Disclosures

No relevant financial relationships

No off-label investigational uses
Objectives

• Explain how the transmission of tuberculosis occurs.

• Name the most common site of tuberculosis disease.
Important Definitions

IGRA: Interferon gamma release assay (blood test)
LTBI: Latent TB Infection, TB Infection, infection
TB: Tuberculosis, active TB disease, TB disease, TB case
TST: Tuberculin Skin Test; Mantoux test
Tubercle bacilli: The *Mycobacterium tuberculosis* that causes TB infection and/or disease
Historical Considerations

- TB is noted in the Bible and has been found in Egyptian mummies
- TB is referred to as “consumption” or the “wasting disease”
- In 1890, Robert Koch announced that he had found a cure for Tuberculosis – 8 years after discovering the cause of TB
- The cure consisted of subcutaneous doses of tuberculin (purified protein derivative – PPD) which was found to be ineffective as a cure but ultimately became a widely-used diagnostic tool for TB
What is TB?

TB is caused by a bacteria called Mycobacterium tuberculosis (MTB)
What is Tuberculosis?

- Tuberculosis is a communicable disease.
- Tuberculosis has infectious and noninfectious stages in the disease process.
- *M. tb* organisms also called tubercle bacilli.
- TB disease is covered by laws that provide for the protection of the public.
Transmission of Tuberculosis
TB is spread by the aerosolization of droplet nuclei containing TB bacilli – “cluster” - .5 microns in size.

Droplet nuclei are expelled when a person with infectious TB coughs, sneezes, speaks or sings.

Transmission occurs when persons with infectious TB expel droplet nuclei into the air. The droplet nuclei float on the air waves, are inhaled, and reach the alveoli of the lungs.
TB is NOT spread by:

- shaking someone’s hand
- sharing food or drink
- touching bed linens, toilet seats, or table tops
- sharing a toothbrush
- kissing
- walking by someone outside
What is the Probability TB Will Be Transmitted?

Infectiousness of person with TB (i.e., number and size of the droplet nuclei the TB patient expels into the air)

Susceptibility of the exposed person

Environmental factors that affect the concentration of organisms (size of and the ventilation in the environment)

Proximity, frequency, and duration of exposure (e.g., close contacts)
Pathogenesis

Droplet nuclei containing tubercle bacilli are inhaled, enter the lungs, and travel to the alveoli.

Tubercle bacilli multiply in the alveoli.
Pathogenesis

A small number of tubercle bacilli enter the bloodstream and spread throughout the body. The tubercle bacilli may reach any part of the body, including areas where TB disease is more likely to develop (such as the brain, larynx, lymph node, lung, spine, bone, or kidney).
**Pathogenesis**

<table>
<thead>
<tr>
<th>Image</th>
<th>Text</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1.png" alt="Image" /></td>
<td>Within 2 to 8 weeks, special immune cells called macrophages ingest and surround the tubercle bacilli. The cells form a barrier shell, called a granuloma, that keeps the bacilli contained and under control (LTBI).</td>
</tr>
<tr>
<td><img src="image2.png" alt="Image" /></td>
<td>If the immune system cannot keep the tubercle bacilli under control, the bacilli begin to multiply (TB disease). This process can occur anywhere in the body.</td>
</tr>
</tbody>
</table>
Central nervous system

Lymphatic system

Joints

Bones

Genitourinary Systems

Pleura

Lungs

Miliary TB

Millet seed like pattern
Pathogenesis Worldwide

• Although incidence and mortality has decreased, tuberculosis remains one of the top 10 causes of death worldwide.
• At least one-third of the world’s population are infected with TB.
• In 2015, approximately 1 million children became ill with TB and 170,000 died.
• TB killed 1.8 million people worldwide in 2015 and 0.4 million were HIV+.
Pathogenesis Worldwide

- In 2015, 35% of HIV deaths were due to TB.
- In 2015, 480,000 cases were MDR-TB
- Sixty percent of the TB cases worldwide were found to be from Indonesia, China, Nigeria and South Africa.
Pathogenesis – United States

• In 2016, 9,287 TB cases were reported to CDC while in 2015, 9,557 cases were reported.

• In 2016, the TB case rate (#cases per 100,000 population) was 2.9 compared to 2015 case rate of 3.0.

• For 2016, 31.6% of the cases were reported as US-born while 67.9% were reported as Foreign-born. The remaining 0.5% were unknown.
So how does this happen?

