

Chapter 10

Medical Mycology

Pharmaceutical Microbiology

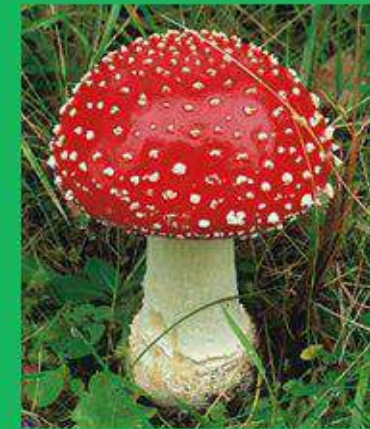
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General Characteristics of Fungi

- The study of fungi is called: **Mycology**.
 - 1. All fungi are **Eukaryotic** organisms living everywhere on earth.
 - 2. Fungi are **Heterotrophic** i.e. depend on other organism for food and are different from plants which are "**Autotrophic**".
- **Heterotrophic organisms are 3 kinds:**
- A) Saprophytic:** the fungus is living on dead organic matter.
 - B) Symbiotic:** the fungus is living together with other organism.
 - C) Parasitic:** the fungus is living in an organism and it is harmful to it e.g. *Candida albican*.
3. Beneficial fungi are important in the production of cheeses and antibiotics e.g. Penicillin.

General Characteristics of Fungi

- Secrete digestive enzymes onto food → **extracellular digestion** → absorption of nutrients
- Digestive enzymes can digest tough substances, such as cellulose in wood
- Cell walls made of **chitin**, a polysaccharide
- **Multicellular**, except for **yeasts** (unicellular)
- Very efficient nutrient transport in hyphae → grow very fast!
- Most are **poisonous** → leave it to the experts to pick the fungus on your plate...



General Characteristics of Fungi

- Fungi are eukaryotic microorganisms (domain eucarya) that occur ubiquitously in nature.
- Only about 200 of the thousands of species have been identified as human pathogens, and among these known pathogenic species fewer than a dozen are responsible for more than 90% of all human fungal infections.

□ The basic morphological element of filamentous fungi is the hypha and a web of intertwined hyphae is called a mycelium. The basic form of a unicellular fungus is the yeast cell.

□ Dimorphic fungi usually assume the form of yeasts in the parasitic stage and the form of mycelia in the saprophytic stage.

□ Filamentous fungi reproduce either asexually (mitosis), by hyphal growth and tip extension, or with the help of asexual spores. Yeasts reproduce by a process of budding.

□ Sexual reproduction (meiosis) on the other hand, produces sexual spores.

□ The cell walls of fungi consist of nearly 90% carbohydrate (chitin, glucans, mannans) and fungi membranes are rich in sterol types not found in other biological membranes (e.g., ergosterol).

Comparison of fungi and bacteria

Feature	Fungi	Bacteria
diameter	4 μm	1 μm
nucleus	eukaryotic	prokaryotic
cytoplasm	with mitochondria and endoplasmic reticulum	without mitochondria and endoplasmic reticulum
Cell membrane	sterol present	sterol absent
Cell wall	chitin	peptidoglycan
spores	sexual and asexual spore for proliferation	spore for survival , not for proliferation
dimorphism	yes	No
metabolism	Require organic carbon and no anaerobes	May do not require organic carbon and maybe anaerobes

General Aspects of Fungal Disease

- Mycoses are classified clinically as follows:
 - ❑ Primary mycoses (histoplasmosis, blastomycoses).
 - ❑ Opportunistic mycoses (surface and deep yeast mycoses, aspergillosis)
 - ❑ Subcutaneous mycoses (sporotrichosis, chromoblastomycosis,)
 - ❑ Cutaneous mycoses (pityriasis versicolor, dermatomycoses).

❑ The natural resistance of the macroorganism to fungal infection is based mainly on effective phagocytosis whereas specific resistance is generally through cellular immunity.

❑ Opportunistic mycoses develop mainly in patients with immune deficiencies (e.g., in neutropenia).

❑ Laboratory diagnostic methods for fungal infections mostly include microscopy and culturing, in order to detect the pathogens directly, and identification of specific antibodies.

