Introduction of medical Fungi

Mycology: is the study of fungi, which are eukaryotic organisms that evolved in tandem with the animal kingdom. However, unlike animals, most fungi are nonmotile and possess a rigid cell wall. Unlike plants, fungi are non-photo synthetic.

Approximately 80,000 species of fungi have been described, but only about 400 are medically important, and less than 50 are responsible for more than 90% of the fungal infections of humans and other animals. Rather, most species of fungi are beneficial to humankind. They reside in nature and are essential in breaking down and recycling organic matter. Some fungi greatly enhance our quality of life by contributing to the production of food and spirits, including cheese, bread, and beer. Other fungi have served medicine by providing useful bioactive secondary metabolites such as antibiotics (eg, penicillin) and immunosuppressive drugs (eg, cyclosporine).

The term mycoses refers to infections that are caused by fungi. Most pathogenic fungi are exogenous, their natural habitats being water, soil, and organic debris. The mycoses with the highest incidence candidiasis and dermatophytosis are caused by fungi that are frequent components of the normal human microbiota and highly adapted to survival on the human host.

mycoses may be classified as superficial, cutaneous, subcutaneous, **or systemic,** invading the internal organs .

Comparison of Fungi and Bacteria

Feature	Fungi	Bacteria
Diameter	About 4µm(candida)	About 1 µm(Sthaphylococcus)
Nucleus	Eukaryotic	Prokaryotic
Cytoplasm	Mitochondria and endoplasmic membrane	Mitochondria and endoplasmic membrane
Cell membrane	Sterols present	Sterol absent except mycoplasma
Cell wall content	Chitin	Peptidoglycan
Spores	Sexual and a sexual for reproduction	Endospores for survival
Thermal dimorphism	Yes(some)	No
Metabolism	Require organ carbon, no obligate anaerobes	Many do not require carbon, many obligate anaerobes

Budding: A common mode of asexual reproduction, typical of yeasts. During mitosis, the parent cell wall protrudes outwardly and enlarges to form a nascent bud that contains the progeny nucleus. A fungal cell may produce single or multiple buds.

Conidia: Asexual reproductive structures (mitospores) produced either from the transformation of a vegetative yeast or hyphal cell or from a specialized conidiogenous cell, which may be simple or complex and elaborate. Conidia may be formed on specialized hyphae,

Hyphae: Tubular, branching filaments (2–10 μm in width) of fungal cells, the mold form of growth. Most hyphal cells are separated by porous cross-walls or septa, but in the Order Mucorales, the hyphae are characteristically sparsely septate. Vegetative or substrate hyphae anchor the colony and absorb nutrients. Aerial hyphae project above the colony and bear the reproductive structures.

Mycelium: Mass or mat of hyphae, mold colony.

Spore: A specialized propagule with enhanced survival value, such as resistance to adverse conditions or structural features that promote dispersion. Spores may result from asexual (eg, conidia, sporangiospores) or sexual .

Yeasts: Unicellular, spherical to ellipsoid (3–15 μm) fungal cells that usually reproduce by budding.

General properties of pathogenic Fungi

1. Fungi have two basic growth forms, as **molds** and **yeasts**.
2. Growth in the mold (or mould) form occurs by the production of multicellular branching cylindrical tubules called **hyphae** that Hyphae are extended by apical elongation due to the production of new cell wall growth at the hyphal tips.
3. The mass of intertwined hyphae that accumulates during active growth is a **mycelium**.
4. Some hyphae are divided into cells by cross-walls or **septa**, which typically form at regular intervals during hyphal growth. However, members of the Order Mucorales produce hyphae that are rarely septated.

