

Lecture 9 & 10

Fungi and their Pathogenesis, Diversity, and Fungal infection

- Additional Notes
- Important
- Explanation
- Examples

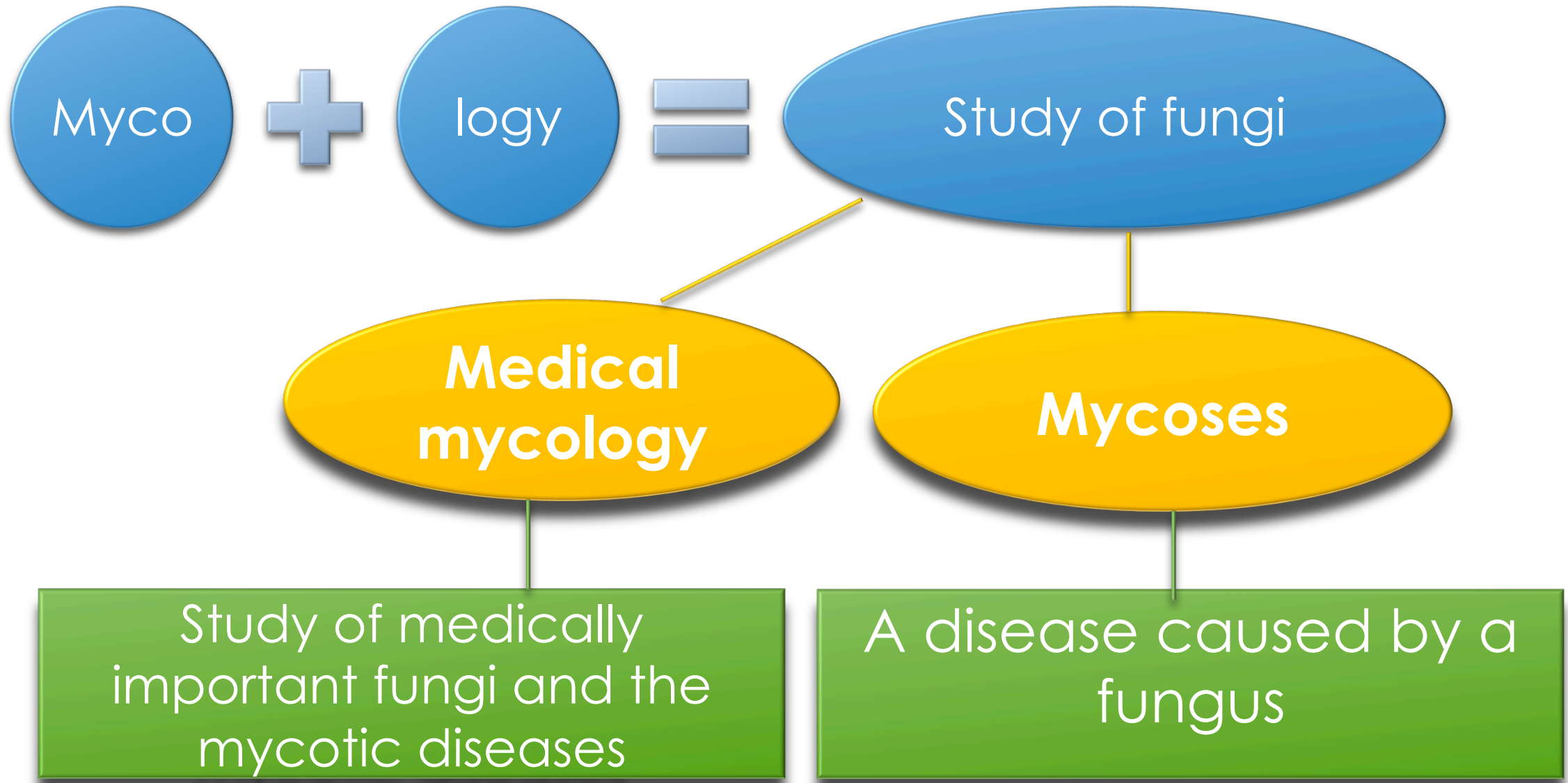
A special thanks goes to Sara AlKharashi for volunteering in doing these two lectures.



OBJECTIVES

- To describe the general characteristics of fungi and recognize a fungus from all other living organisms.
- To establish familiarity with the terminology needed by medical students.
- To know certain fundamental facts about classification reproduction and identification of fungi.
- To provide students with an overview of the common medically important yeasts and mold fungi.
- To provide the students with an overview of the major fungal diseases that threatens human health.
- To give a fundamental knowledge about the antifungal agents, their mechanisms of action, and spectrum.

