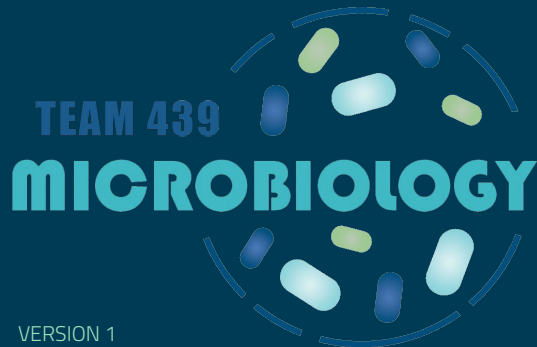


Diversity of Pathogenic Molds & Yeast

(Diversity of Fungi & Fungal Infections)



Objectives

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

Colour index:

- **Red: Important.**
- Grey: Extra info & explanation.
- **Purple: Only in girl's slides.**
- **Green: Only in boy's slides.**
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Any future corrections
will be in the editing
file, so please check it
frequently.

Scan the code
Or click [here](#)



Definitions

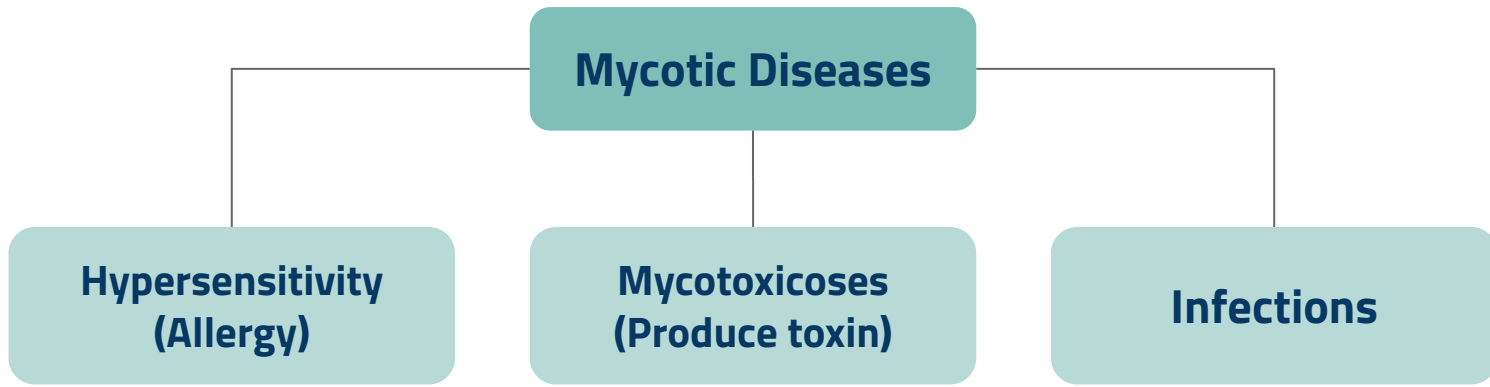
- ★ **Immunocompetent:** healthy person/host with **normal** immune system
- ★ **Immunocompromised/Immunosuppressed:** a person/host with a **weakened** (impaired) immune system
- ★ **Mycosis:** fungal infection

Risk factors (causes) of being immunocompromised:

- ❖ HIV/AIDS
- ❖ Hematopoietic stem cell transplant (HSCT)
- ❖ Solid organs transplantation
- ❖ Malignancies (cancer)
- ❖ Neutropenia (abnormally low concentration of neutrophils)
- ❖ Diabetes
- ❖ Immunosuppressant drugs
- ❖ Many more....

EXTRA: Monotherapy: use of a single drug to treat a disease or condition.



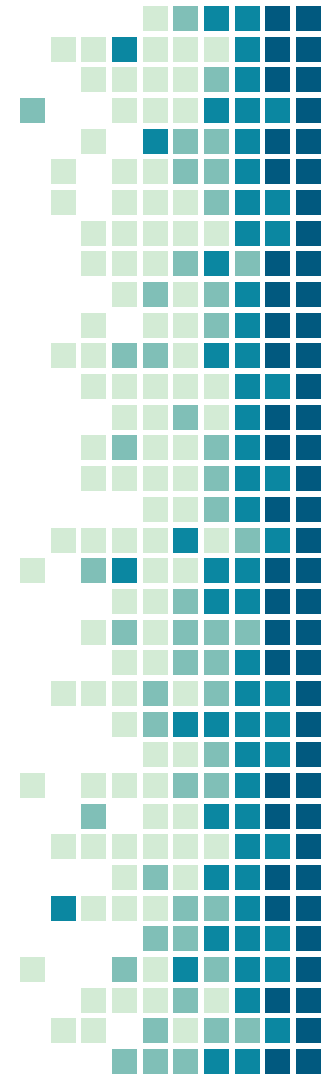


How are infections acquired?

