Tuberculosis Transmission, Pathogenesis, and Infection Control

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Tuberculosis Transmission and Pathogenesis

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DISCLOSURE

• NO relevant financial relationships

• NO conflicts of interest
OBJECTIVES

- Explain how M. tuberculosis is transmitted
- Describe the pathogenesis of M. tuberculosis
- Explain how drug-resistant TB disease develops
- Describe the components of an effective infection control program
- Explain administrative, engineering controls, and respiratory protection
- Describe ways healthcare workers can protect themselves and others from being infected with M. tuberculosis
TRANSMISSION
Droplets

CASE

CONTACT

Droplet Nuclei

- Cough
- Sneezing, talking, singing
- Sneezing produces ~40K droplets
- Coughing produces ~3K droplets = Talking x 5 mins

American Journal of Infection Control. 1998
Droplets

1-5 µm droplets
Stay suspended for hours

Large Infectious Droplets
Small Infectious Droplets

1-3 Feet  3-5 Feet  5-160+ Feet

TB Transmission and Progression

Chronological events after inhalation of M. tuberculosis

- 70% immediate killing of MTB (PPD-)
- 30% primary complex (PPD+)

Immediate killing:
- Stabilization (latency)
- Reactivation (post-primary TB)

Primary complex:
- Localized disease (primary TB)
- Dissemination of MTB
  - Stabilization (latency)
  - Acute disease (meningitis, miliary TB)


Small infiltrate with draining LN
Small calcification
PPD +
Risk Factors for Transmission -- SOURCE

- Location of Tuberculosis
  - Pulmonary/Laryngeal $>$ Extrapulmonary TB

- Bacillary Load
  - Cavitary disease
  - Smear positive

- Treatment
  - Decreases bacillary burden

- Cough

- Duration of Cough
Risk Factors for INFECTION--CONTACTS

• Previous exposure (i.e. hx of LTBI) likely confers protection against infection on reexposure and progression to active disease.

• Duration: Longer is worse

• Proximity: Family members, cohabitants

• Immune Status

• Other Host Factors
## Risk of Reactivation

**Table 3. Relative Risk of Reactivation Tuberculosis among Persons with Medical Conditions That Impair Immune Control of *M. tuberculosis*.**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Study</th>
<th>Relative Risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Advanced HIV infection</td>
<td>Pablos-Mendez et al.\textsuperscript{27} Moss et al.\textsuperscript{26}</td>
<td>9.9 (8.7–11.3)†</td>
</tr>
<tr>
<td></td>
<td></td>
<td>9.4 (3.5–25.1)</td>
</tr>
<tr>
<td>Old, healed tuberculosis</td>
<td>Ferebee,\textsuperscript{13} Ferebee et al.\textsuperscript{20}</td>
<td>5.2 (3.4–8.0)</td>
</tr>
<tr>
<td>Chronic renal failure</td>
<td>Pablos-Mendez et al.\textsuperscript{27}</td>
<td>2.4 (2.1–2.8)†</td>
</tr>
<tr>
<td>Infliximab therapy</td>
<td>Keane et al.\textsuperscript{28}</td>
<td>2.0 (0.7–5.5)†</td>
</tr>
<tr>
<td>Poorly controlled diabetes</td>
<td>Pablos-Mendez et al.\textsuperscript{27}</td>
<td>1.7 (1.5–2.2)†</td>
</tr>
<tr>
<td>Silicosis</td>
<td>Cowie\textsuperscript{29} Corbett et al.\textsuperscript{30} Kleinschmidt and Chuchyard\textsuperscript{31}</td>
<td>1.7 (1.3–2.1)†</td>
</tr>
<tr>
<td>Underweight (≤10 percent below normal)</td>
<td>Palmer et al.,\textsuperscript{22} Edwards et al.\textsuperscript{23}</td>
<td>1.6 (1.1–2.2)</td>
</tr>
<tr>
<td>Gastrectomy</td>
<td>Thorn et al.\textsuperscript{32} Steiger et al.\textsuperscript{33}</td>
<td>1.4 (1.1–1.9)†</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.3 (1.2–1.4)†</td>
</tr>
</tbody>
</table>

* CI denotes confidence interval, and HIV human immunodeficiency virus.  
† The relative risk is estimated, as described in the Methods section.

