

**Diversity  
of Fungi  
and  
Fungal  
Infections**

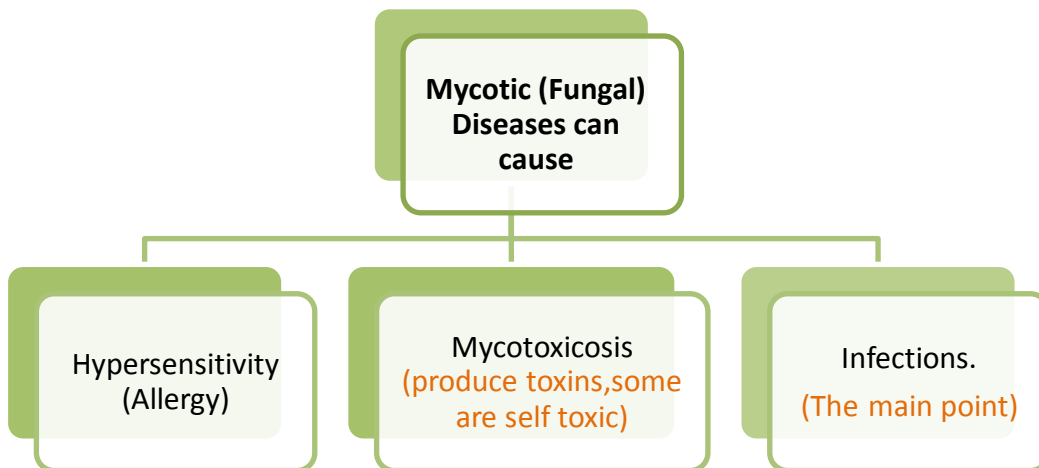
Lecture 11



### Revision on the first fungal lecture:

1. **Fungi** can be **classified** based on morphology to: **Yeast, Filamentous** fungi.
  2. **Yeast** is a **round unicellular** cell and it **replicates** by **budding**.
  3. A hypha is a long, branching filamentous cell and it replicate by spore formation and hyphal fragmentation
  4. We can differentiate between **filamentous** fungi by **microscopic** and **macroscopic appearance** of my **conidia**.
  5. We can differentiate between yeast by chemical substances.
  6. Not all fungi pathogenic most of them are not.
  7. The Normal habitat of **most fungi** is the **soil** ( **where we find it** ).
  8. Not any person that inhale or inject the fungi will get fungi infection.
  9. The fungi have to be Thermo tolerance and have the Ability to survive in tissue environment and the Ability to withstand host defenses to cause a disease.
- 

### Diversity of Fungi and Fungal Infections:



infection is acquired from:

- **Colonization** (normal flora) = development (**over growth**) of normal flora in or on the body (**The normal flora is any organism that lives within the host and cause no harm.**)  
(+) normal flora grows by 1-Antibiotics 2-weak immune system 3-humidity 4- obesity
- **Inhalation** (Airborne) (**carried through the air – spores**)
- **Contact.** (**Direct contact can cause Superficial and Cutaneous mycosis**).
- **Ingestion**
- **Trauma**

❖ The **host** can be ether **healthy** or **immunocompromised**.

- (Immunocompromised = the host who has a malfunction in the immune system - more severe )

| Types of fungal infections (Mycosis)          |                                                                                                                                       |
|-----------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------|
| Mycosis                                       | The effect                                                                                                                            |
| <b>Superficial mycosis</b>                    | Affect the outer layer of the skin or hair shaft, and has <b>No immune response</b>                                                   |
| <b>Cutaneous mycosis</b><br>(Dermatophytosis) | on the keratin of the skin (nail and hair) caused by a group of keratinophilic fungi, called dermatophytes ( <b>immune response</b> ) |
| <b>Subcutaneous mycosis</b>                   | They go to the dermis, subcutaneous, tissues, muscle and may extend to bone and has an <b>immune response</b>                         |
| <b>Systemic mycosis</b>                       | Internal organs and respiratory diseases and it usually caused by <b>primary disease</b> .                                            |
| <b>Opportunistic mycosis</b>                  | if the <b>immune system is compromised</b> by Risk factors : HIV/AIDS, Malignancies, Organs transplantation, Diabetes                 |