Diagnosis

❑ Microscopy. Native preparation: briefly heat material under coverslip with 10% KOH.

❑ Culturing. This is possible on universal and selective mediums. Sabouraud dextrose agar can contain selective agents (e.g., chloramphenicol and cycloheximide)

Biochemical tests

are used to identify yeasts and are generally not as important in mycology as they in bacteriology.

Serology.

By the identification of antibodies to special fungal antigens in patient's serum.

Antigen detection.

By finding of specific antigens in the diagnostic material by direct means using known antibodies, possible in some fungal infections (e.g., cryptococcosis).

Cutaneous (allergy) tests

with specific fungal antigens can be useful in diagnosing a of fungal infections.

Nucleic acid detection.

Combined with amplification, such tests are useful for rapid detection of mycotic diseases in immunocompromised patients.

Therapy

- anti-infective agents are available for specific treatment of fungal infections:

(a) Polyenes. These agents bind to membrane sterols and destroy the membrane structure

1-Amphotericin B. Used In systemic mycoses. Fungicidal activity with frequent side effects.

2-Nystatin Only for topical use in mucosal mycoses.

(b)Azoles. These agents disrupt ergosterol biosynthesis
by inhibiting conversion of lanosterol to ergosterol

Their effect is mainly fungistatic with possible gastrointestinal side effects.

1-Ketoconazole. One of the first azoles. No longer used because of side effects.

2-Fluconazole. Oral or intravenous application. For the treatment of surface and systemic mycoses and cryptococcal meningitis in AIDS patients.

3-Itraconazole. Oral and intravenous application. Use in systemic and cutaneous mycoses and also for the treatment of aspergillosis..

(c) Allylamines. inhibit squalene epoxidase, another enzyme required for ergosterol synthesis.

- Terbinafine. By oral and topical application to treat dermatomycoses.

(d) Echinocandins.

- Inhibit the creation of glucan in the fungal cell wall
- Caspofungin has been approved as a salvage therapy in refractory aspergillosis. It is useful also in oropharyngeal and esophageal candidiasis.

