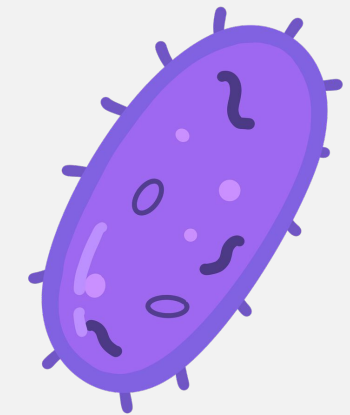
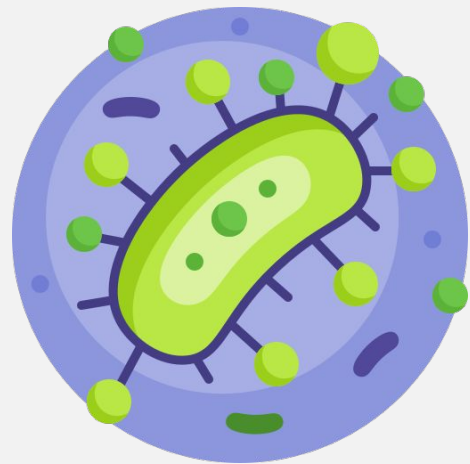


Diversity of pathogenic Molds & Yeasts

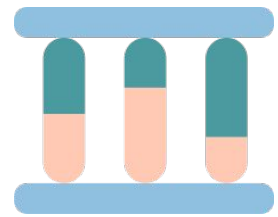
Editing File



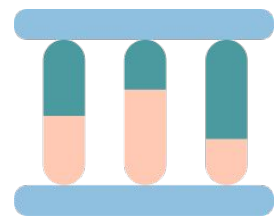
index:

- **Main text.**
- **Important.**
- **In boys slides only.**
- **In girls slides only.**
- **Doctors notes.**
- **Extra info.**

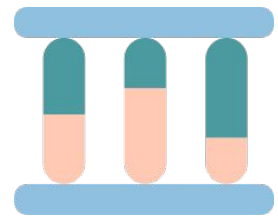
OBJECTIVES



To provide students with an overview of the common medically important yeasts and mold fungi.

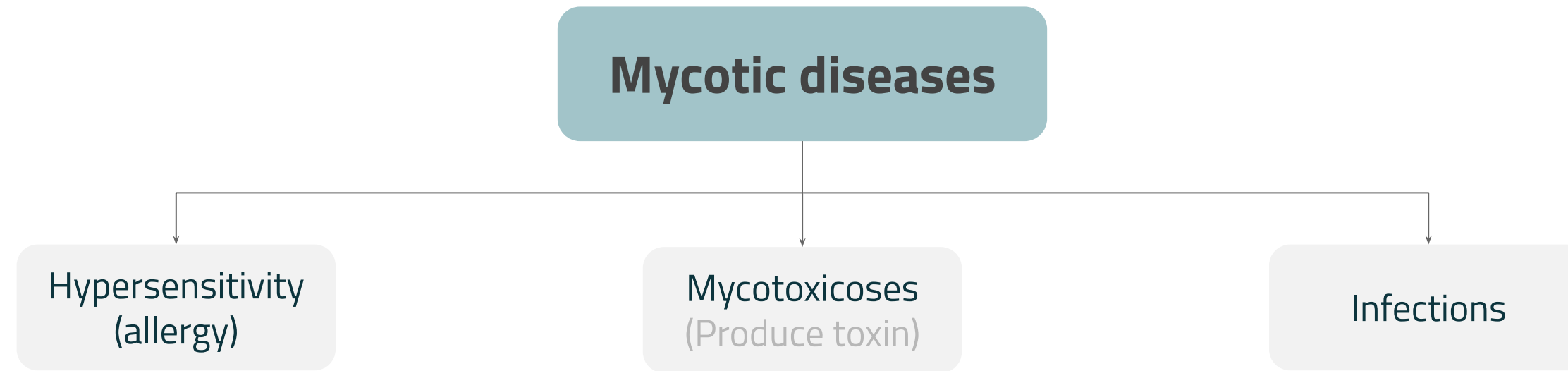


To give a fundamental knowledge about the antifungal agents, their mechanisms of action, and spectrum.



To provide students with an overview of the major fungal diseases that threatens human health.

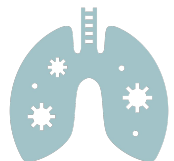
Mycotic diseases



How the infection is acquired?



