DISEASES OF FUNGAL ORIGIN
• Fungi are eukaryotes with cell walls that give them their shape.

• Fungal cells can grow as a multicellular filaments called moulds or as single cells or chains of cells called yeast.
Most yeasts reproduce by budding.

Some yeasts such as Candida albicans produce buds that fail to detach and become elongated, producing a chain of elongated yeast cells called pseudo hyphae.
Structure

• The main body of most fungi is made up of fine, branching, usually colourless threads called **hyphae**.

• An individual fungus filament is called **hypha**

• Several of these these hyphae, all intertwining to make up a tangled web called the **mycelium**

• One major difference is that most fungi have cell walls that contain **chitin**, unlike the cell walls of plants, which contain **cellulose**.
Fungal spores enters through respiratory tract
MORPHOLOGICAL CLASSIFICATION

• A) MOLDS—THEY ARE HYphae IN FORM  Eg..RINGWORM OR DERMATOPHYTES.

• B) YEASTS—SINGLE CELL THAT BUD TO REPRODUCE  Eg. CRYPTOCOCCUS NEOFORMANS.

• C) YEAST LIKE –FORM PSEUDO HYphae  EG.. CANDIDA ALBICANS.

• D) DIMORPHIC FUNGI—FUNGI HAVING YEAST FORM IN TISSUE AND MOULD IN CULTURE EG..BLASTOMYCES DERMATITIDES.
Fungal diseases are classified into 4 groups:

ACCORDING TO PATHOGENICITY:

- Superficial mycoses
- Mucocutaneous mycoses
- Subcutaneous mycoses
- Deep mycoses/SYSTEMIC MYCOSIS
Superficial And Cutaneous Mycoses!!

common and limited to the very superficial or keratinized layers of skin, hair, and nails.

- Piedra – colonization of the hair shaft causing black or white nodules
- Tinea nigra – brown or black superficial skin lesions
- Tinea capitis – folliculitis on the scalp and eyebrows
SUPERFICIAL MYCOSES

• Favus – destruction of the hair follicle.

• Pityriasis:
  • dermatitis characterized by redness of the skin and itching:
CUTANEOUS AND MUCOCUTANEOUS MYCOSES

• Associated with:
  • Skin
  • Eyes
  • Sinuses
  • Oropharynx and external ears
  • Vagina
CUTANEOUS AND MUCOCUTANEOUS MYCOSES

- Ringworm – skin lesions characterized by red margins, scales and itching.
- onychomycosis – chronic infection of the nail bed
  Commonly seen in toes
- Hyperkeratosis – extended scaly areas on the hands and feet
..CUTANEOUS AND MUCOCUTANEOUS MYCOSES
- **Mucocutaneous candidiasis** – colonization of the mucous membranes
  - Caused by the yeast *Candida albicans*
  - Often associated with a loss of immunocompetence
  - Thrush – fungal growth in the oral cavity.
  - Vulvovaginitis – fungal growth in the vaginal canal
    - Can be associated with a hormonal imbalance
SUBCUTANEOUS MYCOSES

• Localized primary infections of subcutaneous tissue: involve lymphatics and rarely disseminate

Can cause the development of cysts and granulomas.
...SUBCUTANEOUS MYCOSES

types:

• Sporotrichosis – traumatic implantation of fungal organisms.

• Paranasal conidiobolae mycoses – infection of the paranasal sinuses
  • Causes the formation of granulomas.

• Zygomatic rhinitis – fungus invades tissue through arteries
  • Causes thrombosis
  • Can involve the CNS.
• Deep mycoses Usually seen in immunosuppressed patients with:
  • AIDS
  • Cancer
  • Diabetes

• Can be acquired by:
  • Inhalation of fungi or fungal spores
  • Use of contaminated medical equipment

• Deep mycoses can cause a systemic infection – disseminated mycoses

• CAN DISSEMINATE TO SKIN!!!!
DEEP MYCOSES
DEEP MYCOSES

• Coccidiomycoses – caused by genus *Coccidioides*.