- ❖ These infections can be seen in both hosts but the damage caused by infection will be more severe in the Immunocompromised host except of the **Opportunistic mycoses we will only see it in**
1. the immunocompromised
  2. if the host who looks healthy but has an immune deficit which is not discovered yet.( like in the HIV patient )

- ❖ The Fungi can be an Opportunistic Fungi or Primary Pathogens

### **Opportunistic Fungi:**

1. normal flora (candida) – the most fungi causes infection
2. fungi in our environment (Aspergillus, Zygomycetes and Cryptococcus)

### **Primary Pathogens:**

1. Endemic: cause diseases by inhalation
2. Dermatophytes: cause diseases by contact

### ❖ **Diagnosis of fungal infection**

- Clinical features (history, risk factors, etc)
- Imaging: x-ray, MRI, CT scan.
- Lab Investigations: Histopathology and Microbiology

### ❖ **Lab Diagnosis:** Direct Microscopy → Culture → Serology → PCR.

# Direct Microscopy :

1. Potassium Hydroxide (10-20% KOH) – ( it isolates the fungus)
2. Fungal stains:

Giemsa Stain, Grocott's Methenamine Silver stain (GMS), India ink

# Culture:

Fungal media: Sabouraud Dextrose Agar (SDA), other media if needed.

# Serology: (Detection of Antigen and/or Antibody in the serum)

# PCR (Polymerize chain reaction) : (Detection of Fungal DNA)

**Notes:**

- ❖ **Among all the fungi "Candida" is number one that well cause fungal infections then "Aspergillus" is number 2.**
- ❖ **Dermatophytes: it cause the systemic mycosis and it is contagious .**

We use Antifungal agents to clear fungal infections (**Mycosis**)

( Antibiotics for bacteria )

| Target (for the antifungi) | Group                 | Mechanism of action                                                                                                                | Antifungal Agents                                                                                         | Spectrum of activity                                                                                                                                                                                                                                                                                               | Comments                                                                                                                                |
|----------------------------|-----------------------|------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------|
| <b>Cell membrane</b>       | Polyenes              | Binds to ergosterol within cell membrane, formation of pores which lead to cell death                                              | Amphotericin B, Nystatin                                                                                  | <b>Broad antifungal spectrum</b> which includes <b>most fungi</b>                                                                                                                                                                                                                                                  | Serious toxic side effects (nephrotoxicity) ( <b>ergosterol is similar to cholesterol of human, so it is serious toxic</b> )            |
|                            | Azoles<br>The largest | Inhibit the synthesis of ergosterol                                                                                                | Ketoconazole<br>Itraconazole<br>Fluconazole<br>Voriconazole<br>Posaconazole<br>Miconazole<br>clotrimazole | Variable antimycotic activity*<br><b>Fluconazole are used to treat the infections that is caused by yeast and has a limited or no activity against mold fungi</b><br><b>Voriconazol</b> is the drug of <b>choice for Aspergillosis</b><br><b>Posaconazole</b> has a broader spectrum of activity than other azoles | Not effective against zygomycosis (except posaconazole)<br>Adverse Effects<br>Drug Interactions                                         |
| <b>Cell wall</b>           | Echinocandins         | Inhibits glucan synthesis, (glucan polymers in the fungal cell wall)<br>Glucan is very important for the rigidity of the cell wall | Caspofungin<br>Micafungin<br>Anidulafungin                                                                | Good activity against <i>Candida spp</i> , <i>Aspergillus spp</i><br>Limited or no activity against other fungi                                                                                                                                                                                                    | Has less toxicity and side effects compared to amphotericin B and azoles<br><br>( <b>less toxic because human cells has no glucan</b> ) |
| <b>DNA/RNA synthesis</b>   | Pyrimidine analogues  | Fungal RNA miscoding<br>Interfering with DNA synthesis                                                                             | Flucytosine                                                                                               | Restricted spectrum of activity<br><i>Candida</i> species<br><i>Cryptococcus neoformans</i>                                                                                                                                                                                                                        | Monotherapy now limited (Resistance)                                                                                                    |