Mycobacteria & Fungal Respiratory Tract Pathogens

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The World Health Organization (WHO) estimates that approximately one-third of the global population is infected with *M. tuberculosis* (TB).

Around **10 million new cases** of TB are being reported each year, **2-3 million deaths** occur each year worldwide. 95% in developing countries.

After emerging (HIV)/AIDS, TB is the **second most common cause of death** in AIDS patients due to an infectious disease.
Mycobacterium Tuberculosis

- **Tubercle Bacilli**. Acid-Fast Bacilli. Widely distributed in Human, Animals, Birds, Environment. TB bacilli grow slowly, Resistant to Dryness, low Acidity. survive years in nature. But Susceptible to UV-light, Heat.

- **M. tuberculosis**. Causes 95% of human TB cases. mostly pulmonary. Respiratory infection. Few cells. Lung positive person may infect hundred of susceptible person. All ages. mostly children. with malnutrition.

- **Optimal conditions for transmission include**: overcrowding, Large cities, poor conditions & Low standard public hygiene.
Acid Fast Bacilli Stained by Ziehl-Neelsen (AF Stain)
Infection With Mycobacteria mostly through RT air droplets

A person may contract pulmonary tuberculosis from inhaling droplets from a cough or sneeze by an infected person.

Granuloma in lung tissue
Pulmonary Infection

- **Primary Tuberculosis**: 90% Pulmonary TB, Children, Asymptomatic, TB Bacilli infect Alveolar macrophages. Develop small lung lesions. Fibrosis, Calcification, Hypersensitivity. Infected person becomes **Positive for Tuberculin Skin test**.

- Few cases Primary TB infection may spread from Lesion by direct extension to lymphatic system, bronchi, blood, Kidneys Gastrointestinal, Meningitis (children). Rarely developing **Military tuberculosis**.

Tuberculin Test

- **Symptomatic/ asymptomatic** infected persons develop positive Tuberculin skin test. Reaction to TB glycerol extract (Mycolic acids + lipoproteins).

- **Mantoux -Tuberculin skin test** Specific TB antigens produced from boiling culture of *M. tuberculosis*.

- The test consists an intradermal injection of 5 tuberculin units (0.1 ml) of PPD in the forearm. The test is read after 48-72 hours.

- **Positive tuberculin:** Indurations, Edema & Erythematic skin > 1 cm, Interpretation

- Vaccination with **BCG** Protection 30-78% result in positive Tuberculin test.
Tuberculin (PPD) Skin Test
Other Human Pathogenic Mycobacteria species

- **M. bovis**: common in domestic animal.. rare human.. Infection.. source: milk, dairy products, meat.. begins mostly intestinal infection.. may spread to other parts.. **Slow grower**

- **Atypical mycobacteria**: Widely distributed in nature.. water, soil, birds, animals , mostly slow grower (1-3 weeks)

- **M. kansasii**: Soil, Photochromogenic, Produce yellow/orange color during incubation in light.. Mostly Lung tuberculosis.. immuno-suppressed persons, AIDS.

- **M. marinum**: Water ,Fish , localized Skin, ulcers-soft tissues, Swimming pool, aquarium granuloma.. Lymph nodes.

- **M. avium complex**: Animals, water,,Skin Lesions, rarely Pulmonary disease..

- **M.ulcernas**: Soil in Tropical countries, Skin lesions, necrosis, More Resistant to anti-tuberculosis drugs..
Rapidly growing Mycobacteria species: Rarely cause skin ulceration, mostly non-pathogens.. *M. smegmatis*.. Found in on extragenital tract.. May contaminate urine culture.

Diagnosis & treatment: Tuberculosis is confirmed by positive Direct AF Smear/ Culture, PCR X-ray, Positive tuberculin Test.

Clinical specimens: Sputum, Urine, CSF, Tissues, Culture Loewenstein-Jensen Agar.. 4-8 Weeks.. No Blood Serological test.

