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Medical Mycology
Fungi were discovered earlier than bacteria and viruses.

In the past, most fungi cause skin infections or cosmetic infections, where bacteria and viruses cause serious fatal diseases, so there was no interest of studying fungi.

In 1980, when HIV infection was discovered, increasing number of immunocompromizing conditions, they found that fungi produce fatal diseases; from that time, fungi return to be in focus again.
Medical Mycology

- It is the science that deals with the study of pathogenic fungi that produce diseases.
Fungi are eukaryotic organisms have true nuclei with definite nuclear membrane, nucleolus, cytoplasmic organelles.

- Amorphous glucans
- Glycoprotein + protein
- Chitin + protein*
- Plasma*

*at hyphal tip
Cell membrane of fungi has **sterols**, which is the target of action of antifungal agents. **Ergosterol** dominates in contrast to cholesterol in mammalian membrane.
Structure

- **Cell wall of fungi lacks:**
  - Peptidoglycan
  - Glycerol & ribitol teichoic acid
  - Lipopolysaccharide

- **Cell wall composed of:**
  - Chitin.
  - Glucan (important for new antifungal agent).
  - Mannan.
Fungal metabolism:

- All fungi are **heterotrophic** organism need to parasite or saprophyte (on plant, animal or human) to obtain organic source of carbon or nitrogen.
- All fungi are **aerobic**.
- Some are **facultative anaerobes**.
- None are **strict anaerobes**.
Fungal metabolism:

- Optimum temperature of growth **25 – 30 °C** (because most are saprophyte live in the environment).
- Some are **thermophilic**, and can grow at higher temperature.
- Fungi can tolerate a wide range of pH **(2 – 9)**, but generally they prefer **acidic** media.
Reproduction

Modes of vegetative reproduction in fungi.
Sexual reproduction:

• Involve the union of 2 nuclei or 2 sex cells or 2 sex organs.
Asexual reproduction:

- It is the **main** method of reproduction.
- It includes:
  - **Fragmentation** of hyphae & each fragment grows into a new individual fungus.
  - **Fission** of cell into 2 daughter cells (similar to binary fission in bacteria).
  - **Budding** of cells, each bud produce new individual (e.g. Candida).
  - **Formation of asexual spores**.
• A single fungus may contain **both** modes of reproduction (sexual and/or asexual).
Fungal Spores

- It is the method of reproduction in fungi unlike bacteria.

- Two types:
  1. Sexual
  2. Asexual
1) Sexual
Sexual reproduction

Spermatization

Spermatia

Receptive hypha

Somatogamy

Hyphae of opposite mating types
**Sexual:**

-Zygospore

zygospore is a special type of chlamydospore arising from sexual conjugation between two fungi.
Basidiospore
Ascospore formation
Oospore

female cell fertilized by male cell.
2) Asexual
2) Asexual:

- Thallospore:
  - Blastospores (by budding from thallus).
Thallospore:

- Arthrospores
Chlamydospores

- spores that arise from the thallus by pulling or swelling of mycelium filaments.
Some fungi during growth form sac filled with spores called sporangium.

Spores inside sporangium called sporangiospores.

Hyphae that carry this sporangium are called sporangiophore.

This sporangium when gets ripping, its wall will be broken and the spores disseminate.
Exogenous asexual spores:

- **Conidia:**
  - These are spores formed at the terminal part of a fertile hypha.
  - **Conidophore:** fertile hypha bearing conidia.

