

Lecture Title: **Diversity of Fungi and Fungal Infections**

(Foundation Block, Microbiology)

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Lecture Objectives..



1. To provide students with an overview of the common medically important yeasts and mold fungi.
2. To provide students with an overview of the major fungal diseases that threatens human health.
3. To give a fundamental knowledge about the antifungal agents, their mechanisms of action, and spectrum.



Mycotic Diseases

- Hypersensitivity (Allergy)
- Mycotoxicoses
- Infections

Mycotic Diseases

How the infection is acquired?

- Endogenous, Colonization (overgrowth of normal flora)
- Inhalation (Airborne)

- Contact
- Trauma

Mycotic Diseases

Healthy host?

OR

Immunocompromised host?



(When,
which type
of infection)

Types of fungal infections (Mycoses)



- Superficial mycoses
- Cutaneous mycosis
- Subcutaneous mycoses
- Systemic mycoses
- Opportunistic mycoses



Types of fungal infections (Mycoses)

Healthy Host

- Superficial mycoses
- Cutaneous mycosis
- Subcutaneous mycoses
- Systemic mycoses

Immunocompromised Host

- Superficial mycoses
- Cutaneous mycosis
- Subcutaneous mycoses
- Systemic mycoses
- **Opportunistic mycoses**



Types of fungal infections - Mycoses

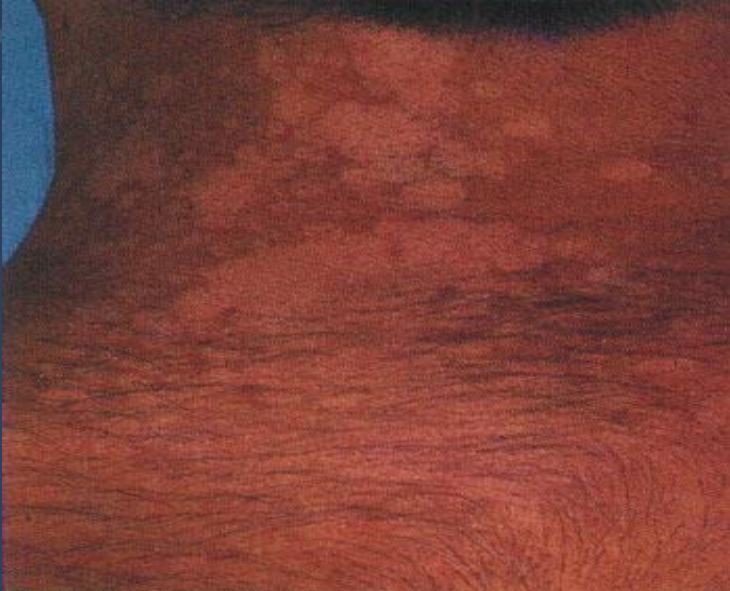
Superficial Mycoses

- Affect the outer layer of the skin or hair shaft
- No immune response

Cutaneous Mycoses

Dermatophytosis

- Infection of the skin, hair or nails caused by a group of keratinophilic fungi, called dermatophytes





Types of fungal infections - Mycoses

Subcutaneous Mycoses

- Fungal infections involving the dermis, subcutaneous tissues, muscle and may extend to bone.
- Usually they are initiated by trauma.





Types of fungal infections - Mycoses

Primary Systemic Mycoses

- Caused by primary pathogens
- Contracted by inhalation, Start as respiratory disease
- Geographically restricted (endemic), north and south America



Types of fungal infections - Mycoses

Opportunistic fungal infections

- Diseases in immunocompromised host
- Risk factors
 - HIV/AIDS
 - Hematopoietic stem cell transplant (HSCT)
 - Solid organs transplantation
 - Malignancies
 - Neutropenia
 - Diabetes

 - Many others

The Fungi

A) Opportunistic Fungi

➤ Normal flora

Candida spp.

Other yeast

➤ Ubiquitous in our environment

Aspergillus spp.

Zygomycetes spp.

Cryptococcus spp.

➤ Other fungi

B) Primary Pathogens

▪ Dermatophytes

▪ Endemic geographically restricted

- *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

- Polyene
- Azole

➤ Cell wall

- Echinocandins
 - Caspofungin
 - Micafungin
 - Anidulafungin

➤ DNA/RNA synthesis

- Pyrimidine analogues
 - Flucytosine



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
- Ketoconazole
- Itraconazole
- Voriconazole
- Posaconazole
- Miconazole, clotrimazole

- **Mechanism of Action**

Inhibits synthesis of ergosterol, the major sterol of fungal cell membrane.

