

- **Fundamental medical mycology, Errol Reiss, H. Jean Shadomy, and G. Marshall Lyon, III :Wiley-Blackwell, Hoboken, NJ,USA, 2011**
- **Textbook of medical mycology ,By: Dr.hamzia Ali Ajah ,2018**

### **Introduction to medical mycology**

#### **MYCOLOGY**

Myco- = fungi - mykes (mushroom)

-logy = the study of

Is the study of fungi, includes their genetic and biochemical properties, their taxonomy, and their use to humans as source for medicinals (e.g., penicillin), food (e.g., beer, wine, cheese, mushrooms ...), as well as their dangers, such as poisoning or infection.

#### **HISTORY**

Mycology was one of the first microbiological sciences, beginning around 1835, when Bassi discovered that some fungi are pathogenic. In 1900, Darling characterized the pathogenic fungus, *Histoplasma capsulatum*. However, the majority of the techniques used today to isolate and identify fungi were developed in the early 1900's by a scientist named Sabouraud. Because of his major contributions in mycology, Sabouraud is called the "Father of Mycology." Medical mycology is a special of medical microbiology concerned with all aspects of diseases in humans and lower animals caused by pathogenic fungi. Mycoses are diseases of humans and lower animals caused by pathogenic fungi.

#### **Definition of fungi.**

The living world is divided into the five kingdoms of Planta, Animalia, Fungi, Protista and Monera. .fungi are eukaryotica, heterotrophic, unicellular to filamentous, rigid cell wall ,spore bearing organisms that usually reproduce by both sexual and asexual means. Further they are insensitive to antibacterial antibiotics.

**a-** Eukaryotic cells contain membrane bound cell organelles including nuclei, mitochondria, Golgi apparatus, endoplasmic reticulum, lysosomes etc.

**b-** Heterotrophic - fungi lack chlorophyll and are therefore not autotrophic (photosynthetic) like plants and algae; rather they are heterotrophic

absorptive organisms that are either saprophytes (living on dead organic matter) or parasites (utilizing living tissue).

c- Like plants, fungi have rigid cell walls and are therefore non-motile, a feature which separates them from animals.

### Structure of Fungi.

Fungi occur in two basic growth forms or stages:

(a) **A unicellular or yeast form** which is defined morphologically, as a single-celled fungus that reproduces by simple budding to form blastoconidia.



Figure 1. Illustration of blastoconidia. Figure 1-2. Illustration of pseudohyphae

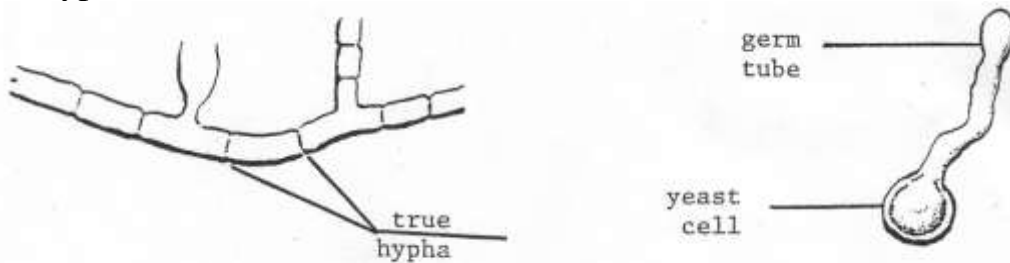


Figure 2. Illustration of true hyphae Figure 1-4. Illustration of germ tubes.

(b) **A filamentous or mould form** which is a vegetative growth of filaments. consist simply of a number of filaments packed tightly together, and reproduction is by spores or conidia. Fungal filaments are known as hyphae and a mass of hyphae collectively make up the mycelium. There are two kinds of hyphae; non-septate (coenocytic) and septate.

Fungi with non-septate hyphae typically belong to the Zygomycetes. Non-septate hyphae are considered to be more primitive because if a hyphal strand is damaged the entire strand dies. Septate hyphae are typically found in the Basidiomycetes and Ascomycetes,

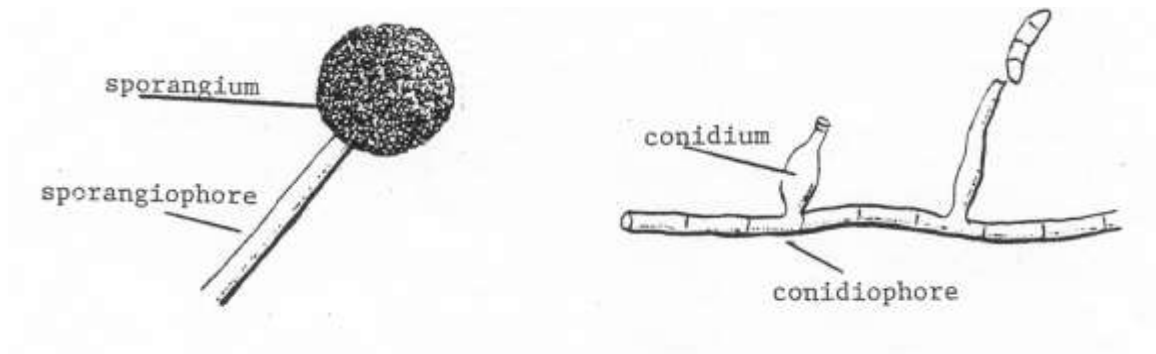


Figure 3. Illustration of sporangium Figure 1-6. Illustration of conidia and and sporangiophore. Conidiophore.