5. Vegetative or substrate hyphae penetrate the supporting medium, anchor the colony, and absorb nutrients.
6. In contrast, aerial hyphae project above the surface of the mycelium and usually bear the reproductive structures of the mold. When a mold is isolated from a clinical specimen, its growth rate, macroscopic appearance, and microscopic morphology are usually sufficient to determine its genus and species.
7. Yeasts are single cells, usually spherical to ellipsoid in shape and varying in diameter from 3 to 15 μm.
8. Most yeasts reproduce by budding, which is initiated by a lateral or terminal protrusion of new cell wall growth that enlarges during mitosis. One or more replicated nuclei enter the nascent bud, which subsequently forms a septum and separates from the parent cell.
9. Some species produce buds that characteristically fail to detach and become elongated; this continuation of the budding process produces chains of elongated yeast cells called **pseudohyphae**.
10. Yeast colonies are usually soft, opaque, 1–3 mm in size, and cream colored. The colonies and microscopic morphology of many species of yeasts appear quite similar, but they can be identified by physiologic tests and a few key morphologic differences. Some species, including several pathogens, are dimorphic and capable of growth as a yeast or mold depending on environmental conditions, such as temperature or available nutrients.

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***Jawetz, Melnick, & Adelberg's Medical Microbiology, Twenty-Seventh Edition,216**

***Review of Medical Microbiology and Immunology,13 ed. 2014**

Fungal Taxonomy, Structure, and Replication

Fungal Taxonomy:

The fungi are classified in their own separate kingdom, Kingdom Fungi.Classic fungal taxonomy depend on **morphology** and **mode of spore production.**

Morphological Classification of Fungi:

Fungi can be divided into four groups each of which have some human pathogenic species.

1. **Moulds:** They are filamentous and mycelial fungi. They grow as long filaments or hyphae which branch and fuse to form a meshwork or mycelium. They reproduce by forming various kinds of spores. On artificial medium they are seen as filamentous mould colony which may be dry and powdery.

2. Yeasts: They are unicellular occurring as spherical or ellipsoidal cells. They reproduce by budding. On solid media they form moist, compact, creamy, mucoid colonies resembling those of staphylococci. *Cryptococcus neoformans* is the only important pathogens.

3. Yeast like fungi: They grow partly as yeasts and partly as long filamentous cells joined, end to end forming a pseudo- mycelium. On solid media moist creamy colored colonies are produced. *Candida albicans* is the example.

4. Dimorphic fungi: They grow in mycelial form at low temperature, i.e. 22°C or in soil whereas growth at 37°C or in animal body occurs in yeast form. The pathogenic members are *Histoplasma capsulatum*, sporotrichum, blastomyces and *Coccidioides immitis.*

Systemic classification:

Based on sexual spore formation fungi are kept in 4 classes as described below:

1. Phycomycetes: They are fungi having non-septate hyphae. They form endogenous asexual spore (sporangiospore) contained within sac-like structure called sporangia (fig.57.3) Sexual spores are also found and are of two kinds: oospore and zygospore.

2. Ascomycetes: They form sexual spores (ascospores) within a sac. This sac is called **ascus**. They include both yeasts and filamentous fungi. They form septate hyphae.

3. Basidiomycetes: They reproduce by means of sexual reproduction. Basidiospores are borne at the tip of basidium. These basidia are sometimes quite large leaf-like structure as in mushroom. They form septate hyphae.

4. Fungi imperfecti: They consist of group of fungi whose sexual phases have not been identified. Fungi of medical importance belong to this group, e.g. *Sporothrix schenkii.*

Structure and reproduction of Fungi:

Fungi may be unicellular or multicellular. The most simple grouping, based on morphology, fungi are either **yeasts or molds.**

A yeast (Figure 57-2), where a progenitor or "mother" cell pinches off a portion of itself to produce a progeny or "daughter" cell. The daughter cells may elongate to form sausage-like pseudohyphae. Yeasts are usually unicellular and produce round pasty تشبه الفطيرة, or mucoid colonies on agar.

Molds, on the other hand are multicellular organisms consisting of threadlike tubular structures called hyphae (see Figure 57-2) that elongate at their tips by a process known as **apical extension**. Hyphae

are either coenocytic (hollow and multinucleate) or septate (divided by partitions or cross-walls) (see Figure 57-2). The hyphae form together to produce a matlike structure حصيرة called a mycelium.

