Tuberculosis

- Causative organism: *Mycobacterium tuberculosis*
  - Strict aerobe
  - Pathogenic strains: hominis, bovis, avium, murine & cold blooded vertebrate strain
- Epidemiology
  - Poverty, crowding, chronic debilitating disease
  - AIDS
Koch’s bacillus

- small slender, rod like bacillus, 4um non-motile, aerobic
- high lipid content
- divides every 16 to 20 hours, an extremely slow rate
- stains very weakly Gram-positive or does not retain dye due to the high lipid & mycolic acid content of its cell wall
- can withstand weak disinfectant and survive in a dry state for weeks.

- demonstrated by
  - Ziehl Neelsen staining
  - Fluorescent dye method
  - Culture in LJ media
  - Guinea pig inoculation
Current Situation

- Two to three million people around the world die of TB each year.
- Someone is infected with TB every second.
- One third of the world population is infected with TB.
- Twenty three countries in south east Asia and sub Saharan Africa account for 80% total cases around the world.
- Number of new cases of TB correlates with economic conditions: the highest incidences are seen in Africa, Asia, and Latin America.
- 70% untreated actively infected individuals die.
Modes of transmission
• Inhalation
• Ingestion
• Inoculation
• Transplacental route

Spread
• Local
• Lymphatic
• Haematogenous
• By natural passages
Pathogenesis

• Anti- mycobacterial CMI, confers resistance to bacteria → development of HS to tubercular Ag
• Bacilli enters macrophages
• Replicates in phagosome by blocking fusion of phagosome & lysosome, continues for 3 weeks → bacteremia but asymptomatic
• After 3 wks, T helper response is mounted by IL-12 produced by macrophages
• T cells produce IFN, activates macrophages → bactericidal activity, structural changes
• Macrophages secrete TNF → macrophage recruitment, granuloma & necrosis
Fate of granuloma

- Caseous material undergo liquefaction---cold abscess
- Bones, joints, lymph nodes & epididymis---sinuses are formed & sinus tract lined by tuberculous granulation tissue
- Dystrophic calcification
Types of TB

- Primary Pulmonary TB
- Secondary TB (miliary, fibrocaseous, cavitary)
- Extra-pulmonary TB (bone, joints, renal, adrenal, skin…)
Primary TB

- Infection in an individual who has not been previously infected or immunised
- Primary complex
  - Sites--- lungs, hilar lymph nodes
    - tonsils, cervical lymph nodes
    - small intestine, mesenteric lymph nodes
Primary TB

In the lung, Ghon’s complex has 3 components:
• Pulmonary component
  - Inhalation of airborne droplet ~ 3 microns.
  - Bacilli locate in the subpleural mid zone of lung
  - Brief acute inflammation – neutrophils.
  - 5-6 days- invoke granuloma formation.
  - 2 to 8 weeks – healing – single round ;1-1.5 cm- Ghon focus.
• Lymphatic vessel component
• Lymph node component
Ghon’s complex
Pulmonary Tuberculosis
Lymphocytes

Giant multinucleated cell (Langhans type)

Aggregation of epithelioid cells
Fate of primary tuberculosis

- Lesions heal by fibrosis, may undergo calcification, ossification
  - a few viable bacilli may remain in these areas
  - bacteria goes into a dormant state, as long as the person's immune system remains active
- Progressive primary tuberculosis: primary focus continues to grow & caseous material disseminated to other parts of lung
- Primary miliary tuberculosis: bacilli may enter circulation through erosion of blood vessel
- Progressive secondary tuberculosis: healed lesions are reactivated, in children & in lower resistance
Secondary tuberculosis

• Post-primary/ reinfection/ chronic TB
• Occurs in immunized individuals.
• Infection acquired from
  - endogenous source/ reactivation
  - exogenous source/ reinfection
• **Reactivation** - when immune system is depressed
  - Common in low prevalence areas.
  - Occurs in 10-15% of patients
  - Slowly progressive (several months)
• **Re-infection** - when large innoculum of bacteria occurs
  - In areas with increased personal contact
Secondary TB

- Sites - Lungs
  - 1-2 cm apical consolidation with caseation
- Other sites - tonsils, pharynx, larynx, small intestine & skin
Fate of secondary tuberculosis

