FUNGI

-Commonly present in nature as saprophytes,
-transiently colonising or etiological agenses.
-Frequently present in biological samples.
-They role in pathogenesis can be difficult to determine.

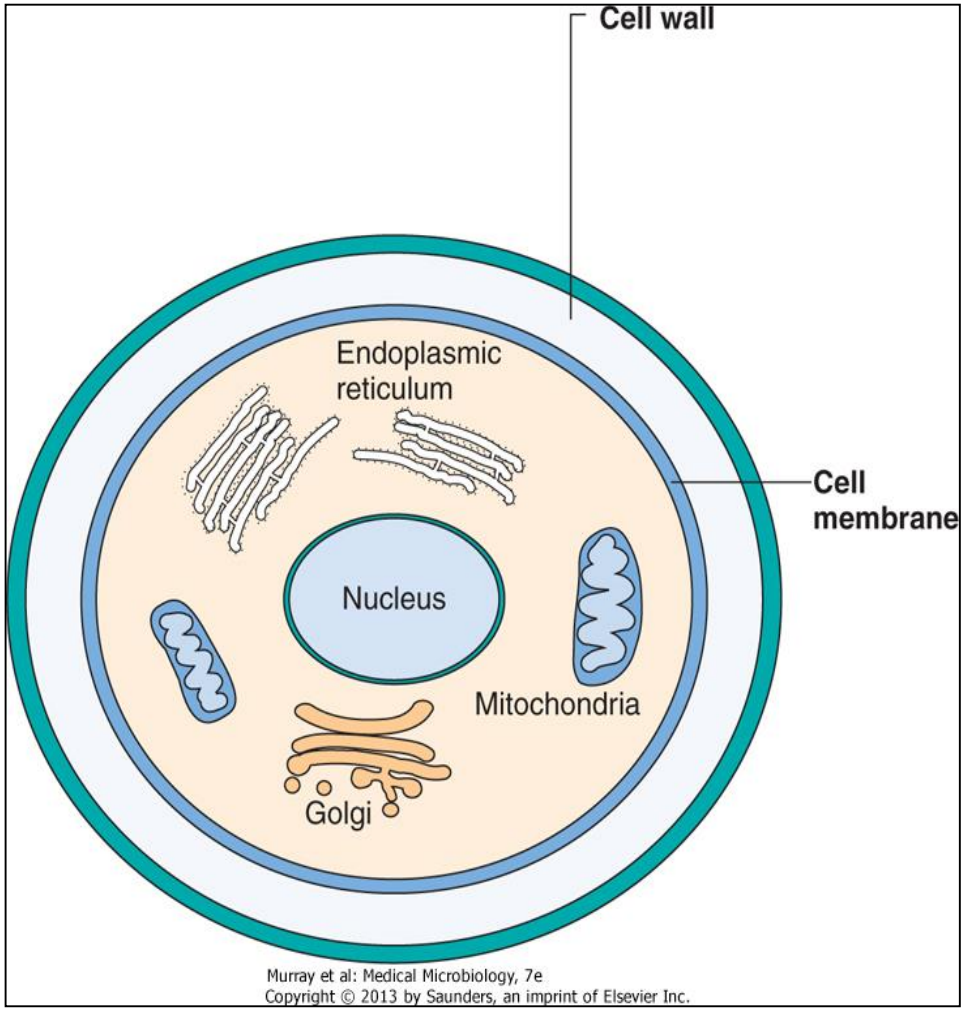
Why Care?

- Fungi are a cause of nosocomial infections.
- Fungal infections are a major problem in immune suppressed people.
- Fungal infections are often mistaken for bacterial infections, with fatal consequences.

Fungal Taxonomy, Structure, and Replication

- Kingdom Fungi.
- eukaryotic
- rigid cell wall
- chitin and glucan
- cell membrane:

- **ergosterol** is substituted for cholesterol (major sterol component)



Fungal Taxonomy, Structure, and Replication

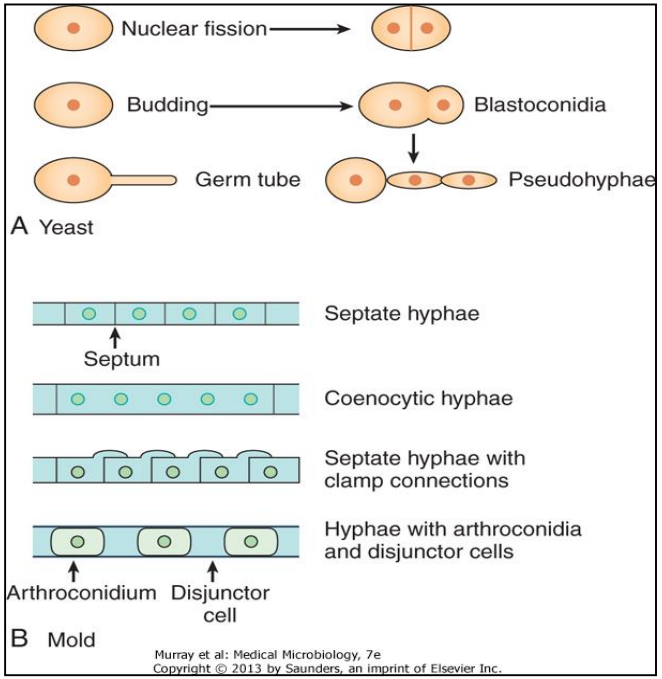
- unicellular or multicellular
- **yeasts** (**pseudohyphae)** or **Molds – hyphae (filamentous, hairy,** or **woolly)**
- Yeast (C. albicans) - one cell, asexual reproduction by budding (blastoconidia) or by division. They can produce filamentous structueres resembling molds – pseudohyphae, elongated cells resembling sausages