Fungi reproduce by formation of spores that may be sexual (involving meiosis, by fusion of the protoplasm and nuclei of two compatible mating types) or asexual (involving mitosis only). The fungi in the Ascomycota, Basidiomycota, Glomeromycota, and Microspora produce both sexual and asexual spores . The form of the fungus producing **sexual spores** is termed the **teleomorph,** and the form producing **asexual spores** is termed the **anamorph**. Asexual spores consist of two general types: **sporangio- spores and conidia**. Sporangiospores are asexual spores produced in a containing structure or sporangia (see Figure 57-3) and are characteristic of genera belonging to the Mucorales, such as *Rhizopus* and *Mucor* spp. Conidia are asexual spores that are borne naked on specialized structures as seen in *Aspergillus* spp. (see Figure 57-3), *Penicillium* spp., and the dermatophytes.

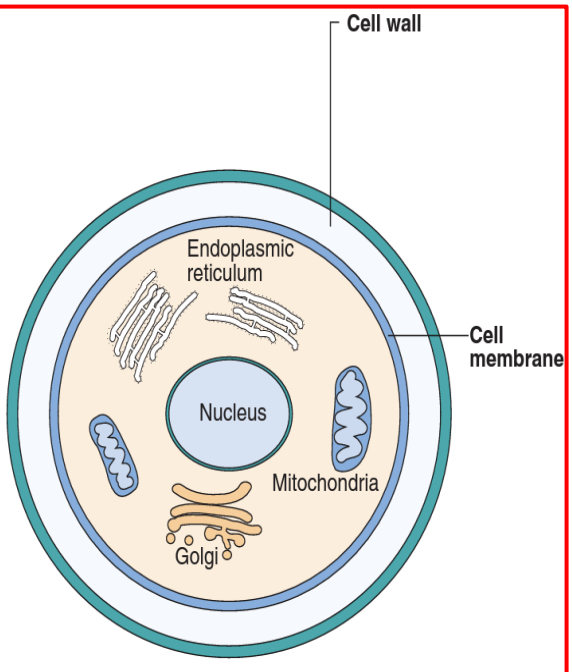


FIGURE 57-1 Diagram of a fungal cell.

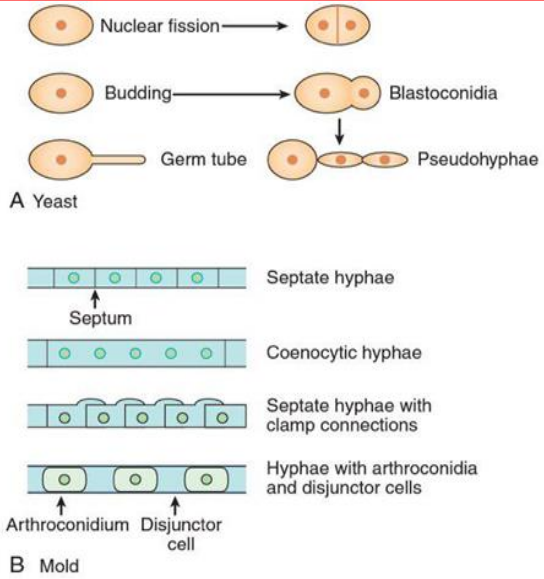


FIGURE 57-2 Fungal cell morphology. **A,** Yeast cells reproducing by nuclear fission and by blastoconidia formation. The elongation of budding yeast cells to form pseudohyphae is shown, as is the formation of a germ tube. **B,** Types of hyphae seen with various molds.

