TB Screening and Prophylaxis

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09/13/2017

No Disclosures
Objectives

- The participant will be able to identify the differences between TB infection and TB disease.
- The participant will have a better understanding of what high risk populations should be screened for latent tuberculosis.
- The participant will be able to identify risk factors associated with developing TB disease after TB infection.
- The participant will understand the utility of screening tools for tuberculosis.
- The participant will know the current treatment options for latent tuberculosis.
Pre-test Question 1

45 yr. old male with PMH of diabetes, hypertension, and rheumatoid arthritis (RA) was sent from rheumatology clinic. He migrated to US from Indonesia 2 yrs ago. His current medications are metformin and lisinopril.

Apart from multiple joint pains, patient denies any shortness of breath, cough, fevers, chest or abdominal pain, fatigue, change in weight or appetite. Due to recent worsening of his RA symptoms, his rheumatologist is considering starting him on infliximab in 4-6 weeks.

On reviewing his previous records, you found that he had a tuberculin skin test done 8 months ago which was 10 mm. His recent HgA1C is 6.9. His recent chest x-ray is negative.

What would you suggest for this patient now?
A. He should have a repeat tuberculin skin test done as previous result was negative

B. He should have quantiferon TB testing done due to negative TST and if positive, he should receive INH for 9 months

C. He has TB disease, he should get combination of anti-tubercular therapy

D. He has TB infection, recommend 12 weekly doses of INH and rifapentine combination

E. No intervention at this point. Recommend to continue his current medications

Pre-test Question 1
What would you suggest for this patient now?
Tuberculosis

- Majority of TB cases caused by M. tb.
- It spread via airborne particles called droplet nuclei.
- Transmission occurs when droplet nuclei inhaled and reach the alveoli of the lungs, via nasal passages, respiratory tract, and bronchi.
The Global Burden of TB, 2014

**Estimated number of cases**

- All forms of TB: 9.6 million
  - 1 million children
  - 3.2 million women
  - 5.4 million men

**Estimated number of deaths**

- 1.5 million*
  - 140,000 in children
  - 480,000 in women
  - 890,000 in men

**HIV-associated TB**

- 1.2 million (12.5%)
- 390,000

**Multidrug-resistant TB**

- 480,000
- 190,000

*Including deaths attributed to HIV/TB

Source: WHO Global TB Report 2015
TB ranks alongside HIV as a leading cause of death

2012, WHO Global Health Observatory

2014, WHO and UNAIDS

In grey: TB/HIV deaths

GLOBAL TB PROGRAMME

World Health Organization
TB incidence: countries and regions

Top 5:
23% in India
10% each: Indonesia & China
5% each: Nigeria & Pakistan
For the first time in 23 years, the number of TB cases in the United States increased in 2015.

A total of 9,557 cases of TB disease were reported in 2015, which represents a 1.6% increase from 2014.

This increase underscores the need for more comprehensive public health approaches in TB prevention and control.
Principles for Stopping TB Transmission
Latent TB Infection (LTBI)

- LTBI is the presence of *M. tuberculosis* organisms (tubercle bacilli) without signs and symptoms or radiographic or bacteriologic evidence of TB disease.
Latent TB Infection (LTBI)

- Tubercle bacilli in the body
- Cannot spread TB to others
- Do not feel sick
- Do not have symptoms
- Normal chest X-ray
- Sputum smears and cultures are negative
- Usually positive skin test
- Not a “case” of TB
- Are at risk for developing TB disease
### LTBI vs. Pulmonary TB Disease

<table>
<thead>
<tr>
<th>Latent TB Infection</th>
<th>Pulmonary TB Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>No symptoms or physical findings suggestive of TB</td>
<td>Symptoms may include one or more of the following: fever, cough, night sweats, weight loss, fatigue, hemoptysis, decreased appetite</td>
</tr>
<tr>
<td>If done, respiratory specimens are smear and culture negative</td>
<td>Respiratory specimens are usually culture positive (smear positive in about 50% of patients)</td>
</tr>
<tr>
<td>Positive TST* or IGRA† result</td>
<td>TST or IGRA is usually positive</td>
</tr>
<tr>
<td>Chest radiograph normal</td>
<td>Chest radiograph is usually abnormal</td>
</tr>
</tbody>
</table>

* tuberculin skin test  
† Interferon-Gamma Release Assay
Risk of TB infection and disease among exposed individuals

Exposure (close contact)

- No Infection: 70%

  Infection: 30%

  Early progression (recent TB ≤ 2 yrs): 5%

  Containment: 95%

    Late progression (reactivation of TB): 5% to 10%

    Continued containment: 90% to 95%
Targeted TB Testing

- Routine TB testing is not recommended.