WHAT IS MYCOLOGY?..



All Eukaryotic organisms
(a true nucleus)

The cell is surrounded by rigid cell wall made of

chitin

complex carbohydrates
(Mannan, glucan)

Characteristics of Fungus

Do not have chlorophyll

Cell membrane

sterol

ergosterol

Heterotrophic

Saprobic

symbiotic

parasitic

WHAT IS A FUNGUS ?

- ✓ **Saprobic** ; feed on dead tissues or organic waste (decomposers)
- ✓ **Symbiotic** ; mutually beneficial relationship between a fungus and another organism
- ✓ **Parasitic** ; feeding on living tissue of a host. (disease)

MORPHOLGY

Yeasts	Filamentous fungi (Hyphae, mycelium)	Dimorphic	
are unicellular organisms	Hyphae are multicellular filamentous structures, constituted by tubular cells with cell walls.	Have two forms depending on change in the environmental factors mold form \leftrightarrow yeast form	
		Yeast	Filamentous
		Parasitic form, Tissue form, Cultured at 37° C	Saprophytic form, Cultured at 25 C

yeast

morphology

Reproduction

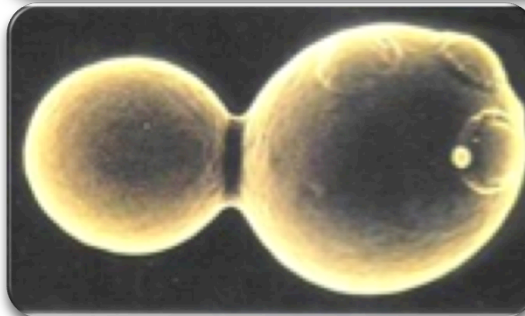
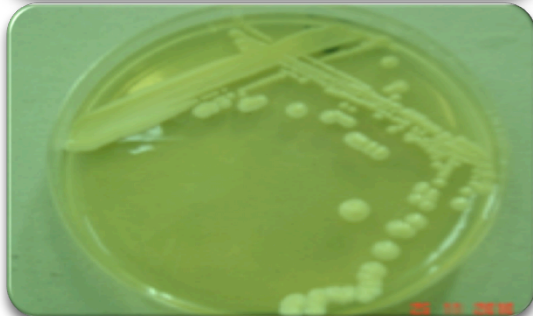
Example

Colony

Asexual;
budding

- *candida albicans*,

- *Saccharomyces cerevisiae*



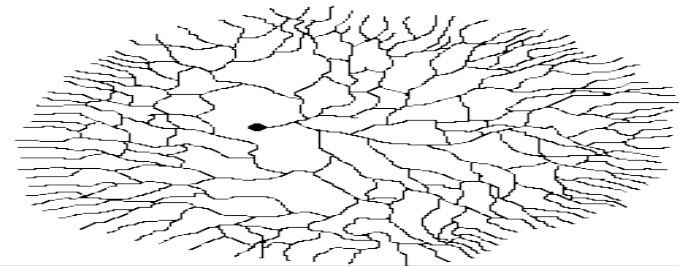
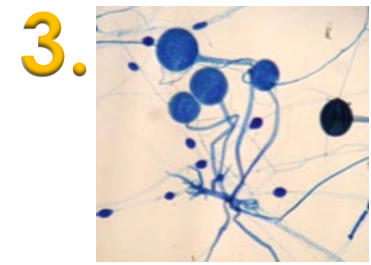
Only mitotic
cell division
Somatic

Filamentous fungi (Mold fungi)

- ✓ **hypha** (plural *hyphae*): is a long, branching filamentous cell, and the main mode of vegetative growth.
- ✓ **Mycelium**: The intertwined mass of hyphae that forms the fungal colony.
- ✓ **Conidia/ Spore** (singular = *conidium*): asexual spores borne externally on hyphae or on a conidiophore.

