Diagnosis & Treatment of Latent TB

James Sunstrum, M.D
Beaumont Health
Disclosures

• None
Learning Objectives

• Describe the current guidelines for LTBI treatment

• Describe monitoring recommendations for patients on LTBI treatment
Number of Active Tuberculosis Cases in New York City, According to Birthplace, 1992–2013.
Foreign-born residents

Metro Detroit’s foreign-born population helps offset slow growth and increase economic power. Detroit lags, with a foreign-born population under 5 percent and limited to a few small areas of the city.

**Key**
- 0% - 1%
- 1.1% - 7%
- 7.1% - 16%
- 16.1% - 24%
- 24.1% - 32%
- 32.1% - 60%

**Average:** 9.3%

Sources: Global Detroit, 2007-11 six-year American Community Survey, 2010 Census

The Detroit News
Transmission

Primary Tuberculosis

Latent Tuberculosis

“Reactivation” Tuberculosis

Skin-test conversion in 6 to 8 weeks

Spontaneous healing in 6 months

Progression after 2 years, 5%

Progression within 2 years, 5%

Progression with concurrent HIV infection, 10% each year

• Within 2 to 8 weeks the immune system produces special immune cells called macrophages that surround the tubercle bacilli
• These cells form a barrier shell that keeps the bacilli contained and under control (LTBI)
TB Pathogenesis (8)

TB Disease

• If the immune system CANNOT keep tubercle bacilli under control, bacilli begin to multiply rapidly and cause TB disease

• This process can occur in different places in the body
# LTBI vs. TB Disease

<table>
<thead>
<tr>
<th>Latent TB Infection (LTBI)</th>
<th>TB Disease (in the lungs)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Inactive</strong>, contained tubercle bacilli</td>
<td><strong>Active</strong>, multiplying tubercle bacilli</td>
</tr>
<tr>
<td>in the body</td>
<td>in the body</td>
</tr>
<tr>
<td>TST or IGRA blood test results</td>
<td>TST or IGRA blood test results</td>
</tr>
<tr>
<td>usually positive</td>
<td>usually positive</td>
</tr>
<tr>
<td>Chest x-ray usually <strong>normal</strong></td>
<td>Chest x-ray usually <strong>abnormal</strong></td>
</tr>
<tr>
<td>Sputum smears and cultures <strong>negative</strong></td>
<td>Sputum smears and cultures may be <strong>positive</strong></td>
</tr>
<tr>
<td>No symptoms</td>
<td><strong>Symptoms</strong> such as cough, fever, weight loss</td>
</tr>
<tr>
<td>Not infectious</td>
<td>Often infectious <strong>before</strong> treatment</td>
</tr>
<tr>
<td>Not a case of TB</td>
<td>A case of TB</td>
</tr>
</tbody>
</table>

Module 1 – Transmission and Pathogenesis of Tuberculosis

Mayo Clinic Center for Tuberculosis
Explaining “Latent” to a Patient

- Dormant
- Trapped or contained
- Not contagious
- Still viable TB bacteria in the body
Alternatives to PPD: Specific Mycobacterial Antigens

- **M. tuberculosis**
  - ESAT-6
  - CFP-10
  - TB7.7

- **BCG**

- **Atypicals**
  - *M. Avium*
  - *M. kansasii*
PPD can React with BCG and Atypical AFB
IGRA Tests More Specific Than PPD
Preferred Tests for Latent TB Infection

**PPD**
- Children <5 years of age

**IGRA**
- Persons who have received BCG vaccination
- People with poor rates of return to read PPD test
Results of Tests for Latent TB Infection

PPD Result is Positive

- > 5mm: HIV+ or immune suppressed, recent TB contact, fibrotic CXR
- >10mm: all others
- >15mm: no known risk for TB

IGRA

- Negative
- Indeterminate
- Positive
Screening for LTBI

TST or PPD

IGRA
Interferon Gamma Release Assays (IGRAs)

- IGRAs detect *M. tb* infection by measuring immune response in blood
- Cannot differentiate between TB and LTBI; other tests needed
- May be used for surveillance/screening, or to find those who will benefit from treatment
- FDA-approved IGRAs are QFT Gold In-Tube and T-Spot. *TB* test
General Recommendations for Using IGRAs

- May be used in place of, but not in addition to, TST
- Preferred when testing persons
  - Who might not return for TST reading
  - Who have received BCG vaccination

- Generally should not be used to test children <5 years of age, unless used in conjunction with TST
General Recommendations for Using IGRAs (cont.)