- Molds(hyphae) – elongation at both ends, can be multinucleated – coenocitic or septated

- **Hyphae - apical extension,**
  - **- coenocytic** (hollow and multinucleate)
  - **- septate** (divided by partitions or cross-walls)

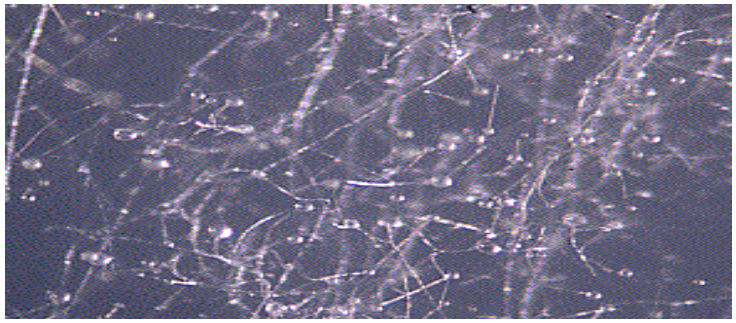
  Mycelium - vegetative hyphae
  - **- aerial hyphae - conidia**

DIMORPHIC FUNGI

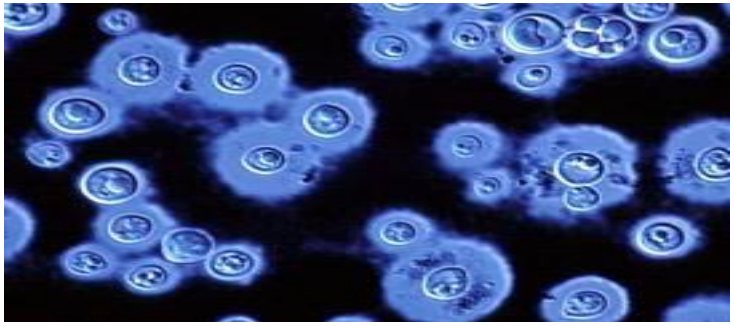


Fungal Morphology

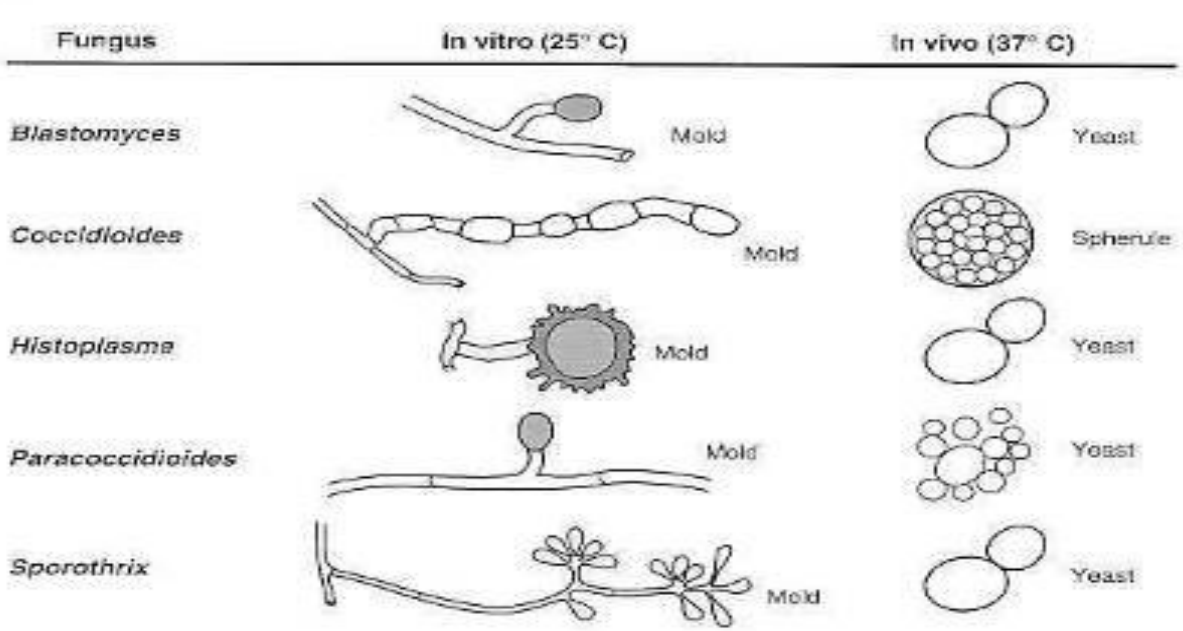
Hypae (threads) making up a **mycelium**



