Mayo Clinic Center for Tuberculosis

TB Transmission and Pathogenesis

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Disclosures

• Relevant Financial Relationships: none

• Off label discussions of rifapentine
Learning Objectives

• Understand the hematogenous phase of TB infection

• Discuss the pulmonary host defense mechanisms that protect against TB

• Discuss the most common immune suppressive condition in TB patients in the United States
March 11, 2015 Detroit Metro Airport

- Flight #456 from Manila
- 60 yr male coughing up blood on flight
- CDC Quarantine Station evaluated
- Sent to our Emergency Room
- Cavitary, smear + TB diagnosed.
- Drug susceptible
Questions about airplane TB Case

• What is risk of transmission to passengers?
• What predisposed him to get active TB?
• How might have this been prevented?
Figure 1: Cabin Air Flow Patterns

Cargo Compartment
The cascade of tuberculosis (TB) transmission and disease.

<table>
<thead>
<tr>
<th>Step 1: Contact</th>
<th>Step 2: Generation of Infectious Particles</th>
<th>Step 3: Infection and Disease Progression</th>
</tr>
</thead>
<tbody>
<tr>
<td>A person with active TB and a susceptible person come into sufficiently close contact for airborne transmission of <em>M. tuberculosis</em> to occur.</td>
<td>The person with active TB aerosolizes particles of appropriate quality (size, etc.) containing bacilli of sufficient number and virulence to transmit infection.</td>
<td>The susceptible host has an immune background that facilitates initial infection, non-sterilization of the corresponding granuloma, and eventual progression to infectious disease.</td>
</tr>
<tr>
<td><strong>Catalyst:</strong> Increased contact rates</td>
<td><strong>Catalyst:</strong> Increased infectiousness</td>
<td><strong>Catalyst:</strong> Increased susceptibility</td>
</tr>
</tbody>
</table>
TB Transmission (3)

- TB is spread person to person through the air via droplet nuclei

- *M. tuberculosis* may be expelled when an infectious person:
  - Coughs
  - Sneezes
  - Speaks
  - Sings

- Transmission occurs when another person inhales droplet nuclei
TB Transmission (2)
Types of Mycobacteria

• *M. tuberculosis* causes most TB cases in U.S.

• Mycobacteria that do **not** cause TB (not airborne person-to-person)
  - e.g., *M. avium* complex
  - *M. kansasii*

*M. tuberculosis*
TB Transmission (4)

Dots in air represent droplet nuclei containing *M. tuberculosis*

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First line of defense – physical & chemical barriers

- Respiratory tract
  - Nose - nasal hair, mucus secretions (phagocytes and antibacterial enzymes), irregular chambers
  - ciliated epithelium (nasal cavity, sinuses, bronchi and trachea)
  - Cough reflexes
  - Alveolar macrophages
TB Pathogenesis
Study Question 1.7

When a person inhales air that contains droplet nuclei containing *M. tuberculosis*, where do the droplet nuclei go? *(pg. 15)*

- Most of the larger droplet nuclei become lodged in the upper respiratory tract, where infection is unlikely to develop.
- However, droplet nuclei may reach the small air sacs of the lung (the alveoli), where infection begins.
Droplet nuclei containing tubercle bacilli are inhaled, enter the lungs, and travel to small air sacs (alveoli)
TB Pathogenesis (5)

Tubercle bacilli multiply in alveoli, where infection begins

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A small number of tubercle bacilli enter bloodstream and spread throughout body.
• Within 2 to 8 weeks the immune system produces special immune cells called macrophages that surround the tubercle bacilli.
• These cells form a barrier shell that keeps the bacilli contained and under control (LTBI).
Tuberculous Granuloma
Caseation Necrosis
TB Pathogenesis (8)
TB Disease

If the immune system CANNOT keep tubercle bacilli under control, bacilli begin to multiply rapidly and cause TB disease.

This process can occur in different places in the body.
This process can occur in different places in the body

- Lungs
- Pleura
- Lymph nodes
- Peritoneum
- Meninges
- Renal
- Fallopian tubes
- Epididymis
- Iritis
- Otitis media
- Synovial fluid
- Skin
- Thyroid
- Adrenal gland
- Liver
- Etc, etc, etc.
Fig. 1 The life cycle of M. tuberculosis.

