Transmission & Pathogenesis of Tuberculosis

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Virtually all \textit{M. tuberculosis} is transmitted by airborne particles that are 1-5 \textmu m in diameter.

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\textit{Mycobacterium tuberculosis} & TB disease

- Acid fast bacillus
- Slow growing
- Intracellular pathogen
- Thick waxy cell wall
- Non-replicating persistence
- Productive cough
- Dramatic weight loss
- Night sweats
- General malaise
- Pulmonary or extra-pulmonary

\textit{Slide courtesy of Joanne Turner, PhD}
The Taxonomic Tree for Selected Mycobacteria and Related Species

ORDER [Actinomycetales]
FAMILY [Mycobacteriaceae, Actinomycetaceae, Streptomycetaceae]
GENUS [Mycobacterium, Nocardia, Actinomyces, Streptomyces]
SPECIES [M. tuberculosis complex, M. leprae, NTM = nontuberculous mycobacteria]

Overview of inhaled mycobacterial diseases
(prototype: M. tb, other major NTM: M. aviumintracellulare Complex and M. kansaii)

The Paradigm: Latent Infection vs. Active Disease
- Inhaled airborne droplet nuclei
- Phagocytosis by alveolar macrophages
- Regional spread
- Dissemination
- Resolution-common development of effective cell-mediated immune response
- Primary active disease (uncommon in healthy host)
- Reactivation disease

Transmission of M. tuberculosis
- M. tb spread via airborne particles called droplet nuclei
- Expelled when person with infectious TB coughs, sneezes, shouts, or sings
- Transmission occurs when droplet nuclei inhaled and reach the alveoli of the lungs, via nasal passages, respiratory tract, and bronchi

Pathogenesis
- Droplet nuclei containing tubercle bacilli are inhaled, enter the lungs, and travel to the alveoli
- Tubercle bacilli multiply in the alveoli
**M. tb infection Pathway**

**Stage 1**
- Spread person to person by aerosol
- Droplet inhaled
- Larger droplets lodge in nose and throat
- Smaller droplets reach alveoli (small air sacs)

**Pathogenesis**
- A small number of tubercle bacilli enter the bloodstream and spread throughout the body
  - Tubercle bacilli may reach any part of the body, including areas where TB disease is more likely to develop
    - Brain, larynx, lymph node, lung, spine, bone, or kidney

**Pathogenesis**
- 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)
- If the immune system cannot keep the tubercle bacilli under control, the bacilli begin to multiply rapidly (TB disease)
  - This process can occur in different areas in the body, such as the lungs, kidneys, brain, or bone

*Slide courtesy of Jordi Torrelles, PhD*
Transmission of Tuberculosis and Progression from Latent Infection to Reactivated Disease

Latent TB Infection (LTBI)

- Granulomas may persist (LTBI), or may break down to produce TB disease
- 2 to 8 weeks after infection, LTBI can be detected via tuberculin skin test (TST) or interferon gamma release assay (IGRA)
- Immune system is usually able to stop the multiplication of bacilli
- Persons with LTBI are not infectious and do not spread organisms to others
**Containment / Latency**

- In some, the granulomas break down, bacilli escape and multiply, resulting in TB disease
- Can occur soon after infection, or years later
- Persons with TB disease are usually infectious and can spread bacteria to others
- Positive \( M.\text{tb} \) culture confirms TB diagnosis

**Transmission of \( M.\text{tb} \)**

- Transmission is airborne from patients with active pulmonary TB
- **Vehicle**: droplet nuclei (1-5 µm)
- **Quantity** of organism high with cavitary disease
- **Environment**: spread is enhanced by crowded, poorly ventilated spaces
- **Bottom line**: duration of exposure and concentration of organisms in the air
- **Host susceptibility increases** risk of infection and disease progression
Risk of Exposure/Transmission

- Congregate settings
  - Hospitals, autopsy suites, long term care facilities
  - Correctional facilities
  - Bars
  - Choirs
  - Airplanes, ships

- Aerosol producing procedures: intubation, bronchoscopy, sputum induction

Who is Infectious?

- Smear + > smear* –
- Cavitary > non-cavitary
- Close contact > casual contact
- Prolonged > brief exposure
- Men > women
- Young > old
- HIV + = HIV –

Smear negative cases can still transmit

Drug Resistant TB

- Transmitted same way as drug-susceptible TB
- MDR-TB and XDR-TB are not more infectious
- Unsuspected or delayed detection of drug resistance may delay start of therapy and prolong period of infectiousness

Sites of Disease

- Lungs (pulmonary): most common site, usually infectious
- Miliary: hematogenous dissemination; rare, but fatal if untreated
- Central nervous system: usually occurs as meningitis, but can occur in brain or spine
**Sites of Disease**

- Outside the lungs (extra-pulmonary): 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

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**Classification System for TB**

- Based on TB pathogenesis (stage of disease)
- Helps clinician track the development of TB in patients
- Persons with class 3 or 5 TB should be reported to health department
- Patients should not be classified as class 5 for more than 3 months

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**LTBI vs. Active TB Disease**

<table>
<thead>
<tr>
<th>LTBI</th>
<th>Active TB Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>No symptoms or physical findings suggestive of TB</td>
<td>Symptoms may include fever, cough, weight loss, night sweats, fatigue</td>
</tr>
<tr>
<td>TST or IGRA usually positive</td>
<td>TST or IGRA usually positive</td>
</tr>
<tr>
<td>Radiograph is typically normal</td>
<td>Radiograph may be abnormal</td>
</tr>
<tr>
<td>Sputum smears &amp; cultures are negative</td>
<td>Sputum smears &amp; cultures may be positive</td>
</tr>
<tr>
<td>Cannot spread to others</td>
<td>May spread TB bacteria to others</td>
</tr>
<tr>
<td>Treat for LTBI to prevent TB disease</td>
<td>Needs treatment for TB disease</td>
</tr>
</tbody>
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**TB Classification System**

<table>
<thead>
<tr>
<th>Class</th>
<th>Stage of Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No exposure, no infection</td>
</tr>
<tr>
<td>1</td>
<td>Exposure, no evidence of infection</td>
</tr>
<tr>
<td>2</td>
<td>TB infection, no disease</td>
</tr>
<tr>
<td>3</td>
<td>TB, clinically active</td>
</tr>
<tr>
<td>4</td>
<td>TB, not clinically active</td>
</tr>
<tr>
<td>5</td>
<td>TB suspect</td>
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Questions?