(e)Others

Griseofulvin. binds to polymerized microtubules and inhibits fungal mitosis

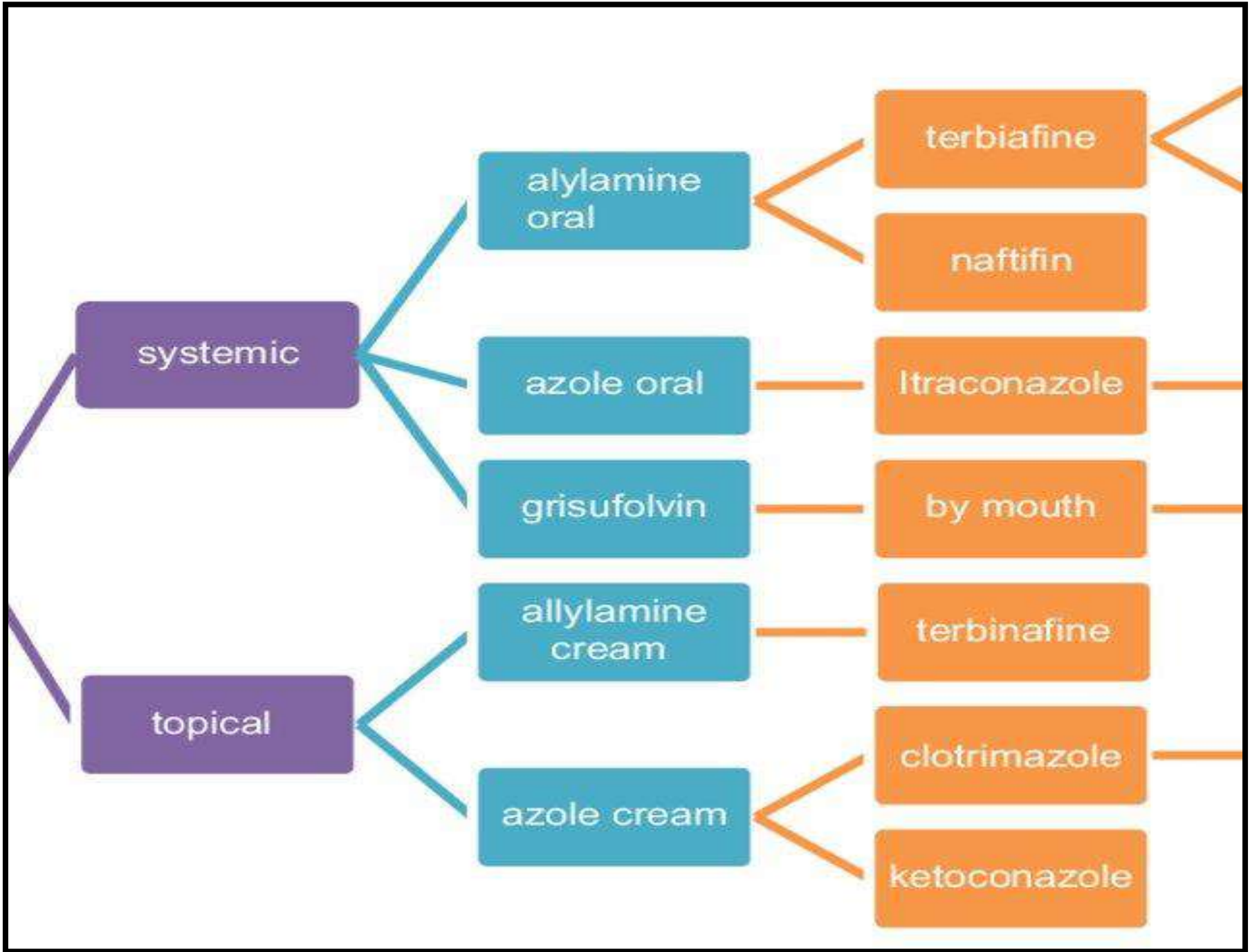
This is an older antibiotic used in treatment of dermatomycoses. (By oral application, therapy must often be continued for months.)

• 5-Fluorocytosine.

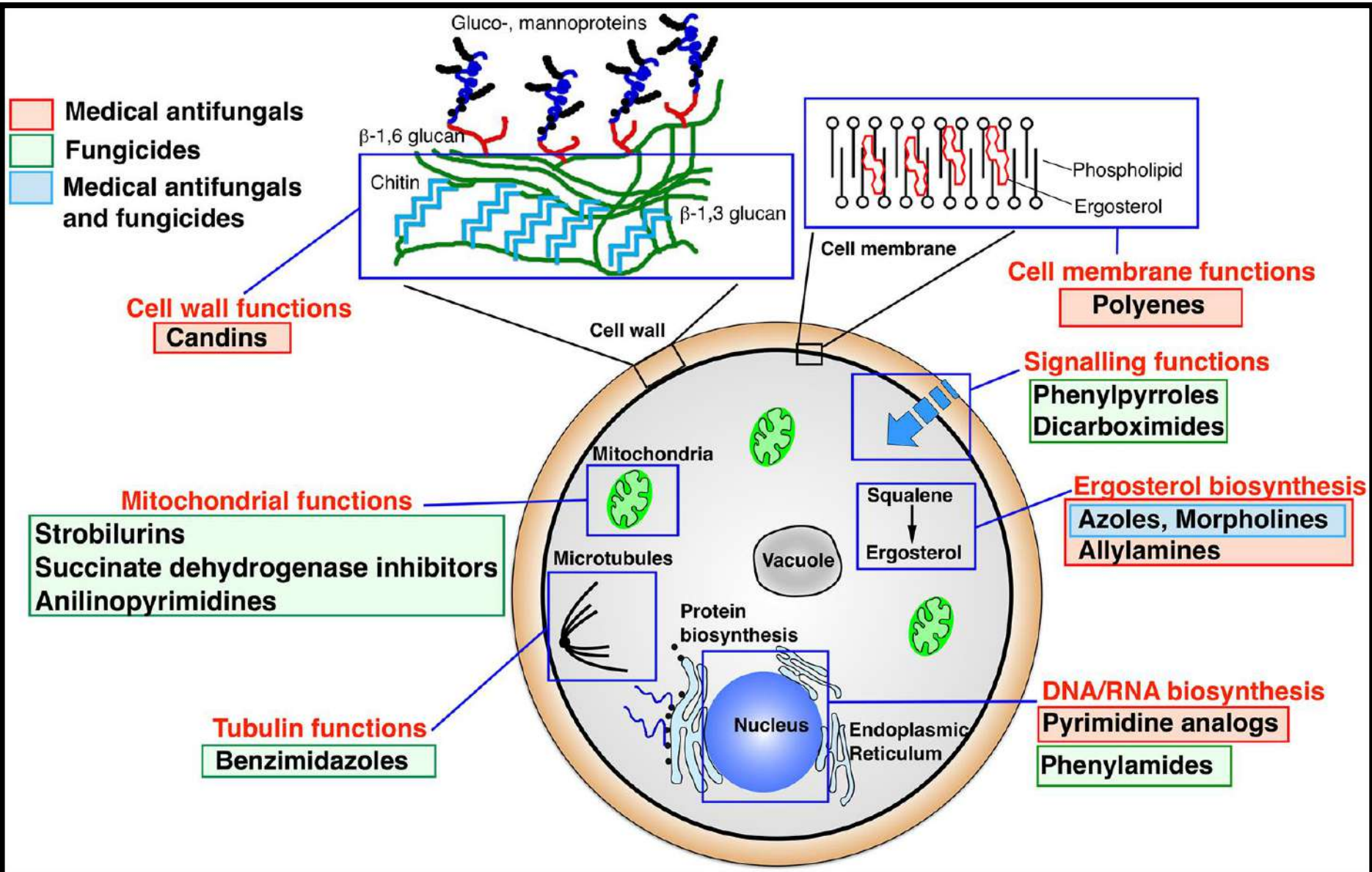
Interferes with DNA synthesis .

