Diagnosis and Medical Management of Latent TB Infection

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Marsha Majors, RN, BSN has the following disclosures to make:

• No conflict of interests

• No relevant financial relationships with any commercial companies pertaining to this educational activity
Special Consideration

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Outcomes of Exposure to *M. tuberculosis*

Inhalation of Droplet Nuclei

Regional replication in lungs, dissemination

~90%  ~5%  ~5%

Killing, containment of organisms  Latent disease  Active disease
Transmission of *M. tuberculosis*

Contacts of Active TB Case

- Among close contacts approximately 30% have LTBI and 1-3% have active TB disease
- Without treatment, approximately 5% of contacts with newly acquired LTBI progress to TB disease within 2 years
- Examination of contacts is one of the most important activities for identifying persons with disease and with LTBI
Treating LTBI

• Prevent progression to active disease
• Interrupt of transmission

• MUST rule out active disease before treating with a single drug

Proper Evaluation of an Adult Contact to a Pulmonary Case of Tuberculosis

• History and Physical Examination
  – Current medical problems (HIV, diabetes, TNF-α agents)
  – Previous exposure to TB, previous TST or IGRA result, previous treatment for LTBI or TB
  – Current symptoms
  – Examination for lymphadenopathy or respiratory findings

• TST or IGRA
Proper Evaluation of a Contact to a Case of Tuberculosis

• Should you get a CXR?
  – Symptoms
  – Positive TST/IGRA result
  – HIV positive or otherwise immunosuppressed

• Cultures?
  – Symptoms
  – Abnormal CXR
  – If you do, wait for the results!!

Before Treatment of LTBI: Exclude Active Tuberculosis!

• Absence of symptoms
• Negative CXR
• Negative medical evaluation
• Order and wait for sputum culture if any question
Ruling out Tuberculosis

Sites of TB Disease

- Lungs
  Extrapulmonary:
  - Larynx
  - Pleural effusion
  - Kidneys
  - Lymphatics
  - Bones & joints
  - Miliary (disseminated)
## Signs & Symptoms

### Pulmonary TB

<table>
<thead>
<tr>
<th>Pulmonary Symptoms:</th>
<th>Systemic Symptoms:</th>
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<tbody>
<tr>
<td>• Productive prolonged cough of over 3 weeks duration</td>
<td>• Fever</td>
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<tr>
<td>• Chest pain</td>
<td>• Chills</td>
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<tr>
<td>• Hemoptysis</td>
<td>• Night sweats</td>
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<tr>
<td></td>
<td>• Appetite loss</td>
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<td></td>
<td>• Weight loss</td>
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<td>• Easy fatigability</td>
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</table>

### Extrapulmonary TB

- More of a diagnostic problem than pulmonary TB
- Involves inaccessible sites = fewer bacteria can cause greater damage
- Bacteriologic confirmation more difficult
- Most forms represent reactivation TB
Evaluation for TB Infection

- Medical history
- Physical examination
- Testing for TB infection
- Chest radiograph
- Bacteriologic or histologic exam

Medical History

- Prior TB exposure, infection or disease
- Past TB treatment
- Demographic factors: country of origin, age, ethnic or racial group, occupation
Medical History

- HIV Infection
- Substance abuse
- Recent infection
- CXR findings suggestive of previous TB
- Diabetes mellitus
- Silicosis
- Prolonged Corticosteroid therapy
- Immunosuppressive therapy
- Cancer of head and neck
- Hodgkin’s
- Leukemia
- End-stage renal disease
- Intestinal bypass
- Gastrectomy
- Chronic malabsorption syndromes
- Low body weight

* Patients who do not know their HIV status should be referred for HIV counseling and testing
Physical Exam

- Cannot be used to confirm or rule out TB
- Can provide valuable information about the client’s overall health

Testing for TB Infection

- A TST or IGRA can help differentiate TB infected from uninfected people
- A negative TST or IGRA does not exclude the diagnosis of TB infection (especially for patients infected with HIV)
Classifying the Tuberculin Reaction
US recommendations

5 mm is classified as positive in

- HIV-positive persons
- Recent contacts of TB case
- Persons with fibrotic changes on chest radiograph consistent with old healed TB
- Patients with organ transplants and other immunosuppressed patients

Classifying the Tuberculin Reaction
US recommendations

10 mm is classified as positive in

- Recent arrivals from high-prevalence countries
- Injection drug users
- Residents and employees of high-risk congregate settings
- Mycobacteriology laboratory personnel
- Persons with clinical conditions that place them at high risk
- Children <4 years of age, or children and adolescents exposed to adults in high-risk categories
Classifying the Tuberculin Reaction
US recommendations

15 mm is classified as positive in

• Persons with no known risk factors for TB

• Targeted skin testing programs should only be conducted among high-risk groups

IFN-γ (gamma) release assays (IGRAs)

Antigen Presenting Cell + Antigen Specific TCell + Antigen

APC processes Antigen

APC presents Antigen to antigen-specific T cell

T cell Produces IFN-gamma

www.cellestis.com
Antigens for Gamma-Release Assays

<table>
<thead>
<tr>
<th>Tuberculosis complex</th>
<th>Antigens</th>
<th>Environmental strains</th>
<th>Antigens</th>
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<tr>
<td></td>
<td>ESAT</td>
<td>CFP</td>
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<tr>
<td>M tuberculosis</td>
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<td>+</td>
<td>M abcessus</td>
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Testing for TB Infection