- CDC discourages use of diagnostic tests for LTBI among individuals and populations at low risk for infection with M. tuberculosis

- Targeted testing should be used to identify and treat persons who are at high risk for developing:
  - Infection with *M. tuberculosis*
  - TB disease once infected with *M. tuberculosis*

- Identifying and treating persons can prevent these persons from developing TB disease in the future.

- This helps to stop the further spread of TB in communities.
Q1. Which of the following is not at high risk for becoming infected with *M. tuberculosis*?

A. Residents & employees of congregate settings

B. Healthcare workers who serve high risk clients

C. Homeless and street drug users

D. People who have unprotected sex **(Correct Answer)**

E. Foreign born patients from TB endemic countries
Who Should Be Tested:

<table>
<thead>
<tr>
<th>Who is considered at risk?</th>
<th>Which countries are considered TB endemic?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Foreign born patients from TB endemic countries, where prior TB exposure is almost certain</td>
<td>All of Asia except Japan</td>
</tr>
<tr>
<td></td>
<td>All of Central and South America</td>
</tr>
<tr>
<td></td>
<td>All of Africa</td>
</tr>
<tr>
<td></td>
<td>All of Eastern Europe</td>
</tr>
</tbody>
</table>
Other Groups At High Risk for TB Infection

- Contacts of persons known or suspected to have infectious TB disease
  - Infants, children, and adolescents exposed to adults at increased risk for infection or disease
- Resident or employee of high-risk congregate setting in places at high risk for TB transmission (e.g., correctional facility, long term care facility, hospital, homeless shelter, residential home for those with HIV)
- Health care workers who serve clients who are at increased risk for TB disease
- Medically underserved, low-income persons
  - Homeless
  - Migrant Workers
  - Illicit drug users
Q2. Which of the following groups are at high risk for developing TB disease after infection with *M. tuberculosis*?

A. Persons on immunosuppressive therapy with TNF-α antagonists or on systemic corticosteroids equivalent to ≥ 15 mg of prednisone per day

B. Persons who were recently infected with *M. tuberculosis* (within the past 2 years)

C. Adolescents exposed to adults in high-risk groups

D. People who live or work in congregate settings whose clients are at increased risk for TB disease

E. All of the above

F. Only A, B and D
Risk Factors for Progression from Latent TB Infection (LTBI) to Active TB Disease

Children younger than 5 years of age

Medical Conditions

- Immunosuppression
- Lymphoma, leukemia
- Head and neck cancer
- Chronic renal failure
- Diabetes
- History of untreated or inadequately treated TB disease
- HIV +/- AIDS
- Malnutrition
- Substance abuse
- Silicosis
- Gastrectomy/ jejunoileal bypass
- Recently infected with \( M. tuberculosis \) (within the past 2 years)
Risk Factors for Progression from Latent TB Infection (LTBI) to Active TB Disease

Immunosuppressive agents

- Steroids (not inhaled)
  - (Prednisone >15 mg/day for 1 month or more)
- Cancer chemotherapy
- Cyclosporine
- Anti-Rheumatics*
  - Etanercept (Enbrel)
  - Infliximab (Remicade)
  - Adalimumab (Humira TM)

Testing for TB infection

- Diagnostic tests that can be used to detect TB infection include:
  - The Mantoux tuberculin skin test (TST)
  - Interferon-gamma release assays (IGRAs)

- A positive TST or IGRA result only indicates if someone has been infected with *M. tuberculosis*.

- These tests cannot identify if a person has TB disease.

- People who are not at high risk for LTBI generally should not be tested. Positive test results in low-risk populations are sometimes inaccurate.
Administering the Tuberculin Skin Testing

- Inject 0.1 ml of 5 TU PPD tuberculin solution intradermally on volar surface of lower arm using a 27-guage needle.

