TB: Transmission, Pathogenesis, & Classification

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Overview

1. TB Transmission and Pathogenesis
   • Latent TB infection (LTBI)
   • Active TB disease

2. Tuberculosis Classifications

3. Strategies for TB Prevention (& Elimination?)
Poll Question!

What is TB? (choose all that apply)

a) TB = **Tuberculosis**

b) An **ancient disease** caused by **mycobacteria**

c) An **airborne disease**

d) A **curable** disease

e) A **preventable** disease
TB = Tuberculosis

Mycobacterium Tuberculosis Complex (MTBC)
Poll Question!

When tubercle bacilli are in the body, but the body's immune system is keeping the bacilli under control and contained, what does the patient have?

a) TB disease
b) Latent TB infection
c) No TB infection or TB disease
d) Don’t know
TB is spread when a person with TB disease coughs, sings, or speaks and you breathe the air contaminated with TB germs. The germs reach your lungs. From there, they can go to other parts of your body.

Your body fights the TB germs. You can take medicine to treat LATENT TB INFECTION and prevent getting TB DISEASE.

Taking your TB medicine is very important. You need to take the medicine to help get better and to prevent the spread of TB germs to others.

You get TB DISEASE when the TB germs multiply and attack your lungs or other parts of your body. When this happens,
- You have a positive TB skin test or TB blood test.
- You feel sick with cough, fever, weight loss, chest pain, or sweating at night.
- You have active TB germs in your body.
- You may give TB germs to others.
- You may have an abnormal chest x-ray.

If your body controls the germs, you have LATENT TB INFECTION. When this happens,
- You may have a positive TB skin test or TB blood test.
- You don't feel sick.
- You don't have TB symptoms.
- You can't give TB germs to others.
- You have a normal chest x-ray.

Taking your TB medicine is very important. You need to take the medicine to help get better and to prevent the spread of TB germs to others.
2 Steps to Prevent M. bovis (cow TB)

Test cows for TB  Pasteurization

Keep your family safe:
Make sure your Queso Fresco is Pasteurized!
Latent TB infection or active TB disease?

What features distinguish one from the other?
Person/Place/Time
The chance of **INFECTION** increases when...

- The concentration of TB bacteria circulating in the air is greater
  - Coughing; smear-positive; cavitary disease
  - Poor ventilation; small enclosed space

- More time is spent with the infectious person (frequency and duration)

- Exposure occurs in an area where the bacteria can easily survive (no ultra violet light)
Not everyone who is exposed to TB will become infected
Pathogenesis

Infection occurs when a person inhales droplet nuclei containing tubercle bacilli that reach the alveoli of the lungs. These tubercle bacilli are ingested by alveolar macrophages. While most bacilli are destroyed or inhibited, a small number may multiply intracellularly and be released when the macrophages die. If alive, these bacilli may spread by way of lymphatic channels or through the bloodstream to more distant tissues and organs (including areas of the body in which TB disease is most likely to develop: regional lymph nodes, apex of the lung, kidneys, brain, and bone). This process of dissemination primes the immune system for a systemic response. Further details about pathogenesis of latent tuberculosis infection (LTBI) and TB disease are described in Figure 1.3.

TB Pathogenesis

Exposure

Infection

Adequate Immunity

Non-specific immunity

Adequate Defenses

Containment (90-95%)

Immunologic defenses

Inadequate Defenses

Inadequate Immunity

Early progression

TB disease (5-10%)

No infection

Adequate Defenses

Inadequate Defenses

TB disease (5-10%)
DISSEMINATION:
Spread of TB to Other Parts of the Body

1. Lungs (~85% all cases)
2. Pleura
3. Central nervous system (spine, brain, meninges)
4. Lymph nodes
5. Genitourinary system
6. Bones and joints
7. Disseminated (miliary)
TB Pathogenesis (3)

No infection

Adequate Immunity

Non-specific immunity

Inadequate Immunity

Infection

Containment (90-95%)