**DIMORPHIC FUNGI:**

This class of fungi is characterized by two forms of growth:

1. Growth as a mold with septate hyphae in their natural reservoir (e.g. soil) or when incubated at 25° C. on conventional fungal media (Sabouraud dextrose or potato dextrose agars).
2. Growth as a yeast in the tissues of an animal/person or when incubated at 37° on enriched media (Brain heart infusion agar)

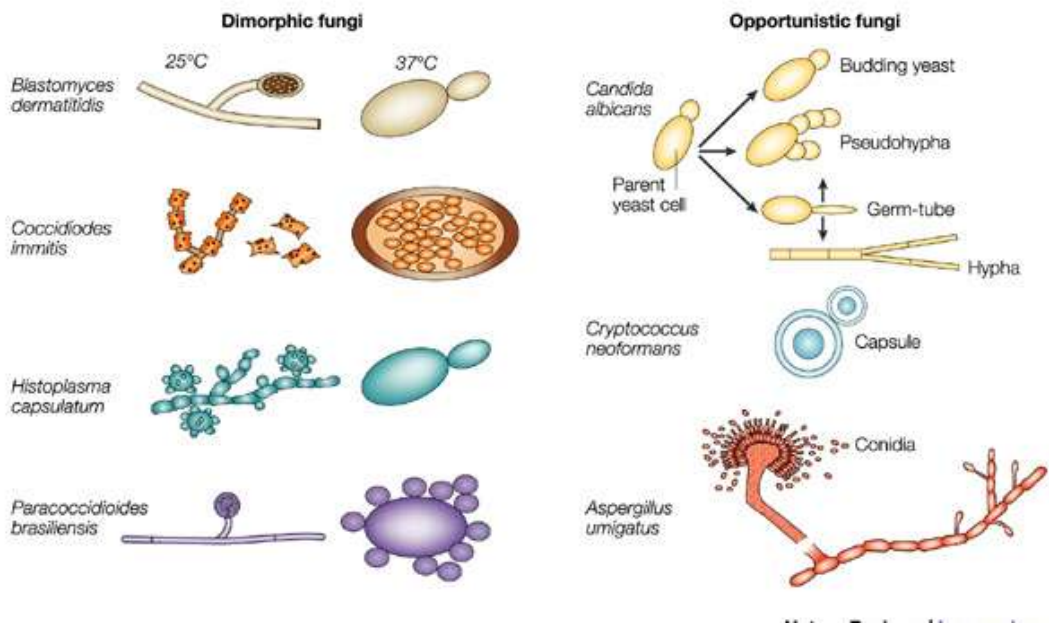


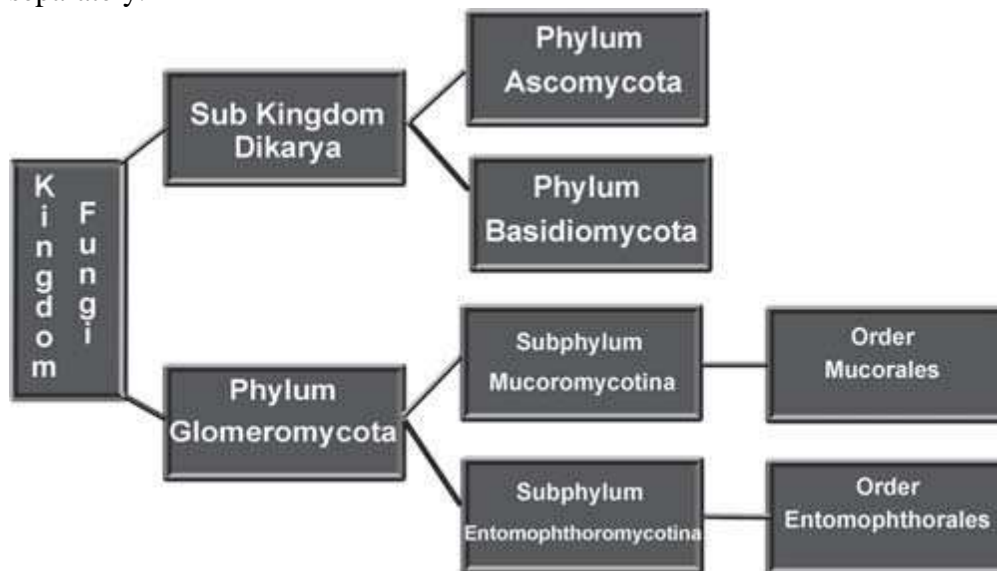
Figure 4: Dimorphism in fungi

**Two basic types of reproductive are found in the fungi:**

- (a) Sexual reproduction is produced by the fusion of two nuclei that then generally undergo meiosis. Sexual methods of reproduction involve plasmogamy (cytoplasmic fusion of two cells), karyogamy (fusion of two nuclei), genetic recombination and meiosis. The resulting haploid spore is said to be a sexual spore, e.g. zygospores, ascospores and basidiospores.
- (b) Asexual reproduction (somatic or vegetative reproduction ) is very common in fungi and occurs by variety of mechanisms. Budding , Fission, Fragmentation of hyphae, Asexual spores