- Produce a wheal 6 to 10 mm in diameter.
Reading the Tuberculin Skin Testing

- Measure reaction in 48 to 72 hours.
- Measure induration, not erythema.
- Record reaction in millimeters, not “negative” or “positive”.
- Ensure trained health care professional measures and interprets the TST.
Interpreting the Tuberculin Skin Testing (PPD)

- A positive TST (PPD) is determined by
  - The size of the induration
  - The patient’s risk factors
# Interpreting Tuberculin Skin Test Reactions

<table>
<thead>
<tr>
<th>5 mm or greater</th>
<th>10 mm or greater</th>
<th>15 mm or greater</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV positive persons</td>
<td>Immigrants from high-prevalence areas</td>
<td>No known risk factors</td>
</tr>
<tr>
<td>Recent contacts of persons with active tuberculosis</td>
<td>Injection drug users</td>
<td></td>
</tr>
<tr>
<td>Fibrotic changes on chest radiograph, consistent with tuberculosis</td>
<td>Residents and employees* of high-risk congregate settings</td>
<td></td>
</tr>
<tr>
<td>Patients with organ transplants and other immunosuppressed patients</td>
<td>Personnel in mycobacteriology laboratories</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Persons with clinical conditions that place them at high risk for progression of disease</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Children: &lt;4 years of age; all exposed to adults at high-risk</td>
<td></td>
</tr>
</tbody>
</table>

(Note: the CDC discourages testing of people at low risk for infection.)
Q3. Which of the following patient has a negative TST reaction?

A. 32 years old, HIV infected, 8 mm of induration
B. 51 years old, has diabetes, 12 mm of induration
C. 26 years old, native of Mexico, 7 mm of induration
D. 69 years old, resident of a nursing home, 11 mm of induration
E. 52 years old, chest x-ray findings suggestive of previous TB, 6 mm of induration
Who needs repeat LTBI testing?

- Healthcare workers
- Close contacts to infectious TB cases
- Frequent travelers to abroad
  - If baseline TST is negative, consider retesting your patients that have extended travel to high risk areas
  - Do symptom review upon return and possibly retesting 8-10 week after return
Q4. What factors can cause false-positive reactions to the TST?

A. Infection with nontuberculous mycobacteria (NTM) (mycobacteria other than M. tuberculosis)

B. BCG vaccination

C. Administration of incorrect antigen

D. All of the above

E. Only B choice is correct
Factors That May Cause False-Positive TST Reactions

- Nontuberculous mycobacteria (NTM)
  - Reactions caused by NTM are usually \( \leq 10 \) mm of induration.

- BCG vaccination.
  - Reactivity in BCG vaccine recipients generally wanes over time; positive TST result is likely due to TB infection if risk factors are present.

- Administration of incorrect antigen.

- Incorrect measuring or interpretation of the TST reaction.
Q5. What factors can cause false-negative reactions to the TST?

A. Recent TB infection (within the past 2-10 weeks)
B. Very young age (younger than 6 months)
C. Recent live-virus measles or smallpox vaccination
D. All of the above

- Recent TB infection (within the past 2-10 weeks): 0%
- Very young age (younger than 6 months): 0%
- Recent live-virus measles or smallpox vaccination: 0%
- All of the above: 0%
## Factors That May Cause False-Negative TST Reactions

<table>
<thead>
<tr>
<th>Possible Cause</th>
<th>People at Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anergy</td>
<td>HIV-infected people, other people with weakened immune systems, severe TB disease, and some viral illness (e.g., measles and chicken pox)</td>
</tr>
<tr>
<td>Recent TB infection</td>
<td>People infected with <em>M. tuberculosis</em> within the past 8 to 10 weeks</td>
</tr>
<tr>
<td>Very young age</td>
<td>Children younger than 6 months</td>
</tr>
<tr>
<td>Recent live-virus measles or small pox vaccination</td>
<td>Any person who will be or recently received a live-virus vaccination</td>
</tr>
<tr>
<td>Incorrect method of giving TST</td>
<td>Any person being tested</td>
</tr>
<tr>
<td>Incorrect interpretation of TST</td>
<td>Any person being tested</td>
</tr>
</tbody>
</table>
Q6. Which of the followings is false regarding Interferon-gamma release assay (IGRA) testing

A. Requires one patient visit to conduct the test
B. Does not cause booster phenomenon
C. BCG vaccination does not cause false-positive result
D. Does not cross react with non tuberculous mycobacterium
Interferon-gamma release assay (IGRA)

- IGRAs are blood tests that measure a person’s immune reactivity to *M. tuberculosis*.

- White blood cells from most patients that have been infected with *M. tuberculosis* will release interferon-gamma (IFN-g) when mixed with *M. tuberculosis* antigens and control substances.

- Can be used in all circumstances in which the TST is currently used, including contact investigations, evaluation of recent immigrants who have had BCG vaccination, and TB testing of health care workers.