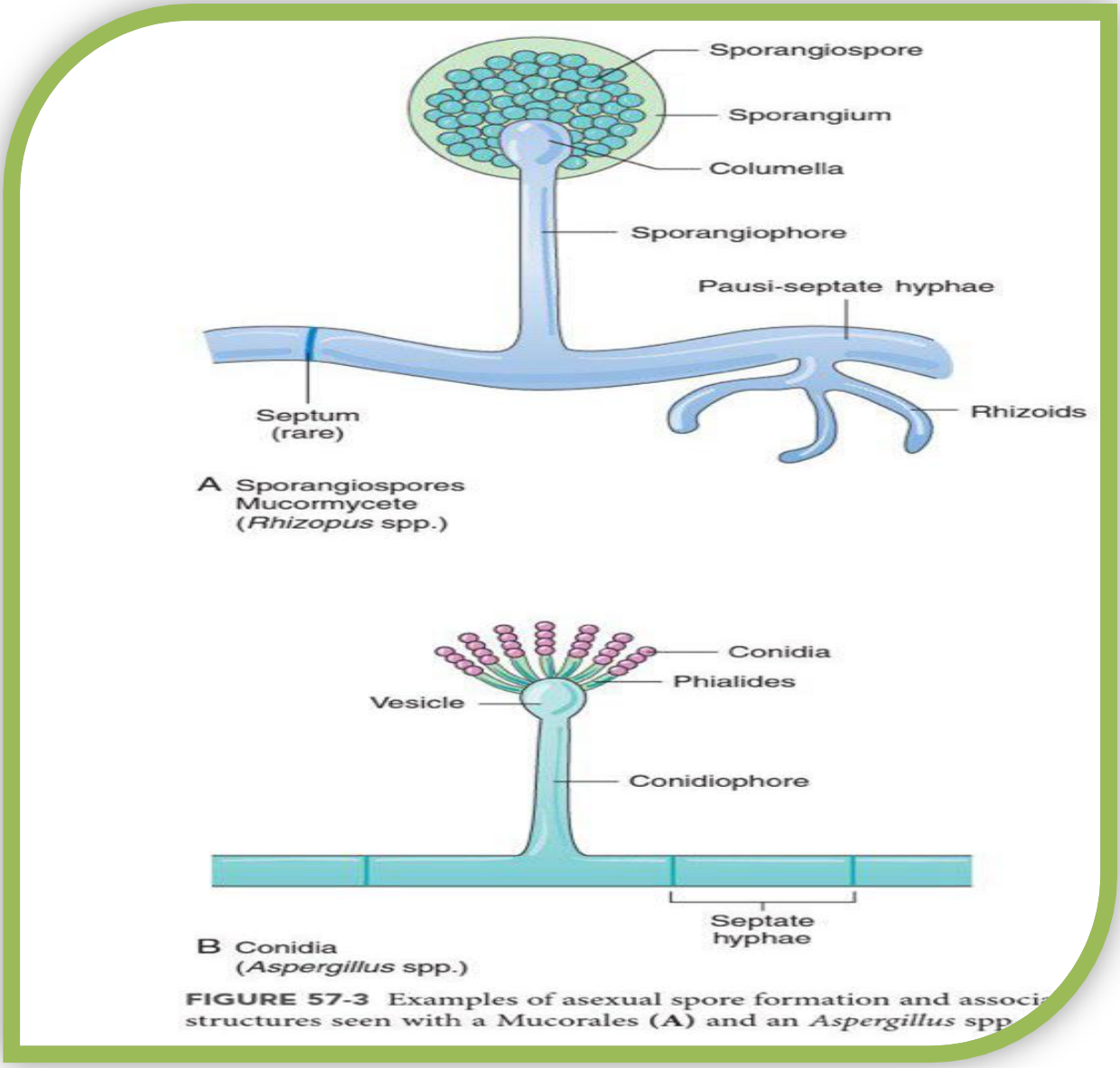


FIGURE 57-3 Examples of asexual spore formation and associ structures seen with a Mucorales (A) and an *Aspergillus* spp

References

***Patrick R. Murray , Kens S. Rosenthal, and Michael A. Pfaller. Medical Microbiology, 2016**

***Satish Gupte, The short text book of Medical Microbiology,10th ed, 2010**

Types of Mycoses

In addition to the formal taxonomic classification of fungi, fungal infections may be classified according to the tissues infected as well as by specific characteristics of organism groups. **These classifications include the superficial, cutaneous, subcutaneous mycoses, the endemic mycoses, and the opportunistic mycoses.**