Endogenous, colonization (Overgrowth of normal flora)



Inhalation (Airborne) **very common** (Usually filamentous spores)



Contact (With infected human/animal)



Trauma (Burns or accidents)

Diagnosis of fungal infections done according to:



Clinical features :
(History , Risk factors , etc)



Imaging :
Good value in diagnosis and therapy monitoring



Lab investigations :
Histopathology , Microbiology

Types of fungal infections (Mycoses):

Healthy host include **only!**:
 1- superficial mycosis
 2- cutaneous mycosis
 3- subcutaneous mycosis
 4- systemic mycosis

And the **immunocompromised** include them all + **opportunistic mycosis**

Mycosis = singular
 Mycoses = plural

**Healthy host
 (Immunocompetent)**

**Immunocompromised
 Host**

**Superficial
 Mycosis**

**Cutaneous
 Mycosis**

**Subcutaneous
 Mycosis**

**Systemic
 Mycosis**

**Opportunistic
 Mycosis**

Affects the outer layer of the **skin** or **hair** shaft

no immune response
 (no redness, no itching, no pain)

a.k.a **Dermatophytosis**
 (very common)

Infection of the **skin, hair, nails** caused by a group of keratinophilic fungi called **Dermatophytes**

Fungal infections involving the **Dermis, Subcutaneous tissues, muscle** and may extend to **Bone**

Usually they are initiated by trauma (like surgeries or car accidents)

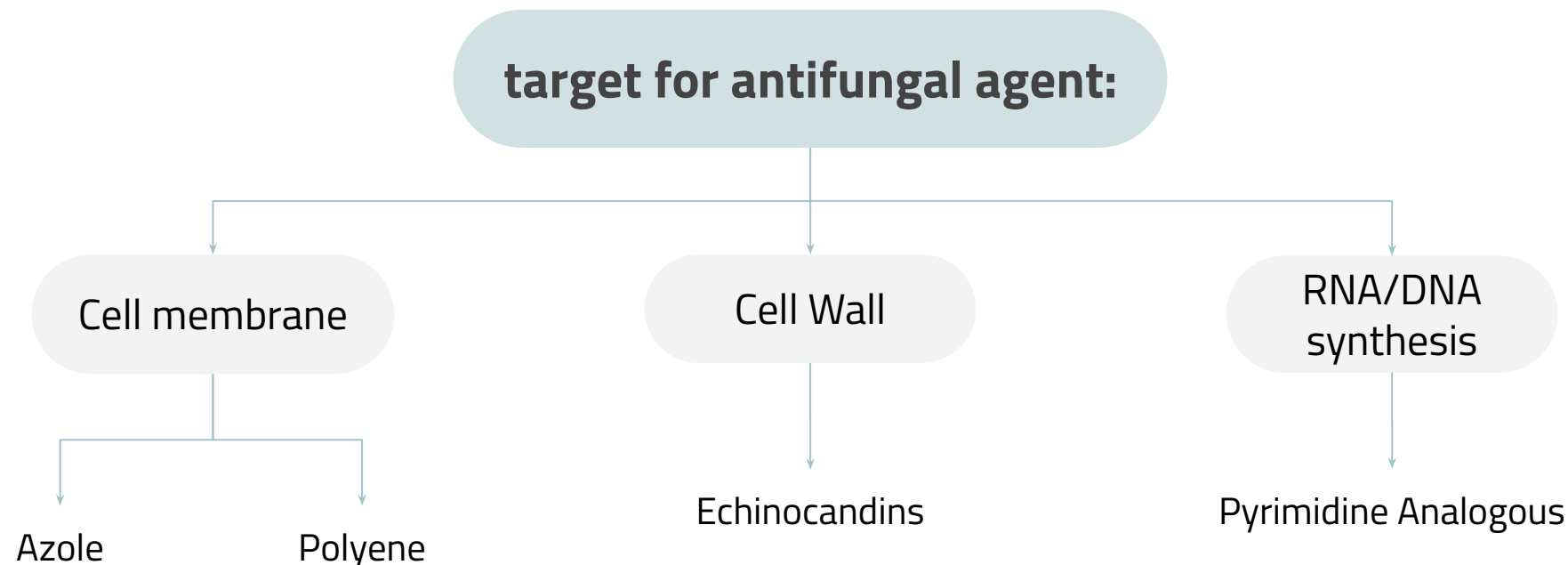
- Caused by primary pathogens
 - Contracted by inhalation, start as (mild) respiratory disease
 - Geographically restricted (endemic) North and South America