Given by oral application in candidiasis, aspergillosis, & cryptococcosis.

The toxicity of amphotericin B is reduced in combination with 5-fluorocytosine.



Map of antifungal agents



Fungi as Human Pathogens

• A. Primary Mycoses

- ❑ Primary systemic mycoses include histoplasmosis, blastomycosis, The natural habitat of these pathogens is soil.
- ❑ Their spores are inhaled with dust, get into the lungs, and cause a primary pulmonary mycosis.
- ❑ Starting from foci in the lungs, the organisms can then be transported, hematogenously or lymphogenously, to other organs
- ❑ The therapeutics used to treat these infections are amphotericin B and azoles.

1. Histoplasma capsulatum (Histoplasmosis)

- Histoplasma capsulatum is the pathogen responsible for histoplasmosis, an intracellular mycosis of the RES
- The natural habitat of H. capsulatum is the soil.
- Spores (conidia) are inhaled into the respiratory tract, are taken up by alveolar macrophages, and become yeast cells that reproduce by budding.
- Over 90% of infections remain clinically silent.
- Treatment with amphotericin B is only indicated in severe infections.

2. Blastomyces dermatitidis

- The pathogens occur in the soil and are transmitted to humans by inhalation.
- The primary blastomycosis infection is pulmonary.
- Secondary hematogenous spread can lead to the skin problems.
- Amphotericin B is the therapeutic agent of choice. **azole derivatives (e.g., itraconazole),**
- Untreated blastomycoses almost always have a lethal **outcome.**

b. Opportunistic Mycoses (OM)