1.Superficial Mycoses

Superficial mycoses are those infections that are limited to the very superficial surfaces of the skin and hair. They are nondestructive and of cosmetic importance only. The clinical infection is characterized by discolorationتغييرلون or depigmentation and scalingتغيير of the skin. **Tinea nigra** caused by ***Hortaea wernecki*** refers to brown or black pigmented macular patches localized primarily **to the palms.**

The clinical entities of **black and white piedra** involve the hair and are characterized by nodules composed of hyphae that include the hair shaft. The fungi associated with these superficial infections include *Piedraia hortae,* and *Trichosporon* spp…..etc

2.Cutaneous Mycoses

Cutaneous mycoses are infections of the keratinized layer of skin, hair, and nails. These infections may stimulate a host response and become symptomatic. Signs and symptoms include itching, scaling,

broken hairs, ringlike patches of the skin, and thickened discolored nails. Infections of the skin involving these organisms are called dermatophytoses. **Tinea unguium** refers to infections of the toes اصابع involving these agents. **Onychomycosis** includes infections of the nails caused by the dermatophytes as well as non dermatophytic fungi (e.g., *Candida* and *Aspergillus* spp.).

3.Subcutaneous Mycoses

Subcutaneous mycoses involve the deeper layers of the skin, including the cornea, muscle, and connective tissue, and are caused by a broad spectrum of taxonomically diverse fungi. The fungi gain access تتمكن من الوصول to the deeper tissues usually by traumatic inoculation and remain localized, causing abscess formation, non-healing ulcers, and draining sinus tracts. The host immune system recognizes the fungi, resulting in variable tissue destruction. Infections may be caused by hyaline molds, such as *Acremonium* spp. and *Fusarium* spp., and by pigmented fungi, such as *Alternaria* spp.Subcutaneous mycoses tend to remain localized and rarely disseminate systemically.

4.Endemic Mycoses

The endemic mycoses are fungal infections caused by the classic dimorphic fungal pathogens *Histoplasma capsulatum, Coccidioides immitis,..etc* . These fungi exhibit thermal dimorphism (exist as yeasts at 37° C and molds at 25° C) and are generally limited to geographic regions .The endemic mycoses are often referred to as

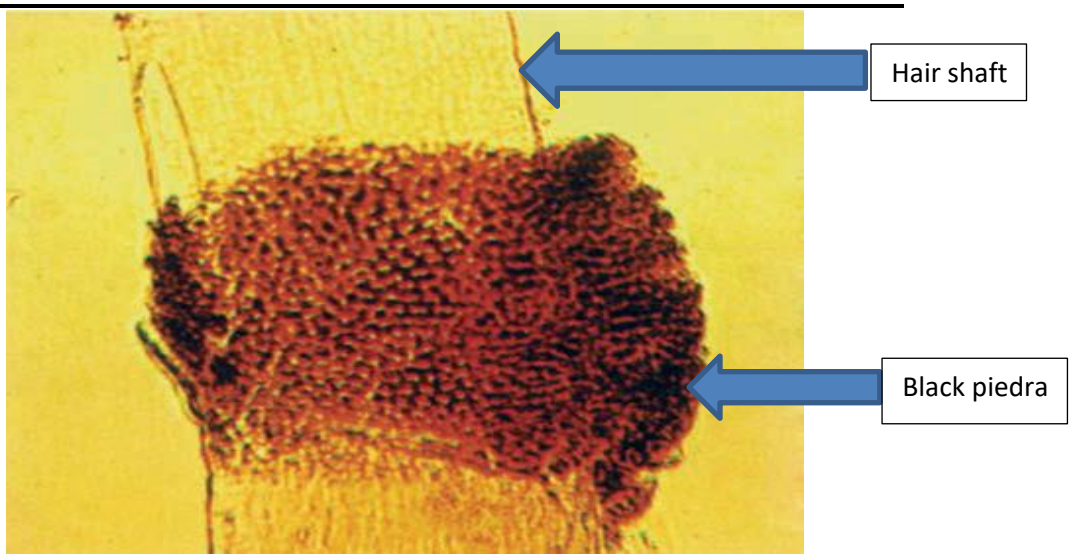
systemic mycoses because these organisms are true pathogens and can cause infection in healthy individuals. All of these agents produce a primary infection in the lung, with subsequent dissemination to other organs and tissues.

