

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

(Foundation Block, Microbiology)

**Lecturer name:**

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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

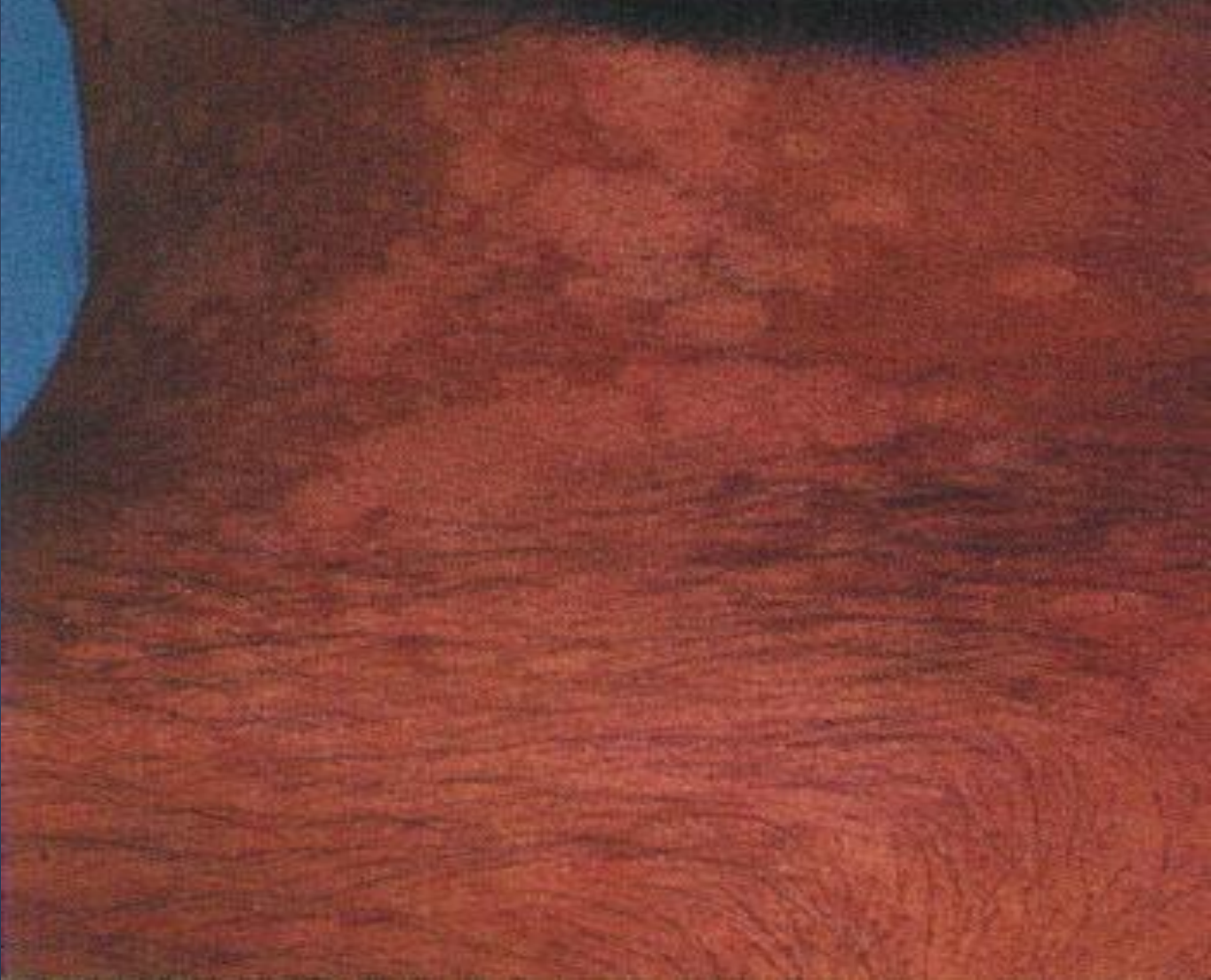
## Cutaneous Mycoses

### Dermatophytosis