- ✓ **Examples:**

1. *Aspergillus*,
2. *Penicillium*,
3. *Rhizopus*



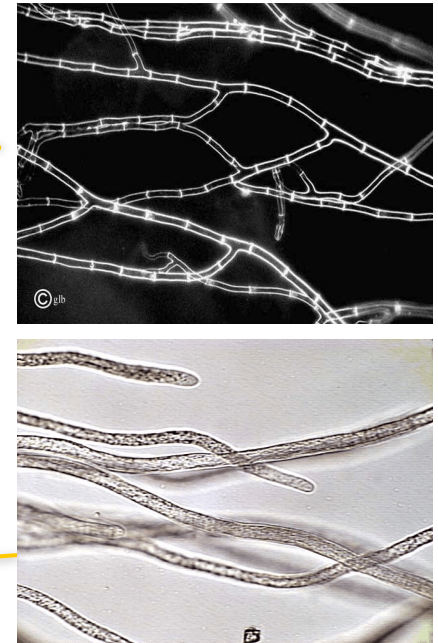
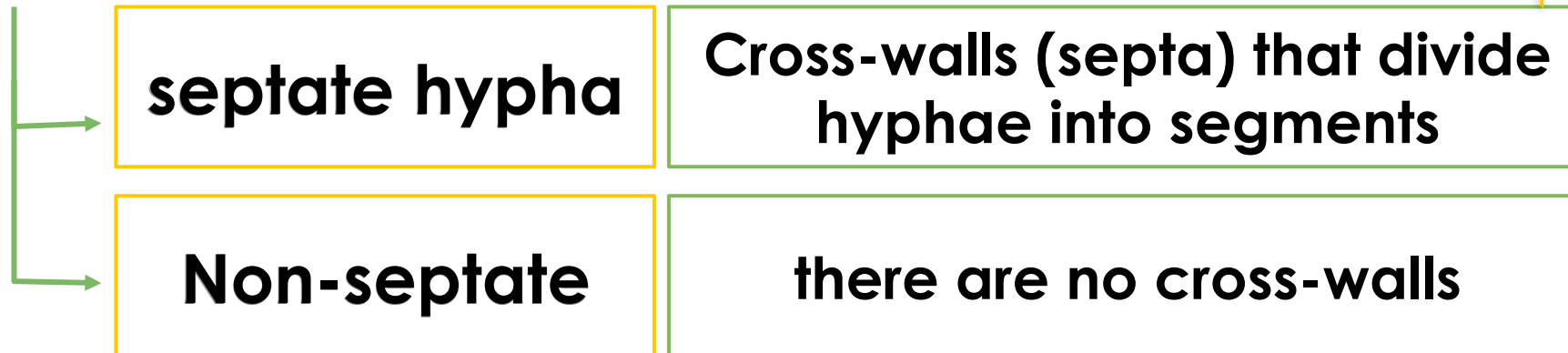
Spore

Hyphal

mycelium

Filamentous fungi (Mold fungi)

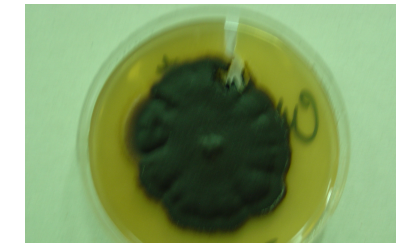
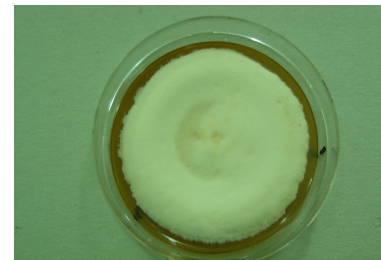
✓ Hypha might be:



✓ Moniliaceous molds

Pigment of hypha might be :

- Hyaline
- lightly pigmented conidia or hyphae
- Colorless



✓ Spores

- These are the small airborne particles by which fungi reproduce.
- They are produced by mitosis and readily disseminate in the air.

Filamentous fungi (Mold fungi)

✓ Reproduction

Asexual		Sexual
Only mitotic cell division		Fusion
Somatic	by hyphal fragmentation	mitosis
Spore formation	<ul style="list-style-type: none">✓ Sporangiospores in sporangia✓ Chlamydospores in or on hyphae✓ Conidia (conidium) on hypha or oconidiophores	meiosis

PATHOGENICITY OF FUNGI

- ✓ **fungi can cause diseases to humans**
 - Cause superficial infections,
 - some can cause allergic reactions
 - Few cause invasive infections
- ✓ **To cause the disease:**
 - Thermotolerance
 - Ability to survive in tissue environment
 - Ability to withstand host defenses

Diversity of Fungi and Fungal Infections

- ✓ **Mycotic Diseases**
 1. Hypersensitivity (Allergy)
 2. Mycotoxicoses
 3. Infections

fungus infections (Mycoses)

acquired

Endogenous, Colonization (overgrowth of normal flora)

Inhalation (Airborne)

Contact

Trauma

Types

1-Superficial mycoses

2- Cutaneous mycosis

3- Subcutaneous mycoses

4-Systemic mycoses

5-Opportunistic mycoses

Types fungal infections (Mycoses)