Yeasts

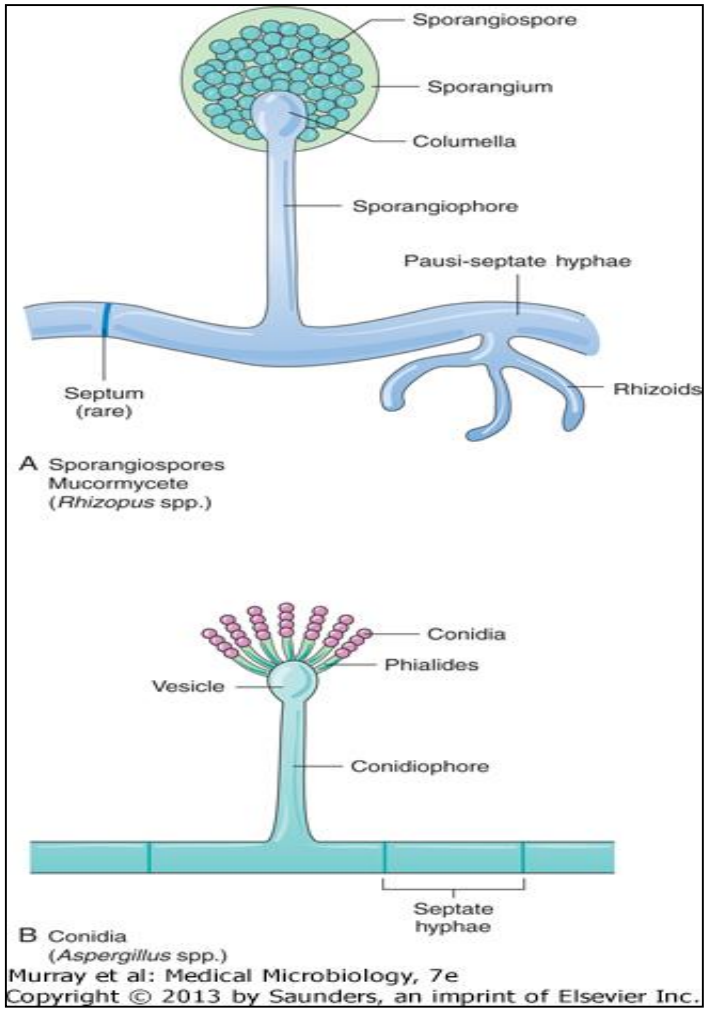


Many pathogenic fungi are **dimorphic**, forming hyphae at ambient temperatures but yeasts at body temperature.



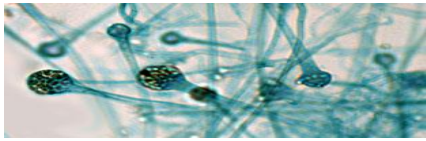
Fungal Taxonomy, Structure, and Replication

- Asexual spores : **sporangiospores** and **conidia**
- Sporangiospores - **sporangia**
- Conidia - borne naked



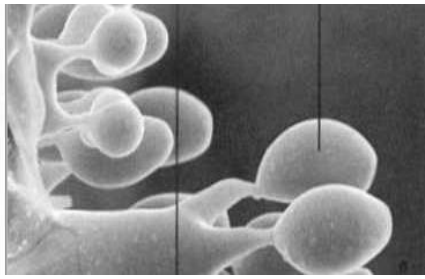
Four major phyla of Fungi

Zygomycota (Mucormycetes)— sexual spores are thick walled resting spores called zygospores (*Rhizopus, Mucor)*

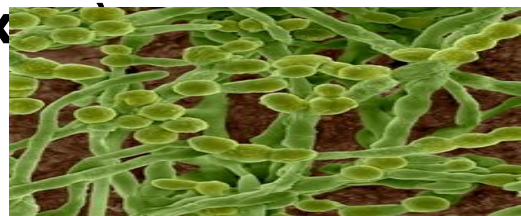


Ascomycota (Euascomycota)—spores borne internally in a sac called an ascus (Dermatophyte*s, Blastomyces, Histoplasma, Aspergillus)*

Basidiomycota—spores borne externally on a club-shaped structure called a basidium *(Cryptococcus, Malassezia, Trichosporon)*