• Primary respiratory infection.
• Leads to fever, erythremia, and bronchial pneumonia.
• Usually resolves spontaneously due to immune defense.
• Some cases are fatal.
DEEP MYCOSES

- Histoplasmosis – caused by *Histoplasma capsulatum*
  - Often associated with immunodeficiency.
  - Causes the formation of granulomas.
  - Can necrotize and become calcified.
  - If disseminated can be fatal.
• Aspergillosis – caused by several species of *Aspergillus*
  • Associated with immunodeficiency.
  • Can be invasive and disseminate to the blood and lungs
    • Causes acute pneumonia
  • Mortality is very high.
    • Death can occur in weeks.
Fungal Diseases of medical importance

- Candidiasis.
- Dermatomycoses
- Respiratory Fungal Infections
Candidiasis

Etiological agent: *Candida albicans*

- Dimorphic fungus of the class Deuteromycetes.
- Grows as yeast or pseudohyphae.
- Spread by contact; often part of normal flora.
- Opportunistic infections common. Vulvovaginitis.
- Oral candidiasis (thrush).
- Intestinal candidiasis.
Candidiasis

• Residing normally in the skin, mouth, gastrointestinal tract, and vagina.

• **DIABETICS AND BURN PATIENTS** susceptible to superficial candidiasis.

• Severe disseminated candidiasis.

• Commonly occurs in patients who are neutropenic due to Leukemia, Chemotherapy, Or Bone Marrow Transplantation, and may cause shock and DIC.
Types of candidiasis

Oral candidiasis (Thrush).
Perlèche (Angular cheilitis).
Candidal vulvovaginitis.
Diaper candidiasis.
Congenital cutaneous candidiasis.
Perianal candidiasis.
Candidal paronychia.
Erosio interdigitalis.
Chronic mucocutaneous candidiasis.
Systemic candidiasis.
Antibiotic candidiasis (iatrogenic candidiasis)
The Vicious Cycle

1. Infection
2. Antibiotics
3. Wipe out friendly bacteria
4. Toxins
5. Weaken the immune system
6. Candida
7. Infection

This cycle continues, affecting the immune system and promoting the growth of toxins and candida.
OPPORTUNISTIC INFECTION BY CANDIDA ALBICANS IN AN AIDS PATIENT
• commonly candidiasis takes the form of a superficial infection on mucosal surfaces of the oral cavity (thrush):

• Clinical features Oral thrush:
  it is a sore mouth, shows white curd like patches of the fungus on the oral mucosa and tongue, which can be scrapped away leaving a raw, tender, bleeding surface behind
found in!!

- Newborns.
- Debilitated people.
- Children receiving oral steroids for asthma.
- Following a course of broad-spectrum antibiotics that destroy competing normal bacterial flora.

- Major risk group includes HIV-positive patients; people with oral thrush for no obvious reason should be evaluated for HIV infection.
• **CANDIDA ESOPHAGITIS**.
  - seen in AIDS patients and in those with hematolymphoid malignancies.
  - present with dysphagia (painful swallowing) and retrosternal pain;
  - endoscopy demonstrates white plaques and pseudo membranes resembling oral thrush on the oesophageal mucosa.

• **CANDIDA VAGINITIS**.
  - common form of vaginal infection in women, especially diabetic, pregnant, or who are on oral contraceptive pills. usually associated with intense itching and thick, curd like discharge.
CUTANEOUS CANDIDIASIS.

- present in infection of the nail ("onychomycosis").
- nail folds ("paronychia")
- hair follicles ("folliculitis")
- moist skin such as armpits or webs of the fingers and toes ("intertrigo"), and penile skin ("balanitis")

- "Diaper rash" is a cutaneous candidial infection seen in the perineum of infants, in the region of contact with wet diapers.
• Invasive candidiasis:
caused by blood-borne dissemination of organisms to various tissues or organs.

• Common patterns include:
  (1) renal abscesses
  (2) (2) myocardial abscesses and endocarditis.
  (3) brain micro abscesses and meningitis,
  (4) endophthalmitis (virtually any eye structure can be involved).
  (5) hepatic abscesses.
TREATMENT!!

Oral and vaginal candidiasis:

1. Topical antifungal agents falls into two groups:
   Polyenes: Amphotericin B, nystatin. Imidazoles: Clotrimazole, Miconazole, econazole

2. Systemic antifungal agents are both triazoles: Flucanazole, itraconazole
Dermatomycoses

- Dermatomycoses are any fungal infection of the skin or hair.

- Caused by many different species and are generally named after the infected area rather than the species that causes it.
DERMATOMYCOSIS/TINEA/RINGWORM

Cause: Several genera of dermatophytic fungi:

- *Trichophyton*.
- *Microsporum*.
- *Epidermophyton*.
- Grow on skin, hair, nails
- Transmitted by contact with infected persons or animals.
Tinea infections: Red, scaly or blister-like lesions; often a raised red ring; “ringworm”

- Tinea pedis
- Tinea corporis
- Tinea capitis
- Tinea barbae
- Tinea cruris
- Tinea unguium
body ringworm Generally restricted to stratum corneum of the smooth skin. Produces concentric or ring-like.