Treatment Multiple Antibiotics: 6-24 Months.. Rifampicin, Isonaized, Pyrazinamid, Ethambutol, development of Multidrug resistant MB tuberculosis.. At present 1-5% worldwide.. Completing treatment is essential for cure
Nocardiosis

- **Nocardia asteroids/ N. barsiliensis.** Aerobic G+ve Pleomorphic Bacilli & Branched short Filaments.. Slightly Acid Fast.. Common as Environmental Saprophytes.

- Human Exogenous Infection.. Mostly **Pulmonary localized abscesses**.. Necrosis.. small Cavities.. spread to Brain, Kidneys.. Common in Immunosuppressed & Lung malignancy

- **Chronic suppuration**.. Abscess.. Granulomas, Draining sinuses containing granules.. Muscles, Bones, Feet, Hands and other body parts.

- **Diagnosis & Treatment:** Sputum/biopsies culture on blood 1-4 weeks at room temperature , Co-trimoxazole, Rifampicin, Amikacin.. 4-6 Weeks.
Respiratory Fungal Agents

- **Fungal respiratory diseases** can be divided into:
- Fungal agents.. Widely distributed in Environment.. Cause mostly infection in immunocompromised individuals.. receiving immunosuppressive therapy.. undergoing bone marrow transplantation or solid-organ transplant .. HIV infection.

- **Clinical presentations**: Fungal respiratory infections are non-specific .. often overlap with other infectious and non-infectious processes.. mostly without fever

- The causative agents can be opportunistic endogenous Yeast or exogenous **filamentous Fungi /Molds**
Yeast Form: Oral Candidiasis

- **Part of oral /intestinal/vaginal flora**... causes characteristic mucosa patches of a creamy-white to grey pseudomembrane composed of **Blastospores** and **Pseudohyphae**.

- **Candidiasis** often develop after long antibiotics treatment.

- Oral candidasis may spread... **Esophagus, Bronchi, Lungs, Gastro-intestinal tract**, or become systemic.. **Candidiaemia** may results in **endocarditis, meningitis**.

- **Systemic Candidiasis** is common in patients with cell-mediated immune deficiency, receiving aggressive cancer, immunosuppression, transplantation therapy.

- **C. albicans, C.glabrata, C. tropicalis, C. krusei**, 
1- Pseudohyphae, Blastospores, Chlamydospores
2- Oral Candida Trush
Candida Pseudohyphae with Blastospores-Gram-stain
Predisposing Factors for the Development of Candidiasis

- **Impaired epithelial barrier**: Burns, Wounds / abrasions, Hydration/maceration, Indwelling catheters, Foreign bodies (Dentures, etc), Increased gastric pH, Cytotoxic/ Antbiotics agents, Radiation

- **Systemic disorders**: Diabetes mellitus, Pregnancy/oral contraceptives, Malnutrition, Malabsorption, Iron deficiency.

- **Malignancy / Haematologic disorders**: Neutropnea / Leukemia, Lymphoma, advanced cancer, AIDS all immunodeficiency conditions.

- **Systemic treatment**: Fluconazole, amphotericin B, Caspofungin.

- **Local Ointment**: Nystatin, micronazole, clotrimazole
Yeast: Cryptococcosis

- Encapsulated *C. neoformans* cause a chronic, subacute - acute pulmonary, systemic or meningitic disease. Meningoencephalitis. Often isolated from Pigeon & Birds excreta.

- Primary pulmonary infections: Mostly pneumonia-like illness, with symptoms such as cough, fever, chest pain. Dissemination may include central nervous system. Lesions in brain, skin, bones and other visceral organs. Common significant opportunistic pathogens in immunodeficient humans, AIDS patients. Diagnosis: Culture + Antigens detection in Serum, CSF & Biopsy.
Cryptococcus detection by India ink test
Molds: Aspergillosis-1

- Most common *Aspergillus* species
  - *A. fumigatus*, *A. flavus*, *A. niger*.
- *Aspergillus* widely distributed in nature. Survive harsh environmental conditions. Found in all dead animal, plants, Grains, soil, spread via small spores that are extremely light and float easily in the air.