5.Opportunistic Mycoses

The opportunistic mycoses are infections attributable to fungi that are normally found as human commensals or in the environment. With the exception of *Cryptococcus neoformans* and *Cryptococcus gattii*, these organisms exhibit inherently low or limited virulence and cause infection in individuals who are weakened, immunosuppressed, or who carry implanted prosthetic devices or vascular catheters. Virtually تقريبا any fungus can serve as an opportunistic pathogen, and the list of those identified as such becomes longer each year. The most common opportunistic fungal pathogens are the yeasts *Candida* spp. and *C. neoformans*, the mold *Aspergillus* spp.,etc. Because of its inherent virulence, *C. neoformans* is often considered a "systemic" pathogen. Although this fungus may cause infection in immunologically normal individuals, it clearly is seen more frequently as an opportunistic pathogen in the immunocompromised population.

***Patrick R. Murray , Kens S. Rosenthal, and Michael A. Pfaller. Medical Microbiology, 2016**

***Satish Gupte, The short text book of Medical Microbiology,10th ed, 2010**



Black piedra. Note invasion by *Piedraia hortae* both within (endothrix) and outside (exothrix) the hair shaft. Dermatophyte invasion would be similar. (**SHERRIS** MEDICAL MICROBIOLOGY, 2014)

Tinea nigra (https://en.wikipedia.org/wiki/Tinea_nigra)

General principle in treatment, antifungal agents

Antifungal therapy has undergone a remarkable transformation in recent years. Once the only area of the agents amphotericin B and 5-fluorocytosine, which were toxic and difficult to use, the treatment of mycotic disease has now been advanced by the availability of several new systemically active agents and new formulations of other older agents that provide comparable if not superior efficacy with significantly less toxicity.

SELECTION OF ANTIFUNGALS

As with all chemotherapy, the selection of antifungal agents for treatment of superficial, subcutaneous, and systemic mycoses involves balancing probable efficacy against toxicity.

The factors to be considered are the following:

(1) The threat of morbidity or mortality posed by thespecific infection, (2) the immune status of the patient.

(3) The toxicity of the antifungal.

(4) The probable activity of the antifungal agent against the fungus. In the case of superficial mycoses, the risks of appropriate therapy are small, and various topical agents may be tried.

Treatment failures are common particularly in the immunocompromised. It is hoped that the addition of the new cell wall active agents to the regimen will have a favorable effect on these outcomes.

The antifungal agents, both systemic and topical (Table 61-1).

Figure(61-1)Show The sites of action of antifungal.

The terminology appropriate for this discussion is summarized bellow:

Antifungal spectrum: Range of activity of an antifungal agent against fungi. A broad-spectrum antifungal agent inhibits a wide variety of fungi, including both yeast like fungi and molds, whereas a narrow- spectrum agent is active only against a limited number of fungi.

Fungistatic activity: Level of antifungal activity that inhibits the growth of an organism. This is determined in vitro by testing a standardized concentration of organisms against a series of antifungal dilutions.

The lowest concentration of the drug that inhibits the growth of the organism is referred to as the **minimum inhibitory concentration (MIC).**

Fungicidal activity: The ability of an antifungal agent to kill an organism in vitro or in vivo.

The lowest concentration of the drug that kills 99.9% of the test population is called the **minimum fungicidal concentration (MFC).**

Antifungal combinations: Combinations of antifungal agents that may be used to (1) enhance efficacy in the treatment of a refractoryمقاوم fungal infection, (2) broadenتوسيع the spectrum of empiricalتجريبي antifungal therapy, (3) prevent the emergence of resistant organisms, and (4) succeed a synergistic killing effect.

Antifungal synergism: Combinations of antifungal agents that have enhanced antifungal activity when used together compared with the activity of each agent alone.

Antifungal antagonism: Combination of antifungal agents in which the activity of one of the agents interferes with the activity of the other agent.

Efflux pumps: Families of drug transporters that serve to actively pump antifungal agents out of the fungal cells, thus decreasing the amount of intracellular drug available to bind to its target.

