



# Microbiology

Doctor 2017 | Medicine | JU

● Sheet

○ Slides

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# Intro to Mycology

\*underlined text was explained in the lecture but is not found in the slides

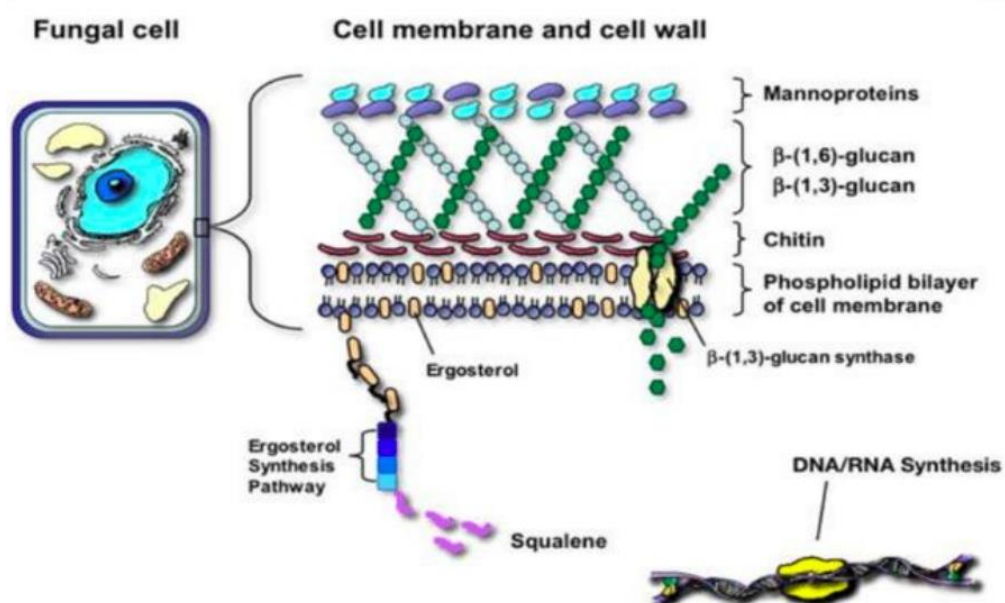
-mycology: the study of the mycoses of man (fungal infections)

-less than 300 species of fungi are pathological to man

-developed in the 1800s before bacteriology

## What is a fungus?

- Eukaryotic, heterotrophic, no chlorophyll
- Produce **hyphae** structures (mold), and **spores** for reproduction
- Grow on dead tissue (**saprophytic**) or on living tissue (parasitic) or symbiont (commensal/part of our normal flora)
- All fungi use organic carbon from decaying matter as food source; they secrete chemotrophic enzymes that degrade organic substances into soluble nutrients, then absorb them
- Have a rigid cell wall made of **chitin**,  **$\beta$ -glucans** and **mannans**, which are polysaccharides and targets for antifungal drugs
- Contain **ergosterol** rather than cholesterol (also target for antifungals)
- Mostly obligate anaerobes
- Can be sexual (teleomorphs) or asexual (anamorphs). The reproductive units are called propagules
- The asexual elements in propagules are called **conidia**; spores can be sexual or asexual, and a single fungus can be seen to reproduce sexually and/or asexually



## Importance of Fungi:

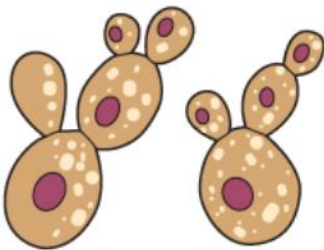
- Often cause damage to crops
- Number of infections are on the rise due to immunosuppressants such as drugs and diseases like AIDS
- Produce antibiotics (penicillin)
- Used in the food industry (bread, cheeses, wine...)

## General Mycology:

Morphologically, fungi can be classified based on their growth into:

### 1. Yeasts:

- a. Round cells that reproduce via budding
- b. Can form long chains of budding cells (pseudohyphae)
- c. Examples include *Candida albicans* (human flora) and *Cryptococcus neoformans* (found in pigeon faeces and soil)
- d. Common cause of infection in immunosuppressed patients
- e. Can infect multiple body systems (arthritis, meningitis, respiratory infections)



Budding yeast cells

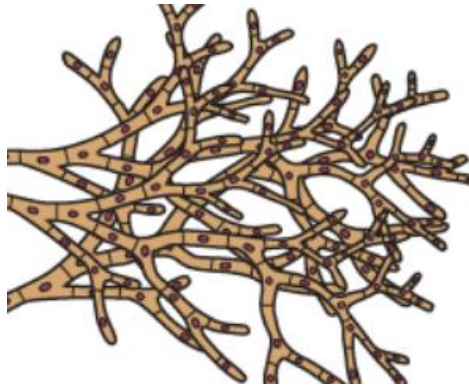


Pseudohyphae

### 2. Molds:

- a. Filamentous fungi with long, branching filaments (hyphae)
- b. Can be septate or non-septate (septate means separation, so non-septates form one long continuous cell with multiple nuclei)
- c. The mycelium is the mass of branching hyphae stereotypical of molds
- d. Can produce asexual spores at tip or sides of hyphae; spores are held in sacs called sporangiospores (e.g. in Dermatophytes (ringworms), Zygomycetes and *Aspergillus*)

- e. The difference between pseudohyphae and real hyphae is that pseudohyphae have no septation (only constriction) and have fragile cell walls



Drawing of a septate mold

### 3. Dimorphic Fungi:

- Can form yeasts or molds dependent on the environment
- Exist as yeasts when grown in tissues or at 37°C (parasitic stage), and molds form at 22°C (saprophytic stage)
- Examples include *Blastomyces dermatitidis*, *Coccidioides immitis* and *Histoplasma capsulatum*
- This dimorphism is reversible and is highly linked to virulence; dimorphism can be blocked biochemically so the fungus doesn't cause disease anymore, and removing the block will make it virulent again

## **Fungal Diseases:**

As stated before, fungal diseases are becoming a growing threat, especially to individuals with a compromised immune system. Fungal diseases can be divided into three classes; allergies, intoxications, and infections.

