign-born patients in 2013 alone (compared to 63% nationally). Virtually all of these patients arrive from the developing world. Although most adult foreign-born patients (and all refugees) are screened for active TB prior to US arrival, none are actually screened for latent disease. At Health Partners Center for International Health (CIH), providers screen foreign born patients for latent TB as part of their new arrival health screening.
- Patients under age 5 have a PPD (TST) placed.
- Patients over age 5 are screened with the QFT-gold blood test.
Current guidelines recommend screening for all foreign-born patients from high-incidence countries that have been in the United States for less than 5 years. However, in 2004 alone, greater than 50% of foreign-born cases of TB were in those who had resided within the U.S. for greater than 5 years. In fact, even in patients who have lived in the U.S. for >20 years, annual rates still far exceed rates of those born in the U.S.

Recent studies have suggested all immigrants should be screened for latent tuberculosis (LTBI) regardless of time of arrival or length of stay in the U.S. Among one study of 123,114 immigrants, of the reported cases of active TB, reactivated LTBI cases were more prevalent in patients screened after 1 year of arrival. However, the overall rate of LTBI reactivation showed no decline throughout years 1-9 after arrival. Therefore, CIH currently screens all foreign-born patients regardless of time since arrival as reactivation (or re-exposure) can occur anytime following arrival.

**Which Test to Order**
QFT-gold testing has demonstrated similar sensitivity to PPD (70-78% vs 77% with PPD) and superior specificity (96-99% vs 59-97% with PPD). The superior specificity is due to the fact that QFT-gold is NOT affected by a patient’s BCG vaccine status. The Bacille Calmette-Guerin (BCG) vaccine is commonly used in TB endemic areas to limit childhood mortality and development of miliary tuberculosis. False-positive TST results in patients who received BCG are common, which is primarily why the use of QFT-gold is recommended in the foreign-born population.

**Indeterminate Results**
Indeterminate results occur for a myriad of reasons. Because patients must have intact cell mediated immunity to mount a response, one cause of such results is immunocompromised states (e.g. HIV). Other confounding conditions may lead to an indeterminate result (e.g. insufficient sample, improper specimen handling, etc.). Regions Hospital reports rates of indeterminate results between 1-2%, with 78% of these results found in the inpatient setting. Thus, it is important to contact the laboratory to discuss the conditions by which the sample was rendered indeterminate.

**When Your Patient Has a Positive Test Result**
The first step in management of a positive TB screening test is to rule out active TB through a thorough history and physical. Once you have determined you are dealing with latent disease it is important to offer reassurance to your patient. Tuberculosis may have significant social, cultural and religious implications based on a patient’s background. The diagnosis can be associated with significant personal stress and social stigma. So please remember, always address a patient’s current understanding of an illness prior to educating on the topic. Most foreign born patients will not be familiar with the concept of latent disease (but most will know something about TB). This is where the sleep analogy can be useful (as above).

After initial counseling, all patients who live in Ramsey or Hennepin Counties with a positive screening test for TB should be referred to the County Public Health Tuberculosis Clinic for treatment of LTBI. Many primary care clinics have the capacity to manage LTBI; however, safety and adherence are significant concerns (especially with the emergence of multi-drug resistant TB). Only ~30-60% of patients complete a 6-month course of therapy. Furthermore, monthly clinical monitoring of patients by the Public Health Department is helpful in avoiding potentially life-threatening side effects of the medications. We do NOT
recommend that you prescribe INH or rifampin for your patient if he or she has latent TB and lives in Ramsey or Hennepin Counties. If your patient lives outside of these counties, referral to your MTM pharmacist is the safest option.

- Referral is available in Epic by typing the word Public Health in the order search field. The order is called “Public Health – TB Order”

**Additional Testing**

Remember: a positive TST or QFT-gold does not distinguish between active tuberculosis and latent infection. Diagnosis of active infection is based on symptoms, chest x-ray findings, and additional testing (including acid-fast bacilli smear and culture). Further testing should be at the discretion of the provider and will vary case by case. For those patients with signs or symptoms of active tuberculosis, contact the public health department or a Health Partners ID physician to discuss next steps (i.e. admission to hospital versus treatment at home).

Of note, recent trends have shown an increase in extra-pulmonary tuberculosis cases. In foreign-born patients presenting to Minnesota providers from 2007-2011, 53% of tuberculosis cases had extra-pulmonary manifestations (most commonly TB of the cervical lymph nodes). Thus, additional testing may be necessary based on a patient’s additional complaints or findings in the setting of positive tuberculosis testing.

**Treatment of Latent Tuberculosis**

It is important to remember that treatment of latent TB is never urgent. If you have suspicion or concern for active disease, this must be ruled out prior to embarking on treatment for latent disease.

Latent tuberculosis may be treated with a variety of drugs based on patient co-morbidities. The gold standard is 9 months of isoniazid therapy. Four months of rifampin therapy may be used as an alternative in patients at higher risk for hepatotoxicity due to INH therapy (i.e.; elderly, known liver disease, etc.), though rifampin is not an option for some patients undergoing HAART.

**Conclusion**

Improved public health systems have markedly decreased rates of active tuberculosis in U.S.-born patients. While this trend has produced improvement in the overall rates of disease, rates amongst foreign-born patients have been relatively unchanged for the past decade. From 2002-2007, over 21,277 foreign-born patients arriving to Minnesota were screened for tuberculosis, and of those screened nearly 40% (and 50% of those from Sub-Saharan Africa) tested positive for latent TB. Thus to match the decrease in active cases seen in US-born patients, providers must continue to pursue excellence in the care of immigrants and refugees by ensuring they have had appropriate screening for and management of latent TB.
References:
7. Tuberculosis http://www.health.state.mn.us/tb

Questions: Please reply to this e-mail, and your questions(s) will be directed to the authors of this Pearl, Matthew Goers, MD and Ann Settgast, MD.

Pearls of Knowledge Archive
All Pearl recommendations are consistent with professional society guidelines, and reviewed by HealthPartners Physician Leadership.

Addendum: February 5, 2015
A SmartSet was developed by the Occupational Medicine department to assist with the evaluation of latent TB infections. The SmartSet is OCCMED LATENT TB #2137

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