Only causes diseases in **Immunocompromised** hosts



Mycotic Disease

Primary Pathogen	Endemic geographically restricted	1- Histoplasma spp 3- Coccidioides spp	2- Blastomyces spp 4- Paracoccidioides spp
	Dermatophytes	(Cutaneous Mycosis)	
Opportunistic Fungi	Normal flora	1- <i>Candida</i> spp	2- and other yeast
	Ubiquitous in our environment: Mound everywhere	1- <i>Aspergillus</i> spp 2- <i>Zygomycetes</i> spp	3- <i>Cryptococcus</i> spp
	Other fungi	—	



❖ Risk factors of being immunocompromised

- 1- **HIV/AIDS**
- 2- Hematopoietic stem cell **transplant** (HSCT)
- 3- Solid organs transplantation
- 4- Malignancies (cancer)
- 5- Neutropenia (abnormally low concentration of neutrophils)
- 6- Diabetes
- Many more....

because the patient will be given medicines to inhibit the immune system

Target for antifungal agent (Cell membrane) :

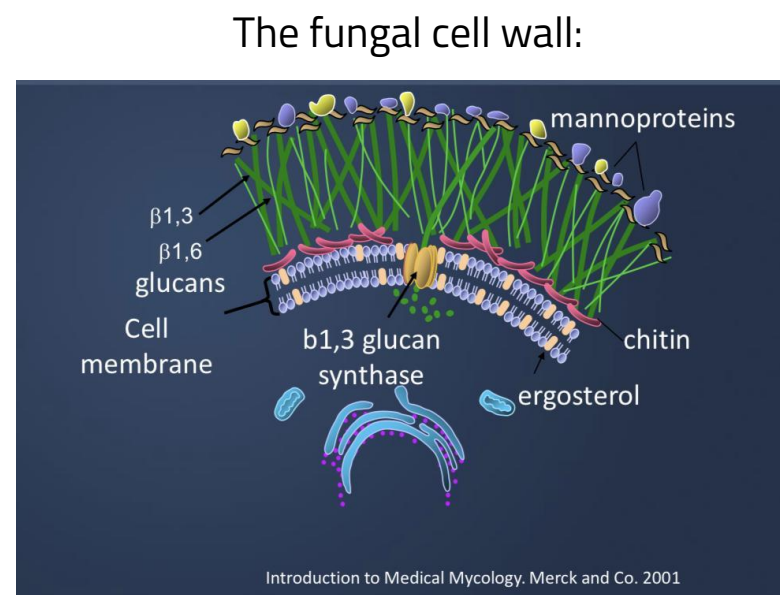
Target	Cell Membrane																										
Group	Polyenes	Azole																									
Antifungal Agents	<ul style="list-style-type: none"> -Amphotericin B (lipid formulations) - Nystatin 	<ul style="list-style-type: none"> - Fluconazole: affects yeast - Itraconazole: affects yeast + mold - Voriconazole: affects yeast + mold - Posaconazole: affects yeast + mold + Zygomycetes (has the broadest spectrum in the azole group, and it is the only azole that affects zygomycetes). - Miconazole - Ketoconazole - Clotrimazole 																									
Mechanism of action	<p>Amphotericin B (MOA):</p> <ul style="list-style-type: none"> ➤ Binds to ergosterol within the fungal cell membrane resulting in formation of pores which permit leakage of intracellular contents, and lead to death . 	<p>(Don't confuse the MOA of azoles with polyenes)</p> <ul style="list-style-type: none"> -Inhibits synthesis of ergosterol (ergosterol is a major sterol in the cell membrane of fungi). 																									
Spectrum of activity	<p>Amphotericin B has a(broad antifungal spectrum which includes most fungi that cause human disease.</p>	<table border="1"> <thead> <tr> <th colspan="5">Azoles spectrum of activity (Just know the fungi that is affected by each azole)</th> </tr> <tr> <th></th> <th>Fluconazole</th> <th>Itraconazole</th> <th>Voriconazole</th> <th>Posaconazole</th> </tr> </thead> <tbody> <tr> <td>Yeast</td> <td>High</td> <td>Low</td> <td>High</td> <td>High</td> </tr> <tr> <td>Mold, e.g: Aspergillus</td> <td>No effect</td> <td>Medium</td> <td>High</td> <td>High</td> </tr> <tr> <td>Zygomycetes</td> <td>No effect</td> <td>No effect</td> <td>No effect</td> <td>Medium</td> </tr> </tbody> </table>	Azoles spectrum of activity (Just know the fungi that is affected by each azole)						Fluconazole	Itraconazole	Voriconazole	Posaconazole	Yeast	High	Low	High	High	Mold, e.g: Aspergillus	No effect	Medium	High	High	Zygomycetes	No effect	No effect	No effect	Medium
Azoles spectrum of activity (Just know the fungi that is affected by each azole)																											
	Fluconazole	Itraconazole	Voriconazole	Posaconazole																							
Yeast	High	Low	High	High																							
Mold, e.g: Aspergillus	No effect	Medium	High	High																							
Zygomycetes	No effect	No effect	No effect	Medium																							