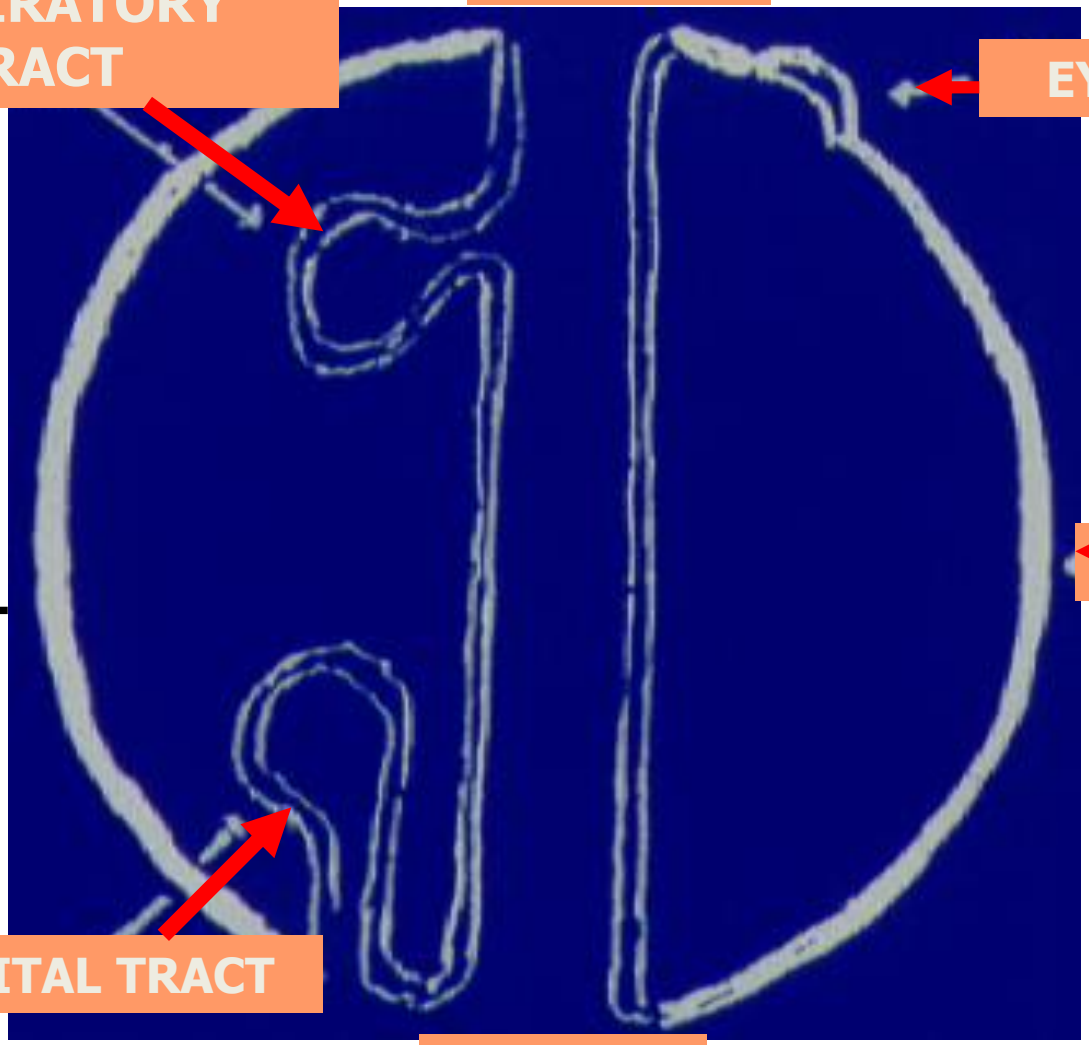


Deuteromycetes or *fungi imperfecti*, have no known sexual state in their life cycle (**is no longer formally accepted as a tax**



PORTAL OF ENTRY

- SKIN
- HAIR
- NAILS
- RESPIRATORY TRACT
- GASTROINTESTINAL TRACT
- URINARY TRACT



Effect of fungi

- Mycetismus – preformed toxins ergotamine alcaloids, psychotropic substances,

- Mycotoxicoses – aflatoxines, chronical exposition

- alergic reaction – air mycelium - alergic pneumonia, rhinitis, bronchial asthma, aleveolitis, atopic reaction
- colonisation and disease – inborne immunity, diseases are short, self limiting infections

  Immunocompetent : superficial, skin, subcutaneous, systemic
  Immunocompromised and AIDS: fungi with low patogenicity – oportunictic mycoses

Patogenic potential of fungi
Tools of pathogenicity

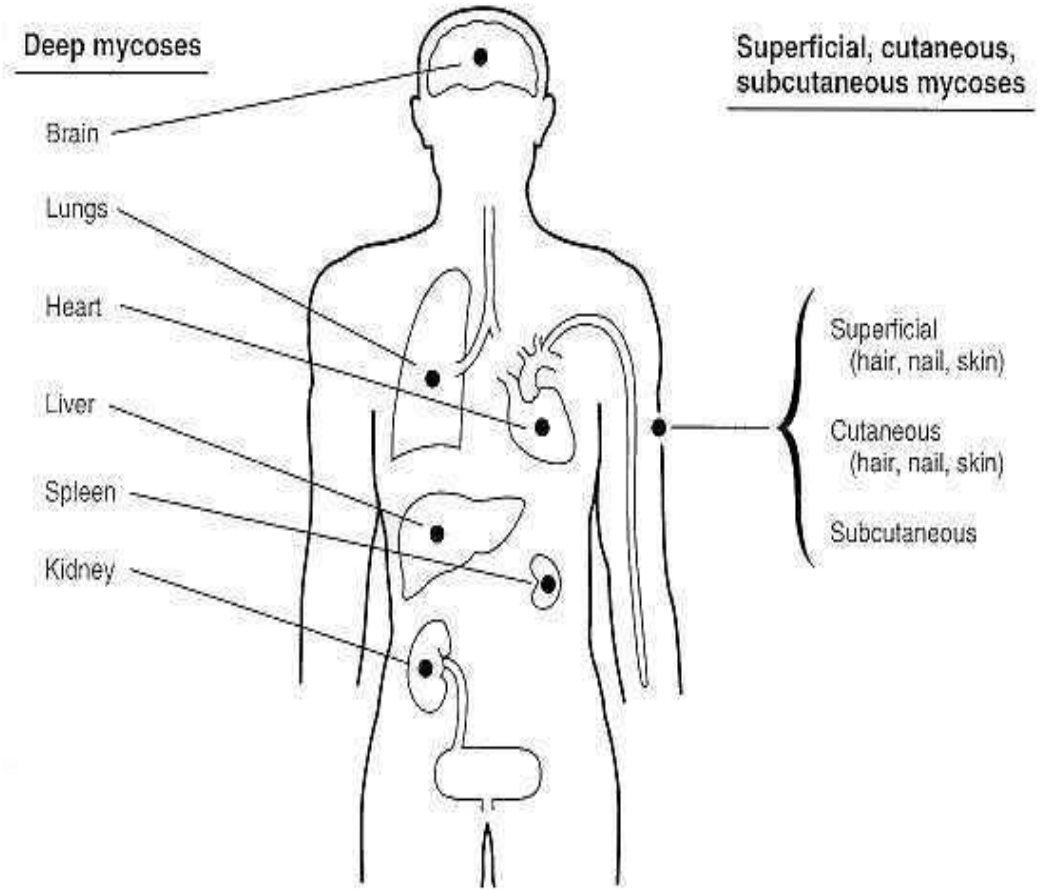
- Usually exogenous – except. Candidosis
- Longlasting exposition of man to fungi,
- Pathogenesis depend on nonspecific immune mechanism – skin, mucous membrane, IDS
- **Dermatophytes** – colonisation of skin, hairs, nails – ensyme keratinase
- **Dimorfic fungi** – as molds in the nature, as yeast in tissues **Candida** – yeast becomes filamentous during invasion of tissue
- **Capsule** - *Cryptococcus neoformans*

