Mayo Clinic Center for Tuberculosis

Tuberculosis Infection, Transmission & Infection Control

Jeremy Clain, MD
Pulmonary & Critical Care Medicine | Mayo Clinic
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Disclosures

• No relevant financial relationships
• No conflicts of interest
Objectives

• Describe the mechanism of person-to-person transmission of Mycobacterium tuberculosis

• Identify the major steps that mediate the process that leads from MTB exposure to infection

• Define the components of an effective TB infection control program

• Describe ways healthcare workers can protect themselves and others from being infected with M. tuberculosis
A Case

OUTBREAK OF TUBERCULOSIS AMONG REGULAR PATRONS OF A NEIGHBORHOOD BAR

SUSAN E. KLINE, M.D., LINDA L. HEDEMARK, M.D., AND SCOTT F. DAVIES, M.D.

Abstract Background. Outbreaks of tuberculosis have been reported in prisons, nursing homes, urban homeless shelters, and other crowded settings. We report a nonresidential outbreak of tuberculosis that originated in a neighborhood bar.

Methods. A homeless patient with highly infectious pulmonary tuberculosis was a regular patron of a neighborhood bar during a long symptomatic interval before diagnosis. We investigated 97 other regular customers and employees of the bar through interviews, tuberculin skin testing, and chest roentgenography. We performed DNA fingerprinting on isolates from the index patient and 11 other patients.

Results. The index patient apparently infected 41 of 97 contacts (42 percent), resulting in 14 cases of active tuberculosis and 27 cases of infection but no disease (indicated by positive tuberculin skin tests). Four other cases of active tuberculosis occurred among regular customers of the bar who were missed by the contact investigation. There were also two secondary cases. Radiographic findings in active cases included upper-lobe disease in seven cases (three cavitary) and negative chest films at the time of diagnosis in four cases. All 12 culture isolates we tested had the same chromosomal-DNA restriction pattern.

Conclusions. The spread of tuberculosis in a neighborhood bar can be a major public health problem. The high rate of infection and disease among the contacts was unexpected and was not due to coinfection with the human immunodeficiency virus. Possible explanations include heavy alcohol use among the contacts, high infectivity of the index case, or both. Sputum cultures must be performed in tuberculin-positive contacts who have symptoms, even if the chest films are normal. (N Engl J Med 1995;333:222-7.)
Case History

• 48-year-old man presented to HCMC in Minneapolis in 1992 with progressive respiratory and symptoms for 6 months

• Symptoms included:
  • Frequent coughing
  • Intermittent hemoptysis
  • 31 kg weight loss

Case Outcome

- Sputum smear densely positive for AFB+ organisms
- Sputum culture positive for MTB

A Case Continues – Contact Investigation

• Patient frequented a neighborhood bar
• 41 of 97 contacts infected
• 20 active cases linked back to the original patient

Figure 2. Flow-Chart Overview of the Contact Investigation and Origin of the 20 Active Cases of Tuberculosis That Resulted from Infection in the Index Patient.

TB Transmission and Pathogenesis

• Questions to consider:
  • What is the difference between being close to an index TB case and being exposed to MTB?
  • What is the risk of MTB infection in an individual who has been exposed?
  • What does it mean to have MTB infection, and how does that terminology relate to active TB case?
Transmission of Mycobacterium Tuberculosis
Transmission

• The most effective means of communicating MTB involve forced expiratory maneuvers, including coughing, sneezing, yelling, singing, and loud talking.

• Once aerosolized, MTB may remain airborne for several hours.

• The bacterium must be transmitted in a droplet small enough to reach the recipient's alveolus (1-5 µm).

• A single bacterium in a small respiratory droplet has more infectious potential than a clump of bacteria in a large droplet.
TB Pathogenesis

Exposure to infectious particles

- Adequate
  - Innate immunity
    - Containment (95%)
      - Adequate
        - Adaptive (T-cell) immunity
          - Continued containment (90%)
            - Adequate
              - Adaptive (T-cell) immunity
            - Inadequate
              - Late progression (5%)
          - Inadequate
            - Early progression (5%)
        - Inadequate
          - Infection (30%)
      - Inadequate
        - No infection (70%)
  - Inadequate
    - Infection (30%)

- Inadequate
  - No infection (70%)
TB Pathogenesis – Exposure & Infection

- Exposure to infectious particles
  - Adequate Innate immunity
    - Containment (95%)
      - Adequate Adaptive (T-cell) immunity
        - Continued containment (90%)
      - Inadequate Late progression (5%)
    - Inadequate Infection (30%)
      - Inadequate Early progression (5%)
  - Inadequate No infection (70%)
MTB: Exposure to Infection (1)

- MTB organisms enter through the upper airways, but establish infection at the level of the alveoli.

- Numerous non-immunologic host defenses protect an exposed individual from infection:
  - Nasal hair
  - Mucus secretions
  - Ciliated epithelium
  - Cough reflexes
MTB: Exposure to Infection (2)

• In addition to mechanical barriers, there are innate immune mechanisms that protect an exposed individual from MTB infection.