من أقدم ال antifungal

Fluconazole Use only with yeast
 Azoles not good to be used with zygomycetes because they are non septate
 (Azoles are not good choice with non septate)

Target for antifungal agent (Cell wall, DNA RNA synthesis) :

Target	Cell wall	DNA/RNA synthesis → Not really common these days
Group	Echinocandins (very toxic because it targets glucan)	Pyrimidine Analogous
Antifungal Agents	(Usually end with -fungi) - Caspofungin. - Micafungin. - Anidulafungin	- Flucytosine (Used with yeast only, candida spp & cryptococcus neoformans)
Mechanism of action	<ul style="list-style-type: none"> ➤ 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, and it helps it to grow & survive 	<ul style="list-style-type: none"> ➤ Fungal RNA miscoding ➤ Interfering with DNA synthesis
Spectrum of activity	<p>Good activity against:</p> <ol style="list-style-type: none"> 1) Candida spp 2) Aspergillus spp 	<p>(Restricted spectrum of activity)</p> <p>Active against:</p> <ol style="list-style-type: none"> 1) Candida spp 2) Cryptococcus neoformans <p>- It has restricted use in monotherapy, because it frequently develops resistance.</p> <p>(Cannot be used alone “mono” because fungi develop resistance, so it is used in combination therapy due to resistance & toxicity).</p>



Summary :

هذا الجدول ملخص للمحاضرة مهم
تمرون عليه

Target	Group	Mechanism of action	Antifungal agents	Spectrum of activity	Comments (very important)
Cell membrane	Polyenes	Binds to ergosterol within the cell membrane, forming pores which lead to cell death	1) Amphotericin B (Only IV administration) 2) Nystatin	Broad antifungal spectrum (includes most fungi) Best in terms of spectrum	Serious toxic side effects (nephrotoxicity) (Toxic to the kidney)
	Azoles	Inhibits the synthesis of ergosterol	1) Fluconazole	Limited/no activity against mould fungi Good activity on yeast	Not effective against zygomycosis (except posaconazole)
			2) Voriconazole	Good activity on Molds (e.g Aspergillosis) & yeast	-Not effective against zygomycosis (except posaconazole)
			3) Posaconazole	Broader spectrum of activity than other azoles Good activity on Molds & Yeast & Zygomycetes	-Adverse effects
			4) Ketoconazole 5) Itraconazole 6) Miconazole 7) Clotrimazole	-	-Drug interactions (toxic to the liver cells)
Cell wall	Echinocandins	Inhibits glucan synthesis	1) Caspofungin 2) Micafungin 3) Anidulafungin	Good activity against : 1) Candida spp 2) Aspergillus spp Limited/no activity against other fung	Less toxic & less side effects compared to amphotericin B & azoles (i.e its the safest)
DNA/RNA synthesis	Pyrimidine analogues	Fungal RNA miscoding or interfering with DNA synthesis	Flucytosine	Restricted to: 1) Candida spp 2) Cryptococcus neoformans	Monotherapy (limited resistance) -Cannot be used alone because fungi develop resistance. -So its used in combination therapy because of its resistance and toxicity.

Quiz

Q1: Subcutaneous mycoses mostly affects which part of the body? Slide 4

- A Dermis (Skin) B Subcutaneous tissues C Nephrons D A & B

Q2: A patient was given an antifungal drug belonging to the polyene family. What is the most suitable mechanism of action of polyene? Slide 6

- A Blocking of G6PD B Block ergosterol synthesis C Binds to ergosterol within the fungal cell membrane D Inhibit cell wall synthesis

Q3: What is the mechanism of action of echinocandins? Slide 7

- A RNA miscoding B Inhibits B-1,3 –D glucan synthase C bind to ergosterol to form pores. D inhibit synthesis of ergosterol.

Q4: Why might a person be considered immunocompromised? Slide 5

- A They recently had a transplant surgery B They are diabetic C They have HIV/AIDS D A & B and C

Q5: Which of the following antifungal agents can be used against Molds & yeast and zygomycetes? Slide 6

- A Fluconazole B Voriconazole C Flucytosine D Posaconazole



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Dana Abu Alamah

Madaen Alarifi

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AlJawharah alyahya

Layal alkhalfah

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Khalid Alghamdi