	1- Superficial Mycoses	2- Cutaneous Mycoses (Dermatophytosis)	3- Subcutaneous Mycoses	4-Primary Systemic Mycoses
Site of affect	outer layer of the skin or hair shaft	skin, hair or nails	the dermis, subcutaneous tissues, muscle and may extend to bone.	Contracted by inhalation, Start as respiratory disease
Cause	No immune response	a group of keratinophilic fungi, called dermatophytes	Usually they are initiated by trauma	Caused by primary pathogens

Types fungal infections (Mycoses)

5- Opportunistic fungal infections

✓ **Diseases in immunocompromised host**

✓ **Risk factors:**

- HIV/AIDS
- Hematopoietic stem cell transplant (HSCT)
- Solid organs transplantation
- Malignancies
- Neutropenia
- Diabetes

The fungi

A) Opportunistic Fungi		B) Primary Pathogens	
Normal flora	<ul style="list-style-type: none">▪ Candida spp.▪ Other yeast	Dermatophytes	
Ubiquitous in our environment	<ul style="list-style-type: none">▪ Aspergillus spp.▪ Zygomycetes spp.▪ Cryptococcus spp	Endemic geographically restricted	<ul style="list-style-type: none">▪ Histoplasma spp.▪ Blastomyces spp.▪ Coccidioides spp.▪ Paracoccidioides spp

Diagnosis of fungal infection

- ✓ **Clinical features** :(history, risk factors, etc)
- ✓ **Imaging** :Good value in diagnosis and therapy monitoring
- ✓ **Lab Investigations:**
 - **Histopathology**
 - **Microbiology**

Antifungal agents

Targets for antifungal agents

Cell membrane	Cell wall	DNA/RNA synthesis
<ul style="list-style-type: none">▪ Polyene▪ Azole	<ul style="list-style-type: none">▪ Echinocandins<ul style="list-style-type: none">✓ Caspofungin✓ Micafungin✓ Anidulafungin	<ul style="list-style-type: none">▪ Pyrimidine analogues<ul style="list-style-type: none">✓ Flucytosine

Antifungal agents

✓ Polyenes

- Amphotericin B, lipid formulations
- Nystatin

Mechanism of Action Amphotericin B (MOA):

- Binds to ergosterol within the fungal cell membrane resulting in formation of pores which permit leakage of intracellular contents, and lead to death .
- Amphotericin B has an broad antifungal spectrum which includes most fungi that cause human disease

✓ AZOLES

- Fluconazole
- Itraconazole
- Posaconazole
- Ketoconazole
- Voriconazole
- Miconazole, clotrimazol

Mechanism of Action

- Inhibits synthesis of ergosterol, the major sterol of fungal cell membrane.
- Inhibits 14- α -sterol demethylase, which is a microsomal CYP450 enzyme.

Antifungal agents

✓ Flucytosine

Mechanism of Action

- Fungal RNA miscoding
- Interfering with DNA synthesis

Spectrum of Activity (Restricted spectrum of activity)

- **Active against**
- ***Candida* species**
- ***Cryptococcus neoformans***
- **Monotherapy : now limited (Resistance)**

✓ Echinocandins

- **Caspofungin**
- **Micafungin**
- **Anidulafungin**

Mechanism of Action

- **Inhibits B-1,3 –D glucan synthase, the enzyme complex that forms glucan polymers in the fungal cell wall.**
- **Glucan polymers are responsible for providing rigidity to the cell wall.**

Good activity against

- ***Candida* spp**
- ***Aspergillus* spp**

Quiz

1.The intertwined mass of hyphae that forms the fungal colony is:

- a) Hypha b) Pseudohypha c) Mycelium

2.Fungi can divide asexually by :

- a) Budding b) Hyphal Fragment c) Both A & B

3. can divide asexually by budding :

- a) Yeast b) Molds c) Both A & B

4.The small airborne particles that are readily disseminated in the air are :

- a) Conidia b) Spores c) Hyphae

5.Subcutaneous mycoses are fungal infections that involve:

- a) Hair b) Skin c) Muscles

Quiz

6..... are examples of opportunistic fungi:

- a) Histoplasma species b) Aspergillus species c) Coccidioides species

7.Echinocandins are active against:

- a) Aspergillus species b) Cryptococcus neoformans c) Blastomyces species

8.Cell membrane is the target for polyene and azole.

- a) T b) F

9.Amphotericin B binds to ergosterol within the fungal cell wall resulting in formation of pores.

- a) T b) F

10.Fungi are prokaryotic organisms.

- a) T b) F

Quiz

11. The cell membrane of the fungus contains ergosterol.

a) T b) F

12. Dermatiaceous molds are hyaline or lightly pigmented conidia.

a) T b) F

13. Candidium is asexual spore.

a) T b) F

14. Thermatolerance is the ability to withstand relatively hot conditions.

a) T b) F