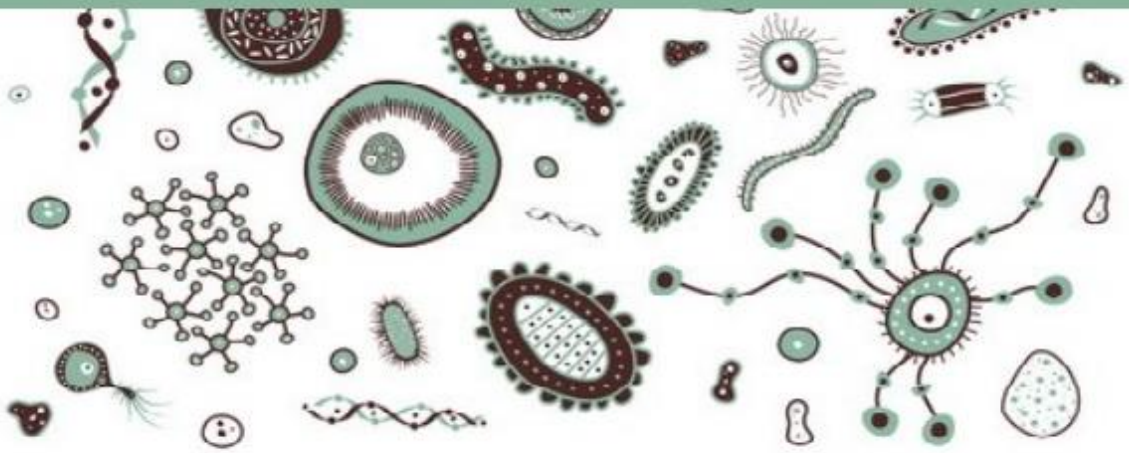
Microbiology



◉ Sheet ○ Slides

Number :18

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Introduction to medical mycology:

First of all, we are not going to cover all the medical mycology in this course. These lectures are not found in any reference, so stick in what is written here...

Mycology: is branch of microbiology that studies fungi.

Historically, Fungi were mistakenly considered as plants. Although fungi are evolutionarily more closely related to animals than to plants, this was not recognized until a few decades ago after some researches related to cell wall, cytoplasm and other organelles. So biologists have accepted that it's a distinct group of microorganism...

1.1 General features of fungi

1-eukaryots: having true nuclei, containing more than one chromosome –unlike bacteria- , for example, most yeasts have 16 chromosomes with 6250 gene → larger number of genes than bacteria.

2-fungal cells are generally **larger** than bacterial cells.

3-We can't use bacterial stains to examine fungi .However , some yeasts appear as a G +Ve if stained with gram stain despite the fact that yeasts have different cell wall structure than bacteria .

4-**fungi reproduce by budding or sporulation,** not binary fission...

5- Relatively nonpathogenic: of 100000 known species, only few are considered as human pathogens "100 human pathogens ".

So fungal infections are rare unlike bacterial infections, if you visited the microbiology department in any hospital, you will notice that only 10% of the specimens are related to fungal infections.

Fungi, however, found mostly in association with plants, not animals.

- ❖ Notice that points 1-5 are differences between fungi and bacteria.

6-fungal infections are called Mycosis. And usually not susceptible for antibiotics.

7-fungi are distributed everywhere: like bacteria, it can be found in soil, water or trees, some of them could be considered as normal flora!

8-aerobic: most of them require oxygen as a final electrons accepter in the ETC... So they can't live in anaerobic conditions.

However, yeasts are considered as facilitative anaerobes, having the ability, to switch between aerobic respiration and anaerobic fermentation, if they have been deprived from Oxygen.

Aspergillus Niger, is a major **exception**, is one of the few filamentous fungi that can survive anaerobic conditions, having the ability to switch between aerobic respiration and anaerobic fermentation (facilitative anaerobe), which is used in industry to produce many organic compounds, like **citrate.**

9-heterotrophes / chemoheterotrophes: can't do photosynthesis, this is one of the **major differences between plant and fungal cells...**

So, they have to "**eat**" in order to acquire inorganic compounds – (like Co2) or organic compounds, like vitamins, minerals, water... etc ...