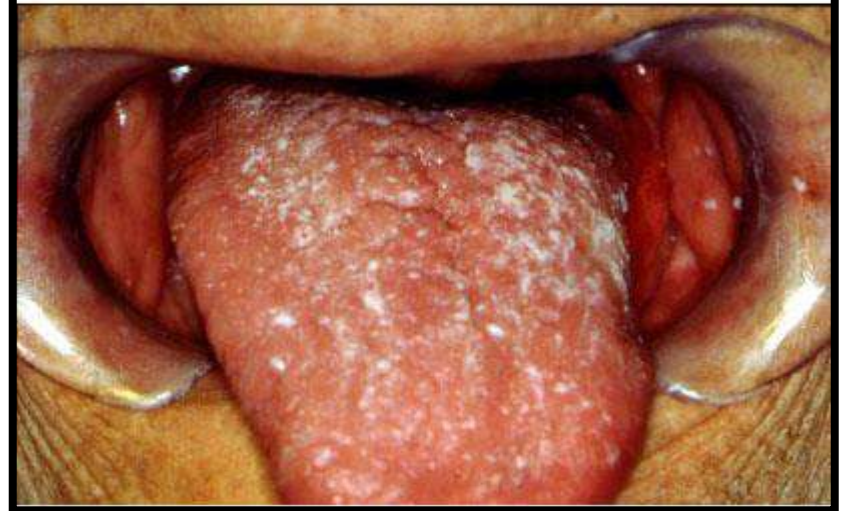
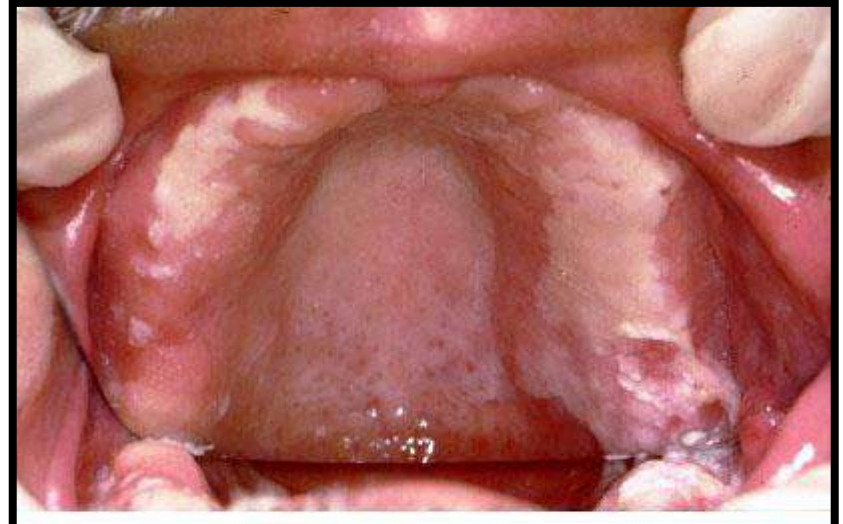
- Opportunistic mycoses (OM) that affect skin and mucosa as well as internal organs are caused by both yeast and molds.
- A precondition for development of such infections is weakness in the host's immune defenses. .
- Candidiasis is an endogenous infection.**
- Other OMs are exogenous infections caused by fungi that naturally inhabit the soil or plants.

□ These environmental fungi usually invade via the respiratory tract. The most important are aspergillosis, and cryptococcosis.

□ All OMs have a primary infection focus, usually in the upper or lower respiratory tract.

□ From this focus, the pathogens can disseminate hematogenously and/or lymphogenously to infect additional organs.

1- Candidiasis



1-Candida (Soor)

- ❑ At least 70% of all human Candida infections are caused by C. albicans. Gram staining of primary preparations reveals C. albicans to be a Gram-positive, budding, oval yeast .
- ❑ Candida is a normal inhabitant of human and animal mucos(commensal).
- ❑ Candiadeses usually develop in persons whose immunity is compromised,

In oral cavity infections, a white, stubbornly adherent coating is seen on the tongue.

Candida can spread to cause secondary infections of the lungs, kidneys, and other organs. Candidial endocarditis are observed in drug addicts.

• Therapy.

Nystatin and azoles can be used in topical therapy.