*__Primary pathogens__ - *Histoplasma capsulatum, Blastomyces dermatitis, Coccidioides immitis*

* **Oportunistic pathogens** - *Aspergillus, Candida, Mucor*

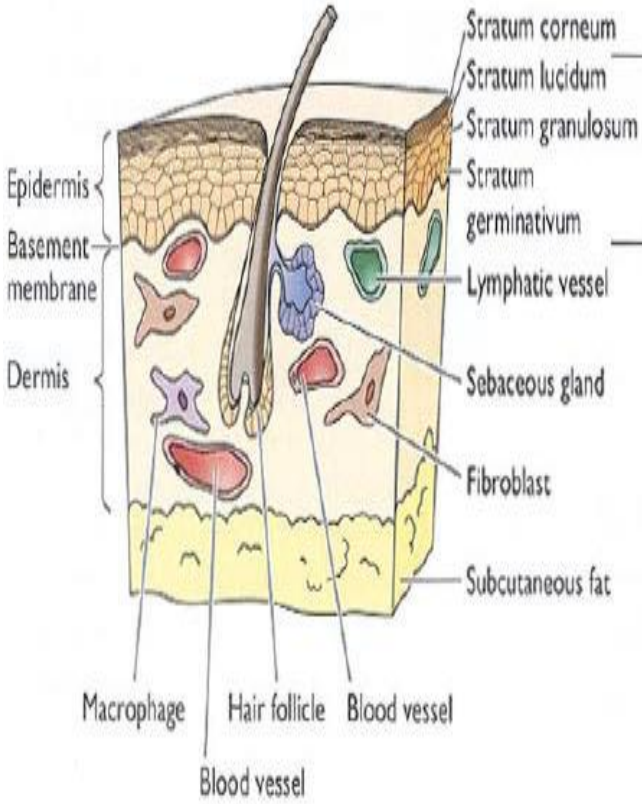
Mycoses:

- Superficial
- Cutaneous
- Subcutaneous
- Systemic
- Opportunistic



Mycoses

- **<u>Superficial mycoses</u>** - limited to the keratinized outermost layers of the skin and hair shafts (asymptomatic, cosmetic significance - pigments produced by the fungi-black, brown, green, DO NOT elicit an immune response because the fungi colonize tissues that are nonliving).
- **<u>Cutaneous mycoses</u>**-restricted to the keratinized layers of the skin and its appendages (hair and nails), **Dermatophytes** (various immune responses may be evoked)
- **<u>Subcutaneous mycoses</u>** - dermis, subcutaneous tissues, muscle, fascia, bones(rare) saprophytic fungi - they live in soil and on vegetation



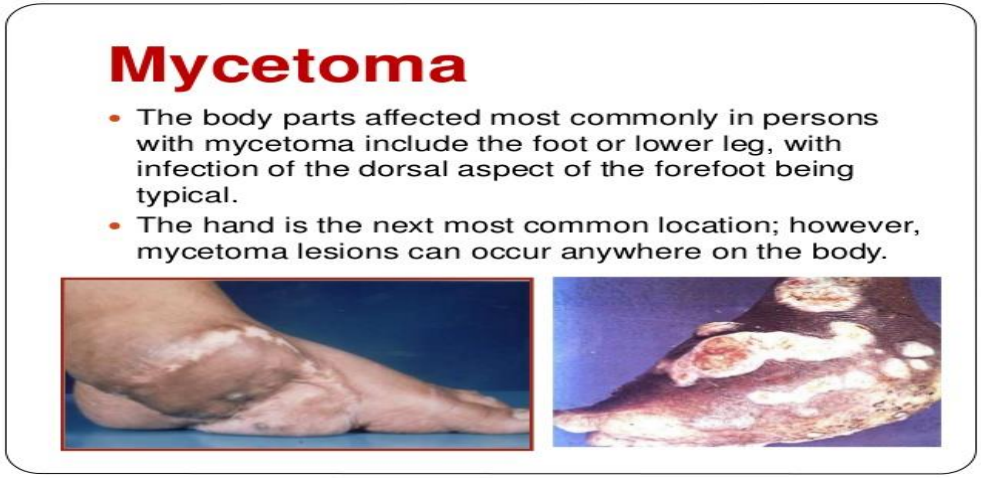
-Eumycotic mycetoma - *Acremonium sp., Aspergillus nidulans, Madurella grisea, Madurella mycetomatis, Scedosporium apiospermum*