- They do not help differentiate latent tuberculosis infection (LTBI) from tuberculosis disease.
Interferon-gamma release assay (IGRA)

- Two Food and Drug Administration (FDA) approved IGRA's are commercially available in the U.S.:
  - QuantiFERON®-TB Gold-in-tube test (QFT-GIT)
  - T.SPOT®.TB test (T-Spot)

**Interpretation of IGRA Test Results**

<table>
<thead>
<tr>
<th>IGRA Test</th>
<th>Results Reported as</th>
</tr>
</thead>
<tbody>
<tr>
<td>QFT-GIT</td>
<td>Positive, negative, indeterminate</td>
</tr>
<tr>
<td>T-Spot</td>
<td>Positive, negative, indeterminate, borderline</td>
</tr>
</tbody>
</table>

Note: Laboratory should provide both quantitative and qualitative results
# Advantages of Using the QFT-G Compared to Using the TST

<table>
<thead>
<tr>
<th>QFT-G Result</th>
<th>TST</th>
</tr>
</thead>
<tbody>
<tr>
<td>Requires 1 patient visit to conduct the test</td>
<td>Requires 2 patient visits to conduct the test (3 to 4 visits if 2 step testing)</td>
</tr>
<tr>
<td>Results can be available in 24 hours</td>
<td>Results are available 48 to 72 hours later</td>
</tr>
<tr>
<td>Does not cause booster phenomenon</td>
<td>Can cause booster phenomenon</td>
</tr>
<tr>
<td>Not as likely to have incorrect reading</td>
<td>More likely to have incorrect reading</td>
</tr>
<tr>
<td>BCG vaccination does not cause false-positive result</td>
<td>BCG vaccination can cause false-positive result</td>
</tr>
<tr>
<td>Specificity of IGRA testing is 98–100 %</td>
<td>Specificity of TST is 85-88 % for TST</td>
</tr>
</tbody>
</table>
Disadvantages and limitations of IGRAs

- Blood samples must be processed within 8-30 hours after collection while white blood cells are still viable.
- Errors in collecting or transporting blood specimens or in running and interpreting the assay can decrease the accuracy of IGRAs.
- Cost of IGRA testing varies but is usually in the range of $160-$230, versus the cost of TST at approximately $10-$15.
- Limited data on the use of IGRAs for:
  - Children younger than 5 years of age;
  - Persons recently exposed to *M. tuberculosis*;
  - Immunocompromised persons (including corticosteroids or TNF-α antagonists),
  - Persons with certain blood disorders, cancers, diabetes, silicosis, or severe kidney disease
  - Serial testing.
2010 CDC Guidelines

IGRA can be used in all circumstances in which the TST is currently used. Routine testing with both TST and IGRA is **not** recommended.

- IGRA preferred, but TST is acceptable:
  - Low likelihood to return for TST reading (e.g. homeless, drug abusers)
  - Prior BCG vaccination (improve acceptance of LTBI treatment)
- TST preferred, but IGRA is acceptable:
  - Children < 5 yrs.
- Either TST or IGRA may be used without preference
  - Recent TB contacts with active case
    - (repeat testing 8-10 weeks after end of exposure if initial test was negative)
  - Periodic screening of HCW
- Both TST and IGRA can be considered
  - High risk of TB infection and progression, and risk of poor outcome
    - HIV
    - Immunosuppressed patients
Q7. 25-yr-old physician from China has pre employment TST of 20 mm induration. He has no significant past medical history including no history of TB disease or known TB exposure. He is currently asymptomatic and denies smoking or illicit drug use. His chest x-ray is normal. He is not currently on any medications. What would you do?

A. Repeat TST in one month

B. Perform interferon-gamma release assay

C. Offer treatment for latent TB infection

D. No treatment needed, patient had BCG vaccination
Evaluation of Persons with Positive TB Test Results

Person has a positive test for TB infection

Rule out TB disease

Consider treatment for LTBI

If person refuses or is unable to receive treatment for LTBI, follow-up TST or IGRA and serial chest radiographs are unnecessary

Person accepts and is able to receive treatment of LTBI

Develop a plan of treatment with patient to ensure adherence

Educate patient about the signs and symptoms of TB disease
Q8. All of the following regimens are used for LTBI treatment except:

A. Isoniazid

B. Isoniazid & rifapentine

C. Rifampin

D. Rifampin and Pyrazinamide

Correct answer: D. Rifampin and Pyrazinamide
## Treatment Regimens for Latent TB Infection