Adequate Defenses

Immunologic defenses

Inadequate Defenses

Late progression

TB disease (5-10%)
Risk Factors for Progression of Infection to TB Disease

• 10% of adults infected with TB who have a normal immune systems develop TB at some point in their lifetime

• Highest risk: Recent infection (within 1-2 years of infection)

• Conditions/treatment that impairs immune control of *M. tb*

<table>
<thead>
<tr>
<th>Condition (partial list)</th>
<th>TB risk^a</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV/AIDS</td>
<td>10 - 100</td>
</tr>
<tr>
<td>Organ-transplant recipients</td>
<td>20 - 70</td>
</tr>
<tr>
<td>Chronic renal failure requiring dialysis</td>
<td>6.9 - 52.5</td>
</tr>
<tr>
<td>TNF-alpha blockers</td>
<td>1.6 - 25.1</td>
</tr>
<tr>
<td>Silicosis</td>
<td>2.8</td>
</tr>
<tr>
<td>Fibronodular disease on CXR</td>
<td>6 - 19</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1.6 - 7.83</td>
</tr>
<tr>
<td>Smoking</td>
<td>2 – 3.4</td>
</tr>
</tbody>
</table>

^a Relative risk of TB compared to the general population


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<th>Risk Factor</th>
<th>Risk of Developing TB Disease</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td>TB infection and no risk factors</td>
<td>About 10% over a lifetime</td>
<td>For people with TB infection, no risk factors, and no treatment, the risk is about 5% in the first 2 years after infection and about 10% over a lifetime.</td>
</tr>
<tr>
<td>TB infection and diabetes</td>
<td>About 30% over a lifetime</td>
<td>For people with TB infection, diabetes, and no LTBI treatment, the risk is about 30% over a lifetime (3 times as high as those with no risk factors).</td>
</tr>
<tr>
<td>TB infection and HIV infection</td>
<td>About 7% to 10% PER YEAR</td>
<td>For people with TB infection, untreated HIV infection and with no LTBI treatment, the risk is about 7% to 10% PER YEAR, a very high risk over a lifetime.</td>
</tr>
</tbody>
</table>

## Risk of Progression from TB Infection to Disease by Age

<table>
<thead>
<tr>
<th>Age at Primary Infection</th>
<th>No Disease (%)</th>
<th>Pulmonary TB (%)</th>
<th>Miliary or Central Nervous System TB (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth -12 months</td>
<td>50</td>
<td>30-40</td>
<td>10-20</td>
</tr>
<tr>
<td>1-2 years</td>
<td>75-80</td>
<td>10-20</td>
<td>2-5</td>
</tr>
<tr>
<td>2-5 years</td>
<td>95</td>
<td>5</td>
<td>0.5</td>
</tr>
<tr>
<td>5-10 years</td>
<td>98</td>
<td>2</td>
<td>&lt;0.5</td>
</tr>
<tr>
<td>&gt;10 years</td>
<td>80-90</td>
<td>10-20</td>
<td>&lt;0.5</td>
</tr>
</tbody>
</table>

Adapted from Marias et al Am J Resp Crit Care 2006;173:1078-1093
Natural History of TB: Timeline

Months since initial infection with MTB

1 2 3 4 5 6 7 8 9 10 11 12
2 yr 3 yr 4 yr

19
<table>
<thead>
<tr>
<th>Person with LTBI</th>
<th>Person with TB Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Has a small amount of TB bacteria in his/her body that are alive but <strong>inactive</strong></td>
<td>Has a large amount of <strong>active</strong> TB bacteria in his/her body</td>
</tr>
<tr>
<td>Cannot spread TB bacteria to others</td>
<td>May spread TB bacteria to others</td>
</tr>
<tr>
<td>Does not feel sick, but may become sick if the bacteria in his/her body become active</td>
<td>May feel sick, and may have symptoms such as a cough, fever, and/or weight loss</td>
</tr>
<tr>
<td>Usually has a positive TB skin test or TB blood test result indicating TB infection</td>
<td>Usually has a positive TB skin test or TB blood test result indicating TB infection</td>
</tr>
<tr>
<td>Chest radiograph is typically <strong>normal</strong></td>
<td>Chest radiograph may be <strong>abnormal</strong></td>
</tr>
<tr>
<td>Sputum smears and cultures are <strong>negative</strong></td>
<td>Sputum smears and cultures may be <strong>positive</strong></td>
</tr>
<tr>
<td>Should consider treatment for LTBI to prevent TB disease</td>
<td>Needs treatment for TB disease</td>
</tr>
<tr>
<td>Does <strong>not</strong> require respiratory isolation</td>
<td>May require respiratory isolation</td>
</tr>
<tr>
<td>Is not a TB case</td>
<td>Is a TB case</td>
</tr>
</tbody>
</table>