-is a chronic, suppurative infection of the subcutaneous tissue and contiguous bone

- the feet are the most comon site for infection

- showing numerous draining sinuses, destruction of bone, distortion of the foot, and hyperplasia at the openings of the sinus tracts

Lab. Dg.: Direct Microscopy: Serosanguinous fluid containing the granules should be examined using 10% KOH



Systemic fungal infections

Natural immunity is high; physiologic barriers include:

1. Skin and mucus membranes
2. Tissue temperature-fungi grow better at less than 37°C
3. Redox potential- *in vivo* conditions too reducing for most fungi

Infection requires a large inoculum and a susceptible host

1. infection often occurs in *endemic areas*
2. most infections are *asymptomatic* or self-limiting
3. in immune-compromised hosts, infections are more often fatal (AIDS)

Systemic fungal disease is most often associated with four organisms

1. *Coccidioides immitis*
2. *Histoplasma capsulatum*
3. *Blastomyces dermatitidis*
4. *Paracoccidioides brasiliensis (S. America)*

Opportunistic Mycoses

do not normally cause disease in healthy people,

cause disease in people with weakened immune defenses (immunocompromised people).

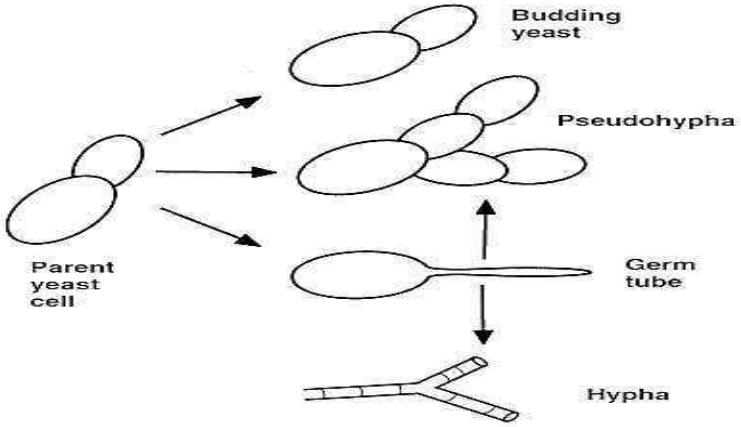
Weakened immune function may occur due to
-inherited immunodeficiency diseases,
-drugs that suppress the immune system (cancer chemotherapy, corticosteroids, drugs to prevent organ transplant rejection),
-radiation therapy,
-infections (e.g., HIV),
- cancer,
-diabetes,
-malnutrition.

The most common infections are:
Aspergillosis
Candidiasis
Cryptococcosis
Pneumocystis carinii
Zygomycosis

Candidiasis

C. albicans is a member of the indigenous microbial flora of humans.

1. Found in the gastrointestinal tract, upper respiratory tract, buccal cavity, and vaginal tract.
2. Growth is normally suppressed by other microorganisms found in these areas.
3. Alterations of gastrointestinal flora by broad spectrum antibiotics or mucosal injury can lead to gastrointestinal tract invasion.
4. Skin and mucus membranes are normally an effective barrier but damage by introduction of catheters or intravascular devices can permit *Candida* to enter the bloodstream.



In vitro (25° C): mostly yeast;

In vivo (37° C): Yeast, and pseudohyphae

Note difference from other fungi

Conventional Laboratory Diagnosis

- **Conventional Microbiologic Methods** Direct microscopy (Gram, Giemsa, and calcofluor white stains)
- Culture
- Identification
- Susceptibility testing
- **Histopathologic Methods** Routine stains (H&E)
- Special stains (GMS, PAS, Mucicarmine)
- Direct immunofluorescence
- In situ hybridization
- **Immunologic Methods**
- Antibody
- Antigen
- **Molecular Methods**
- Direct detection (nucleic acid amplification)
- Identification
- Strain typing
- **Biochemical Methods** Metabolites
- Cell wall components
- Enzymes