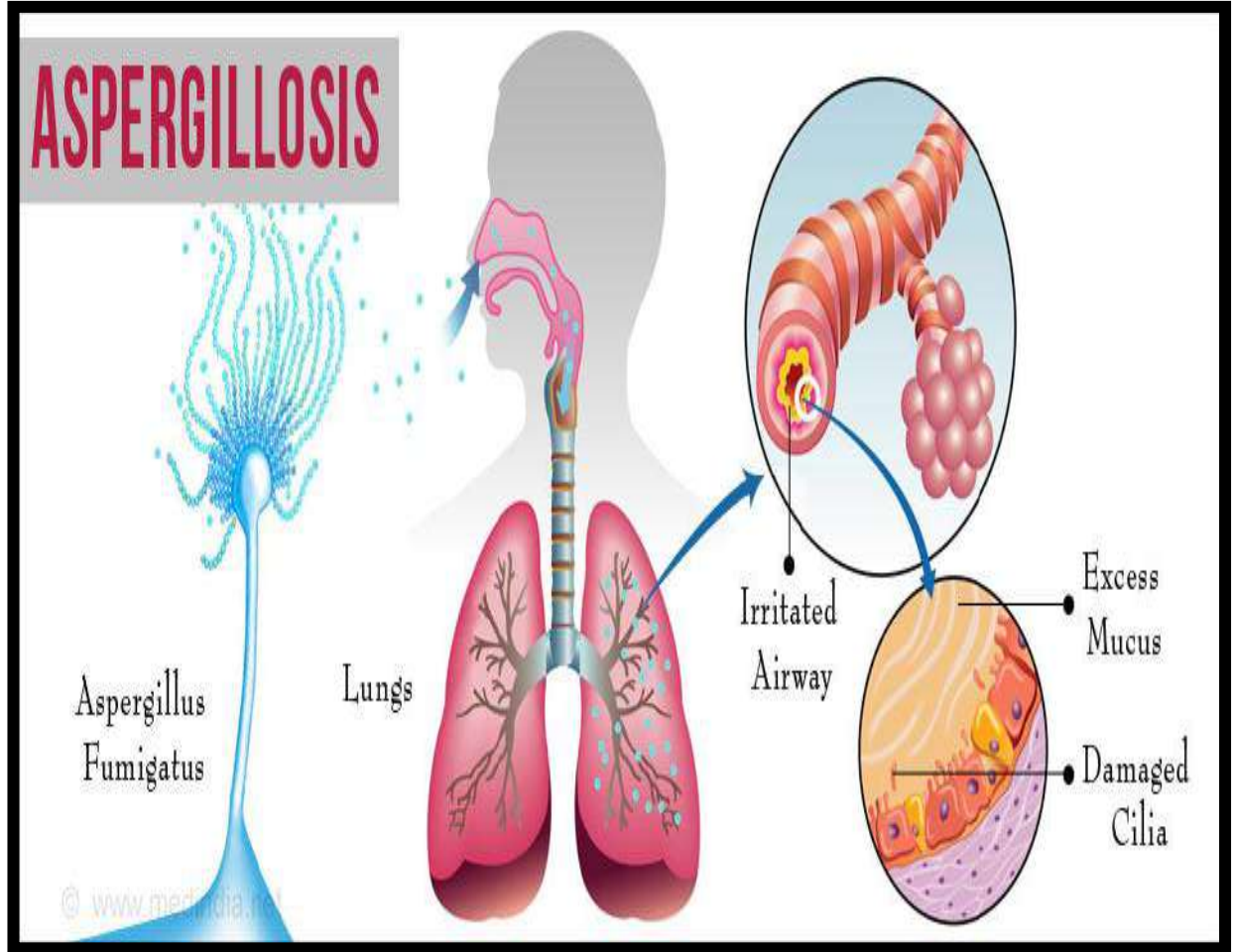
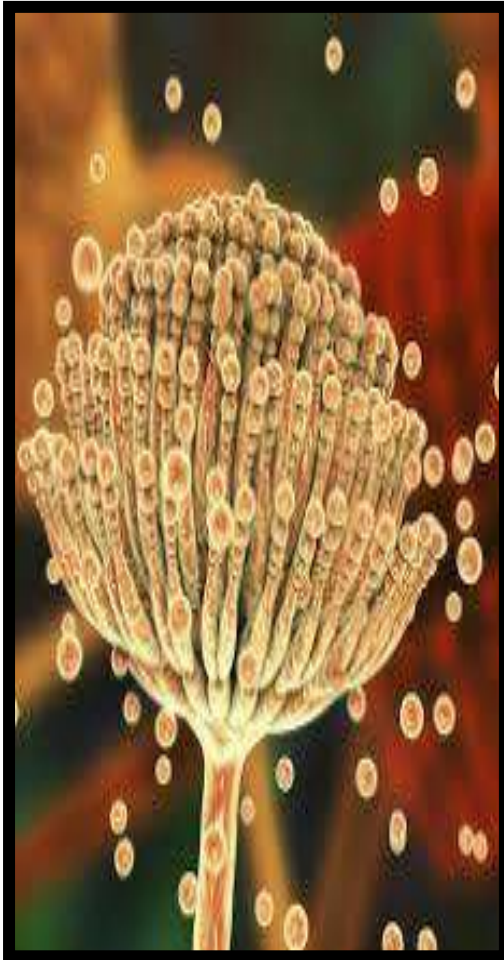
In cases of deep candidiasis, amphotericin B is still the agent of choice, often administered together with 5-fluorocytosine.