Diagram showing different types of conidia and macroconidia.
Microconidia

- Unicellular, asexual external spores.
Macroconidia:

- Multicellular,
Endogenous:

- **Normal flora** and it is the main source in nosocomial infection (because those people in hospitals are immunocompromized).
Source of infection (cont.):

- **Exogenous:**
  - This is the main source of fungal infection mainly from the environment.
  - Few fungal infections are communicable between human or between animals.
Mode of transmission:

- Respiratory tract (air borne infection).
- GIT (food & water borne infection).
- Blood stream injection.
- Skin = contact.
- Most fungal diseases are not communicable between human or animals.
Most fungi are opportunistic:

- Produce diseases in immunocompromized patients.
- Little is primary pathogen (cause disease in person with intact immune system).
Steps of infection:

• I. Adherence:
  – By adhesions, e.g. *Candida*, but filamentous fungi have no adhesions.
  – *Fibrinonectin* of epithelial cell is the receptors.
  – Virulence usually associated with adherence.
ii. Invasion:

- **Mechanical trauma** to skin or mucosal surface is an essential step in fungal infection, because most of the infective element in fungi is the spore and it is non-invasive.

- Some fungi have invasive power like Candida by the formation of hyphae and pseudohyphae.
iii. Phagocytic interactions:

- Some fungi especially dimorphic fungi show resistance to phagocytic killing.
- Some fungi are capsulated and can resist phagocytosis (Cryptococcus).
Immunity to fungal infections

- Innate immunity:
  - Non-specific works against all microorganisms.
Immunity to fungal infections (cont.)

- **Acquired immunity:**
The main immunity is cellular immunity because fungi stay inside the host cell. Antibodies have limited role in some fungal diseases.
Fungal Classification

a. According to morphology:
Moulds (Filamentous fungi):

- Grow with formation of hyphae, which may be septated or non-septated.
Moulds (Filamentous fungi):

– **Vegetative mycelium:**
  - Some hyphae will penetrate the media.
  - Some hyphae present at the surface of the media.

– **Aerial mycelium:**
  - Some hyphae may be directed upward & carry the different types of spores that produced by this fungus.
Yeasts

– **Unicellular** fungi (rounded or oval in shape).
– Reproduce by **budding**.
– The only example of pathogenic yeasts is **Cryptococcus neoformans**.
Yeast-like

- Unicellular fungi (rounded or oval in shape).
- Reproduce by budding.
- But during infection it produces **pseudohyphae**.
- Example: Candida.
Dimorphic fungi:

- Can grow as **yeast** during infection in the body & on incubating culture at 37 ºC.
- Can grow as **moulds** or filaments when inoculated at room temperature.
- Example: Histoplasma capsulatum.
Fungal Classification

B-According to nature of their sexual spores:
Phycomycetes (Zygomycetes):

- Sexual spores are of 2 types:
  - zygospores & oospores.
  - Usually non-pathogenic.
Ascomycetes

Sexual ascospores.

Some are pathogenic.
Basidiospores

- Sexual basidiospores.
- Non-pathogens.
Perfect or sexual state not present or not discovered, so can't be placed within one of the above three classes.

Most of pathogenic moulds, yeasts, yeast-like and dimorphic fungi belong to this group.

**Fungi imperfecti**

- **Kingdom Mycota**
  - Sexual reproduction not identified:
    - Fungi Imperfecti or Dueteromycetes, e.g., Cercospora Fusarium
  - Sexual reproduction identified:
    - Primitive Fungi Oomycota (Mycelium Aseptate)
    - Advanced Fungi Eumycota (Mycelium Septate)

  - **Phycomycetes** (Algal Fungi), e.g., Phytophthora albugo
  - **Zygomycetes** (Conjugation Fungi), e.g., Mucor rhizopus
  - **Ascomycetes** (Sac Fungi), e.g., Yeast candida
  - **Basidiomycetes** (Club Fungi), e.g., Puccinia agaricus
Human mycosis terminology
A. Anatomical terminology
(According to the site of infection):

- Dermatomycosis: Fungal infection of the skin.
- Pulmonary mycosis: Fungal infection of the lung.
- Cardiovascular mycosis: Fungal infection of the cardiovascular system.
B. Mycological terminology (According to the etiology):

- **Candidiasis (= Candidiosis):** Fungal infection by Candida.

- **Aspergillosis:** Fungal infection by Aspergillus.

- **Cryptococcosis:** Fungal infection by Cryptococcus.