### 1. Allergies

- Spores are constantly in the air and molds can grow on any moist, organic surface
- Inhalation of spores or toxins can cause an allergic reaction, with symptoms such as asthma and eosinophilia
- In the nasal area, they manifest as allergic rhinitis. In the bronchial area, they cause asthma. In the alveolar area, it appears as allergic alveolitis
- Example: *Aspergillus fumigatus*

## 2. Toxins (mycotoxicosis)

- a. Most common toxins are aflatoxins, which are produced by some fungi (like Aspergillus species), and these fungi grow on foods such as corn, peanuts, and tree nuts
- b. Intoxication results from ingestion of aflatoxins on food
- c. Aflatoxins are metabolized in the liver to epoxide, which is a carcinogen
- d. B1 aflatoxin causes a mutation in the p53 tumor suppressor gene, which can cause uncontrolled growth in hepatocytes (hepatocellular carcinoma)

## 3. Infections (mycoses)

- a. Most frequent
- b. Can be mild or deadly infections depending on the immunity of the host
- c. Fungal infections are becoming more common due to increased use of antibiotics, corticosteroids, and cytotoxic drugs (immunosuppressant)

Infections can be classified according to the tissue that has infection:

- **Superficial and cutaneous;** infection in the epidermis, mucosa, nail, or hair
  - May or may not cause tissue destruction and immune response
  - No living tissue invasion is involved
  - E.g. Pityriasis versicolor and Tinea nigra (superficial), cutaneous candidiasis and dermatophytes (cutaneous)
  - The difference between cutaneous and superficial is that in cutaneous infections, pathological changes take place due to fungus or its metabolites, while in superficial infections, there are no pathological changes
  - Signs and symptoms of cutaneous infection: itching, scaling and broken hair
- **Subcutaneous;** infection is limited to sub-cutaneous tissue such as basement membrane, without spread to other tissues
  - E.g. chromoblastomycosis and mycetoma (Madura foot)
  - Acquired through skin cuts/abrasions
- **Systemic (endemic);** infections affecting body systems that can disseminate
  - E.g. coccidioidomycosis, histoplasmosis, paracoccidiomycosis and blastomycosis
- **Opportunistic;** cause infections in immunocompromised patients
  - E.g. Cryptococcus and candida species

## **Diagnosis of Fungal Infection:**

Diagnosis is based on a combination of clinical observation and laboratory investigation. The clinical observation is mainly seeing if the patient responds to antibacterial antibiotics.

## **Laboratory Investigation:**

- Recognition of fungus using microscopy
- Isolation of fungus in culture
- Use of serological test (blood sample) [antigen-antibody interaction]
- Using PCR to recognize fungal DNA
- Types of specimens:
  - Skin, nails, and scalp scrapings with hair stubs
  - Suspected candida infections should be taken from mucosal swabs
  - Subcutaneous infections need skin, crusts, pus, or biopsies (excised tissue)
  - Systemic infections require specimens from site of infection (biopsies and fine-needle aspirations)
- Stains and microscopy
  - Can be examined using wet mount after digestion using potassium hydroxide (a strong alkali that digests the surrounding tissue, making fungi more prominent/visible)
  - Calcoflour can be added to wet mount, because it and KOH bind to the cell wall and can be detected using fluorescent microscopy
  - Use of special stains: methylene blue, lactophenol blue, PAS and ink
- Cultures; relatively easy to grow, and are the most sensitive means of diagnosis
  - Sabouraud dextrose medium is used and can be paired with chloramphenicol and cycloheximide to prevent bacterial and saprophytic contaminations, respectively

## **Therapy:**

- Antifungal agents are dependent on the presence of ergosterol in fungi
- Polyenes such as amphotericin B (used as IV in systemic mycoses) and nystatin (topical) are fungicidal drugs; they bind to membrane sterols and destroy membrane structure

- Azoles such as ketoconazole, fluconazole, itraconazole, voriconazole and posaconazole are fungistatic; they disrupt ergosterol synthesis. Azoles are hepatotoxic, so patient's liver functions must be monitored during their use
- Other drugs include:
  - Griseofulvin (used to treat superficial mycosis)
  - 5-fluorocytosine [5-FC] (inhibits fungal RNA/DNA synthesis)
  - Allylamines e.g. terbinafine/Lamisil (used to treat dermatophytes)
  - Echinocandins e.g. Caspofungin (inhibit synthesis of glucans)

The following slide wasn't explained in the lecture:

## Spore types

- Conidial Asexual spores | Formed off of hyphae | Common | Airborne
- Blastoconidia: "Buds" on yeasts (asexual budding daughter yeast cells)
- Arthroconidia: Asexual spores formed by a "joint"
- Spherules and Endospores (Coccidioides): Spores inside the spherules in tissues