Imaging Reports & TB

What key words make you “think TB”? 
- Cavity
- Miliary pattern
- RUL (upper lobe preference)
- Hilar adenopathy (pediatric)
  - Enlarged lymph nodes

What other words might indicate (pulmonary) TB?
- Pleural effusion
- Pneumonia
- Infiltrate
- Opacities
- Ground glass
- Tree and bud
- Nodules
- Reticulonodular
- Granulomas
- Necrosis

Latent TB: Calcified granuloma/nodule

“Old TB”
Scaring
Fibrosis (can also be present with active TB)
Pleural thickening

Radiographic evidence of surgical interventions? Ex: plombage or lobectomy

Key: stable abnormalities
Make sure to get X-ray at end of treatment to know “new normal”
• Q: Will all TB patients present with a cavity?
  – A: No. There are a wide range of radiographic presentations with TB disease.

• Q: Does a cavity automatically mean the patient has TB?
  – A: No. TB is a possible cause of cavitary disease. Collect sputum to rule out TB.

**X-rays are just one tool**

**Rule of thumb: If signs/symptoms or abnormal x-ray, collect sputum**

**Look at whole picture**
LTBI or TB?

Latent TB Infection

Is not currently sick. Can be treated to prevent future illness

Tuberculosis (TB)
LTBI or TB?

Latent TB Infection

Tuberculosis (TB)

Collected specimens may culture out *M.tb*
LTBI or TB?

Latent TB Infection

Tuberculosis (TB)

May require respiratory isolation precautions
**LTBI or TB?**

**Latent TB Infection**

**Tuberculosis (TB)**

May feel sick and may have symptoms such as a cough, fever, and/or weight loss
Latent TB Infection

Is not contagious. There is no risk of spreading TB to others at this point in time.

Tuberculosis (TB)
Latent TB Infection

Never treat with a single drug. Standard treatment starts with four drug therapy: (RIPE).

Tuberculosis (TB)
TB Spectrum: Infection to Disease

While the spectrum reflects disease progression, treatment is still for “LTBI” or “TB Disease”

Subclinical = Asymptomatic Disease

<table>
<thead>
<tr>
<th>TB Spectrum</th>
<th>LTBI</th>
<th>Subclinical TB disease</th>
<th>Active TB disease</th>
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<th>Asymptomatic “Immune sensitized to Mtb” or “Latent infection”</th>
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<th>Asymptomatic “Subclinical, bacteriologically positive disease”</th>
<th>Symptomatic “Clinical bacteriologically negative disease”</th>
<th>Symptomatic “Clinical bacteriologically positive disease”</th>
<th>Symptomatic “Clinical smear positive/extensive disease”</th>
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<tbody>
<tr>
<td>Smear</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Culture</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Molecular (Xpert)</td>
<td>-</td>
<td>-/-/+</td>
<td>-/+</td>
<td>-/+</td>
<td>-/+</td>
<td>-/+</td>
</tr>
<tr>
<td>CXR (Pulmonary TB)</td>
<td>Normal</td>
<td>Minimal abnormalities</td>
<td>Minimal abnormalities</td>
<td>Extensive abnormalities/ cavities</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Identification</td>
<td>LTBI screening</td>
<td>Active Case Finding</td>
<td>Passive Case Finding</td>
<td></td>
<td></td>
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<td>Current management approach</td>
<td>1HP, 3HP (weekly), 3HR, 4R, 6H, 9H</td>
<td>Observation or 2HRZ(E)/4HR</td>
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<td></td>
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https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964(22)00112-8/fulltext
What are the classifications for TB?
Poll Question!