Azoles—Spectrum of Activity

	Fluconazole	Itraconazole	Voriconazole	Posaconazole
Yeast	+++	+	+++	+++
Mold , e.g <i>Aspergillus</i>	--	++	+++	+++
<i>Zygomycetes</i>	-	-	-	++

Flucytosine

- **Mechanism of Action**

Fungal RNA miscoding

Interfering with DNA synthesis

- **Spectrum of Activity** (Restricted spectrum of activity)

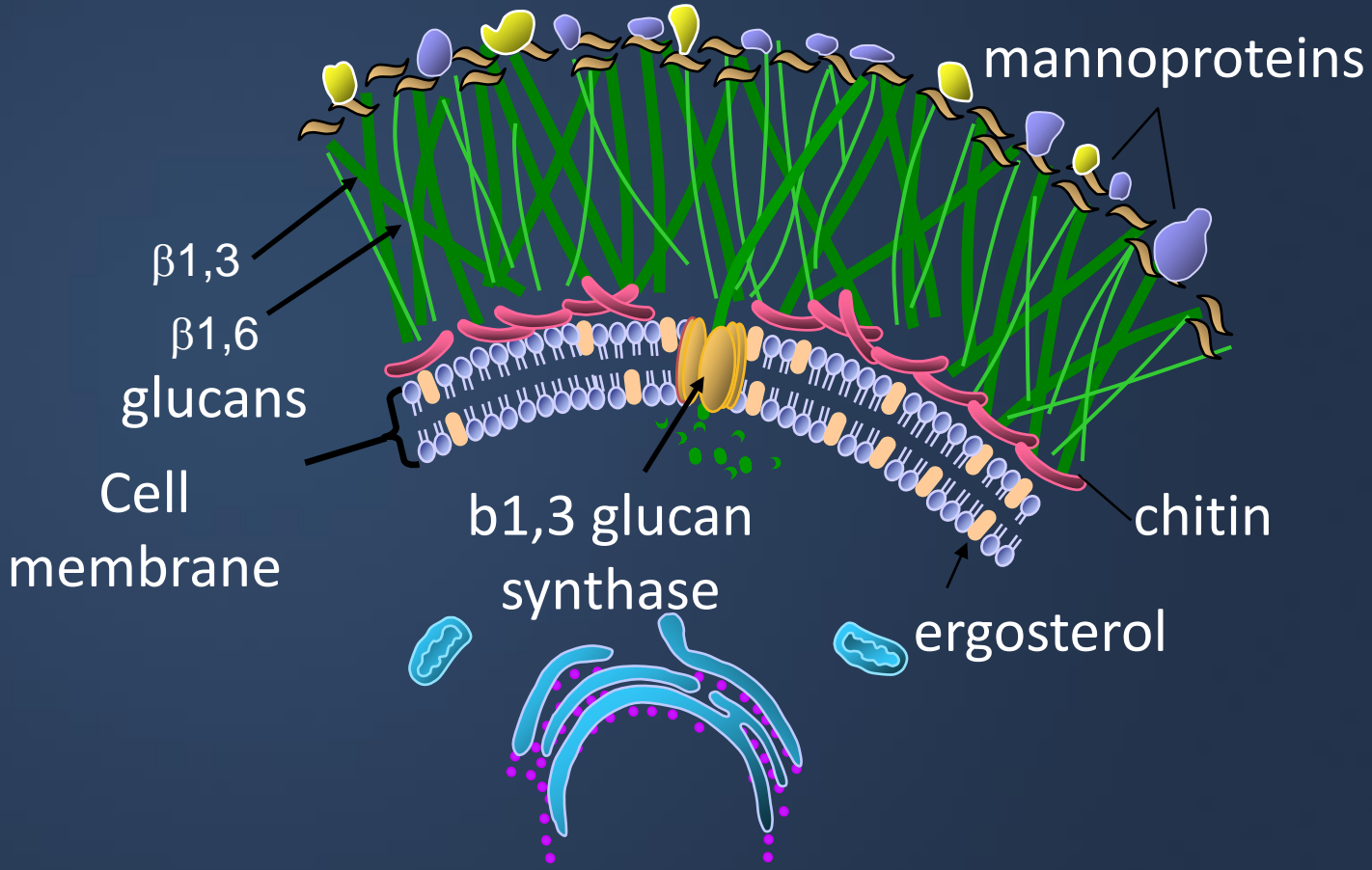
Active against

Candida species

Cryptococcus neoformans

Monotherapy : now limited (**Resistance**)

The Fungal Cell Wall



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

Target	Group	Mechanism of action	Antifungal Agents	Spectrum of activity	Comments
Cell membrane	Polyenes	Binds to ergosterol within cell membrane, formation of pores which lead to cell death	Amphotericin B, Nystatin	Broad antifungal spectrum which includes most fungi	Serious toxic side effects (nephrotoxicity)
	Azoles	Inhibit the synthesis of ergosterol	Ketoconazole Itraconazole Fluconazole Voriconazole Posaconazole Miconazole clotrimazole	Fluconazole has a limited or no activity against mould fungi Voriconazol is the drug of choice for Aspergillosis Posaconazole has broader spectrum of activity than other azoles	Not effective against Zygomycosis (except posaconazole) Adverse Effects Drug Interactions
Cell wall	Echinocandins	Inhibits glucan synthesis, (glucan polymers in the fungal cell wall)	Caspofungin Micafungin Anidulafungin	Good activity against <i>Candida spp</i> , <i>Aspergillus spp</i> Limited or no activity against other fungi	Less toxicity and side effects compared to amphotericin B and azoles
DNA/RNA synthesis	Pyrimidine analogues	Fungal RNA miscoding Interfering with DNA synthesis	Flucytosine	Restricted spectrum of activity <i>Candida</i> species <i>Cryptococcus neoformans</i>	Monotherapy now limited (Resistance)

Thank You 😊

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