• Ultimately, about 30% of exposed individuals will develop MTB infection.
TB Pathogenesis – Exposure & Infection

- Exposure to infectious particles
  - Innate immunity
    - Adequate: Containment (95%)
    - Inadequate: Infection (30%)
  - Inadequate: Infection (30%)
  - Adequate: Containment (95%)
    - Adequate: Adaptive (T-cell) immunity
      - Inadequate: Late progression (5%)
    - Inadequate: Early progression (5%)
  - Continued containment (90%)

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Primary Infection with M. Tuberculosis

Latent Tuberculosis Infection (LTBI)

- Individual has been exposed to and infected with MTB
- Adaptive immune system has been activated, with involvement of multiple cell types
- Represents a containment phase, with relatively stable bacterial numbers
- Since the adaptive immune system has been engaged, immune-based tests for TB infection (TST, IGRA) are positive
# LTBI versus TB Disease

<table>
<thead>
<tr>
<th>A Person with LTBI</th>
<th>A Person with TB Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Has no symptoms</td>
<td>Has symptoms</td>
</tr>
<tr>
<td>Does not feel sick</td>
<td>Usually feels sick</td>
</tr>
<tr>
<td>Cannot spread TB bacteria to others</td>
<td>May spread TB bacteria to others</td>
</tr>
<tr>
<td>Usually has a skin test or blood test result indicating TB infection</td>
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</tr>
<tr>
<td>Has a normal chest x-ray and a negative sputum smear</td>
<td>May have an abnormal chest x-ray, or positive sputum smear or culture</td>
</tr>
<tr>
<td>Needs treatment for latent TB infection to prevent TB disease</td>
<td>Needs treatment to treat TB disease</td>
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CDC.gov
TB Pathogenesis – After Primary Infection

- Exposure to infectious particles
- Innate immunity
  - Adequate: No infection (70%)
  - Inadequate: Infection (30%)
- Adaptive (T-cell) immunity
  - Adequate: Containment (95%)
  - Inadequate: Early progression (5%)
- Continued containment (90%)
  - Adequate: Adaptive (T-cell) immunity
  - Inadequate: Late progression (5%)
Natural History of TB Infection

• Early progression (5%)
  • Diagnosis of TB disease within 2 years of MTB exposure

• Late progression (5%)
  • Diagnosis of TB disease more than 2 years after MTB exposure

• Sustained containment (90%)
  • Never diagnosed with TB disease
Reactivation Tuberculosis

Classical Tuberculosis Granuloma

Reactivation Tuberculosis

Process Not Limited to Airways

• During primary infection, small numbers of MTB organisms spill into the blood and lymph
• Can deposit in any organ in the body
• Reactivation TB can occur in pulmonary and extrapulmonary locations
Risk Factors for Progression to Active TB

• Immunosuppression
  • Disease, especially HIV
  • Medications, especially TNF inhibitors and prolonged corticosteroid therapy

• Diabetes mellitus
• Advanced renal failure
• Substance abuse
• Silicosis
Summary of TB Pathogenesis: Exposure, Infection, Containment, Progression

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<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>
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<td><strong>Catalyst:</strong> Increased infectiousness</td>
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Back to Minneapolis 1992
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Figure 2. Flow-Chart Overview of the Contact Investigation and Origin of the 20 Active Cases of Tuberculosis That Resulted from Infection in the Index Patient.
# TB Infection Control

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Factors That Increase Risk of Infection

• Details of the contact/exposure
  • Proximity of contact
  • Duration of exposure
  • Procedural setting (intubation, bronchoscopy, sputum induction, chest PT, administration of nebulized medications, irrigation of TB abscess)

• Features of TB index case
  • Pulmonary or laryngeal involvement
  • Cavitary disease
  • AFB smear positive
  • Short time to culture positivity
Principles of TB Infection Control

• Identify potential TB cases early
• Reduce potentially hazardous contacts to individuals undergoing TB evaluation or early treatment of established TB disease
• Treat TB systematically
Principles of TB Infection Control

- Identify
- Isolate
- Treat
Components of TB Infection Control Programs

• Administrative measures
• Environmental measures
• Personal protective measures
TB Infection Control: Administrative Measures

- Management measures that are intended to reduce the risk or exposure to persons with infectious TB
- Create a framework that promotes TB case identification and isolation, and facilitates effective treatment
- Provide a structure to allow individuals to make good choices for patient care and personal safety
Administrative Measures – TB Control

• Establish appropriate laboratory processing, testing, and reporting of results

• Implement effective work practices for managing patients who may have TB disease

• Educate, train, and counsel health care workers, patients, and visitors about TB infection and TB disease

• Test and evaluate workers who are at risk for exposure to TB disease

• Coordinate local and state efforts
TB Infection Control: Environmental Measures

• Environmental controls aim to prevent the spread and reduce the concentration of infectious droplet nuclei

• Consist of primary and secondary controls
Primary Environmental Controls

- Target the source of infection
- Utilize two levels of ventilation:
  - Local exhaust ventilation (hoods, tents, or booths)
  - General ventilation to dilute and remove contaminated air
Secondary Environmental Controls

- Target the environment adjacent to the source of infection
- Utilize two strategies:
  - Control airflow to prevent contamination of air
  - Clean the air by using high efficiency particulate air (HEPA) filtration or ultraviolet germicidal irradiation
TB Infection Control: Personal Measures

- Personal protective measures are most effective in the setting of appropriate administrative and environmental controls
- Personal measures include interventions for both the index patient and for health care workers and visitors
Respiratory Protection Equipment

- Health Care Worker/Visitor
  - N95 Respirator

- Patient
  - Surgical Mask
N95 Respirators

• Designed to filter out droplet nuclei expelled into the air from a patient

• Only effective if it fits properly

• Also only effective if actually worn when during potential exposure:
  • During interaction with patient in airborne isolation room
  • In rooms where cough- or aerosol-producing procedures are done
  • During transport of potentially infectious patient
  • In homes of individuals with active TB
Summary

• Mycobacterium tuberculosis is transmitted in small respiratory droplets, 1-5 µm in size

• The risk of MTB infection following TB case exposure is about 30%

• On a population basis, the risk of developing TB disease from TB infection is about 10%, with host factors adjusting individual risk

• TB infection control depends on administrative, environmental, and individual protective measures
Thank you!
clain.jeremy@mayo.edu