Exposure to person with infectious TB

- TB Infected
  - TB Infection
  - TB Disease

- Not TB Infected
Latent TB Infection (LTBI)

- Referred to as: Infection, TB infection, Latent TB Infection, and/or LTBI
- 2 to 8 weeks after infection, LTBI can be detected by administering and reading a TST or interferon-gamma release assay (IGRA)
- The immune system is usually able to contain and stop the multiplication of bacilli by encapsulating the bacilli
- Persons with LTBI are not infectious and do not spread organisms to others
TB Disease

- Referred to as Active TB, TB disease, TB Case
- The immune systems for some persons are unable to contain the bacilli, so they begin to multiply, resulting in TB disease
- Can occur soon after infection, or years later
- Persons with TB disease are usually infectious and can spread bacilli to others
- Positive *M. tb* culture confirms TB diagnosis
TB Infection  vs TB Disease

- Organism is contained
- Not ill; inactive or latent
- Not contagious
- Lifetime risk of progressing to active disease
- Treatable – to prevent progression to disease
  (+) TST/IGRA & (-) CXR

- Organism is not contained
- Ill – usually in lungs
- Contagious
- Active TB disease; TB Case
- Treatable to progress to noninfectious and cure
  (+)/(-) TST/IGRA & (+)/(-) CXR
Sites of TB Disease

- **Pulmonary**: Lungs; most common site; usually infectious
- **Miliary**: occurs when bacilli spread to all parts of the body; rare, but fatal if untreated
- **Central nervous system**: usually occurs as meningitis, but can occur as lesions in the brain or spine
Sites of TB Disease

Extrapulmonary: Outside the lungs; usually not infectious, unless person has

- Concomitant pulmonary disease,
- Extrapulmonary disease in the oral cavity or larynx, or
- Extrapulmonary disease with open site, especially with aerosolized fluid.

Extrapulmonary TB can be anywhere: kidney, bladder, knee, wrist, uterus…
Risk of Progressing to TB Disease

Normal Immune System

• Untreated, 5% of infected persons with normal immune system develop TB in first 1–2 years post infection, another 5% later in life

• Thus, about 10% of infected persons with normal immune system will develop TB at some point in life if not treated for TB infection
Risk of Progressing to TB Disease
Weak Immune System

- Persons with a weak immune system are at increased risk of progressing from TB infection to TB disease

- HIV infection highest risk factor: risk of developing TB disease is 7%–10% each year;
- Children <5 years of age at increased risk
- Other immune compromising conditions:
  - Using a TNF-alpha inhibitor
  - Diabetes Mellitus
  - Chemotherapy
  - Organ transplant recipients
Who should we be concerned about their TST status?

Those persons who are a highest risk of progressing to TB disease once TB infected:

• Persons at risk of exposure to person known to have TB disease

OR

• Persons who once infected have medical conditions associated with an increased risk of progression from TB infection to TB disease.
Specifically

Those persons who have been recently TB infected:

- Contacts to known TB cases
- Immigrants from high endemic areas
- Children < 5 years of age
- Groups with high rates of transmission: homeless, injection drug users, persons with HIV
- People who work or reside in facilities where TB is common: hospitals that care for persons with TB disease, homeless shelters, correctional facilities and other congregate settings (nursing homes, CRCFs, residential homes for persons with HIV, other locally defined facilities)
Specifically

Persons who once infected have medical conditions associated with an increased risk of progression from TB infection to TB disease:

- HIV
- Substance abusers
- Diabetes Mellitus
- Silicosis
- Organ transplantation
- Severe kidney disease
- Cancers of head and neck
- Low body weight
- Conditions that require prolonged use of corticosteroids or other immunosuppressive agents (TNF-α inhibitors, cancer chemotherapy)
## In Conclusion

<table>
<thead>
<tr>
<th><strong>Person with LTBI (Infected)</strong></th>
<th><strong>Person with TB Disease (Infectious)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Has a small amount of TB bacteria in his/her body that are alive, but inactive</td>
<td>Has a large amount of active TB bacteria in his/her body</td>
</tr>
<tr>
<td><strong>Cannot</strong> spread TB bacteria to others</td>
<td>May spread TB bacteria to others</td>
</tr>
<tr>
<td>Does <strong>not</strong> feel sick, but may become sick if the bacteria become active in his/her body</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 TB skin test or TB blood test reaction indicating TB infection</td>
<td>Usually has a TB skin test or TB blood test reaction indicating TB infection</td>
</tr>
<tr>
<td>Radiograph is typically normal</td>
<td>Radiograph may be abnormal</td>
</tr>
<tr>
<td>Sputum smears and cultures are negative</td>
<td>Sputum smears and cultures may be positive</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>Not a TB case</td>
<td>A TB case</td>
</tr>
</tbody>
</table>
Romance is in the air

...but so is tuberculosis, I mean, if you really think about it.

https://friendorfoebia.files.wordpress.com/2011/01/romance.jpg?w=630
Questions?
References

http://www.cdc.gov/mmwr/preview/mmwrhtml/rr4906a1.htm.


CDC. *Treatment of Tuberculosis.* MMWR. 2003; 52 (No. RR-11) 
http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5211a1.htm

http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5905a1.htm?s_cid=rr5905a1_e.

CDC. Guidelines for Preventing the Transmission of Mycobacterium Tuberculosis in Health-care settings. MMWR 2005; 54, RR-17.
References

Curry International TB Center: www.currytbcenter.ucsf.edu
Heartland National TB Center: www.heartlandntbc.org
Mayo Clinic Center for Tuberculosis: http://centerfortuberculosis.mayo.edu
Rutgers Global Tuberculosis Institute: www.globaltb.njms.rutgers.edu
Southeastern National Tuberculosis Center https://sntc.medicine.ufl.edu