### Classification of Fungi.

The higher level classification of kingdom Fungi was revised by Hibbett et al. (2007). These revisions take into account *cladistic analysis*. The largest category of fungi pathogenic for humans is the subkingdom *Dikarya*, consisting of two phyla: *Ascomycota* and *Basidiomycota*. (The familiar phylum *Zygomycota* is not considered a valid taxon because it is not *monophyletic*.) Fungal pathogens previously classed in the *Zygomycota* are now found in the phylum *Glomeromycota*, subphylum *Mucoromycotina* and subphylum *Entomophthoromycotina*. In summary, the phyla and subphyla are constructed based on the the result of cladistic analysis and the mode of sexual reproduction: the *Mucoromycotina*, *Ascomycota*, and *Basidiomycota* (Figure 1-22). The *Entomophthoromycotina* formerly classed with the *Zygomycota* are now considered separately.



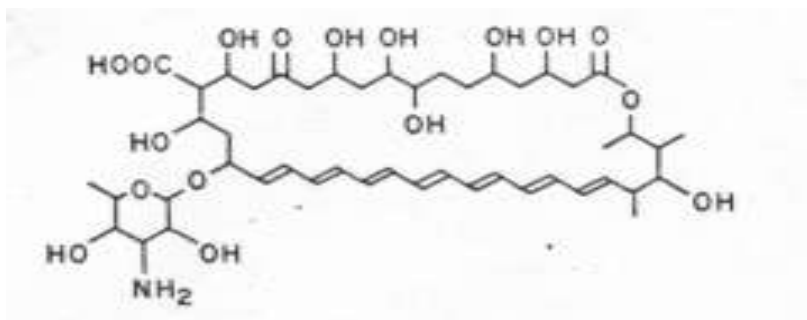
**Figure 5:** A higher level classification of the kingdom Fungi: phyla and subphyla containing pathogenic fungi (Hibbett *et al.*, 2007).

## Antifungal agent

An antifungal agent is a drug that selectively eliminates fungal pathogens from a host with minimal toxicity to the host.

### 1-Polyene Antifungal Drugs

Amphotericin, nystatin, and pimaricin interact with sterols in the cell membrane (ergosterol in fungi, cholesterol in humans) to form channels through which small molecules leak from the inside of the fungal cell to the outside.



Amphotericin B

### 2-Azole Antifungal Drugs

Fluconazole, itraconazole, and ketoconazole inhibit cytochrome P<sub>450</sub>-dependent enzymes (particularly C14-demethylase) involved in the biosynthesis of ergosterol, which is required for fungal cell membrane structure and function. **Antifungal Azoles** are synthetic drugs

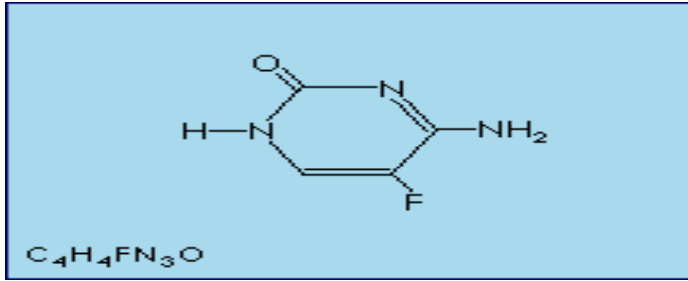
with broad-spectrum fungistatic activity. Azoles can be divided into two groups: the older *imidazole agents* (**clotrimazole, ketoconazole, miconazole**) in which the five-member azole nucleus contains two nitrogens and the newer *triazole compounds* (**fluconazole, itraconazole, and voriconazole**), in which the azole nucleus contains three nitrogens.

### 3-Allylamine and Morpholine Antifungal Drugs

Allylamines (naftifine, terbinafine) inhibit ergosterol biosynthesis at the level of squalene epoxidase. The morpholine drug, amorolfine, inhibits the same pathway at a later step.

### 4-Antimetabolite Antifungal Drugs

5-Fluorocytosine acts as an inhibitor of both DNA and RNA synthesis via the intracytoplasmic conversion of 5-fluorocytosine to 5-fluorouracil.



## Lab Diagnoses of Mycoses

- Clinical presentation
  - History (risk factors)-Physical Exam (lesions,ets)
  - Mould or Yeast? -Septate hyphae?
- Culture of organism (days to weeks)

Media Most Frequently Used for the Cultivation of Fungi.

- (1) Sabouraud's Dextrose Agar (SDA).
  - (2) Sabouraud's Dextrose Agar with antibiotics
  - (3) Brain Heart Infusion Agar (BHIA) ,Problem, contaminating bacteria
- Serology-Antibody or Antigen tests
  - Molecular Biology-PCR