- **Histoplasmosis:** Fungal infection by Histoplasma.
Types of human mycosis
Infection restricted to uppermost **horny** layer of skin, hair and nails e.g. **Pityriasis versicolor**.
2 - **Cutaneous mycosis:**

- Ringworm fungi.
- Candidiasis of skin, mucosal surfaces.
3- Subcutaneous mycosis (Implantation mycosis):

- Most of fungi are **non invasive**.
- Occurs by implantation of spores into wounds.
- e.g. **Mycetoma** (madura foot), **thorn pricks** mycosis.
4- **Systemic mycosis:**

- Multi organs affected.

**Mode of infection:**
- Inhalation of spores of saprophytic fungi.
- Spread of local mycosis.

**Examples:**
- Cryptococcosis.
- Histoplasmosis.
- Candidiasis.
5- Opportunistic mycosis:

- **Fungal infection by:**
  - **Fungal** flora (Candida).
  - Saprophytic fungi in the environment (Aspergillus).

- **This infection occur in:**
  - Immunocompromised host (Both innate and acquired immunity).
  - Opportunistic conditions like:
    - Diabetic patients.
    - Cancer patients.
    - Corticosteroid & other immunosuppressive therapy (e.g. Cytotoxic drugs).
    - Prolonged antibiotic therapy.
Diagnosis of fungal infections
1. Direct Microscopic Preparation:

- A) Unstained preparation
- Important and rapid method of diagnosis of fungal infections.
- Scraping of lesion or bits of exudates (e.g. sputum, pus).
  - Put on clean slide.
  - Add drop of KOH (10–30\%).
  - Put cover slip.
  - Gentle heating for 5–10 minutes (not direct heating).
  - Examine by high power lens of the microscope.
  - Find diagnostic fungal elements.
1. Direct Microscopic Preparation:

- **b) Stained preparation:**

  - Rapid and easy.
  - Cover slip preparation (KOH) may be stained with Lactophenol cotton blue.
  - India ink preparation is used for demonstration of *Cryptococcus neoformans*.
  - Its positivity not more than 30%.
2. Culture for isolation of fungi:

- **Sabouraud`s dextrose agar (SDA):**
  - Composed of agar + dextrose + peptone.
  - Disadvantage: Bacteria can grow on it.
2. Culture for isolation of fungi:

- **SDA + Chloramphenicol (0.05%)**: Chloramphenicol is added to inhibit bacterial growth.
2. Culture for isolation of fungi:

- **SDA + Chloramphenicol + Cyclohexamide (0.5%)**: Cyclohexamide is added to inhibit the growth of saprophytic fungal contaminants.
2. Culture for isolation of fungi:

- **Blood agar:**
  - Some fungi as yeast, and yeast like (Candida and Cryptococcus) grow rapidly as bacteria after 4 weeks from incubation.
Growth is identified by:

- **Macroscopic characters**: e.g. colour from both sides (recto–verso examination), shape, size and texture of the colony.
- **Microscopic stained preparation**.
- **Biochemical reaction**: Sugar fermentation and assimilation (especially in yeast).
3. Microculture:

- Used to:
  - See whole morphological details of fungi.
  - Prevent disturbing fungal morphology.

- It has 2 types:
  - Direct evaluation of a culture in an open petri dish under the microscope.
  - Slide culture technique.
4. Histopathology:

**Yeast cells:**

- They may be intracellular small yeast: e.g. *Histoplasma capsulatum*.
  - They may have a large distinguishing capsule: e.g. *Cryptococcus*. 
4. Histopathology:

- **Spherules:**
  - Intact spherules are large **sac-like structure** filled with **sporangiospores**.