- ❖ **Yeasts**, like heterotrophic bacteria, require complex organic compounds for growth, mainly carbohydrates.

- **Filamentous fungi** are more similar to chemoheterotrophes, having the ability to utilize some inorganic compounds like Co2...

Notice that eating in general is divided into digestion and absorption.

Higher eukaryotes, like humans, have an internal digestive system that digest food internally. However, **fungi don't depend on an internal digestive system**. They, instead, liberate some enzymes, that will hydrolyze carbohydrates... and these monomers will be absorbed internally. So, in general, **fungi eat only by absorption, without digestion.**

1.2 Classification of fungi

Fungi is divided into two major classes,

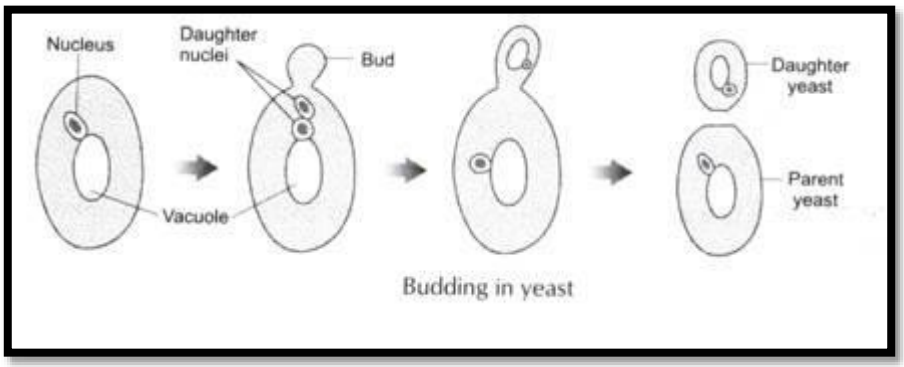
1-unicellular cells "yeasts": yeasts are spherical unicellular organisms, having true nucleus, which means that fungi belong to eukaryotes...

- One of the most known yeasts, is baker's yeast *Saccharomyces cerevisiae" which* is highly important in baking (fermentation of sugars → carbon skeleton (ethanol) + Co2 "causes enlargement of Dough "). we can also use it in industry to produce variety of vitamins "provitamin D " and some pharmacological products by genetic engineering like hormones "insulin" , vaccines "habitats B vaccine "

Yeasts Reproduce by budding

- The difference between both, binary **fission** is the division of a cell to give two **equal** cells...

In budding: **bulging** on the surface of the cell → flow of the **cytoplasm** → **enlargement** of the bulge with the time because of the flow of the cytoplasm → the nucleus will start division and DNA replication ending by **two separated nuclei** → one of these nuclei will **migrate** to the daughter cells → daughter cells will be **separated gradually** "usually, when daughter cell is separated, it's as large as mother cell .. so the **major difference between binary fission and budding , that daughter cells in budding mature and separate gradually** " .



Notice that, budding is considered as a special type of **mitoses**.

2-filamintous fungi "molds " : multicellular fungi which are mixtures of many small and large morphological structures (so we have central filaments , vertical filaments , at the end of these filaments we have what we call a head projecting structure "vesicle" , which carries the spores)