Echinocandins can be used in severe oropharyngeal and esophageal candidiasis.

2-Aspergillus (Aspergillosis)

- ❑ Aspergilloses are most frequently caused by Aspergillus fumigatus. Aspergilli are ubiquitous in nature. They are found in large numbers on rotting plants.
- ❑ Sabouraud agar is suitable for selective culturing.

2-Aspergillosis



Pathogenesis and clinical pictures.

- The main portal of entry for this pathogen is the bronchial system, but the organism can also invade the body through injuries in the skin or mucosa.
- Acute, invasive pulmonary aspergillosis is seen in patients suffering from neutropenia or AIDS or following organ transplants .
- Of all fungi, aspergilli are most frequently responsible for various forms of sinusitis.
- In persons with atopic allergies, asthma may be caused by an allergic aspergillus alveolitis

C. Cutaneous Mycoses

□ Dermatophytes are classified into

Trichophyton, Microsporum and Epidermophyton

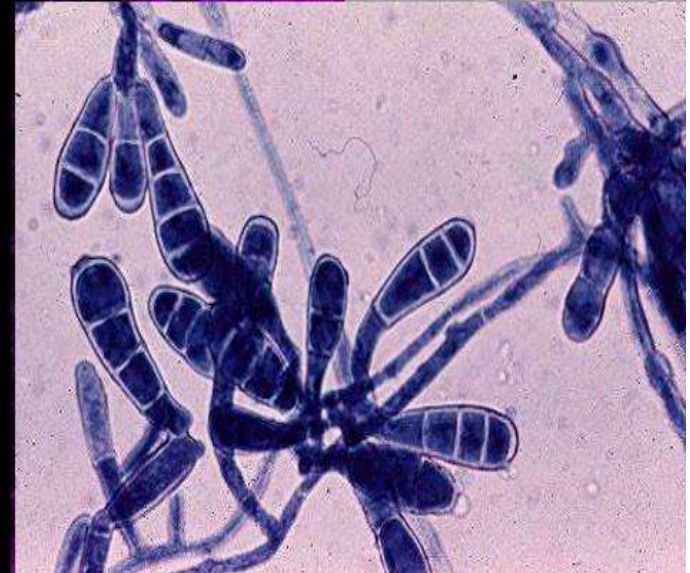
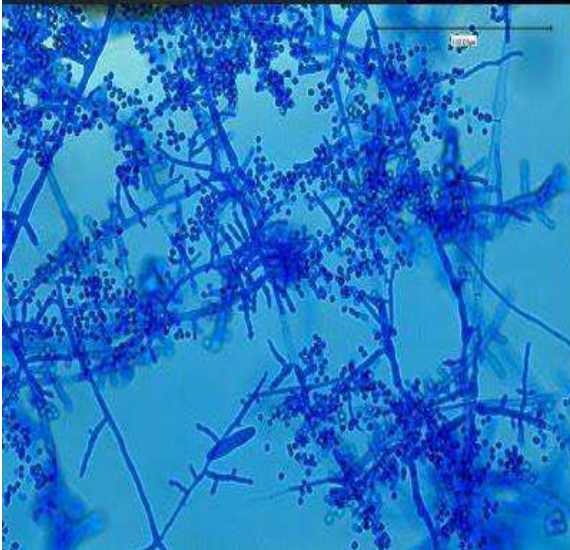
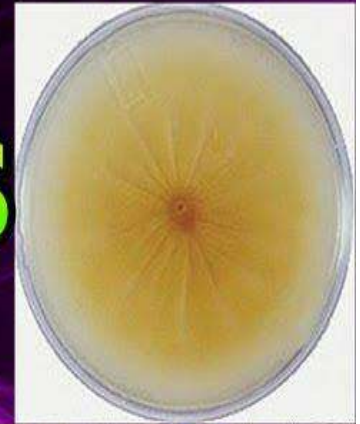
□ Some dermatophyte species are anthropophilic, others zoophilic.