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













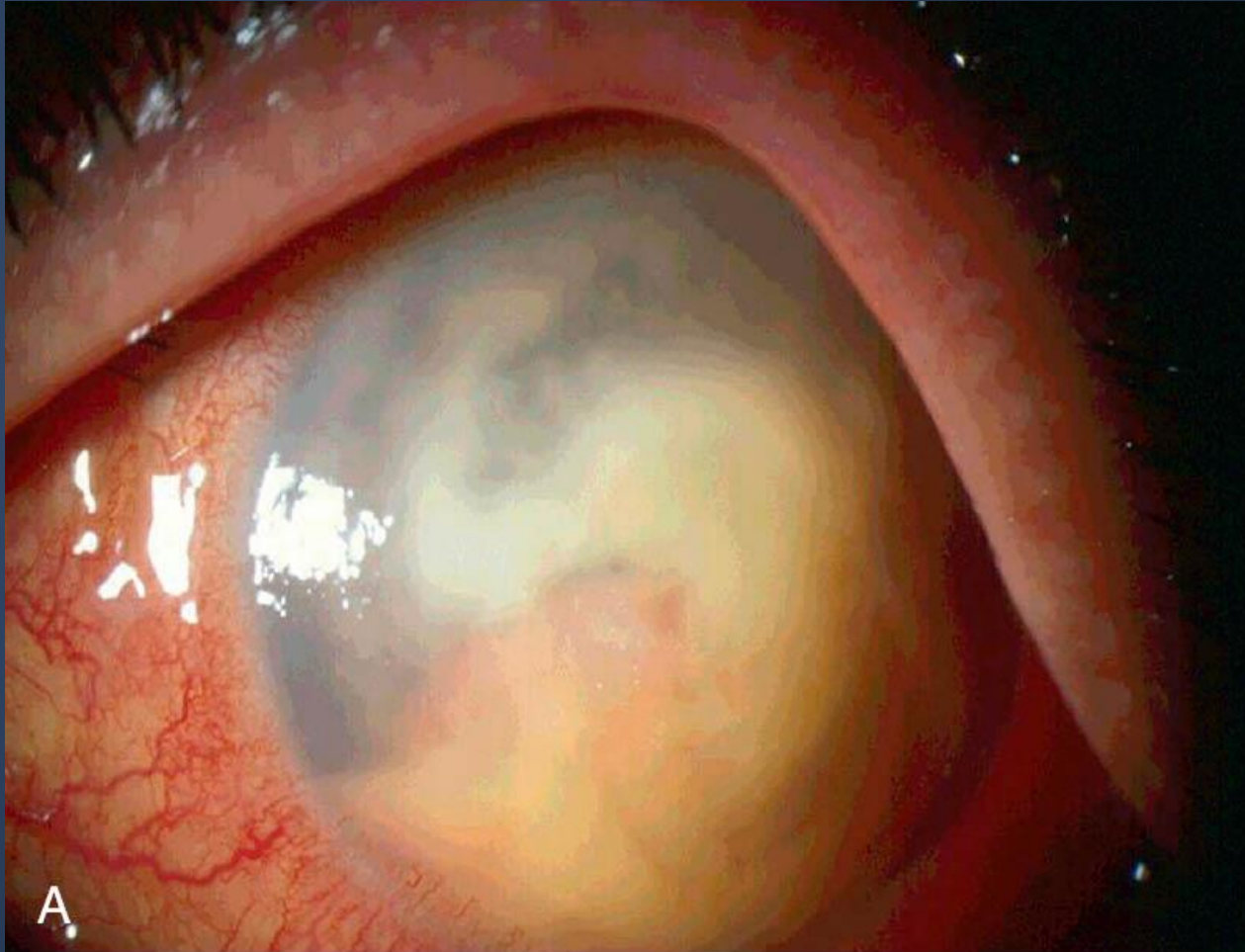


# Types of fungal infections - Mycoses

## 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)

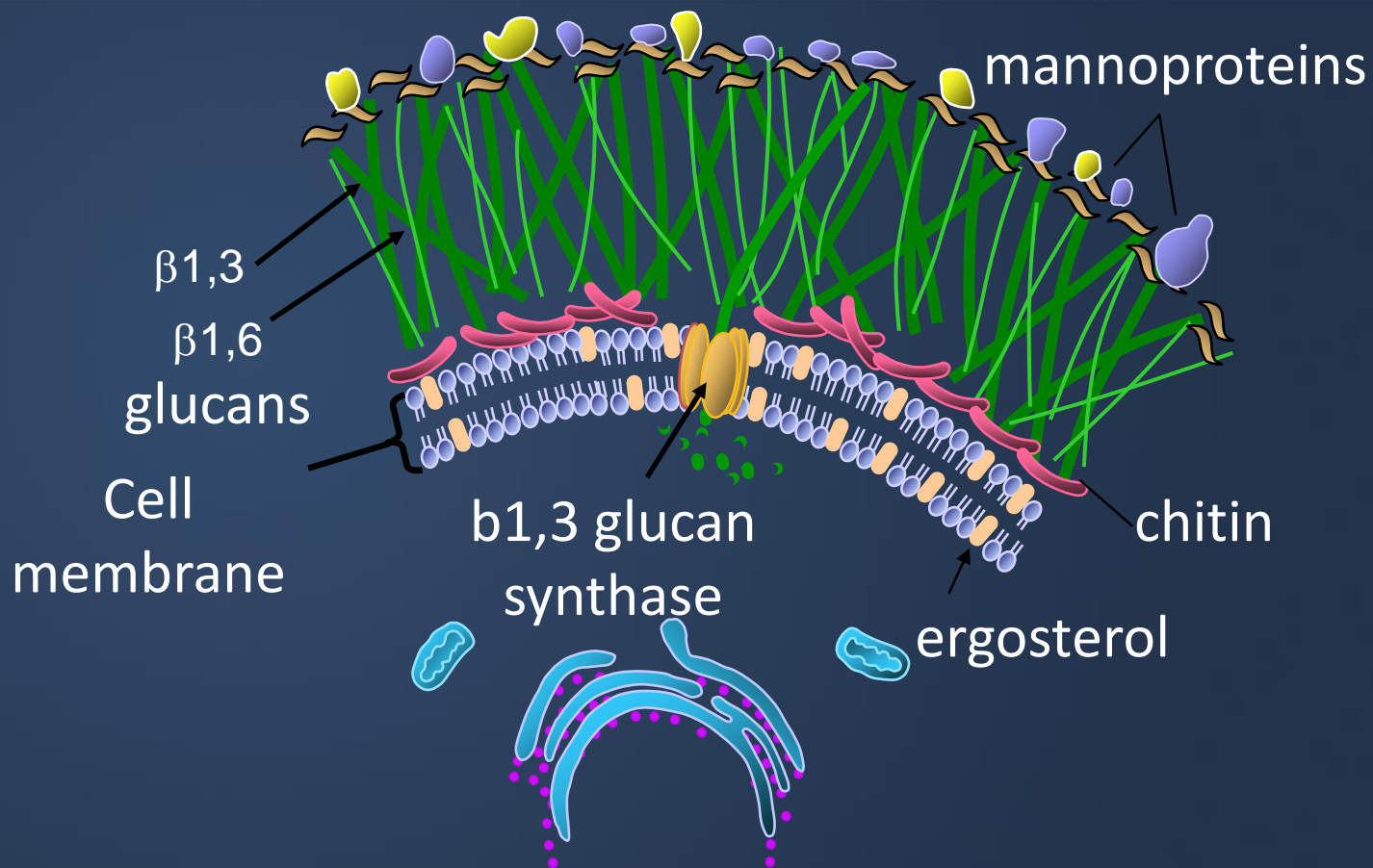
Active against

*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	<b>Fluconazole</b> has a limited or no activity against mould fungi <b>Voriconazol</b> is the drug of choice for Aspergillosis <b>Posaconazole</b> 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 😊

(Foundation Block, Microbiology)

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**Oct-2019**