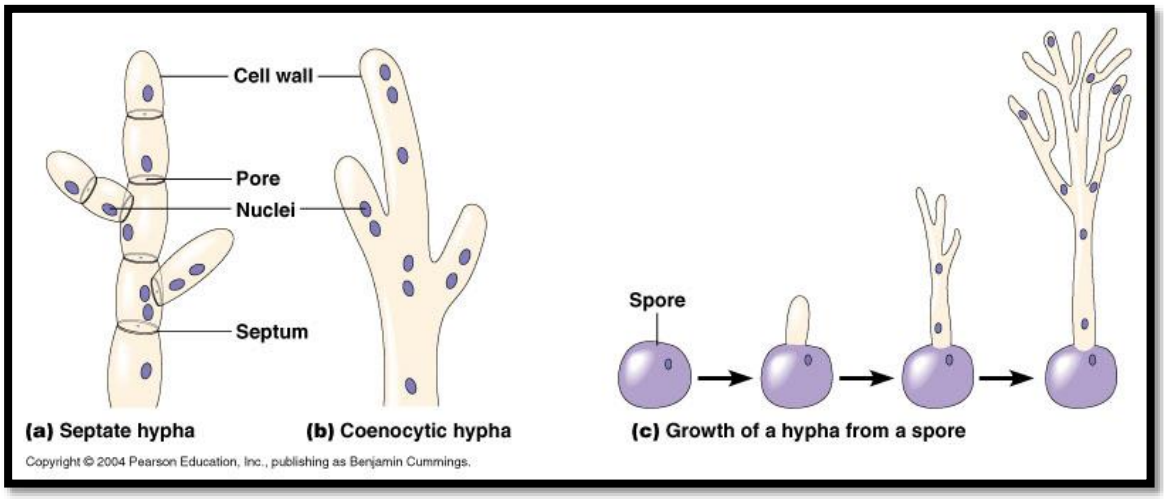
- Filaments are used for absorption of water and some nutrients. In gross examination, these filaments appear like plant roots, so they though in the past that fungi belong to plants...

- They are called molds "العفن "because **they can infect any type of food that contain sugars and / or protein,** especially fruits and bread. These molds are very important in the nature, in what we call **recycling of the organic compounds,**

especially cellulose, by degrading these macromolecules into smaller and simpler organic compounds like alcohols.

Molds reproduce, usually by **sporulation**:

When we say molds, we actually mean “filamentous fungi “, as a conclusion molds are composed from many filaments or “Hyphae” ... the life cycle of these molds depends on these hyphae :



1-At first, **we have a horizontal Hyphae**, composed of tube-like structure.

2-during replication, other horizontal filaments are projecting from the first filaments, **these filaments will start branching "like a tree"**, ending by **vertical filaments**...

Note … we have two types of hypha (septated, coenocytic)... (Seen in the figure)

3-At the end, these filaments are going to form heads, or *“**vesicles**”*, these vesicles are going to form other morphological units … that will carry **spores**.

We call small spores “microconidium”, while large spores "macroconidium”.

4-each of these spores , can grow up into a tube-like structure "Hyphae" , if it reached an appropriate environment … it will repeat the life cycle again and again and again and again and again and again :p …

To sum up:

Horizontal filaments → **vertical** filaments → spores **carried** on the vesicle → liberation and **spreading** of these spores → each **spore gives me one hyphae** → collection of all these hyphae "**mycelium**"

Due to the fact that we cant use gram stain or any biochemical tests to classify these molds , we depend on some morphological features (i.e. type of filaments, type of fragmentation of theses filaments, presence of different branching, number of branching, the number of spores and the size of the spores. Etc, / **type of the mycelium**)

❖Mycelium?!

-it's the collection of all filaments …

-Vegetative mycelium: horizontal filaments (tube-like structure) which means the presence of filaments inside the medium -which could be soil, plants or whatever. They're responsible for absorption of nutrients and support the growth of the second type of mycelium (over-the-medium-areal mycelium). More like the roots of a tree, that's why in the past filamentous fungi were classified as plants.