Left: A patient showing the disseminated stage of disease (coccidioidomycosis).
Top right: spherules.
Bottom right: chains of arthrospores interspersed with empty cellular compartments.
4. Histopathology:

- *Hyphae:*
  - They may be **brown** in colour or **non-coloured**.
  - They may be **septated** or **non-septated**.
4. Histopathology:

• **Granules:**
  – They are tightly packed masses of **hyphae or filaments**, which are surrounded by **tough outer rind**.
4. Histopathology:

- *Combination of yeast cells and hyphae:* As in Candida.
5. Woods light:

- Helps in clinical diagnosis.
- Long wave ultraviolet rays (black rays) which when come in contact with mycotic areas of skin and hair produce fluorescent colours.
- **Disadvantage:** it occurs in some mycotic infections only.
6. Indirect method of diagnosis:

• Detection of circulating antibodies (Serological diagnosis):
  • It has limited role.
  • Used in diagnosis and follow up of Cryptococcus and Candida with limits.
Tests used for detecting fungal antibodies:

Step 1
Microbial antigen is dried on a glass slide and treated with a chemical fixative.

Step 2
Dilutions of patient serum are incubated with the antigen on the slide, and then rinsed.

Step 3
A fluorescein-labeled antibody (conjugate) is added.
Fungal skin tests:

- It has **no value** in diagnosis.
- It does not differentiate between active and past infection.
- Mainly used for **epidemiological study**.
- It is observed by formation of **induration and swelling** due to reaction between injected antigen and T cells.
- *e.g.* Histoplasmin, Candidin, Tricophytin tests.
Antifungal therapy

• **Topical antifungals:**
  – Polyenes e.g. nystatin, fungizone
  – Azoles (e.g. miconazole, Ketoconazole, econazole, clotrimazole).
  – Miscellaneous e.g. tolanftate, allylamine, iodine.
Systemic antifungals:

- **Polyenes** (e.g. Amphotericin-B).
- **5-flucytosine.**
- **Azoles** (e.g. itraconazole, fluconazole).
- **Terbinafine.**
- **Griseofulvin**
- **Iodine.**

**New antifungal**

- Echinocandins e.g. caspofungin
- New triazole e.g. voriconazole
Mechanism of action of antifungal

Cell membrane
Polyenes
Azoles

Nucleic acid synthesis
5-Flucytosin
Griseofulvin

Cell wall
Cuspofungin
1) Polynes

- Bind to **ergosterol** in the fungal cell membrane → altered permeability → leakage of $K^+$, $Mg^{++}$, Sugar → Cell death
- It is **fungicidal**, has broad Spectrum usage until now
- **Hepatotoxic** and **nephrotoxic**
- **Lipid preparations** (as liposomal amphotericin-B) are more tolerable and less toxic.
2) Azole

- Inhibits ergosterol biosynthesis via binding to cytochrome p-450 dependent enzyme 14α demethylase → accumulation of 14α sterol → depletes sterols.

- Hepatotxic, spermatogenesis inhibitor so its usage restricted

- Fluconazole crosses blood brain barrier so used in treatment of cryptococcal meningitis.
3) Criseofulvin

- Exact mechanism is unknown
- Inhibit nucleic acid synthesis
- Have antimitotic activity by inhibiting microtubules assembly "microtubules called cytoskeleton that support shape, transport of substrates of eukaryotic cell"
- Inhibit synthesis of cell wall chitin.
4) 5- Flucytosin:

- Deaminated in cell to **5- fluorouracil**, which replace uracil base in RNA → **disruption of protein synthesis.**
How to select proper antifungal drug?

- We can select proper antifungal drug via susceptibility testing method e.g.
- *Broth dilution method*
- *Agar diffusion method*
I. Superficial fungal infection
A. Ring worm fungi
(Tinea = dermatophytosis)

**Dermatophytosis**

- Fungal infection by dermatophytes of keratinous structures (skin, hair, nails)
A. Ring worm fungi

Common clinical types:

1. Tinea Corporus:

- Dermatophyte infection of the **glabrous** skin (**trunk, back, dorsum of the hand**).
Fungal infection of the skin of the scalp and hair.

This takes 3 forms of hair involvement:

• a) **Endothrix:**
  – There is abundant fungus growth inside the hair shaft.

• b) **Ectothrix:**
  – The spores surround the hair shaft from outside lead to weakness and falling of the hair.