- Clients who have a + TST result, a positive IGRA result or symptoms suggestive of TB (regardless of TST results) should be evaluated with an chest x-ray

- If abnormalities are noted, or the client has symptoms suggestive of extrapulmonary TB, additional diagnostic tests should be conducted
No CXR study shows findings specific for TB

Cavitary process likely to be TB

Common mimics of TB =

- Non-tuberculous mycobacteria (NTM)
- fungal infection
- bacterial abscesses
- necrotic neoplasm (especially lung neoplasm)

Chest Radiograph (CXR)

- Cannot confirm diagnosis of TB disease
- Abnormalities often seen in apical or posterior segments of upper lobe or superior segments of lower lobe
- May have unusual appearance in HIV positive persons (with HIV positive patients, any finding can be significant)
CXR - special situations

• Pregnant women who are highly suspicious and being evaluated for active disease should undergo a CXR without delay, even during the first trimester

• Patients suspected of extrapulmonary TB should have a CXR to R/O pulmonary TB

Differences In Adult and Pediatric TB
**Reactivation Disease**

- Occurs years after primary infection
- Typical of adult disease
- Occasionally seen in teens
- Often cavitary disease
- High numbers of organisms (AFB +)
- Usually symptomatic and contagious

**Primary Disease**

- Typical of childhood TB
- Usually not cavitary
- Classic x-ray: pulmonary infiltrate with or without hilar adenopathy, but may be nonspecific
- Low numbers of organisms
  - AFB smears negative in 95% of cases
  - Culture negative in 60% of cases
- Most children <12 yrs not contagious
- Often asymptomatic (50%)
Adult TB Disease

- **Pulmonary**: 85%
- **Extrapulmonary**: 15%

CDC
Pediatric TB Disease

- Pulmonary: 75%
- Extrapulmonary: 25%

Extrapulmonary TB Disease

Adults
- Lymphatic: 40%
- Other: 18%
- GU: 16%
- Bone/Joint: 10%
- Miliary: 9%
- Meningeal: 5%

Children
- Lymphatic: 67%
- Pleural: 14%
- Other: 5%
- Bone/Joint: 4%
- Miliary: 5%
- Meningeal: 6%

CDC
Common symptoms of TB disease in children

• Cough and/or respiratory distress
• Pulmonary findings on examination
• Lymphadenopathy or lymphadenitis
• S/Sx of meningitis including seizures
• Persistent fever (FUO)
• Weight loss or failure to thrive
• Unlike adults, up to 50% of children with TB disease have no symptoms

If in doubt....

• Get an MD evaluation
• Collect cultures and wait
• Re-evaluate....either disease will declare itself or the patient will convince you they don’t have TB
Proper evaluation Contacts < 5 years old

- TST
- CXR
- Rule out active disease
- Window prophylaxis
  - Treatment for LTBI during the period between TST screenings

HIV positive Contacts of an Active Pulmonary Case

- TST or IGRA
- CXR (regardless of symptoms)
- A complete course of LTBI treatment
  - Once disease ruled out
  - Regardless of TST/IGRA results
  - Regardless of CD4 count
HIV-infected persons, regardless of age, should be treated for LTBI if they have no evidence of active TB and exhibit the following characteristics:

1) a positive diagnostic test for LTBI and no prior history of treatment for active or latent TB (A1);
2) a negative diagnostic test for LTBI but are close contacts of persons with infectious pulmonary TB (AII); and
3) a history of untreated or inadequately treated healed TB (i.e., old fibrotic lesions on chest radiography) regardless of diagnostic tests for LTBI (AII).
Regimens for Treating LTBI

- 9-month regimen of isoniazid (INH) is the preferred regimen

- 6-month regimen of INH is less effective but may be used if unable to complete 9 months

- Rifampin (RIF) given daily for 4 months is an acceptable alternative when treatment with INH is not feasible. *Remember: rifampin interacts with LOTS of stuff, check!*

- In situations where Rifampin cannot be used, rifabutin may be substituted (e.g., HIV-infected persons receiving protease inhibitors, patients receiving methadone).

‘3HP’

- New LTBI treatment approved by the CDC

- Recommended to be given by DOT only

- INH 900 mg + rifapentine 900 mg once weekly for 12 weeks

- Note:
  - INH tablets are 300 mg
  - Rifapentine tablets are 150 mg
  - Total pill burden: 9 pills (plus vitamin B₆)
INH for LTBI

The most important thing for you to do when treating a patient for LTBI with INH is to counsel them to STOP the medication if they notice side effects and come in for a blood draw.

Routine blood work while on LTBI treatment

- HIV positive patients
- Patients with other co-morbid conditions
- Patients with baseline laboratory abnormalities
- Substance abusers (especially alcohol)

- Not necessary for children or otherwise healthy adults
MDR Contacts

• Based on the susceptibility pattern of the index case
• Risk/benefit weighed in each case
• No window prophylaxis under 5 y/o

• Call for help!! (1-800-TEX-LUNG)

Thank you for your attention!

Questions?

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