- Heal with fibrous scarring & calcification
- Progressive secondary pulmonary tuberculosis:
  - fibrocaseous tuberculosis
  - tuberculous caseous pneumonia
  - miliary tuberculosis
Fate of secondary tuberculosis

• Fibrocaseous tuberculosis:
  - massive caseation which may break into a bronchus to produce- cavitary/open TB,
  - endobronchial or endotracheal TB
  - or remain as soft caseous lesion- non-cavitary

Complications:
  a) aneurysm of arteries– hemoptysis
  b) bronchopleural fistula
  c) tuberculous empyema

• Tuberculous caseous pneumonia: caseous material may spread to rest of the lung
Miliary TB

- Millet like, yellowish, firm areas without caseation
- Extensive spread through lympho-hematogenous route
- Low immunity
- Pulmonary involvement via pulmonary artery
- Systemic through pulmonary vein:
  - LN: scrofula, most common
  - kidney, spleen, adrenal, brain, bone marrow
Signs and Symptoms of Active TB

- Pulmonary: cough, hemoptysis, dyspnea
- Systemic:
  - fever
  - night sweats
  - loss of appetite
  - weight loss
  - chest pain, fatigue
- If symptoms persist for at least 2 weeks, evaluate for possible TB infection.
Diagnosis

- Sputum- Ziehl Neelsen stain – 10,000 bacilli, 60% sensitivity
  - release of acid-fast bacilli from cavities intermittent.
  - 3 negative smears : low infectivity
- Culture most sensitive and specific test.
  - Conventional Lowenstein Jensen media- 10 wks.
  - Liquid culture: 2 weeks
- Automated techniques within days
  - PCR should only be performed by experienced laboratories (10 bacilli)
- PPD for clinical activity / exposure sometime in life
- X-ray chest
- FNAC
PPD Tuberculin Testing

• Read after 72 hours.
• Induration size - 5-10 mm
• Does not d/s b/w active and latent infection
• False +: atypical mycobacterium
• False -: malnutrition, HD, viral, overwhelming infection, immunosuppression
• BCG gives + result.
Tuberculosis

Atypical mycobacteria
- Photochromogens---M. kansasii
- Scotochromogens---M. scrofulaceum
- Non-chromogens---M. avium-intracellulare
- Rapid growers---M. fortuitum, M. chelonei

5 patterns of disease
- Pulmonary—M. kansasii, M. avium-intracellulare
- Lymphadenitis---- M. avium-intracellulare, M. scrofulaceum
- Ulcerated skin lesions----M. ulcerans, M. marinum
- Abscess---- M. fortuitum, M. chelonei
- Bacteraemias---- M. avium-intracellulare as in AIDS
A 32-year-old woman has had a chronic cough with fever for the past month. On physical examination, she has a temperature of 37.5°C, and on auscultation of the chest, crackles are heard in all lung fields. A chest radiograph shows many small, ill-defined nodular opacities in all lung fields. A transbronchial biopsy specimen shows interstitial infiltrates with lymphocytes, plasma cells, and epithelioid macrophages. Which of the following infectious agents is the most likely cause of this appearance?

(A) *Staphylococcus aureus*
(B) *Plasmodium falciparum*
(C) *Candida albicans*
(D) *Mycobacterium tuberculosis*
(E) *Klebsiella pneumoniae*
(F) *Cytomegalovirus*
## Infectious Granulomatous Diseases

### Examples of Diseases with Granulomatous Inflammations

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<tr>
<th>Disease</th>
<th>Cause</th>
<th>Tissue Reaction</th>
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| Tuberculosis    | *Mycobacterium
tuberculosis* | Noncaseating tubercle (granuloma prototype): a focus of epithelioid cells, rimmed by fibroblasts, lymphocytes, histiocytes, occasional Langhans giant cell; caseating tubercle: central amorphous granular debris, loss of all cellular detail; acid-fast bacilli |
| Leprosy         | *Mycobacterium
tuberculosis* | Acid-fast bacilli in macrophages; non-caseating granulomas                        |
| Syphilis        | *Treponema
pallidum*    | Gumma: microscopic to grossly visible lesion, enclosing wall of histiocytes; plasma cell infiltrate; central cells are necrotic without loss of cellular outline |
| Cat-scratch disease | Gram-negative
c bacillus  | Rounded or stellate granuloma containing central granular debris and recognizable neutrophils; giant cells uncommon |