• c) **Favic type:**
  – Some fungal mycelia are present inside the shaft with air space.

**A. Ring worm fungi**

**Common clinical types:**

2. **Tinea Capitis:**

Fungal infection of the skin of the scalp and hair.

This takes 3 forms of hair involvement:

• a) **Endothrix:**
  – There is abundant fungus growth inside the hair shaft.

• b) **Ectothrix:**
  – The spores surround the hair shaft from outside lead to weakness and falling of the hair.

• c) **Favic type:**
  – Some fungal mycelia are present inside the shaft with air space.
A. Ring worm fungi

Common clinical types:

3. Tinea Barbae:

- Fungal infection of the beard and moustache skin area in male.
Ring worm of the foot. It is an infection of the feet or toes with dermatophyte fungus, which includes the soles, nails and interdigital peeling.

- A. Ring worm fungi

Common clinical types:

4. Tinea Pedis (Athlete's foot):
A. Ring worm fungi
Common clinical types:

5. Tinea Manum:

– Fungal infection of the palm of the hand and inter-digital areas.
A. Ring worm fungi
Common clinical types:

7. Tinea cruris

— Fungal infection of the crural area and perineum.
A. Ring worm fungi

Common clinical types:

7. Tinea Unguim:

— Fungal infection of the nail of the hand.
Epidemiology

According to the source of infection
1- Anthroprophilical:

- From human to human.
- e.g. Epidermophyton flocosum.
2- Zoophilic:

– From animal to human.
– e.g. **Microsporum canis**.
3- Geophilic:

– Spores found in soil.

– e.g. Microsporum gypseum.
Pathogenesis:

1. Infective stage is **arthrospore** of fungus or keratinous material containing fungus element.
2. Needs **direct or indirect contact** (indirect by the use of the same items of the patient).
3. Need slight **trauma**.
4. Active infection restricted to the **basal keratinocytes of the epidermis**.
Dermatophytes include 3 genera:

- 1. Epidermophyton. e.g. E. flocosum.
- 2. Trichophyton. e.g. T. rubrum.
- 3. Microsporum. e.g. M. canis.
Diagnosis of dermatophyte infection:
Diagnosis of dermatophyte infection:

2. Wood's light (negative result doesn't exclude fungal infection).
3. Direct examination by KOH preparation:
   Diagnostic element in skin & nail is the septated hyphae and arthrospores.
   Diagnostic element in hair is the endothrix, ectothrix or favic.
Diagnosis of dermatophyte infection:

4. Culture:

- On Sabouraud's dextrose agar with chloramphenicol & actidion (cyclohexamide).
- Dermatophyte test medium that is yellow in colour (if turned red, this indicate positive test).
Macroscopic examination.

Microscopic examination: In order to differentiate between the three genera of dermatophytes according to the type of macroconidia present.
Microsporum: Spindle shape, multicellular with rough surface.
Diagnosis of dermatophyte infection: 
**Growth is examined by:**

Epidermophyton: 
Clup shape (racket) with smooth surface.
Diagnosis of dermatophyte infection:

Growth is examined by:

**Trichophyton:**

- pencil shape with smooth surface.
Treatment

• **A. Systemic agents (oral):**
  - Griseofolvin (drug of choice).
  - Itraconazole.
  - Allylamine (Lamisil).
  - Ketoconazole (not used now).
• **B. Topical agents:**
  - White field.
  - Clotrimazole (Canesten).
  - Miconazole (Daktarin).
• **Prophylaxis against Tinea pedis:**
  • Keep the feet dry.
  • Rub between toes by dry piece of gauze & alcohol.
B. *Pityriasis versicolor* (Tinea versicolor)
**Pityriasis versicolor**

**Definition:**

- Chronic superficial fungal infection of the **upper most** horny layer of the epidermis.
- Main area affected is the **trunk** but it can appear in any site of the skin.
- Infection causes nothing except **loss of the normal skin pigmentation** may result in hypo- or hyper-pigmentation (blotchy appearance).
Etiology:

—Caused by yeast flora called *Pityrosporum orbicularis*. 
Diagnosis:

- Direct microscopic examination of skin scrapping by KOH preparation.
- Diagnostic element is short angular hyphae & yeast cells (spaghetti & meat ball appearance).
Treatment:

- Any topical azole is effective (e.g. Miconazole, Clotrimazole).
- If the infection is recurrent or widely diffused in the trunk: Selenium blue Shampoo (1% selenium sulfide).
Candidal infection
Source of infection:

- **Endogenous**: (autoinfection): Present as normal flora in oral cavity, GIT, female genital tract and skin which is the major source of infection.

- **Exogenous**: By sexual intercourse.
Pathogenesis and virulence factors:

- **Adhesin**: Colonization on the mucosal surface.
- **Pseudohyphae**: Inflammation and tissue destruction.
- **Protease enzyme**: Invasion.
- **Endotoxin like**: Releasing of histamine leading to clinical reaction.
- **Resistance to intracellular killing of phagocytes**.
Predisposing factors:

- Extreme of age.
- Pregnancy and diabetes.
- Prolonged use of antibiotics, steroids or immunosuppressive drugs.
- Traumatic conditions such as catheter or IV lines.
Immunity:

- Cell mediated.
- Humoral immunity has a limited role.
Causative agents:

- **Candida albicans.**
- **Non-albicans Candida:**
  - Candida tropicalis.
  - Candida glabarata (doesn’t cause pseudohyphae).
Clinical manifestations of diseases caused by Candida:

- **Mucocutaneous infection:**
- **Oral thrush:** In the mouth (cheesy covering layer), mouth angles: (stomatitis), at the lips (cheilitis).
- **Vaginitis:** White-milky discharge and itching.
Clinical manifestations of diseases caused by Candida:

**Cutaneous infections:**

- **Skin:** Napkin area in baby, axilla, groin, submammary folds, characterized by **Satellite lesions**, redness, itching and red follicles.
- **Nail:** Onychia and paronychia.
Clinical manifestations of diseases caused by Candida:

**systemic infections:**

- Urinary tract infection.
- Endocarditis.
- Meningitis.
- Septicemia, fungemia.
Laboratory diagnosis of Candidiasis:
A. Direct:

1. **Microscopic examination:**
   - Unstained preparation or stained preparation (KOH) **lactophenol-cotton blue** stains.
   - For detection of **yeast cells** and **pseudohyphae**.
2. Culture:

– On SDA medium.
– The suspected growth is identified by:
  
  • **Macrosopic appearance** of the colonies after 24 – 48 hours are white, smooth, creamy and have characteristic yeast odour.
2. Culture:

- **Microscopic appearance**: Spherical or oval cells.
  - Gram film shows Gram-positive yeast.

- **Microculture**: Rice agar tween plates for demonstration of chlamydomospores (in C. albicans).
2. Culture:

- The suspected growth is identified by:
  - **Biochemical reactions**: Sugar fermentation and assimilation for species differentiation.
  - **Germ tube formation**: The ability of Candida to form filamentous growth after 2 – 4 hours when cultivated on human serum at 37ºC (in C. albicans).
  - **Chlamydospores formation** on Potato Carrot Bile (PCB) medium (in C. albicans).
• **B. Indirect:**

• **1. Skin test:** No value in diagnosis.

• **2. Serological test:**
  – Ag detection: Important in immunocompromized patients.

• **3. Histopathology:**
  – Diagnostic element is Yeast cell & Pseudohyphae.