David G. Russell et al. Science 2010;328:852-856
## LTBI vs. TB Disease

<table>
<thead>
<tr>
<th>Latent TB Infection (LTBI)</th>
<th>TB Disease (in the lungs)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Inactive</strong>, contained tubercle bacilli in the body</td>
<td><strong>Active</strong>, multiplying tubercle bacilli in the body</td>
</tr>
<tr>
<td>TST or blood test results usually positive</td>
<td>TST or blood test results usually positive</td>
</tr>
<tr>
<td>Chest x-ray usually <strong>normal</strong></td>
<td>Chest x-ray usually <strong>abnormal</strong></td>
</tr>
<tr>
<td>Sputum smears and cultures <strong>negative</strong></td>
<td>Sputum smears and cultures may be <strong>positive</strong></td>
</tr>
<tr>
<td><strong>No symptoms</strong></td>
<td><strong>Symptoms</strong> such as cough, fever, weight loss</td>
</tr>
<tr>
<td><strong>Not infectious</strong></td>
<td><strong>Often infectious</strong> before treatment</td>
</tr>
<tr>
<td><strong>Not a case</strong> of TB</td>
<td><strong>A case</strong> of TB</td>
</tr>
</tbody>
</table>

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Conditions with increased probability of LTBI progression to TB disease

- HIV
- Substance abuse
- Chest X-ray findings of previous TB
- Recent TB infection
- Prolonged corticosteroid therapy >30 days
- TNF inhibitors

- Organ transplant
- Silicosis
- Diabetes mellitus
- Severe kidney disease
- Certain types of cancer
- Certain types of intestinal disease
- Low body weight
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Mycobacterial Burden

- Incubating: $10^3-10^4$
- Latent: $10^4-10^5$
- TB scar: $10^6$
- Active: $10^9-10^{11}$
Transmission

Primary Tuberculosis

Latent Tuberculosis

“Reactivation” Tuberculosis

Skin-test conversion in 6 to 8 weeks

Spontaneous healing in 6 months

Progression within 2 years, 5%

Progression after 2 years, 5%

Progression with concurrent HIV infection, 10% each year

Overview of the possible phases in the course of pulmonary tuberculosis (TB) and corresponding potential prevention and control measures.

Progression to TB Disease (4)

TB and HIV

In an HIV-infected person, TB can develop in one of two ways:

- Person with LTBI becomes infected with HIV and then develops TB disease as the immune system is weakened
- Or:
- Person with HIV infection becomes infected with *M. tuberculosis* and then rapidly develops TB disease

Image credit: Mississippi State Department of Health

Module 1 – Transmission and Pathogenesis of Tuberculosis

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His aunt has TB. 22 yr male with (AIDS).

PPD zero mm. What to do?
6 weeks later, admitted with suspect *Pneumocystis pneumonia*. Miliary TB diagnosed.
TB Transmission (5)

• Probability that TB will be transmitted depends on:
  • Infectiousness of person with TB disease
  • Environment in which exposure occurred
  • Length of exposure
  • Virulence (strength) of the tubercle bacilli

• The best way to stop transmission is to:
  • Isolate infectious persons
  • Provide effective treatment to infectious persons as soon as possible
MDR-TB
Boeing 747-100
Passengers and Flight Crew on Flight 4 Who Had Positive Tuberculin Skin Tests

Fig. 2  Assessing whether contact-tracing is needed

Physician diagnoses a TB case with history of recent long-distance air travel

Public health authority notified of a TB case with history of recent long-distance air travel

Flight(s) occurred within the past 3 months?

YES → Was the patient likely to have been infectious at the time of travel?

YES → Public health authority contacts the airline to verify TB patient was on aircraft

Was the patient on the aircraft?

YES → Was the total flight duration ≥8 hours?

YES → Public health authority, in cooperation with the airline company, gathers contact details of passengers sitting in the same row and in the two rows in front of and behind the TB case

NO → No further action needed
Major Migration Flows: 1990s

4 x increase in volume as compared to 1960-75

Source: Population Action International 1994
CDC Quarantine Station

• Passengers in adjacent rows notified
• 8 cities across USA.
• No evidence of transmission on flight
• Investigation took ~12 weeks to complete.

• Local Health Dept:
• 3 household contacts IGRA +
What predisposed him to getting active TB?

- Endemic country
- Diabetes mellitus
How might have this been prevented?

• Screen immigrants from endemic countries for latent TB
• IGRA preferable
• Treat latent TB
An appropriately fitted respirator (mask) will prevent the transmission of TB to the healthcare worker.
A person who inhales TB bacteria always becomes infected.

A. True
B. False
If a contagious TB patient is aboard an airplane, the entire plane will become infected.

A. True
B. False
Granulomas are only found with TB infection

A. True
B. False
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