Transmission and Pathogenesis of Tuberculosis

Journey of the TB bacillus

Objectives

• Describe the basic pathophysiology and transmission of *Mycobacterium tuberculosis* and use this knowledge to inform clinical care

• Identify features that increase an individual’s risk of progression from TB infection to active TB disease
**M. tuberculosis complex (M.tb)**

**The etiology**

- *M. tuberculosis*
- *M. africanum*
- *M. canettii* (rare)
- *M. bovis* (cattle)
- *M. orygis* (herd animals)
- *M. microti* (rodents)
- *M. caprae* (sheep/goats)
- *M. pinnipedii* (seals/sea lions)
- *M. suricattae* (meerkats)
- *M. mungi* (mongoose)

**Characteristics of M. tuberculosis**

- Slightly curved, rod shaped bacilli
- 0.2 - 0.5 microns in diameter; 2 - 4 microns in length
- Thick lipid (mycolic acid) cell wall
- Acid fast bacilli (AFB) - resists decolorization with acid/alcohol
- Multiplies slowly (~ every 18-24 hours)
- Aerobic and non-motile
- Metabolism can slow to the point of dormancy and remain in this state for decades
Transmission of TB

Transmission of TB
Transmission and Pathogenesis
Transmission Factors

The likelihood of transmission relates directly to:

- Bacteria load and index case factors
  - Sputum smear (+)
  - Cavitation on chest X-ray
  - Symptoms (e.g., cough) and social activities
- A contact’s exposure time
  - On average, 1-5% of household contacts are found on initial evaluation to have active TB
  - 20-30% of close contacts may have TB infection
- Environmental factors

Transmission ➔ Infection

- Inhaled droplet nuclei containing TB bacilli travel to alveoli
- Bacilli are engulfed by local macrophage
  - Killed by macrophage (no infection)
  - Multiply and overwhelm the macrophage ➔ disseminate to other sites
DISSEMINATION: Spread of TB to Other Parts of the Body

1. Lungs (85% all cases)
2. Pleura
3. Central nervous system • spine, brain, meninges
4. Lymph nodes
5. Genitourinary system
6. Bones and joints
7. Disseminated (miliary)

TB Pathogenesis

- About 3 weeks after infection, a cell-mediated TH1 response is mounted, activating macrophages to become bactericidal
- Mature TH1 cells, both in lymph nodes and in the lung, produce IFN-gamma
- IFN-gamma stimulates formation of the phagolysosome in infected macrophages, creating an inhospitable acidic environment for *M.tb*
TB Pathogenesis (2)

- Immune system activated
  - Granuloma formation may occur containing the bacilli (latent TB infection)
  - Unable to contain and progression to primary tuberculosis occurs (~ 5%)

Primary Tuberculosis

- Tuberculosis that results from the initial *M. tuberculosis* infection
- Radiological features depend on:
  - Age
  - Underlying immune status
  - Prior TB exposure
- Distribution: Any lobe (slight lower lobe predominance)
- Presentations include:
  - Air-space consolidation
  - Cavitation is uncommon (< 10%)
  - Miliary pattern
  - Adenopathy is common (esp. in children and persons with HIV)
Latent TB infection (LTBI) or active TB disease?
What features distinguish one from the other?
Latent TB Infection (LTBI)

- Inactive tubercle bacilli in the body
- Tuberculin skin test or interferon-gamma release assay (IGRA) test results usually positive
- Chest x-ray usually normal
- Sputum smears and cultures negative
- No symptoms
- Not infectious
- Not a case of TB

Active TB Disease

- Active tubercle bacilli in the body
- Tuberculin skin test or interferon-gamma release assay (IGRA) test results usually positive
- Chest x-ray may be abnormal
- Sputum smears and cultures may be positive
- Symptoms such as cough, fever, weight loss
- May be infectious before treatment
- A case of TB


TB Pathogenesis: Infection-Disease Spectrum

PPD=purified protein derivative; TST= tuberculin skin test; IGRA= interferon gamma release assay; CM= central memory; EM= effector memory

Can this be TB?

Typical Pattern: Reactivation, Post-primary TB

Distribution
- Apical / posterior segments of upper lobes
- Superior segments of lower lobes
- Isolated anterior segment involvement is unusual (think M. avium complex or other disease)

Reactivation/Post-primary TB

Patterns of disease
- Air-space consolidation
- Cavitation, cavitary nodule
- Endobronchial spread
- Miliary
- Bronchostenosis
- Tuberculoma
- Pleural effusions
TB Risk Assessment

- Evaluate for risk factors that increase chance:
  - that person may have LTBI (high prevalence)
  - for progression of LTBI to disease (high risk)
High prevalence for LTBI

- Known contact to person with TB disease
- Persons who live or spend time in certain congregate settings
  - nursing homes,
  - correctional institutions,
  - homeless shelter,
  - drug treatment centers
- Persons born in countries with high prevalence of TB

High Risk for Progression

Persons more likely to progress from LTBI to TB disease include:

- Newly infected close contacts
- HIV-infected persons
- Persons with a history of prior, untreated TB or fibrotic lesions on chest radiograph
- Underweight or malnourished persons
- Injection drug users
- Extremes of age (very young or very old)
High Risk for Progression (2)

Persons with certain medical conditions such as:
- Silicosis
- Diabetes mellitus
- Chronic renal failure or on hemodialysis
- Solid organ transplantation
- Carcinoma of head or neck
- Gastrectomy or jejunoileal bypass

High Risk for Progression (3)

Persons taking immunosuppressive agents:
- Steroids
- Cancer chemotherapy
- Cyclosporine

Persons taking blocking agents against Tumor Necrosis Factor-Alpha; some examples include:
- Etanercept (Enbrel®)
- Infliximab (Remicade®)
- Adalimumab (HumiraTM)
- Golimumab (Simponi®)
- Certolizumab pegol (Cimzia®)
Take home points

• People with latent TB infection (LTBI) can be treated to prevent development of TB disease
  – This is a critical aspect to achieve TB Elimination
• Detecting LTBI early and providing treatment helps prevent new cases of TB disease
• You too can be a part of halting TB’s journey here in the U.S. -
  1) Know risks for infection and disease
  2) Encourage and facilitate testing and treatment

Questions?