- Endogenous, colonization (Overgrowth of normal flora).
- Inhalation (**Usually filamentous spores**).
- Contact (With contaminated soil, infected human/animal).
- Trauma (Burns or accidents).

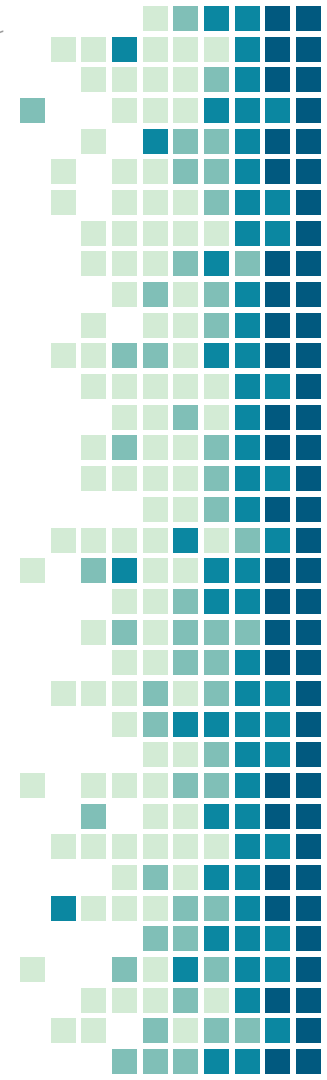
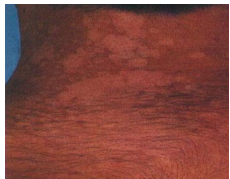
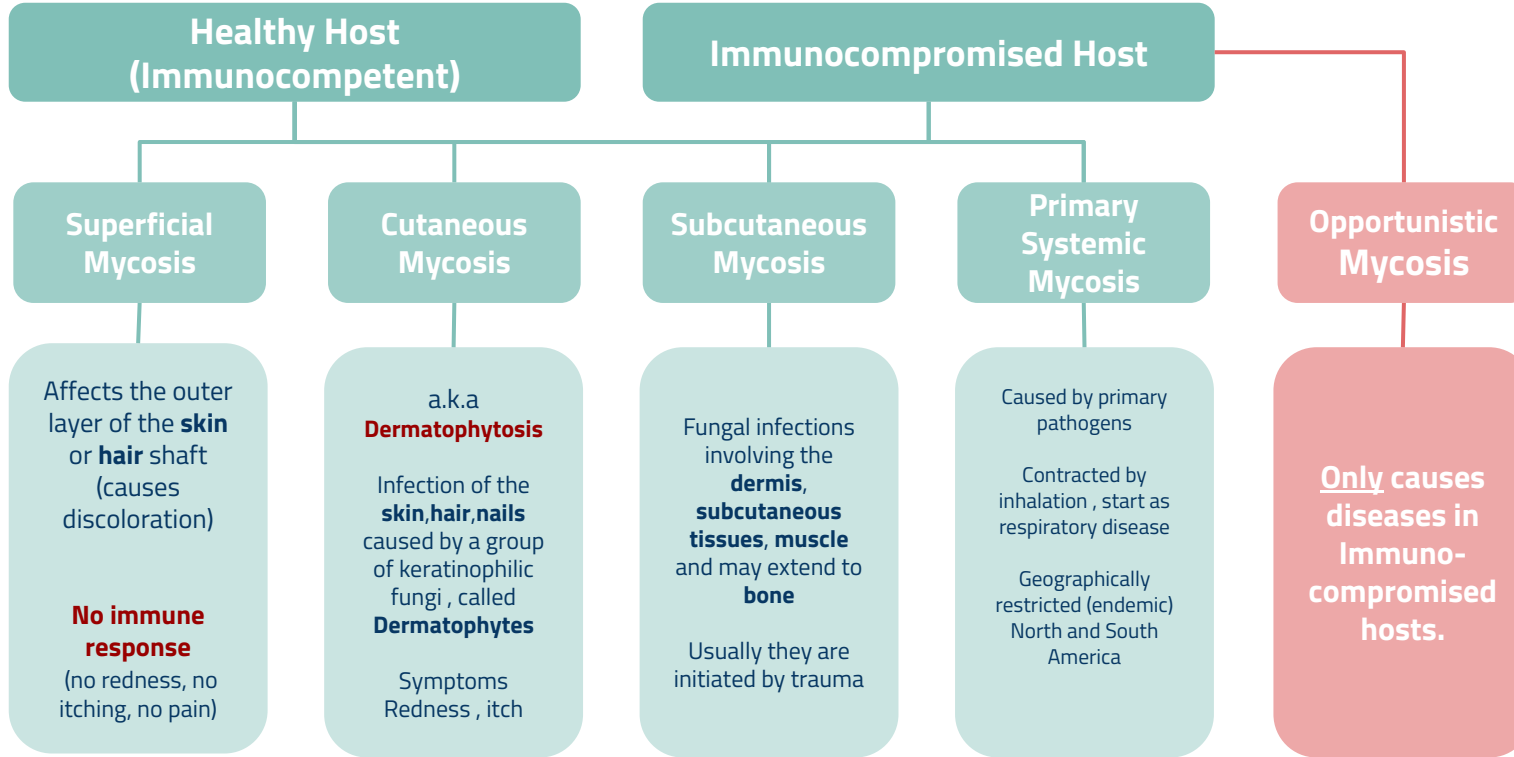
Diagnosis of fungal infections done according to:

