Tuberculosis

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Surat
Global Emergency

- Tuberculosis kills 5,000 people a day
- 2.3 million die each year
• Tuberculosis is infectious disease caused by *Mycobacterium tuberculosis*.

**Types**

• Pulmonary TB
  – Primary TB
  – Secondary TB
• Milliary TB
• Extra-pulmonary TB
TRANSMISSION

Respiratory transmission.

- Conditions for transmission:
  - overcrowding
  - poor personal hygiene
  - poor public hygiene
  - Immuno compromised
Transmission

• Respiratory transmission
• Patients with the active disease expel bacilli into air by:
  – coughing
  – sneezing
  – Shouting
• Bacilli multiply in 4 -6 weeks
• May spreads throughout the body.
• The bacilli implant in areas of high partial pressure of oxygen:
  – lung
  – renal cortex
  – reticuloendothelial system
Coughed out active Bacilli

Inhaled by Surrounding Person

Remain in Air

No Phagocytosis

No Infection

Phagocytosed by Macrophage

Latent Infection

Bacteria lives in Granuloma

Activate in Life time / Immuno compromised

Active Disease
Risk of infection

• Exposure to amount TB bacilli
• Frequency of exposure to TB bacilli
• Duration of exposure to a person with Pulmonary TB
• Untreated AFB smear positive Pulmonary TB cases are the most infectious
Risk factors for disease

- Development of disease depends on individual susceptibility
- HIV increases the risk of getting TB disease
- 10% Life time risk of TB in HIV negative
- 10% Annual risk of TB in HIV positive
TB Pathogenesis

- Bacterial entry
- T Lymphocytes.
- Macrophages.
- Epitheloid cells.
- Proliferation.
- Central Necrosis.
- Giant cell formation.
- Fibrosis.
Morphology of Granuloma

1. Rounded tight collection of chronic inflammatory cells.
2. Central Caseous necrosis.
3. Active macrophages - epithelioid cells.
4. Outer layer of lymphocytes & fibroblasts.
5. Langhans giant cells – joined epithelioid cells.
PATHOGENESIS

1. Droplet nuclei containing tubercle bacilli are inhaled, enter the lungs, and travel to the alveoli.

2. Tubercle bacilli multiply in the alveoli.

3. A small number of tubercle bacilli enter the bloodstream and spread throughout the body. The bacilli may reach any part of the body, including areas where TB disease is more likely to develop (such as the lungs, kidneys, brain, or bone).

4. Macrophages form a hard shell & keeps bacilli under control.

5. Hard shell breaks down and tubercle bacilli escape and multiply (in this example, TB disease develops in the lungs).
Types of tuberculosis

• **Primary tuberculosis:**
  – develops in a previously unexposed person
  – And therefore person is not sensitized.

• **Secondary tuberculosis:**
  – develop in previously infected person.
  – And therefore person is previously sensitized.

• **Miliary Tuberculosis:**
  – Consolidation scattered through the lung parenchyma.
Primary tuberculosis

• Infection of an individual who has not been previously infected or immunized.

• Pathogenesis:
  – Inhalation of bacilli
  – Implant in the distal airspaces
  – Development of Sensitization
  – Gray-white inflammatory consolidation
  – “Ghon focus”
Primary tuberculosis - Ghon’s Complex

- Pulmonary component (Ghon’s Focus)
- Lymph node component
  - Hilar & Tracheo-bronchial
- Lymphatic component
Fate of primary tuberculosis

- Heal by fibrosis → calcification
- Progressive primary tuberculosis
- Primary miliary tuberculosis
Secondary tuberculosis

• Infection of an individual who has been previously infected or sensitized

• The infection may be acquired from
  – Endogenous source:
    • Reactivation of dormant primary complex
  – Exogenous source
Fate of secondary tuberculosis

• Heal with fibrous scarring and calcification
• Progressive pulmonary TB
• Tuberculous caseous pneumonia
• Miliary tuberculosis
Cavitary Secondary TB
Cavitary Secondary TB

- Due to high oxygen tension
- Favourable environment for bacilli
- In Open Tuberculosis
  - Bacilli implant on the mucosal lining of air passages
  - Producing endobronchial / endotracheal TB
Miliary pulmonary tuberculosis

• **Pathogenesis:**
  • Organisms drain in lymphatic
  • Spread in lymphatic ducts
  • Organism enter into right side of heart through venous return
  • Enter in Pulmonary arteries
  • Make microscopic scattered lesion in lung parenchyma
  • Granuloma & Caseous necrosis formation.
Pulmonary TB Clinical features