Fungi thrive in warm, moist areas.

RISK FACTORS:

• Long-term wetness of the skin (such as from sweating).
• Minor skin and nail injuries.
• Poor hygiene.
• can spread, by direct contact with an area of ringworm or if you touch contaminated items such as:
  • Clothing.
  • Combs.
  • Pool surfaces.
• also spread by pets (cats are common carriers).
Tinea Corporis

**Symptoms:**
MAY INCLUDE ITCHING.

- The rash begins as a small area of red, raised spots and pimples.
- The rash slowly becomes ring-shaped, with a red-colored, raised border and a clearer center. The border may look scaly.
- The rash may occur on the arms, legs, face, or other exposed body areas.
Treatment

• **TOPICAL THERAPY:** should be applied for at least 2 weeks.

• Topical azoles and allylamines high rates of clinical efficacy.

• These agents inhibit the synthesis of ergosterol, a major fungal cell membrane sterol.

• **SYSTEMIC THERAPY:** may be indicated for tinea corporis in extensive skin infection. immunosuppression, resistance to topical antifungal therapy.
Tinea Cruris

- Tinea cruris, a pruritic superficial fungal infection of the groin and adjacent skin.

- second most common clinical presentation for dermatophytosis.

Tinea cruris is a contagious infection transmitted by:

fomites, or by autoinoculation from a reservoir on the hands or feet (tinea manuum, tinea pedis, tinea unguinum.)
Tinea Pedis

dermatophyte infection of the soles of the feet and the interdigital spaces.
commonly caused by *Trichophyton rubrum*, a dermatophyte.

- The fungus thrives in warm, moist areas.

Risk factors.
- Wear closed shoes, especially if they are plastic-lined
- Feet wet for prolonged periods of time
- Sweat a lot.
- Develop a minor skin or nail injury.
- Athlete’s foot is contagious, and can be passed through direct contact, or contact with items such as shoes, stockings, and shower or pool surfaces.
Symptoms

• The most common symptom is cracked, flaking, peeling skin between the toes or side of the foot.

Other symptoms:
• Red and itchy skin
• Burning or stinging pain
• Blisters that ooze or get crusty
• If the fungus spreads to your nails, become discolored, thick, and even crumble.
• Athlete’s foot may occur at the same time as other fungal skin infections such as ringworm or jock itch.
Tinea Pedis Treatment

• Tinea pedis can be treated with topical or oral antifungals or a combination of both.

• Topical agents are used for 1-6 weeks.
Tinea Versicolor

- A fungal infection of the skin caused by *Malassezia furfur*.

- characterized by finely desquamating, pale tan patches on the upper trunk and upper arms that may itch and do not tan.

- In dark-skinned people the lesions may be depigmented.

- The fungus fluoresces under Wood's light and may be easily identified in scrapings viewed under a microscope.
Treatment:
Non pharmacologic therapy:
Sunlight accelerates repigmentation of hypopigmented areas.

Pharmacological treatment:

Topical treatment: selenium sulfide 2.5% suspension, applied daily for 10mts for 7 consecutive days.
Antifungal topical agents: miconazole, clotrimazole.
Oral treatment:
ketoconazole 200mg qd/5days or single 400mg- dose Fluconazole: 400mg single dose Triconazole: 200mg/od/5days
Onychomycosis

- Onychomycosis is a **fungal** infection of the toenails or fingernails.

- **Cause:** Onychomycosis causes fingernails or toenails to thicken, discolor, disfigure, and split.

- **Fingernail** infection may cause psychological, social, or employment-related problems.
Onychomycosis Symptoms & Signs

• usually symptomless unless the nail becomes so thick it causes pain when wearing shoes.

• As the nail thickens, onychomycosis may interfere with standing, walking, and exercising.

• Severe cases of Candida infections can disfigure the fingertips and nails.
Treatment of dermatophytes:

Dermatophytes can be treated either topically or systemically.

Commonly used topical agents:

I. Imidazoles: (clotrimazole, econazole, miconazole, sulconazole, and tioconazole) fungistatic

MOA: They inhibit C-14 α demethylase (a cytochrome p450 enzyme), thus blocking the demethylation of lanosterol to ergosterol, this disrupts membrane structure and function, and thereby inhibits fungal cell growth.
2. Terbinafine:

Drug of choice for treating dermatophytes especially onychomycosis.

MOA: terbinafine inhibits fungal squalene epoxidase, thereby decreasing the synthesis of ergosterol, and also the accumulation of toxic product amount of squalene results in death of fungal cell.
Griesofulvin; first orally administered treatment for dermatophytosis.