May be used in place of TST to test recent contacts of infectious TB

- Detect *M. tb* infection with greater specificity than TST
- Data are limited on ability to predict subsequent TB
- In contact investigations, confirm negative via retest 8–10 weeks postexposure
- Use same test for repeat testing to reduce misclassification errors
Tuberculosis Screening Flowchart

Clinical or epidemiologic risk factor for tuberculosis

- No
  - No tuberculin test

- Yes
  - Tuberculin test
    - Or IGRA
      - Negative
        - High-risk exposure within 3 mo
          - No
            - Treatment of latent tuberculosis not indicated
          - Yes
            - Evaluate for treatment of latent tuberculosis infection
      - Positive
        - Chest radiography clinical evaluation
          - Symptoms (e.g., fever, cough, weight loss) or abnormal chest radiograph
            - Evaluate for active tuberculosis
Chapter 5.
Treatment for Latent Tuberculosis Infection
Refer to experienced clinic for LTBI treatment

• Infectious Disease physicians
• Local TB Clinics:
  • Wayne County TB Clinic 734-727-1130
  • City of Detroit TB Clinic 313-577-9827
  • Oakland County Health Dept 248-858-8991
Treatment for Latent TB Infection (LTBI)

- Over 11 million persons in U.S. estimated to have LTBI (4% of population)
  - 5%-10% will develop TB disease if untreated

- Treatment of LTBI essential to controlling and eliminating TB disease

- Reduces risk of LTBI to TB disease progression

- Use targeted testing to find persons at high risk for TB who would benefit from LTBI treatment

- Several treatment regimens available
LTBI Treatment Regimens

Isoniazid (INH)

- **9-month daily regimen is preferred: 270 doses within 12 months**
  - Effective for HIV-infected as well as HIV-uninfected persons
  - Can be given twice weekly via DOT: 76 doses within 12 months
  - Preferred for children 2–11 years of age
LTBI Treatment Regimens

INH (cont.)

- 6-month regimen also generally acceptable: 180 doses within 9 months
  - Can be given twice weekly via DOT: 52 doses within 9 months
  - Shorter regimen not recommended for children, immunosuppressed persons, persons whose x-rays suggest previous TB
LTBI Treatment Regimens

INH-rifapentine (RPT) regimen (12-dose regimen)

- INH and RPT given in 12 once-weekly doses under DOT
LTBI Treatment Regimens

Dosage for 12-dose INH and RPT:

- **Isoniazid**: 15 mg/kg rounded up to the nearest 50 or 100 mg, with a **900 mg** maximum

- **Rifapentine**:
  - 10.0-14.0 kg: 300 mg
  - 14.1-25.0 kg: 450 mg
  - 25.1-32.0 kg: 600 mg
  - 32.1-49.9 kg: 750 mg
  - > 50.0 kg: **900 mg** maximum
Adverse Reactions to INH

Use of INH is associated with some adverse reactions:

- Peripheral neuropathy – give vitamin B<sub>6</sub> if patient has risk factors, or if signs/symptoms develop

- Fatal hepatitis – pregnant/postpartum women at increased risk; monitor closely

- Elevated liver enzymes – discontinue INH if liver enzyme levels exceed 3X normal with symptoms, or 5X upper limit of normal with no symptoms
  - Closely monitor if signs/symptoms of liver injury, or liver enzyme levels are elevated but less than above
Rifampin (RIF)

- Alternative to INH is 4 months daily RIF: 120 doses within 6 months
- Should not be used in HIV-infected persons being treated with some antiretroviral therapy (ART)
LTBI Treatment Regimens for Specific Situations (cont.)

Pregnancy and Breast-Feeding

- 9 months of INH daily or twice weekly; give with vitamin B$_6$
- If cannot take INH, consult with TB expert
- 12-dose INH-RPT regimen not recommended for pregnant women; its safety in pregnancy is not known
- Women at high risk for progression to TB disease, especially HIV infected or diabetic, should not delay LTBI treatment; monitor carefully
- Breast-feeding not contraindicated
Patient Monitoring

Before starting treatment for LTBI, clinicians should

- Exclude possibility of disease (symptoms, chest radiograph)
- Determine if patient has history of prior treatment for LTBI or disease
- Determine if any contraindications to treatment
- Obtain information about current and previous drug therapy, including adverse reactions
- Recommend HIV testing, unless the patient declines (opt-out screening)
Patient Monitoring (cont.)

Establish rapport with patient and emphasize

- Benefits of treatment
- Importance of adherence to treatment regimen
- Possible adverse side effects of regimen
- Establishment of optimal follow-up plan
Patient Monitoring (cont.)

- Baseline laboratory testing not routinely indicated for all patients

- Baseline hepatic measurements are indicated for
  - Patients with a liver disorder or liver disease
  - Patients with HIV infection
  - Pregnant women and those in immediate postpartum period

- Patients with abnormal baseline tests should be monitored regularly
Patient Monitoring (cont.)

At least monthly, evaluate for

- Adherence to prescribed regimen
- Signs and symptoms of TB disease
- Signs and symptoms of adverse effects, especially hepatitis
  - Jaundice, loss of appetite, fatigue, and/or muscle and joint aches
Resources

- Mobile App for IOS, Android: CDC LTBI
- www.cdc.gov/tb
- www.michigan.gov/tb
Mayo Clinic Center for Tuberculosis