TB5 is the American Thoracic Society classification given to a confirmed case of tuberculosis.

a) True
b) False
c) Don’t know
TB Classification Scheme & Definitions

<table>
<thead>
<tr>
<th>Class</th>
<th>Stage of Disease</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No TB exposure,</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Not infected</td>
<td>No history of TB exposure. Negative tuberculin skin test (or IGRA)</td>
</tr>
<tr>
<td>1</td>
<td>Exposure, no</td>
<td>History of TB exposure. Negative tuberculin skin test (or IGRA)</td>
</tr>
<tr>
<td></td>
<td>evidence of</td>
<td></td>
</tr>
<tr>
<td></td>
<td>infection</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Latent TB infection, no disease</td>
<td>Positive tuberculin skin test (or IGRA). No clinical, bacteriologic, or radiographic evidence of TB</td>
</tr>
<tr>
<td>3</td>
<td>TB, clinically active</td>
<td><em>M. tuberculosis</em> cultured (if performed). Clinical, bacteriologic, or radiographic evidence of current TB disease</td>
</tr>
<tr>
<td>4</td>
<td>TB, not clinically active</td>
<td>History of episode(s) of TB OR Abnormal but stable radiographic findings, positive tuberculin skin test, negative bacteriologic studies (if done) AND no clinical or radiographic evidence of current disease</td>
</tr>
<tr>
<td>5</td>
<td>TB suspect (TB Suspected)</td>
<td>Diagnosis pending. TB disease should be ruled in or out within 3 months</td>
</tr>
</tbody>
</table>

5: TB suspected (until otherwise categorized)

Does not have LTBI or TB disease (neg TST and/or IGRA and no symptoms)

0: No History of Exposure
Example: in Contact Investigation (CI) not true exposure

1: History of Exposure:
In CI, final TST/IGRA should be at least 8 weeks after last exposure

2: LTBI (no disease)
- Positive TST/IGRA
- No clinical or xray evidence of TB disease
- No bacteriological evidence of TB (if done)

3: TB, clinically active

4: TB, not clinically active (past history of active disease, and currently no active disease)
# CDC TB Classifications: Immigrants and Refugees

<table>
<thead>
<tr>
<th>Classification</th>
<th>Description</th>
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<tbody>
<tr>
<td>No TB</td>
<td>Normal TB screening examinations</td>
</tr>
<tr>
<td>Class A TB with waiver</td>
<td>[Active] TB disease and have been granted a waiver</td>
</tr>
<tr>
<td>Class B0 TB, Pulmonary</td>
<td>Diagnosed with TB and completed directly observed therapy prior to immigration.</td>
</tr>
<tr>
<td>Class B1 TB, Pulmonary (PTB)</td>
<td>Applicants who have signs or symptoms, physical exam, or chest x-ray findings suggestive of tuberculosis disease, or have known HIV infection, but have negative AFB sputum smears and cultures and are not diagnosed with tuberculosis disease.</td>
</tr>
<tr>
<td>Class B1 TB, Extra-pulmonary (EPTB)</td>
<td>Evidence of EPTB without pulmonary involvement. The anatomic site of infection should be documented.</td>
</tr>
<tr>
<td>Class B2 TB, LTBI Evaluation</td>
<td>Applicants who have a positive IGRA or TST but otherwise have a negative evaluation for tuberculosis.</td>
</tr>
<tr>
<td>Class B3 TB, Contact Evaluation</td>
<td>Recent contact of a known TB case.</td>
</tr>
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Adapted from: [https://www.cdc.gov/immigrantrefugeehealth/panel-physicians/tuberculosis.html](https://www.cdc.gov/immigrantrefugeehealth/panel-physicians/tuberculosis.html)
# How does the classification match up?

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Real Question: “Is this a class 5 or class 3?”