• **4. New tests for diagnosis:**
  – Detection of β-glucan antigen.
  – D-arabinol marker.
  – PCR.
  – Biofilm by scanning electron microscope.
Treatment:

1. Superficial:
   - Topical polyene, nystatin & amphotericin B.
   - Topical imidazole as micronazole, clotrimazole.

2. Deep systemic infection:
   - Amphotericin B.
   - Fluconazole, Itraconazole.
   - Caspofungin.
   - Lipid preparation; liposomal Amphotericin B.
II. Subcutaneous Mycosis
A. Mycetoma
(Madura foot = Maduromycosis)
Definition:

- Chronic granulomatous infection, which produce tumour-like lesion and sinus tract formation, with the presence of pus containing granules affecting foot, SC tissue, fascia and bone.
A. Mycetoma (Madura foot = Maduromycosis)

Etiology:

(1) Bacterial:

– Actinomycotic (Actinomadura, Nocardia, Streptomyces).

– The granules contain very fine delicate filaments.

– Usually the pyogenic abscess has one tract.
A. Mycetoma

Etiology:

(2) Fungal (Eumycotic):

– Most saprophytic fungi can produce mycetoma e.g. Madurella.

– The granules contain large coarse septated hyphae.

– Usually the lesion has many sinuses.
A. Mycetoma
Diagnosis:

KOH preparation.
If it is: Bacterial:
Fine branching filament.
Eumycotic: Coarse septated hyphae.
### A. Mycetoma

**Treatment:**

- **Bacterial (Actinomycotic):**
  Antibacterial antibiotic.

- **Eumycotic:**
  - Amputation of the affected part.
  - Antifungal agents can be used to prevent the amputation or to minimize it e.g. Itraconazole, Amphotericin B.
B. Sporotrichosis
B. Sporotrichosis

Definition

- **Subcutaneous** fungal infection, characterized by mobile tender **nodules** forming **ulcer**, may be followed by **chronic** sporotrichosis in the form of **multiple** hard nodules along lymphatic channels.
B. Sporotrichosis

**Etiology:**

- *Sporothrix schenckii* (A dimorphic fungus).
B. Sporotrichosis

**Diagnosis:**

1. **Sample:** Exudates from lesion or LN aspirate.

2. **Direct film:**
   - In pus: Cigar shaped yeast.
   - In tissue: Asteroid body (fungus surrounded by eosinophilic infiltration).
B. Sporotrichosis

Diagnosis:

3. Culture:
   - At 37 °C on enriched media giving **gray** colonies.
   - Identified microscopically as Gram-positive **cigar shaped budding yeast**.
   - At 27 °C on Sabouraud`s dextrose agar: **wrinkled white to black colonies.**
     Identified microscopically as **branching septated hyphae carry pyriform conidia**.
III. Systemic Mycosis
The organism is **misnamed** because infection is not in the plasma cells but in the **macrophages**, and it is **not capsulated**.

A. *Histoplasma capsulatum*
A. *Histoplasma capsulatum*

Microbiological characters:

1. **Dimorphic fungi:**
   - i.e. two morphological forms:
   - **Yeast:** during infection and cultures at 37 ºC
   - **Mould:** in cultures at 25 ºC produce *microconidia* and *macroconidia* with septated hyphae.

2. Smallest yeast cell, reproduce by budding.

A. Histoplasma capsulatum

Pathogenesis:

- Infection of reticuloendothelial system and grow intracellularly in phagocytic macrophage.
- Primary lesion is in the lung, which leads to calcified nodule and positive Histoplasmin skin test.
- **Immunity:** Cell-mediated immunity.
A. Histoplasma capsulatum

**Epidemiology:**

- **Restricted** geographical distribution.
- Source of infection: **Soil** containing bird or bat droppings.
- No case-to-case transmission.
A. Histoplasma capsulatum

**Clinical picture:**

**Asymptomatic** or respiratory infection giving flue like symptoms in immunocompetent patient.

**Chronic lesion** in lungs leads to tuberculosis like picture.

**Disseminated infection:** appears as febrile illness and enlargement of reticuloendothelial organs.
A. Histoplasma capsulatum

Diagnosis:

- **Direct examination** of sputum is useless as the organism present in few numbers.
- **Histological examination** of bone marrow to demonstrate intracellular yeast in macrophages.
- **Culture**.
- **Serology**.
- **Skin test**: Histoplasmin test; of epidemiological value only.
A. Histoplasma capsulatum