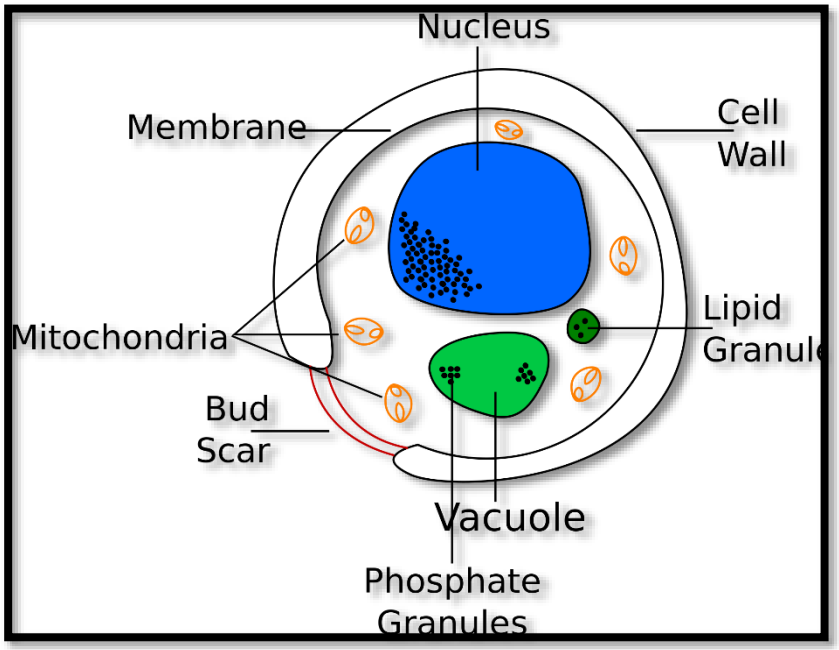
Filaments might not be divided by presence of septa (singular; septum) it might be elongated without any presence of crosswords. In some types of fungi it might be divided and you might recognize the presence of crossword between one cell and the other.

-Areal mycelium: the filaments and the spores which grow over the medium (over the surface of soil or culture media) so it will be

exposed to the air, more like the branches of a tree. It's often recognized by eyes.

Areal mycelium projects over the surface of its media (whether soil, culture media...) - you'll recognize it with your eyes, you may observe different colors, due to the color of spores (red, black…).

1.3 Basic structure of fungi...



1-Cell wall:

As shown in this picture, fungi have special cell walls composed mainly of **complex polysaccharide**, especially chitin (polymer of N- acetyl-glucosamine), this chitin might be associated with few amounts of specific types of sugar; called glucan and mannan, and this is implied also to multi-cellular fungi. So it's a very simple structure, similar to the plants cell wall, of course in plants cell wall mainly it's composed of cellulose rather than chitin.

2-cellular membrane:

Cell membrane of the fungi (whether unicellular "yeast" or multicellular), is composed mainly of lipo-phosphate associated

with certain amount of complex lipids known as **Ergosterol**, while our human cells has cholesterol.

- **Ergosterol …!**

-Contribute rigidity of the cell membrane → survive in harsh conditions.

-Maintains the function of the cell membrane.

3- Inside the cytoplasm we have a true nucleus with true nuclear membrane, a mitochondria and an endoplasmic membrane, thus fungi is considered as eukaryotic cells. Also, there are certain substances like phosphate, lipids and glycogens packed in granules "known as lipid granules "

Note: in filamentous fungi, you can see filaments projecting from cell wall.

However, **Filaments can curry spores only in aerobic conditions**. (That's why we said that almost all filamentous fungi are obligate aerobes).

1.4 Some examples ….

Candida …!

We said that only few species of fungi are related to human cells... let's talk about one of the most famous examples for human-related fungi … "candida", that is considered as an opportunistic pathogen due to the fact that they're found in few numbers in the oral cavity, intestine, mucosa of the vagina (especially in young ladies, which can increase or decrease due to variety of conditions), etc

Cryptococcus neoformans

Only one type of yeasts is encapsulated, known a *Cryptococcus neoformans*, which is an obligate pathogen that could reach the lungs and sinuses causing some chronic infections

Note: these two examples will be covered in details next...

Mushrooms...

Mushrooms are considered as special type of fungi, it's somewhat similar to filamentous fungi. With eukaryotic cells and filaments, at the head of the mushroom, we have a collection or a "nest "of filaments, also called the cap.