- Low grade fever (evening rise)
- Sweating
- Cough (productive)
  - Dry
  - Purulent
  - Haemoptysis
- Weight loss
- Loss of appetite
- Lymphadenopathy
• Non immunocompromised patients
  – 10% latent infections turns to active TB in life time.
• HIV patients
  – 10% of turns to active TB each year.
Cervical
Supra clavicular
Potts spine
Supra renal tuberculosis
Axillary tuberculosis
Diagnosis of TB

- Zeil Nielson Stain
  - For Acid Fast Bacilli
- Adenosine deaminase test
- Culture most sensitive and specific test.
  - Conventional media = 3-6 weeks.
  - Automated techniques within = 9-16 days
- PCR
- Mantoux test
Diagnosis

- Clinical history
- Signs of fever, pleural rub, crackles
- Investigations:
  - X ray chest
  - Intradermal PPD
  - Mantoux
  - ZN staining
  - PCR
  - DNA probing
Mantoux test

• Infection with mycobacterium tuberculosis leads delayed hypersensitivity reaction which can be detected by Mantoux test

• About 2 to 4 weeks after infection, intracutaneous injection of purified protein derivative (PPD) of M.tuberculosis induces a visible and palpable induration that peaks in 48 to 72 hours
PPD Tuberculin Testing

- Sub cutaneous
- Weal formation
- Itching – no scratch.
- Read after 72 hours.
- Induration size.
- 5-10-15mm
Induration Size & Interpretation

- Less than 5 mm
  - No exposure to tubercular bacilli.
- Between 5-9 mm
  - Due to Atypical mycobacteria
  - BCG vaccination.
  - May in HIV or Immunosupression patient
- 10 mm or more
  - Tubercular disease
Classification of Drugs

• 3 Groups of Drugs
  – First Line:
    • Most effective and have lowest toxicity.
    • Isoniazid Rifampin
  – Second Line:
    • Less effective and more toxic effects
    • p-amino salicylic acid, Streptomycin, Ethambutol
  – Third Line
    • Least effective and most toxic.
    • Amikacin, Kanamycin, Capreomycin, Viomycin, Kanamycin, Cycloserine
<table>
<thead>
<tr>
<th>Drugs</th>
<th>Short</th>
<th>Dose (mg)</th>
<th>Dose for pediatric (mg/kg)</th>
<th>Common Side effects</th>
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</thead>
<tbody>
<tr>
<td>Isoniazide</td>
<td>H</td>
<td>600</td>
<td>10-15</td>
<td></td>
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<tr>
<td>Rifampicin</td>
<td>R</td>
<td>450</td>
<td>10</td>
<td>Reddish / Orange color urine</td>
</tr>
<tr>
<td>Pyrazinamide</td>
<td>Z</td>
<td>1500</td>
<td>35</td>
<td></td>
</tr>
<tr>
<td>Ethambutol</td>
<td>E</td>
<td>750</td>
<td>15</td>
<td>Impaired vision</td>
</tr>
<tr>
<td>Streptomycin</td>
<td>S</td>
<td>1200</td>
<td>30</td>
<td>Ototoxicity</td>
</tr>
</tbody>
</table>

**RNTCP** = Revised National Tuberculosis Control Programme

**DOTs** = Direct Observation Therapy
<table>
<thead>
<tr>
<th>Category</th>
<th>Type of Patient</th>
<th>Regimes</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>✔ New Sputum smear Positive</td>
<td>2(HRZE)3</td>
</tr>
<tr>
<td></td>
<td>✔ Seriously ill sputum smear-negative</td>
<td>4(HR)3</td>
</tr>
<tr>
<td></td>
<td>✔ Seriously ill Extra-pulmonary</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>✔ Sputum smear-Positive Relapse</td>
<td>2(HRZES)3</td>
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<tr>
<td></td>
<td>✔ Sputum smear-Positive Failure</td>
<td>1(HRZE)3</td>
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<tr>
<td></td>
<td>✔ Sputum smear-Positive Treatment After default</td>
<td>5(HRE)3</td>
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<tr>
<td>III</td>
<td>✔ Sputum smear-Negative Not seriously ill</td>
<td>2(HRZ)3</td>
</tr>
<tr>
<td></td>
<td>✔ Extra-pulmonary, Not seriously ill</td>
<td>4(HR)3</td>
</tr>
</tbody>
</table>
Drug Interaction

- Competition between Isoniazid and Phenytoin (anticonvulsant).
- They both compete for drug metabolism enzymes.
- Phenytoin interferes with metabolism of isoniazid by reduction in excretion or enhancement of effect of isoniazid.
WARNING!

Rifampin and Isoniazid are the most effective drugs when used together. These 2 drugs should never be given alone! They are always used in combination because resistance occurs to one drug alone very rapidly.
"Troubles are often the tools by which God fashions us for better things."

Exams...!

- Henry Ward Beecher
Thank you