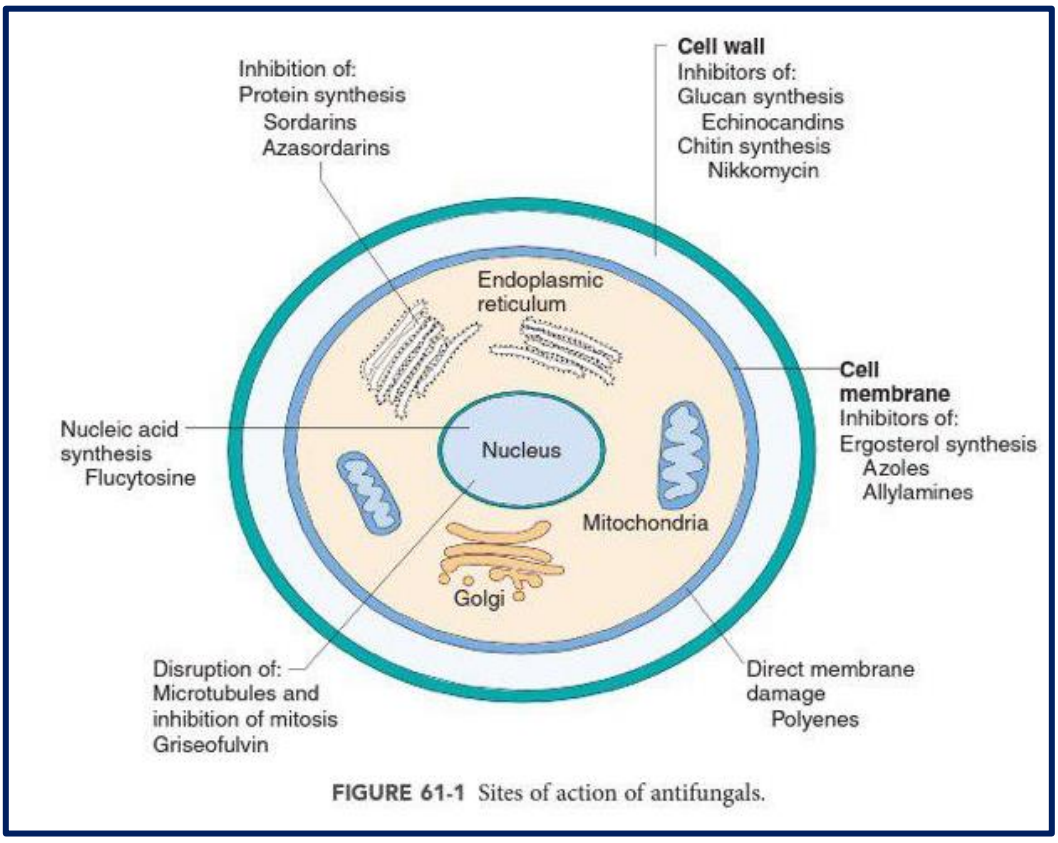


FIGURE 61-1 Sites of action of antifungals.

Systemic and Topical Antifungal

Antifungal agents	Route	Mechanism of action
Allylamines Naftifine	Topical	Inhibition of squalene epoxidase
Antimetabolite Flocytosine	Oral	Inhibition of DNA and RNA synthesis
Imidzoles Bifonaole	Oral, topical	Inhibits lanosterol 14-α-demethylase enzyme
Triazoles Fluconazole	Oral, IV	Same as imidazoles but more specific binding to target
Echinocandins Capsofungin	IV	Inhibition of fungal cell wall glucan synthesis
Polyenes Amphotericin B Nystatin	IV Oral, suspension topical	Binds to ergosterol, causing direct oxidative membrane damage

RESISTANCE TO ANTIFUNGAL AGENTS

MECHANISMS OF RESISTANCE

The same resistance mechanisms observed in bacteria are also found in fungi. A major addition is the much greater use of metabolic means such as efflux pumps and changes in synthetic pathways by fungi. The most glaring difference is the complete absence of enzymatic inactivation of antifungals as resistance mechanism. Perhaps, related to this is the absence in fungi of powerful means for gene transfer such as conjugation and transposition.