1) **Allergic Bronchopulmonary**: Presence of conidia or fungal filaments in lung tissues, Sinuses. Often associated with **Allergic reaction**. Eosinophilia. Asthma.

3) **Mycotoxicosis** due to ingestion of contaminated foods with fungal toxin *A. flavus*. Produce Aflatoxins. Liver cirrhosis. Death
Aspergillosis-2

3) **Pulmonary Aspergilloma** (Fungus Ball). Invasive Aspergillosis. Pre-existing lung cavity, inflammatory, granulomatous, necrotizing disease of lungs. May spread to other organs. Causing mostly Thrombosis. **Rhino-cerebral lesions** rarely systemic and fatal disseminated disease.

- **Treatment:** Fluconazole, Itraconazole, Caspofungin Amphotericin B.

Dimorphic Fungus: **Histoplasmosis-1**


- The primary site of infection is usually **Lung**. Inhalation dust with microconidia. Phagocytosed by macrophages, obligate intracellular parasites. Causing slight inflammatory reaction. Most cases of **histoplasmosis** are asymptomatic/subclinical, benign as Flu-like syndrome.

- Few may develop chronic **progressive lung disease**. Granuloma & fibrosis, chronic cutaneous or systemic disease involve any internal organ. **Fatal systemic disease**.

- All infected persons become positive by histoplasmin skin test.
Histoplasma capsulatum in infected White Blood cells

H & E stained peripheral blood smear of a patient showing the yeast phase of Histoplasma capsulatum within white blood cells. MMRC-UTMB 1996
**Coccidioidomycosis & Blastomycosis**


- Respiratory infection.. inhalation of microconidia, often resolves rapidly leaving the patient with a strong specific immunity to re-infection.

- Some individuals the disease may progress to a chronic pulmonary condition or a systemic disease involving the meninges, bones, joints, subcutaneous, cutaneous tissues.. Antigen Skin test positive.. Not significant in diagnosis.
Laboratory Diagnosis

- **Direct microscopy and culture** should be performed on all specimens (sputum, bronchial washings, CSF, pleural fluid tissue biopsies from various visceral organs).

- Wet mounts in 10% KOH with india ink. Ovoid-budding yeast cells (b) Gram-stain smear.

- Cultures on **Sabouraud dextrose agar** should be maintained for one month at 25C. Fungal growths & Wet Mount. Identification produces hyphae-like conidio-phores & Spores. Color of fungal growth

- **Serological tests** are of limited value. Not significant

- Detection of Histoplasm antigen in blood & urine is significant
Pneumocystis (carinii, Rats type)
P. jiroveci (Human type)

- Small Yeast like Cells ..No filaments or Capsules

- **Pneumocystis** infection occurs by inhalation contaminated dust .. It is commonly found in the lungs of healthy individuals. .without symptoms

- Asymptomatic Infection mostly started in children & increased in Adults .. Worldwide.

- Clinical Disease occurs only associated with both decrease of cellular immunity and humoral immunity, suppressed immunity .

- **Infectious trophic form** of the organism attaches to the lung alveoli.. Encyst & multiple in host tissues.
Pneumocystis-2

- **Clinical disease**.. *Pneumonia*. Organism is usually found in the interstitial fluid in the lungs, Lung tissue.. of *immunocompromised patients*. AIDS.. may disseminate to other internal body organs.. Associated with high mortality.

- Sputum /lung biopsy specimens are usually used for PC detection.

- **Silver – Giemsa-**, Stain.. Immunofluorescent **Antigen (IFA)**.. Treatment: *Cotrimoxazole* alone or with intravenous Pentamidine in sever cases.