PATHOGENESIS
Chronological events after inhalation of M. tuberculosis

- 70% immediate killing of MTB (PPD-)
- 30% primary complex (PPD+)

Immediate killing of MTB

- Stabilization (latency)

Primary complex

- Localized disease (primary TB)
- Dissemination of MTB

Dissemination of MTB

- Stabilization (latency)
- Acute disease (meningitis, miliary TB)

Reactivation (post-primary TB)

Pathogenesis of M. Tb

Macrophage Immunoevasion and Immunosuppression

Immunological Reviews

Mayo Clinic Center for Tuberculosis
The Spectrum of Granulomata

The Importance of Cell-Mediated Immunity

TB Drug Resistance
Mutation Prevalence Rates

- INH: 1 in $10^6$ bacilli
- Rifampin: 1 in $10^8$ bacilli

- Resistance to INH AND Rifampin $\sim 1 \times 10^{14}$
- Total number of bacilli in lung cavity (2.5cm) $\sim 1 \times 10^8$
TB Drug Resistance

• Primary resistance
  • No hx of treatment
  • Presumably infected with a resistant MTb strain

• Acquired resistance
  • Acquired resistance develops during therapy for TB
  • Multiple reasons

Tuberculosis Drug Resistance: A Global Threat
Jean B. Nachega and Richard E. Chaisson
Reasons for MDR-TB

- “Mismanagement” of TB treatment
  - Inappropriate or incorrect use of antituberculars
  - Ineffective formulations (use of single drugs, bad storage conditions)
- Poor adherence
- Person-to-Person Transmission
- Premature treatment interruption

Source: WHO
Mechanism of TB Drug Resistance

• **Spontaneous and Random mutations** in the bacterial chromosome

• **NOT** due to acquisition of genes or plasmids from other mycobacteria
INFECTION CONTROL of TB
Components of Effective Program

• Early/Prompt detection of TB disease
• Isolation of those who are suspected of having TB disease (e.g., airborne precautions)
• Treatment of those suspected of having TB disease

Source: CDC
TB Infection Control Measures

- Administrative controls
- Environmental controls
- Use of respiratory protective equipment
Administrative Controls

• Point person for TB infection control
• Conduct TB risk assessment of the setting
• Ensuring availability of lab processing and testing
• Education of health care workers, patients, visitors
• Coordinating efforts between local and state health departments and healthcare setting
Environmental Controls

http://qualitair.ca/en/Products/Isolation-rooms/Product/Hepa-Net-II
Environmental Controls

http://qualitair.ca/en/Products/Isolation-rooms/Product/Hepa-Net-II
Respiratory Protection Controls

• Implementation of respiratory-protection program

• Train HCWs on respiratory protections and perform mask fitting

• Educate patients on respiratory hygiene (including how to cover cough)
N95 Respirator for HCW

Surgical Mask for Patient

CDC

Shutterstock.com
Powered air-purifying respirators (PAPR)

Source: CDC
Question

• A visitor is here to see her mother who is in airborne isolation for suspected pulmonary tuberculosis. The daughter should wear which of the following for her protection?
  • 1) Powered air-purifying respirator (PAPR)
  • 2) N95 particular respirator
  • 3) Surgical mask
  • 4) No protection needed as she will only be visiting for 45 minutes
Question

A visitor is here to see her mother who is in airborne isolation for suspected pulmonary tuberculosis. The daughter should wear which of the following for her protection?

1) Powered air-purifying respirator (PAPR)
2) N95 particular respirator
3) Surgical mask
4) No protection needed as she will only be visiting for 45 minutes
Wear your protective equipment when you are...

- In the room with a patient with known or suspected TB
- Accompanying a patient with known or suspected TB (ie transport staff)
- Present for a procedure that will induce coughing or aerosolization
Definition of “Non-Infectious”

- 3 consecutive negative AFB sputum smears collected in 8-24 hour intervals (one AM) AND
- Compliant with an adequate treatment regimen for 2 or more weeks AND
- Symptoms improved (eg less cough, no fever)
Contact Investigations

• Performed to identify secondary cases of active/latent TB

• In a healthcare facility, really need to look for those patients who were previously undiagnosed and may have exposed others prior to diagnosis.
  • AFB smear positive: Infectious 3 months prior to 1st smear-positive sputum or 3 months prior to onset of symptoms whichever is earlier
  • AFB smear negative: Infectious 1 month prior to onset of symptoms

• TST/IGRA screening at baseline (if none prior) and then 8-10 weeks post end of exposure
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QUESTION

A patient with which of the following medical conditions is at highest risk for reactivation of Tuberculosis?

a) HIV Infection  
b) End Stage Renal Disease  
c) Silicosis  
d) Gastrectomy
QUESTION

Acquired TB drug resistance is most likely due to which of the following?

a) Acquisition of plasmid from other mycobacteria
b) Acquisition of a resistance gene from other bacteria
c) Poor efficacy of antitubercular agent to reach site of infection
d) Spontaneous mutations in the mycobacterial chromosome
Questions/Comments??

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