Scenario: Professor X is moving out of state. They are on treatment and cultures just came back confirming pulmonary TB. You are transferring their care and the receiving jurisdiction asks “Is this a class 5 or class 3?” (polling question):

a) Class 5
b) Class 3
c) ????
What public health strategies can prevent & (eventually) eliminate TB disease?
Priority Strategies for TB Prevention & Control

1. Early and accurate detection, diagnosis, and reporting of TB cases leading to initiation and completion of treatment

2. Identification of contacts of patients with infectious TB and treatment of those at risk with an effective drug regimen

3. Identification of other persons with latent TB infection at risk for progression to TB disease and treatment of those persons with an effective drug regimen

4. Identification of settings in which a high risk exists for transmission of Mycobacterium tuberculosis and application of effective infection-control measures

TB is spread when a person with TB disease coughs, sings, or speaks and you breathe the air contaminated with TB germs. The germs reach your lungs. From there, they can go to other parts of your body.

Your body fights the TB germs. You can take medicine to treat LATENT TB INFECTION and prevent getting TB DISEASE.

If your body controls the germs, you have LATENT TB INFECTION. When this happens,
- You may have a positive TB skin test or TB blood test.
- You feel sick with cough, fever, weight loss, chest pain, or sweating at night.
- You have active TB germs in your body.
- You may give TB germs to others.
- You may have an abnormal chest x-ray.

You get TB DISEASE when the TB germs multiply and attack your lungs or other parts of your body. When this happens,
- You have a positive TB skin test or TB blood test.
- You feel sick with cough, fever, weight loss, chest pain, or sweating at night.
- You have active TB germs in your body.
- You may give TB germs to others.
- You may have an abnormal chest x-ray.

Taking your TB medicine is very important. You need to take the medicine to help get better and to prevent the spread of TB germs to others.

TB is Curable

- Early detection: If diagnosed & treated early, it decreases risk of becoming infectious
- TB is reportable to public health
- Appropriate treatment is part of infection control
- Case management includes following criteria for release from Airborne Isolation
- Public health rules vary by state/jurisdiction
TB is spread when a person with TB disease coughs, sings, or speaks and you breathe the air contaminated with TB germs. The germs reach your lungs. From there, they can go to other parts of your body. Your body fights the TB germs.

You can take medicine to treat LATENT TB INFECTION and prevent getting TB DISEASE. If your body controls the germs, you have LATENT TB INFECTION. When this happens,
- You may have a positive TB skin test or TB blood test.
- You don’t feel sick.
- You don’t have TB symptoms.
- You can’t give TB germs to others.
- You have a normal chest x-ray.

You get TB DISEASE when the TB germs multiply and attack your lungs or other parts of your body. When this happens,
- You have a positive TB skin test or TB blood test.
- You feel sick with cough, fever, weight loss, chest pain, or sweating at night.
- You have active TB germs in your body.
- You may give TB germs to others.
- You may have an abnormal chest x-ray.

TB is Preventable

- Contact Investigations help to find the most vulnerable to developing TB (recently infected), but it only works if treatment is taken.

- Targeted testing followed by treatment of LTBI can prevent someone from developing TB disease and passing it onto friends and family (and coworkers and patients!)
TB is spread when a person with TB disease coughs, sings, or speaks and you breathe the air contaminated with TB germs. The germs reach your lungs. From there, they can go to other parts of your body. Your body fights the TB germs.

You can take medicine to treat LATENT TB INFECTION and prevent getting TB DISEASE.

If your body controls the germs, you have LATENT TB INFECTION. When this happens,
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- You have active TB germs in your body.
- You may give TB germs to others.
- You may have an abnormal chest x-ray.

Taking your TB medicine is very important. You need to take the medicine to help get better and to prevent the spread of TB germs to others.

You can take medicine to treat LATENT TB INFECTION and prevent getting TB DISEASE.

Interventions to Decrease Risk of Spreading TB

- Cough policy
- Environmental controls
- Administrative controls
- Public health rules vary by state/jurisdiction

Who are your partners?
Final Polling Question!

What is your personal experience with TB? Do you know someone who had TB? (select all that apply)

a) A patient
b) A friend
c) A family member
d) No one I know personally