Diagnosis of Tuberculosis

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Outcomes of Exposure to *M. tuberculosis*

Inhalation of Droplet Nuclei

Regional replication in lungs, dissemination

- ~90% Killing, containment of organisms
- ~5% Latent disease
- ~5% Active disease
Transmission of *M. tuberculosis*
Sites of TB Disease

- Lungs

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

Pulmonary Symptoms:

• Productive prolonged cough of over 3 weeks duration
• Chest pain
• Hemoptysis

Systemic Symptoms:

• Fever
• Chills
• Night sweats
• Appetite loss
• Weight loss
• Easy fatigability
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

- 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
Medical History

* 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 may help differentiate infected from uninfected people with signs and symptoms.

- A negative TST or IGRA does not exclude the diagnosis of TB (especially for patient’s with severe TB illness or infection with HIV).
Classifying the Tuberculin Reaction

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

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

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)
### Antigens for Gamma-Release Assays

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<tr>
<th>Tuberculosis complex</th>
<th>Antigens</th>
<th>Environmental strains</th>
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Testing for TB Infection

- Clients who have a positive 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
CXR – HIV infected persons

- May cause infiltrates without cavities in any lung zone
- May cause mediastinal or hilar lymphadenopathy with or without infiltrates or cavities

In HIV-infected persons almost any abnormality on CXR may indicate TB
Primary Tuberculosis in an HIV positive patient
Miliary Tuberculosis
CXR – old healed TB

- Dense nodules, with or without visible calcification (hilar or ↑ lobes)
- Smaller nodules with or without fibrotic scars (↑ lobes, often with volume loss)

Old healed TB nodules & fibrotic lesions have well-demarcated sharp margins
CXR – old healed TB

• Nodules & fibrotic lesions may contain slowly multiplying bacilli = potential for progression

• CXR consistent with old TB and + TST = high priority for LTBI treatment

Calcified nodular lesions (calcified granuloma) pose a very low risk for future progression
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.
Bacteriologic and histologic Examinations

When lung or larynx is site of disease:

- 3 sputum specimens for AFB smear and culture
- Collected 8-24 hours apart with at least 1 early morning specimen

Specimens should be obtained in an isolated, well-ventilated area or sputum collection booth
Bacteriologic and histologic Examinations

- Sputum collection should be directly supervised
- For patients unable to cough up sputum, deep coughing may be induced
Bacteriologic and histologic Examinations

Bronchoscopy

• Bronchial washings
• Brushings
• Biopsy specimens

Sputum collected after bronchoscopy may also be useful for a diagnosis
Bacteriologic and histologic Examinations

Extrapulmonary Specimens

- Urine
- Cerebrospinal fluid *
- Pleural fluid *
- Pus
- Biopsy specimens

*recovery poor

Do NOT collect specimens in Formalin
Laboratory Examination

**AFB Smear**

- First clue
- presumptive diagnosis only

**Fluorochrome staining preferred method**

- Results available in 24 hours
- Many patients have negative AFB smears
Laboratory Examination

Cultures

Used to confirm diagnosis

- Perform on ALL specimens regardless of AFB results
- Results available in 10 to 14 days (on liquid media, e.g. BACTEC)

TB may be diagnosed on the basis of signs and symptoms in the absence of a + culture
Laboratory Examination

• Nucleic acid probes ID species in 2 to 4 hours

• HPLC are equally rapid and can ID most species

• Solid mediums and conventional tests can take 6 to 12 weeks
Laboratory Follow-up

- Monitor sputum cultures at least monthly until negative cultures are obtained.

- Culture conversion = 1st negative culture in a series of previously positive cultures (all subsequent cultures must remain negative).
Questions?