<table>
<thead>
<tr>
<th>Drug(s)</th>
<th>Duration</th>
<th>Interval</th>
<th>Minimum Doses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isoniazid</td>
<td>9 months</td>
<td>Daily (AII)</td>
<td>270 doses within 12 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Twice weekly (BII)</td>
<td>76 doses within 12 months</td>
</tr>
<tr>
<td></td>
<td>6 months</td>
<td>Daily (BI)</td>
<td>180 doses within 9 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Twice weekly (BII)</td>
<td>52 doses within 9 months</td>
</tr>
<tr>
<td>Isoniazid &amp; Rifapentine</td>
<td>3 months</td>
<td>Once weekly</td>
<td>12 doses within 16 weeks</td>
</tr>
<tr>
<td>Rifampin</td>
<td>4 months</td>
<td>Daily (BII)</td>
<td>120 doses within 6 months</td>
</tr>
</tbody>
</table>
Latent TB Infection Treatment Regimens – Isoniazid (INH)

- 9-month regimen of isoniazid (INH) is one of the preferred regimens
  - 6-month regimen is less effective but may be used if unable to complete 9 months
- May be given daily or intermittently (twice weekly)
- Use directly observed therapy (DOT) for intermittent regimen
- Preferred regimen for children 2-11 years of age
Latent TB Infection Treatment Regimens – Isoniazid (INH) and Rifapentine (RPT)

- 3-month regimen of INH and RPT is an option equal to 9-month INH regimen for treating LTBI in certain groups
  - Otherwise healthy people
  - 12 years of age and older
    - who were recently in contact with infectious TB
    - who had tuberculin skin test conversions
    - positive blood test for TB infections
- Given once a week for 3 months - 12 doses within 4 months
- Must use directly observed therapy (DOT)

*MMWR. Recommendations for Use of an Isoniazid–Rifapentine Regimen with Direct Observation to Treat Latent Mycobacterium tuberculosis Infection
http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6048a3.htm?s_cid=mm6048a3_w
Q9. Isoniazid and Rifapentine is not recommended for which of the following?

A. Children younger than 12 years of age
B. HIV-infected people taking antiretroviral therapy
C. Pregnant women
D. Women expecting to be pregnant within the 12-week regimen
E. People presumed to be infected with INH or rifampin-resistant *M. tuberculosis*
F. All of the above
Latent TB Infection Treatment Regimens – Rifampin

- Rifampin (RIF) given daily for 4 months is an acceptable alternative
  - who cannot tolerate INH
  - who have been exposed to INH-resistant TB
- In situations where RIF cannot be used
  - HIV-infected persons receiving protease inhibitors
    - Rifabutin may be substituted
- RIF daily for 4 months - 120 doses within 6 months
Laboratory Monitoring

- Baseline liver function tests (e.g., AST, ALT, and bilirubin) are not necessary except for patients with risk factors:
  - HIV infection
  - History of liver disease
  - Regular alcohol use
  - Pregnancy or in early postpartum period
Laboratory Monitoring

- Repeat laboratory monitoring if patient has:
  - Abnormal baseline results
  - Current or recent pregnancy
  - Symptoms of adverse reaction
  - Liver enlargement or tenderness during examination
Monthly Evaluation

- At least once a month, the patient should be evaluated for:
  - Adherence to the prescribed regimen
  - Signs and symptoms of TB disease
  - Signs and symptoms of adverse effects, especially hepatitis (i.e., jaundice, loss of appetite, fatigue, and/or muscle and joint aches).
Summary: Meeting the Challenge of TB Prevention

For every patient:

- Assess TB risk factors
- If risk is present, perform TST or IGRA
- If TST or IGRA is positive, rule out TB disease
- If TB disease is ruled out, initiate treatment for LTBI
- If treatment is initiated, ensure completion
45 yr. old male with PMH of diabetes, hypertension, and rheumatoid arthritis (RA) was sent from rheumatology clinic. He migrated to US from Indonesia 2 yrs ago. His current medications are metformin and lisinopril.

Apart from multiple joint pains, patient denies any shortness of breath, cough, fevers, chest or abdominal pain, fatigue, change in weight or appetite. Due to recent worsening of his RA symptoms, his rheumatologist is considering starting him on infliximab in 4-6 weeks.

On reviewing his previous records, you found that he had a tuberculin skin test done 8 months ago which was 10 mm. His recent HgA1C is 6.9. His recent chest x-ray is negative. What would you suggest this patient now?
Post-test Question
What would you suggest this patient now?

A. He should have a repeat tuberculin skin test done as previous result was negative
B. He should have quantiferon TB testing done due to negative TST and if positive, he should receive INH for 9 months
C. He has TB disease, he should get combination of anti-tubercular therapy
D. He has TB infection, recommend 12 weekly doses of INH and rifapentine combination
E. No intervention at this point. Recommend to continue his current medications
“THINK TB” and “TB RISK”

At Risk Populations

Thanks