□ The dermatophytes are filamentous fungi. They grow readily on fungal nutrient mediums at 25–30 °C.

□ After 5–14 days, cultures with a woolly appearance, in different colors,

Microscopic & Colony Characteristic Of

Dermatophytes



Dermatomycoses are infections that are transmitted directly by human contact, animal-human contact or indirectly on inanimate objects (clothes, carpets, moisture, and dust in showers, swimming pools, wardrobes, gyms).

The localization of the primary foci corresponds to the contact site.

Thus feet, uncovered skin (hair, head, facial skin) are affected most frequently.

Different species can cause the same clinical picture.

Frequent dermatomycoses include:

Tinea pedis (athlete's foot): Affects mainly the lower legs.

Tinea versicolour : Affects the neck and back

Tinea capitis: Affects scalp hair.

Tinea corporis (ringworm):. Affects hairless skin.

Tinea cruris : Affects the groins

Tinea barbae: Beard ringworm

Tinea unguium(Onychomycosis) : Affects the nail

Tinea Manum : Affects the hands

1- Tinea pedis (Athelets foot)



Plantar-type athlete's foot



Therapy

- ❑ Terbinafine once daily for one week
- ❑ Plantar-type athlete's foot is more resistant to topical treatments due to the presence of thickened hyperkeratotic skin on the sole of the foot.
- ❑ Keratolytic and humectant medications such as urea, salicylic acid (Whitfield's ointment), and lactic acid are useful adjunct medications and improve penetration of antifungal agents into the thickened skin.
- ❑ Fluconazole or itraconazole may also be taken orally for severe athlete's foot infections.

2-Tinea versicolour



Therapy

Type of treatment (reference)	Drug	Dosage	Duration of treatment
Topical therapy ⁵⁹	Ketoconazole 2% shampoo	Applied to affected areas and washed off after 5 min	Topical therapy (days to weeks)
Systemic therapy ⁶⁰	Itraconazole	Single 400-mg dose	NA
Dermatophytosis ⁶¹⁻⁶⁵	Terbinafine	250 mg/d	1 to 2 wk
	Fluconazole	150 mg/wk	2 to 4 wk
	Itraconazole	200 mg/d	1 to 2 wk
	Griseofulvin	250 mg 3 times/d	2 wk

3-Tinea capitis



Therapy

Tinea Capitis Treatment

- **Must treat hair follicle**
 - Topical not effective
 - Systemic agents
- **Griseofulvin for children ;12.5 mg/kg.**
- **Imidazoles, terbinafine.**
- **Steroids for inflamed lesions like Kerion.**
- **Treat until no visual evidence, culture (-)... plus 2 weeks**
 - Average of 6-8 weeks of treatment.

4- Tinea unguem (onychomycoses)



Healthy nail with
pinkish hue

Yellow
discolored nail

Yellow, brittle and
crumbling nail

Increasing severity of nail fungus infection

Therapy

Type of Treatment	Recommendation
Oral	Continuous therapy (terbinafine) or pulse therapy (itraconazole) for 12 weeks
Topical	Daily for at least 48 weeks, perhaps longer until new nail fully grows
Device	Evidence does not support use of laser therapy for onychomycosis
Manage recurrence/ reinfection	Consider prophylactic antifungal use Maintain proper foot hygiene Wear the correct size shoes Avoid at-risk environments (eg, public showers [gyms] and swimming pools) Sanitize shoes and socks

In your opinion , bacteria is more dangerous
or fungus ?

The end of medical

mycology