(Facility) IHS Chest Clinic Guidelines

Latent Tuberculosis Infection

Who to test:

1. Contact of a person with active pulmonary tuberculosis (TB) disease
2. Person with suspected active TB disease
3. Chest X-ray consistent with healed TB and never treated before.
4. Immunosuppressed: HIV, transplant, prolonged steroid treatment, treatment with anti-TNF agents.
5. Certain conditions: Diabetes mellitus (DM), chronic kidney disease (CKD), low body weight (10% below ideal), silicosis, gastrectomy, adrenoleukodystrophy (ALD).

How to test:

1. If available, the Interferon Gamma Release Assay (IGRA) testing is preferred over the Tuberculin Skin Test (TST) if age over 5 years old meeting some of these criteria:

    a. Likely to be infected with TB
    b. Low or intermediate risk of disease progression
    c. TB testing is deemed to be warranted
    d. History of BCG or have received BCG vaccination
    e. Unlikely to return to have a skin test read

2. Low risk persons who do not meet the criteria above, are tested anyway, and are found to be IGRA or TST positive should have a confirmatory test and only be considered to be TB infected if both tests are positive

Who to treat:

--do not treat every positive TST or IGRA patient. Only treat those with these risk factors:

1. Persons at personal risk for exposure to TB
   a. *These two groups are at risk*
      i. *Health Care personnel with direct patient contact* (doctors, nurses, pharmacists, radiology and lab techs, custodians, food services, clinic secretaries, etc.)
      ii. *Residential Congregate Setting facility employees and residents* (Long Term Care Facilities, corrections facilities, homeless shelters, etc.)
   b. Persons in this category should be screened once at the time of hire and not annually. Only Health Care Personnel with high risk of exposure such as pulmonologists and respiratory therapists or those working in a unit where tuberculosis has been spread before require annual testing.
   c. Health Care Personnel are considered at risk for tuberculosis if they resided for 1 or more months in a country with a high rate of TB or are

immunosuppressed (HIV, transplant, TNF antagonist/steroid Rx) or are a close contact of a case of infectious tuberculosis since the last test. These personnel require treatment for LTBI if either the TST or the IGRA is positive.

d. Health Care personnel who are asymptomatic and not high risk should be treated for LTBI only if both the TST and the IGRA are positive.

2. Patients at personal risk for reactivating TB:
    a. 5 mm TST cutoff:
        i. HIV positive
        ii. Contact of active TB case
        iii. Fibrotic changes on Chest X-Ray consistent with prior TB
        iv. Immunosuppressed (>15 mg prednisone/d for >1 month, received an organ transplant, TNF-alpha inhibitor, etc.). Some experts recommend sending an IGRA in addition to performing a TST and Chest X-ray on patients who are being prescribed a TNF alpha inhibitor.
    b. 10 mm TST cutoff:
        i. Recent immigrant
        ii. Injectable drug use
        iii. Resident at jail, nursing home, hospital, shelter
        iv. DM, CKD, lymphoma/leukemia, unexplained weight loss, silicosis, gastrectomy, age <4 years old, ALD
    c. IGRA positive with any of the above risk factors

How to treat Latent TB:

Preferred Adult Regimens:

1) **First choice:** A twelve-week course of isoniazid (INH) 900 mg PO weekly and rifapentine 900 mg PO weekly (750 mg weekly if <50 kg) is the IHS combination of choice.
2) Alternate regimens:
    a. Rifampin 600 mg PO daily for 4 months preferred for patients with liver disease.
    b. INH 300 mg PO daily for 9 months preferred for HIV positive patients who are taking antiretroviral medications that have clinically significant interactions with rifampin or rifapentine.
3) Special considerations:
    a. Supplement INH with pyridoxine 50 mg PO daily
    b. INH can be given 900 mg PO 2 or 3 times a week as DOT
    c. Rifampin *cannot* be given intermittently like INH

Consider Directly Observed Therapy (DOT) in most patients to ensure adherence to the treatment regimen, eradication of disease, and safety of the patient.

Monitoring for toxicity

a. Monitor the patient for symptoms of toxicity and physical exam monthly
    i. INH: rash, neuropathy, N/V, anorexia, jaundice, lupus-like illness
    ii. Rifampin/rifapentine: rash, flu-like illness, jaundice, bleeding
b. Monitor LFTs at baseline and periodically for patients if the patient:
    i. Has underlying hepatic disease (hepatitis, cirrhosis)
    ii. Has HIV
    iii. Is pregnant or postpartum within 3 months
    iv. Consumes alcohol regularly
    v. Is taking other medications with potential hepatotoxicity
c. If patient has risks for liver disease or has abnormal liver function tests (LFT)s at baseline, monitor the LFTs and CBC monthly (do not rely on symptoms and signs alone due to the high prevalence of non-alcoholic steatohepatosis (NASH) and ALD in this population)
d. Testing is recommended any time during treatment if the patient has symptoms suggestive of hepatitis (e.g., fatigue, weakness, malaise, anorexia, nausea, vomiting, abdominal pain, pale stools, brown urine, chills, or jaundice).