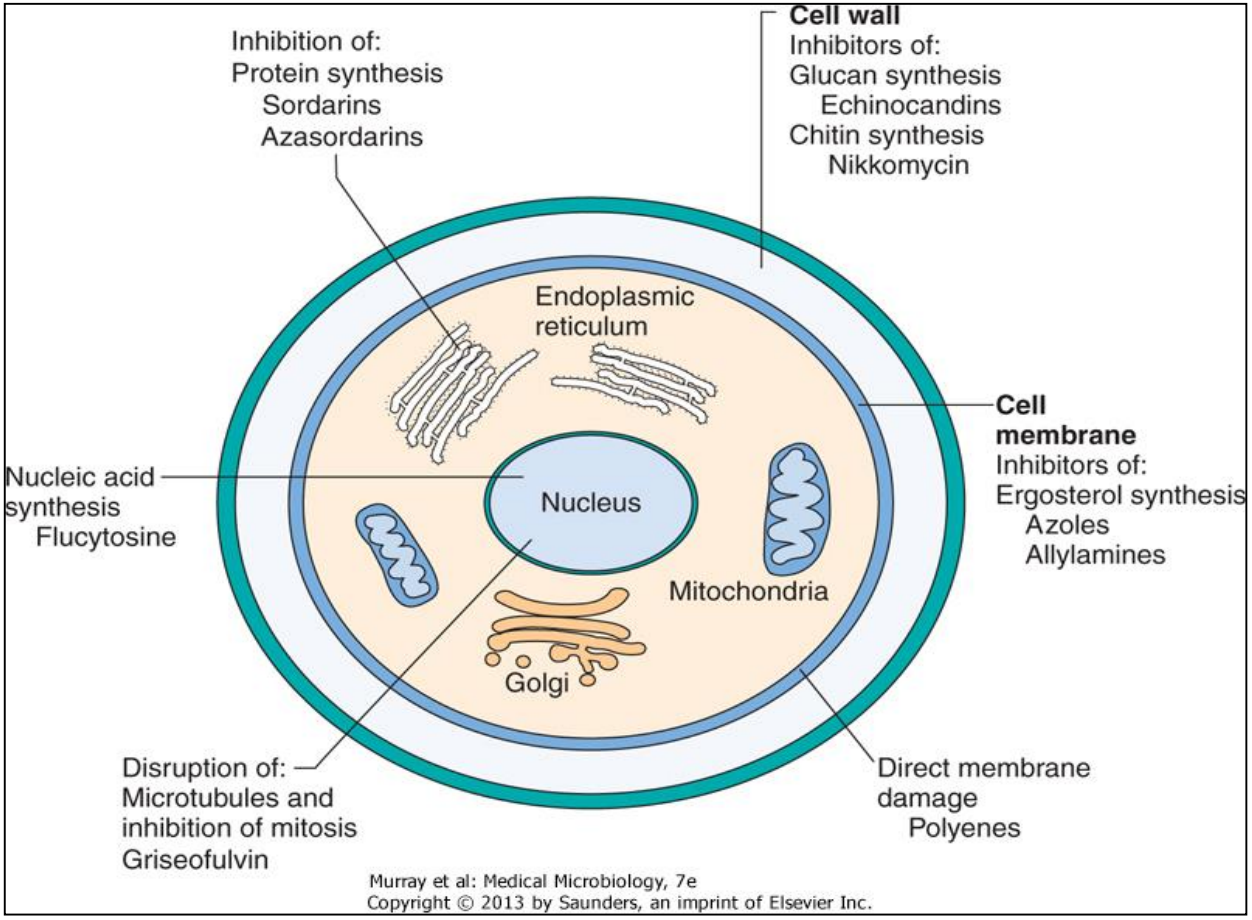
Culture

- substrates or chromogens
- direct detection of specific enzymatic activities
- CHROMagar
- selective

Cultivation media

- Selective
- Sabouraud agar - dextrose, pepton, less agar, pH 5,5 – acid environment and high concentration of glc
- Saprophytic bacteria and fungi can overgrow pathogenic – addition of chloramphenicol (against bacteria) and cyclohexamid (aganinst saprophytic fungi).
- Recommendation of cultivation on media with and without ATB, always in 25 and 37*C (some fungi do not grow at 37+ *H. capsulatum)*
- Identification: all are G+, yeat are growing as bacterial colonies, fungi – longer – several days and even weeks, microscopy – rice agar block - morphology

Antifungal Agents



Target- differences in membrane sterol (ergosterol vs. cholesterol)
- Azoles
- Polyenes
- Allylamines

Target - cell wall biosynthesis (caspofungin)

Target - fungal tubulin (griseofulvin)

Target - fungal nucleoside metabolism. (flucytosine)

Because they are eukaryotic, fungi are biochemically similar to the human host.
Therefore it is difficult to develop chemotherapeutic agents that will destroy the invading fungus without harming the patient.

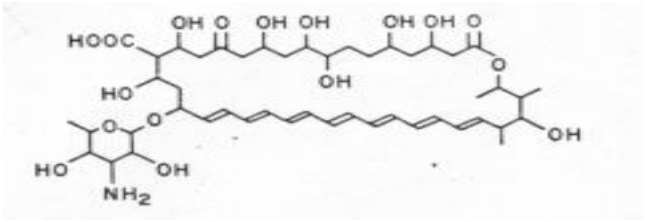
Antimycotics

- Polyens - amfotericin B, nystatin
- Azoles – interference with ensymes depending on cytochromes and acting during demetylation of lanosterol to ergosterol - miconazol,ketoconazol, flukonazol,
- Nucleotides – inhibition of DNA a RNA synthesis - 5 fluorocytosin
  Grisanes – inhibition of the function of microtubules
- KJ – activation of lysosomal ensymes
- Longlasting therapy, monitoring of the patient
- Susceptibility testing – not standardised

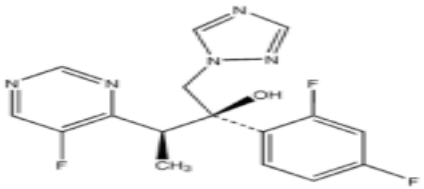
Antifungal Agents

Amphotericin

Member of polyene class of antibiotics. Antifungal effect due to interaction with sterols in membrane, making membranes leaky. Has high affinity for ergosterol, but also binds to cholesterol - severe side effects.



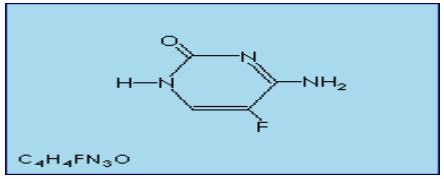
Azole antifungal agents Have 5-membered organic rings that contain either two or three nitrogen molecules (the imidazoles and the triazoles respectively).. Two important triazoles are itraconazole and fluconazole. The azole antifungal agents inhibit cytochrome P450-dependent enzymes involved in the biosynthesis of cell membrane sterols.