**Treatment:**

• Amphotericin B, followed by itraconazole.
B. Cryptococcus neoformans
B. Cryptococcus neoformans

Morphology:

- Capsulated yeast.
- Urease positive.
B. Cryptococcus neoformans

Pathogenesis:

- Infection occurs by inhalation of spores of cryptococcus, which lead to pulmonary infection.
- Most infection is unrecognized and self-limiting.
- Capsule is the determinant of virulence.
- Immunity:
  - Cell-mediated immunity (in immunocompromized patients).
  - Humoral (opsonizing antibodies against capsule).
B. Cryptococcus neoformans

**Epidemiology:**

– One of the *opportunistic mycosis*.
– Source of infection: *Pigeon or birds* droppings and *soil* contaminated with them.
– Human infection mostly *by inhalation*.
– No case-to-case transmission.
B. Cryptococcus neoformans

Clinical picture:

- Pneumonia, infection starts in the lung.
- Then followed by meningitis.
- In heavy infection disseminated skin and bone infections occur.
B. Cryptococcus neoformans

Diagnosis:

– **In Cryptococcus meningitis:**
  – CSF:
    ✷ Increased pressure of CSF.
    ✷ Decreased glucose and increased protein.
    ✷ Increased cell count > 100, mostly lymphocytes.
    ✷ India ink preparation: yeast cell surrounded by huge capsule.
  – **Culture** and identification of growth.
  – Detection of Cryptococcus antigen in CSF by latex agglutination.
B. Cryptococcus neoformans

Treatment:

• **Amphotericin B**, followed by **fluconazole** (Can cross blood brain barrier).
C. Aspergillosis
C. Aspergillosis

– It is the fungal infection by Aspergillus spp.
– It is a *saprophytic* organism.
– Produces *spores* carried by air.
– Aspergillosis can be produced in immunocompromized patients as well as immunocompetent persons.
C. Aspergillosis
Causes:

– *A. fumigatus*, *A. niger*, and *A. flavus*. 
C. Aspergillosis

Clinical forms:

- **Granulomatous lesion:** Chronic infection in the lung.
- **Fungal ball in old TB cavity (Aspregilloma):** Mass formation in the lung, which may be mistaken with bronchogenic carcinoma.
  - **Allergic type:** Asthma and farmer's lung.
- **Acute pneumonia** in immunocompromized patients.
C. Aspergillosis

Mode of transmission:

- Environmentally by inhalation of spores.
C. Aspergillosis

Diagnosis:

• KOH preparation of sputum:
  Hyaline, septated hyphae or dichotomously branched hyphae.

• Culture on SDA and examination of growth by:
  – Macroscopically: Black (A. niger), green-orange or white colonies.
  – Microscopically: septated filaments with characteristic aspergillar heads.
C. Aspergillosis

Treatment:

– Antifungal drugs in disseminated lesions like: Amphotericin B, Itraconazole, Voriconazole.

– Surgical removal of fungal ball.
Mycotoxicosis
Fungi can generate substances with direct toxicity for humans and animals.

Ingestion of these toxins leads to mycotoxicosis, the severity depends on the amount and type of ingested mycotoxin.
Mycotoxicosis

General criteria of mycotoxicosis:

• Non-transmissible.
• No effect of antifungal drugs.
• Seasonal.
• Associated with food ingestion.
• The degree of toxicity depends on many host factors.
• Examination of the food reveals fungal growth.
Mycotoxicosis
Types of mycotoxins:

– There is a large number of mycotoxins according to the fungus producing it. e.g. aflatoxin, ochratoxin, amatoxin, and phallotoxin.
Mycotoxicosis

Aflatoxin:

– Produced by **Aspergillus flavus**.

– Effects of aflatoxins on man:

  • **Initiate liver cell carcinoma** (Its metabolite binds DNA preventing base pairing leading to frame shift mutation).

  • **Immunosuppression**.

  • **Gastroenteritis**.
Thank you