Dose: 500-1000mg daily, given in one dose or divided dose if required.

MOA: cause disruption of the mitotic spindle and inhibition of fungal mitosis.

Treatment for 6 to 12 months:

Duration of treatment: Skin or hair infection: 4-12 weeks.
Finger nail infection: 6 month.
Toe nail infection: more than one year.
Side effects of Treatment of dermatophytes:

Mild: headache, gastrointestinal side effects, hypersensitivity reaction

Moderate: exacerbation of acute intermittent porphyria, precipitation of SLE, Contraindicated in pregnancy
Ecological Groups of Dermatophytes
Geophilic

Species usually recovered from the soil. Occasionally infect humans and animals.
Anthropophilic fungi

- primarily parasitic to man.
- dermatophytes restricted to human hosts.
- produce a mild, chronic inflammation
• Zoophilic organisms found primarily in animals.
• cause marked inflammatory reactions in humans.
Respiratory Fungal Infections

Histoplasmosis

- *Histoplasma capsulatum*, an ascomycete
- Airborne infection
- Transmitted by inhalation of spores in contaminated spores
- Associated with chicken & bat droppings
- Respiratory tract symptoms; fever, headache, cough, chest pains
Respiratory Fungal Infections

Blastomycosis

- *Blastomyces dermatitidis*, an ascomycete
- Associated with dusty soil & bird droppings.
- Skin transmission: via cuts & abrasions.
- Raised, wart-like lesions.
- Airborne transmission: via inhalation of spores.
- Respiratory tract symptoms.
- Occasional internal infections with high fatality rate.
Respiratory Fungal Infections

Cryptococcosis

- *Cryptococcus neoformans*
- A yeast of class Basidiomycetes
- Soil; esp. contaminated with bird droppings
- Airborne to humans.
- Gelatinous capsules resist phagocytosis.
- Respiratory tract infections.
- Occasional systemic infections involving brain & meninges.
Cryptococcus neoformans is present in the soil and in bird (particularly pigeon droppings).

Morphology.
• Cryptococcus has yeast but not pseudohyphal or hyphal forms.
• The 5- to 10-μm Cryptococci yeast has a highly characteristic thick gelatinous capsule.
• Capsular polysaccharide stains intense red with periodic acid-Schiff and mucicarmine in tissues.
• Can be detected with antibody-coated beads in an agglutination assay.
India ink preparations create a negative image, visualizing the thick capsule as a clear halo within a dark background.

Although the lung is the primary site of infection, pulmonary involvement is usually mild and asymptomatic, even while the fungus is spreading to the CNS.
• The major lesions caused by C. neoformans are in the CNS, involving the meninges, cortical gray matter, and basal nuclei.

• the gelatinous masses of fungi grow in the meninges or expand the perivascular Virchow-Robin spaces within the gray matter, producing the so-called soap-bubble lesions.
CRYPTOCOCCUS MICROABSCESSES
Life cycle of *C. neoformans*
Can manifest with involvement of !!

• Skin.
• Mucosa.
• Organs...liver, spleen, adrenals.
• Bones.
• Disseminated form can mimic like Tuberculosis.
Laboratory Diagnosis.

- **CSF** Microscopic observation under India Ink preparation
- **Direct microscopy - Gram staining**
- Cultures on Sabouraud dextrose agar,
- Serological tests for detection of Capsular antigen
- CSF findings mimic like Tuberculosis
- IN CSF - latex test for detection of Antigen
- Blood cultures,
- ELISA
LABORATORY DIAGNOSIS OF FUNGAL DISEASE.

SPECIMEN COLLECTION:

- SKIN SCRAPINGS
  - Nail clippings/scrapings
  - Hair
  - Exudates
  - Biopsy materials.
  - Respiratory
  - Body fluids.CSF.
Laboratory Diagnosis of Mycoses

I. DIRECT EXAMINATION:

* 10-30% KOH
* Histological stains- H&E, PAS
* India Ink
* Wet mount
Laboratory Methods for Diagnosis of Mycoses

II. Isolation & Culture

SDA

Media with/without antibiotics

• Macroscopic examination of culture
• Microscopic examination
Laboratory Methods for Diagnosis of Mycoses

• III. Biochemical Tests:
  * Rapid kits for yeasts
  * Urea test

• IV. Special Tests:
  * In-vitro hair perforation test
    * Germ tube test
  * Chlamydoconidia formation test
V. SEROLOGICAL TESTS:

• LATEX AGGLUTINATION.
• CFT.
• PRECIPITATION