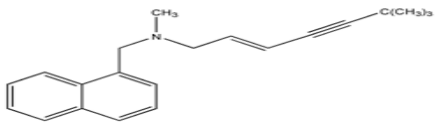
voriconazole

5-fluorocytosine (5FC)

Fungi (but not humans) deaminate 5FC to 5-fluorouracil which blocks RNA and DNA synthesis.



Allylamines Highly hyrophobic antifungal that accumulates in skin and nails. Blocks ergosterol biosynthesis via inhibition of squalene epoxidase (terbinafine/Lamasyl)



terbinafine

ANTIFUNGAL AGENTS

Topical Antifungal Agents

- Topical treatment is **useful in superficial** fungal infections *confined to the stratum* corneum, squamous mucosa, or cornea, including dermatophytosis (ringworm), candidiasis, tinea versicolor, piedra, tinea nigra, and fungal keratitis.
- **Unsuccessful for mycoses** of the **nails** (onychomycosis) and **hair** (tinea capitis)
- No place in subcutaneous mycoses, such as sporotrichosis and chromoblastomycosis.
- **Efficacy of topical agents** depends not only on the type of lesion and the mechanism of drug action, but also on the viscosity, hydrophobicity, and acidity of the formulation.

OTHER TOPICAL ANTIFUNGALS

Drug	Use	Dose
Tolnaftate	drug for tinea cruris and tinea corporis for 1-3 weeks	1% lotion/ cream
Ciclopirox olamine	newer drug effective in tinea infections, pityriasis versicolor and dermal candidiasis; used for onychomycosis, vaginal candidiasis	1% cream, 1% topical solution, 1% vaginal cream
Undecylenic acid	It is fungistatic. Used for tinea pedis, nappy rash and tinea cruris	
Benzoic acid	It has antifungal and antibacterial property. It is fungistatic-weaker than tolnaftate. On hyperkeratotic lesions, it is used in combination with salicylic acid	
Butenafine	Efficacy in tinea cruris/ corporis/pedis is similar to that of topical terbinafine	1% cream; apply locally once/ twice daily.
Quiniodochlor	Weak antifungal and antibacterial activity. It has been used for dermatophytosis, mycosis barbae, seborrhoeic dermatitis, infected eczema, furunculosis and pityriasis versicolor	3% / 4% / 8% cream
Sodium thiosulfate	weak fungistatic, active against *Malassezia furfur*	Karpin Lotion 20%.

Systemic antifungal therapy should be strongly considered, especially in a patient who is at high risk for disseminated fungal infection, if:

- Fever persists despite antibacterial agents and negative blood cultures
- High-grade funguria occurs in the absence of a bladder catheter
- Funguria persists after removal of a bladder catheter
- Fungus is cultured from at least two body sites
- Visceral fungal lesions are confirmed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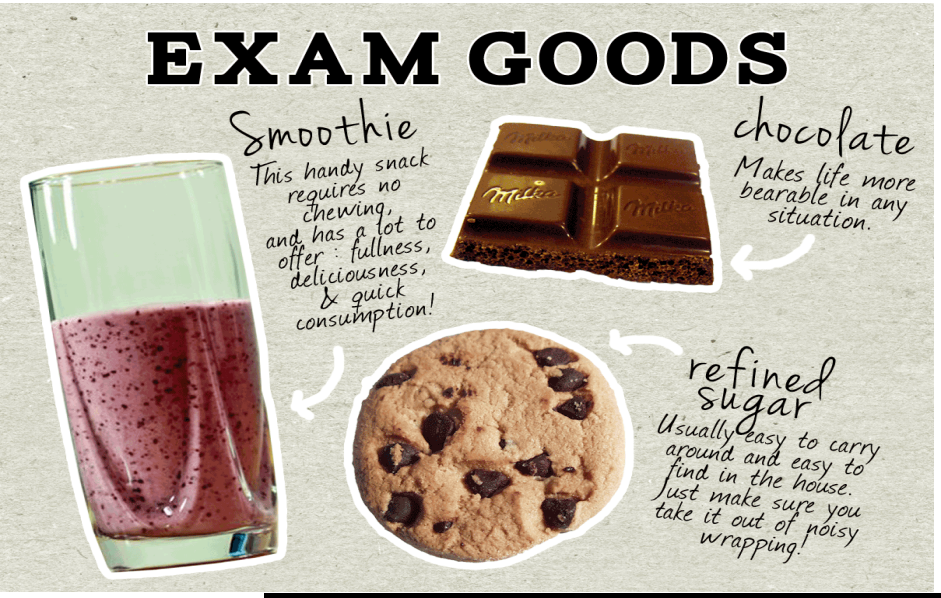
THE END


EXAM GOODS
Smoothie
This handy snack requires no chewing, and has a lot to offer : fullness, deliciousness, & quick consumption!
chocolate
Makes life more bearable in any situation.
refined sugar
Usually easy to carry around and easy to find in the house. Just make sure you take it out of noisy wrapping!

All the Best


1 DAY BEFORE THE EXAM
What my parents think I do
MEDICAL ADDICTS
What my batch mates think I do
What my best-friend thinks I do
What I think I should do
What my teachers think I do
What actually I do