****Active TB treatment****

1) *Treat with 4 drugs: INH, rifampin, ethambutol (EMB), pyrazinamide (PZA)*
   a. Treat 2 weeks in the hospital with **daily** therapy then
   b. Continue for 6 weeks with 4 drugs ***always*** with home based **daily** DOT (daily is defined as every day, Monday through Friday)
   c. Stop EMB when the culture results show sensitivity to the other 3 drugs
   d. Stop PZA when 8 weeks of therapy are completed
   e. Continue therapy for 6 months total with INH and rifampin three times weekly if cultures collected at 8 weeks are subsequently negative and there were no cavities on the Chest X-ray (***alway***s use DOT for the duration)
   f. Continue therapy with INH and rifampin three times weekly for 9 months total if there were cavities on the first Chest X-ray and the week 8 culture is positive (***alway***s use DOT for the duration)
   g. Consider treating immunocompromised patients for 9 months
   h. Check HIV serology for every case of active TB
   i. Monitor for treatment success by checking a monthly sputum for Acid-Fast Bacilli smear and culture for the duration of therapy and at completion
   j. Obtain a follow-up chest x-ray at 2 months and at the completion of therapy.

2) *Monitoring for toxicity*
   a. Monitor for INH and rifampin toxicity as above
   b. Monitor for EMB toxicity with a baseline color vision test and repeat as needed
   c. Monitor for PZA toxicity by following for hepatotoxicity and gout

3) *Managing hepatotoxicity*
   a. Stop INH, RIF, PZA and EMB if the ALT and AST are 5 times greater than normal regardless of symptoms
   b. Stop INH, RIF, PZA and EMB if the ALT and AST are 3 times greater than normal and the patient has symptoms
   c. If drugs are stopped, wait until the LFTs are almost normal (<2 times the upper limit of normal) then re-challenge sequentially with the 3 drugs to determine which drug is the cause of toxicity:
      i) Inpatient Higher risk re-challenge: INH daily for 3 days then change to Rifampin daily for 3 days then change to PZA daily for 3 days. ***Check LFT's daily***. Ethambutol can be started with the initial INH challenge since it is not hepatotoxic and continued during the re-challenge with rifampin and pyrazinamide as a second drug
      ii) Outpatient Lower Risk re-challenge: Give EMB and rifampin daily for one week. If tolerated and LFTs are normal after one week add on INH for one week. If tolerated and LFTs normal after one more week consider adding PZA and checking labs in one week
      iii) Call for infectious disease consultation in the event of toxicity

Contact Investigations:

1) Test all family and social circle contacts with a TST (IGRA testing is occasionally used in school or hospital outbreak testing on Navajo)
2) Repeat TST at 8-10 weeks on all contacts who are initially PPD negative
3) Get Chest X-rays on the close home contacts to rule out active TB
4) Offer INH to the TST-positive (**greater than 5 mm**) adults and children who have not been treated for latent TB previously
5) Offer INH to TST-negative children less than 5 years old with a clear Chest X-ray. Repeat TST at 8-10 weeks and if TST-negative, stop INH
6) Offer INH to HIV positive or other substantially immune-compromised contacts even if TST is negative
7) Test all TST-positive contacts for HIV

How to run a Facility IHS Chest Clinic:

1) Designate 1 – 2 clinics per month as the local Service Unit Chest Clinic
2) Run the chest clinic in conjunction with the Service Unit TB technician
3) The TB technician should:
   a. check that the appropriate blood work has been drawn
   b. perform a screening review of symptoms
   c. estimate the degree of adherence
   d. Make phone calls or home visits to all patients who miss appointments
   e. Give DOT to all cases of active TB and to high risk contacts such as dialysis patients or HIV positive patients
4) The Chest Clinic clinician should:
   a. Monitor for signs and symptoms of toxicity
   b. Check the LFT's and CBCs that are ordered
   c. Review the duration of therapy at each visit (e.g., "5 of 9 months of INH completed")
   d. Check an HIV serology on every active case of TB and every case of Latent TB if the patient gives verbal informed consent
5) Carefully document when treatment for TB is completed in the EHR or paper problem list to avoid confusion in the future

When to call Infectious Diseases consultant:

1) HIV co-infection
2) Transplant patient
3) Drug-drug interactions (especially with Rifampin)
4) Possible drug resistance
5) Drug toxicity on treatment for TB

****Courtesy of Dr. Jonathan Iralu (IHS Chief Clinical Consultant, Infectious Disease), June 2019.*