Entsar Hamed Ahmed Tuberculosis

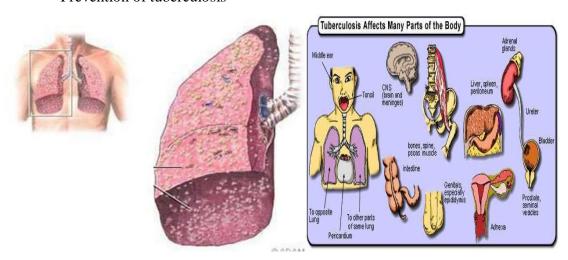
Tuberculosis

Entsar Hamed Ahmed

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Objectives

- General characters of the genus Mycobacteria
- Pathogenesis of human tuberculosis
- Diagnosis of active tuberculosis disease
- Diagnosis of latent tuberculosis infection
- Prevention of tuberculosis



Human tuberculosis

- It is primarily a disease of the lungs (Pulmonary TB)
- May spread to other sites (Extra-pulmonary TB) in one third of cases.
- May proceed to a disseminated infection (Miliary tuberculosis)

MYCOBACTERIUM

Genus Features

- Acid fast rods with waxy cell wall
- Obligate aerobe
 - Cell wall
 - Unique: high concentration of lipids containing long chain fatty acids called mycolic acids
 - Wall makes mycobacteria highly resistant to desiccation and many chemicals (including NaOH used to kill other bacteria in sputa before

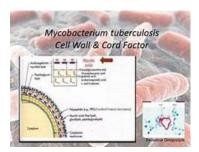
neutralizing and culturing)

• Sensitive to UV

Species of Medical Importance

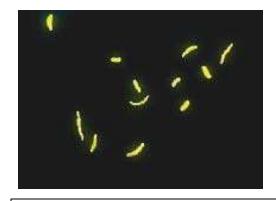
- M. tuberculosis
- M. leprae
- M. avium-intracellulare
- M. kansasii
- M. marinum
- M. ulcerans

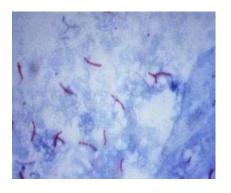
♣ Mycobacterium tuberculosis



Distinguishing Features

- Auramine-rhodamine staining bacilli (fluorescent apple green); no antibody involved
- Acid fast (Ziehl Neelsen stain)





Auramine-rhodamine staining

Ziehl – Neelsen stain

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• Aerobic, slow growing on Lowenstein-Jensen medium; new culture systems (broths with palmitic acid) faster.

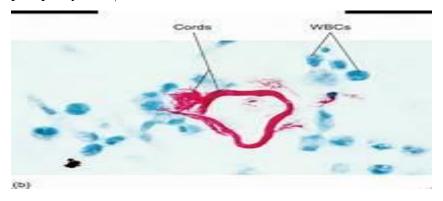
- Produces niacin
- Produces a heat-sensitive catalase: catalase-negative at 68.0°C (154.4 F) (standard catalase test); catalase active at body temperature

Reservoir: human lungs

Transmission: respiratory droplets

Pathogenesis

- Facultative intracellular organism (most important)
- Sulfatides (sulfolipids in cell envelope): inhibit phagosome-lysosome fusion, allowing intracellular survival (if fusion occurs, waxy nature of cell envelope reduces killing effect)
- Cord factor (trehalose dimycolate): causes serpentine growth in vitro; inhibits leukocyte migration; disrupts mitochondrial respiration and oxidative phosphorylation



• **Tuberculin** (surface protein) along with mycolic acid □delayed hypersensitivity and **cell-mediated immunity** (CMI): granulomas and caseation mediated by CMI; no exotoxins or endotoxin; damage done by immune system.

Disease(s)

Primary pulmonary TB

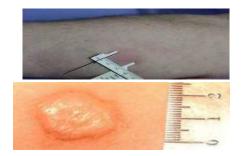
- Symptoms can include fever, dry cough
- Organisms replicate in naive alveolar macrophages, killing the macrophages until CMI is set up (Ghon focus)
- Macrophages transport the bacilli to the regional lymph node (Ghon complex)
 and most people heal without disease
- Organisms that are walled off within the Ghon complex remain viable unless treated

Reactivational TB

- Symptoms can include fever, hemoptysis, night sweats, weight loss
- Erosion of granulomas into airways (high oxygen) later in life under conditions of reduced T-cell immunity can lead to mycobacterial replication and disease symptoms
- Complex disease with the potential of infecting any organ system
- May disseminate (miliary TB): kidneys, GI tract, brain, spine

Diagnosis

- **Microscopy of sputum:** screen with auramine-rhodamine stain (fluorescent apple-green); no antibody involved; very sensitive; if positive, confirm with acid fast stain
- PPD skin test (Mantoux): measure zone of induration at 48–72 hours; positive if:
 - – ≥5 mm in HIV positive or anyone with recent TB exposure; AIDS patients have reduced ability to mount skin test.
 - ≥10 mm in high-risk population: IV drug abusers, people living in poverty, or immigrants from high TB area
 - ≥15 mm in low-risk population
 - Positive skin test indicates only exposure but not necessarily active disease



- Quantiferon-TB Gold Test: measures interferon-gamma production when leukocytes exposed to TB antigens. Used for the diagnosis of latent tuberculosis.
- Slow-growing (3–6 weeks) colonies on Lowenstein-Jensen medium (faster new systems)
- Organisms produce **niacin** and are **catalase-negative** (68°C)

Prevention Always Better than Treatment

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General Measures

- 1. Early case finding and effective treatment.
- 2. Proper infection control measures in hospitals
- 3. Avoid overcrowding.
- 4-Treatment of latent tuberculosis.
- 5-UV light or HEPA (high efficiency particulate air) filter used to treat potentially contaminated air

BCG Vaccine.

• Bacille Calmette-Guérin (BCG) vaccine containing live, attenuated organisms may prevent disseminated disease;

Mycobacteria Other than Tuberculosis (MOTTS)

Distinguishing Features

- Atypical mycobacteria
- Noncontagious
- Found in surface waters, soil, cigarettes

Recall Question

Which of the following diagnostics tests is intended for latent tuberculosis infection?

- A. Sputum smear microscopy
- B. Polymerase chain reaction (PCR)
- C. Interferon-gamma release assay (lGRA)
- D. ELISA for TB antibodies