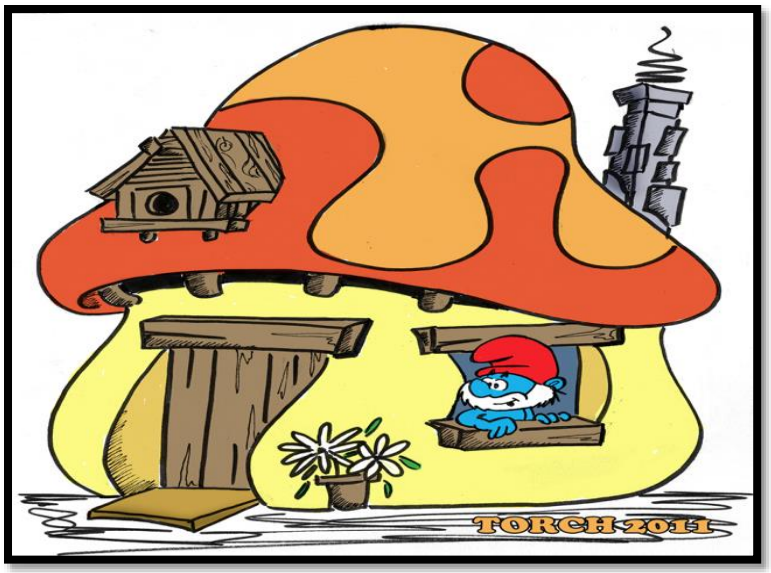
Mushrooms are rich in sugars and carbohydrates, they contain also small amounts of fatty acids, so some of them are used as a food.

However, some wild mushrooms are poisonous, causing death in few hours.

As a general role:

If the head was white, **brown**, **having no other color** → nontoxic

Other color → **white** + **red** / **white** + **dark blue** → toxic → death in few hours.



1.5 Fungi related to human pathology "introduction"

1-Candida …… “Again -_- !! “

As we know, Yeasts candida are commensals, being part of our normal flora (found in mouth ... intestines … vagina. etc.).

Because it **reproduces by budding**, it cannot attach to mucosal membrane, so usually **does not cause inflammation** in the mucosa.

However , it can only attach to mucosa loosely in **immunocompromised patients** , or if there’s **any disturb in the equilibrium of the normal flora**, it may produce filaments “ **Pseudohyphae** “ and attach to the mucosa , causing irritation of the mucosal cells , due it’s antigenic cell wall , causing inflammation → **erythematic lesions**

Note: in the lab, the presence of yeast in a specimen is not considered usually as a pathologic condition, unless they told you that these specimens are brought from inflammatory site.

2- Cryptococcus neoformans.

3-True fungi

Second type of filamentous fungi, usually called **true fungi**, which may cause infections...

The infecting is developed by **implanting** of small segment of the hyphae in a damaged tissue, if managed to grow, the growth pattern will be different from typical filamentous fungi “not associated with production of vertical filaments and spores “

It will produce a network of filaments, causing what we call a **granuloma lesion**, so there’s no typical inflammation reaction like what we recognize in bacteria.

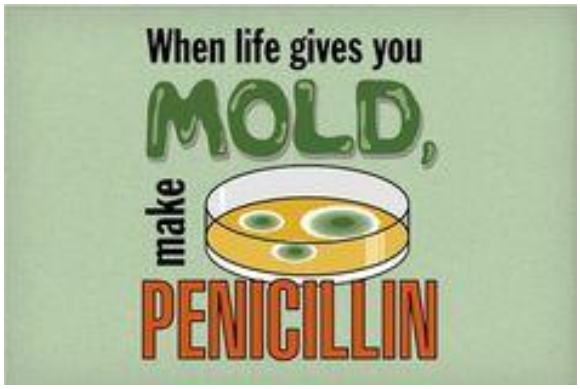
1.6 Anti fungal drugs

Studying antifungal drugs is much easier than antibacterial drugs, because we have only 3-4 groups of antifungal drugs... examples:

1- **Nystatin**: used topically, causing damage to **Ergosterol** → affect the cell membrane**.**

2- **Amphotericin B:** which binds with Ergosterol, forming a transmembrane channel that leads to monovalent ion (K^+, Na^+, $H^+$and Cl^-) leakage, which is the primary effect leading to fungal cell death. (Used in **systemic infections** , blood infections , meningitis) , highly toxic

3- **Azoles**: **these drugs doesn't act directly on Ergosterol.** instead , they inhibit some enzyme that are essential for synthesis of Ergosterol (ends by suffix –zole , like : **Clotrimazole , Posaconazole , Ravuconazole** , etc) .



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