- Clinical features : (History , Risk factors , etc)
- Imaging : Good value in diagnosis and therapy monitoring
- Lab investigations : Histopathology , Microbiology



Types of fungal infections (Mycoses):

Mycosis = singular
Mycoses = plural



Fungi

*spp= species

Primary pathogens

Opportunistic Fungi

Endemic geographically restricted

- Histoplasma spp
- Blastomyces spp
- Coccidioides spp
- Paracoccidioides spp

Dermatophytes

(Cause cutaneous infection)

Normal flora

- Candida spp
- Other yeast

Ubiquitous in our environment (found everywhere)

- Aspergillus spp
- Zygomycetes spp
- Cryptococcus

Other Fungi

- Antifungal agents for fungi.
- Antibiotics for bacteria

Targets for Antifungal Agent

Cell Membrane

Polyene

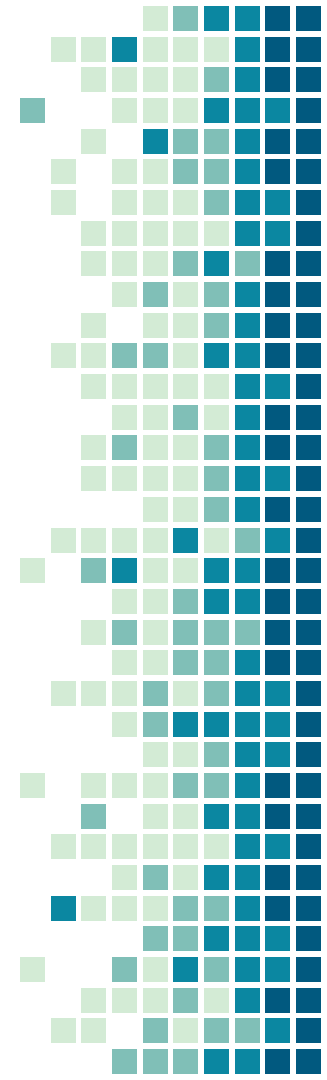
Azole


Cell Wall

Echinocandins

DNA/RNA Synthesis

Pyrimidine Analogous



Target	Cell Membrane																															
Group	Polyenes	Azole																														
Antifungal Agents	<ul style="list-style-type: none"> - Amphotericin B (lipid formulations). - Nystatin  <p>Scan or Click</p>	<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 M.O.A	<p>Amphotericin B (MOA):</p> <p>➤ Binds to ergosterol within the fungal cell membrane resulting in formation of pores which permit leakage of intracellular contents, and lead to death .</p>	<p>(DON'T CONFUSE THE MOA OF AZOLES WITH POLYENES).</p> <p>➤ Inhibits synthesis of ergosterol (ergosterol is a major sterol in the cell membrane of fungi).</p>																														
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" data-bbox="1122 799 1922 871">Azoles—Spectrum Of Activity</th> </tr> <tr> <th colspan="5" data-bbox="1122 871 1922 879">Just know the fungi that is affected by each azole</th> </tr> <tr> <th data-bbox="1122 879 1271 926"></th> <th data-bbox="1271 879 1439 926">Fluconazole</th> <th data-bbox="1439 879 1599 926">Itraconazole</th> <th data-bbox="1599 879 1767 926">Voriconazole</th> <th data-bbox="1767 879 1922 926">Posaconazole</th> </tr> </thead> <tbody> <tr> <td data-bbox="1122 926 1271 972">Yeast</td> <td data-bbox="1271 926 1439 972">High</td> <td data-bbox="1439 926 1599 972">Low</td> <td data-bbox="1599 926 1767 972">High</td> <td data-bbox="1767 926 1922 972">High</td> </tr> <tr> <td data-bbox="1122 972 1271 1038">Mold e.g aspergillus</td> <td data-bbox="1271 972 1439 1038">No effect</td> <td data-bbox="1439 972 1599 1038">Medium</td> <td data-bbox="1599 972 1767 1038">High</td> <td data-bbox="1767 972 1922 1038">High</td> </tr> <tr> <td data-bbox="1122 1038 1271 1085">Zygomycetes</td> <td data-bbox="1271 1038 1439 1085">No effect</td> <td data-bbox="1439 1038 1599 1085">No effect</td> <td data-bbox="1599 1038 1767 1085">No effect</td> <td data-bbox="1767 1038 1922 1085">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
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Target	Cell Wall	DNA/RNA Synthesis
Group	<p style="text-align: center;">Echinocandins (very toxic because it targets glucan)</p>	<p style="text-align: center;">Pyrimidine Analogous</p>
Antifungal Agents	<p style="text-align: center;">(usually end with -fungin)</p> <ul style="list-style-type: none"> - Caspofungin. - Micafungin. - Anidulafungin 	<ul style="list-style-type: none"> - Flucytosine (Used with yeast only, candida spp & cryptococcus neoformans)
Mechanism of Action M.O.A	<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>

Target	Group	Mechanism of action	Antifungal Agents	Spectrum of Activity	Comments
Cell membrane	Polyenes	Binds to ergosterol within the cell membrane, forming pores which lead to cell death	1) Amphotericin B 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) -Not effective against zygomycosis (except posaconazole) -Adverse effects -Drug interactions (toxic to the liver cells)
			2) Voriconazole	Good activity on Molds (e.g Aspergillosis) & yeast	
			3) Posaconazole	Broader spectrum of activity than other azoles Good activity on Molds & Yeast & Zygomycetes	
			4) Ketoconazole 5) Itraconazole 6) Miconazole 7) Clotrimazole	-	
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 fungi	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.

MCQs

1-Which of the following antifungal agents can be used against yeast and molds?

- a) Fluconazole
- b) Itraconazole
- c) Voriconazole
- d) Both b and c

2-Which of the following antifungal agents is the safest to use on a patient?

- a) Amphotericin B
- b) Fluconazole
- c) Miconazole
- d) Micafungin

3-Why might a person be considered immunocompromised?

- a) They recently underwent transplant surgery
- b) They have used immunosuppressive medication
- c) They are diabetic
- d) All of the above

4-Candida albicans is an opportunistic fungus which affects mainly people with which defect?

- a) Liver disorder
- b) Kidney disorder
- c) Blood cell disorder (immunosuppressed)
- d) Heart disorder

5-Subcutaneous mycoses mostly affects which part of the body?

- a) Skin & underlying tissue
- b) Heart
- c) Brain
- d) Nephrons

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

- a) Blocking of G6PD
- b) Block ergosterol synthesis
- c) Disruption of the cell membrane by binding to ergosterol
- d) Inhibit cell wall synthesis



MCQs

7- An immunocompetent person enters the hospital and is diagnosed with a fungal infection. What is the least likely type?

- a) Superficial mycoses
- b) Cutaneous mycosis
- c) Systemic mycoses
- d) Opportunistic mycoses

8- Which antifungal drug will act by inhibiting DNA and RNA synthesis?

- a) Flucytosine
- b) Fluconazole
- c) Caspofungin
- d) Nystatin

9- A patient enters the hospital with small patches on the skin, according to the patient they are painless but you observe some discoloration. What is this type of fungal infection called?

- a) Superficial mycoses
- b) Subcutaneous mycosis
- c) Cutaneous mycoses
- d) Systemic mycoses

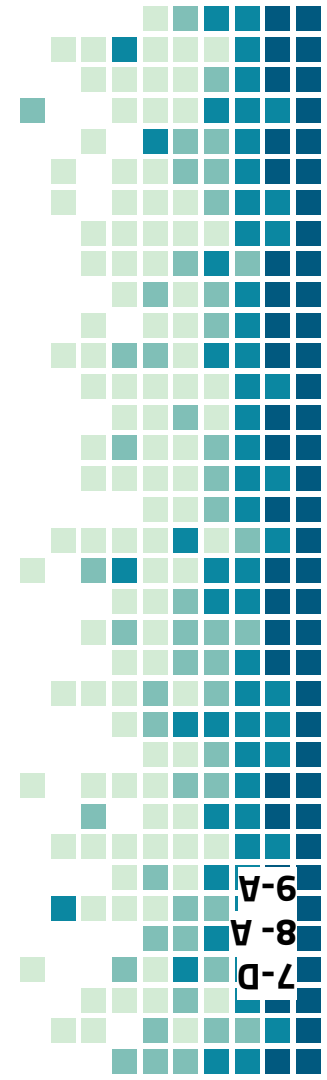
SAQ

Q1- Name an antifungal agent with a broad spectrum of action.

Amphotericin B or Nystatin

Q2- Describe the mechanism of action of Anidulafungin. Slide 8/9

Q3- What are the symptoms of dermatophytosis? Slide 5



7-D
8-A
9-A

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