Polyene Resistance

Because amphotericin B binds directly to the cytoplasmic membrane, the only means to resist this action is to change the membrane composition. The uncommon strains that have been studied show a decrease in the ergosterol content of the membrane. This limits the primary binding sites.

Flucytosine Resistance

Flucytosine requires a permease for entry into the cell and then multiple enzymes to modify it to the active metabolites. Mutation in any one of these enzymes renders the drug ineffective.

This happens readily under the selective pressure of 5FC use. It is one of the few antimicrobials in which emergence of resistance *during* therapy of an acute infection is predictable. It is the reason its use is limited to combinations with other antifungals.

Azole Resistance

There are four major mechanisms of resistance that cross all the azole agents. The two most prominent are efflux pumps and altered target. The efflux pumps transport drug that has entered the cell back outside. Some pumps act for all azoles and others act on only one.

Alteration of subunits of the demethylase enzyme by mutation decreases the affinity of the azole for its enzyme target. Multiple mutations can have an additive effect.

Two metabolic mechanisms compensate for the drug's presence without altering its target or directly inactivating it. Upregulation of the target demethylase allows its action to

continue despite binding of some of the enzyme by the azole. Some resistant strains have been shown to accomplish ergosterol synthesis by an alternate pathway, thus bypassing the azole affected mechanism.

Echinocandin Resistance

Although the echinocandins are relatively new, resistance has already been observed with their use. The mechanism is altered target. Mutations in subunits of the glucan synthetase target have been correlated with increases in MIC of up to a thousandfold.

***Patrick R. Murray , Kens S. Rosenthal, and Michael A. Pfaller. Medical Microbiology, 2016**

*** SHERRIS MEDICAL MICROBIOLOGY,6th ed.2014**

Aspergillus

Etiology: Aspergillus fumigatus

Aspergillus fumigatus is a species of fungus in the genus *Aspergillus*, and is one of the most common *Aspergillus* species to cause disease in individuals with an immunodeficiency.

Scientific classification

Kingdom: Fungi
Division: Ascomycota
Class: Eurotiomycetes
Order: Eurotiales
Family: Trichocomaceae
Genus: *Aspergillus*
Species: *A. fumigatus*
Binomial name *Aspergillus fumigatus*(Fresenius 1863)

Pathogenesis:

Aspergillus fumigatus is the most frequent cause of invasive fungal infection in immunosuppressed individuals, which include patients receiving immunosuppressive therapy for autoimmune or neoplastic disease, organ transplant recipients, and AIDS patients. *A. fumigatus* primarily causes invasive infection in the lung and represents a major cause of morbidity and mortality in these individuals. Additionally, *A. fumigatus* can cause chronic pulmonary infections, allergic bronchopulmonary aspergillosis, or allergic disease in immunocompetent hosts.

Laboratory diagnosis:

Specimen:

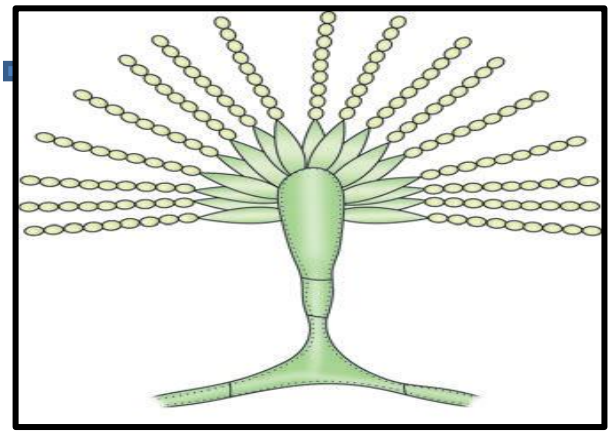
1. Exudate
2. Sputum
3. Lung biopsy.

Direct microscopic examination: KOH preparation of the specimen shows septate filamentous hyphae.

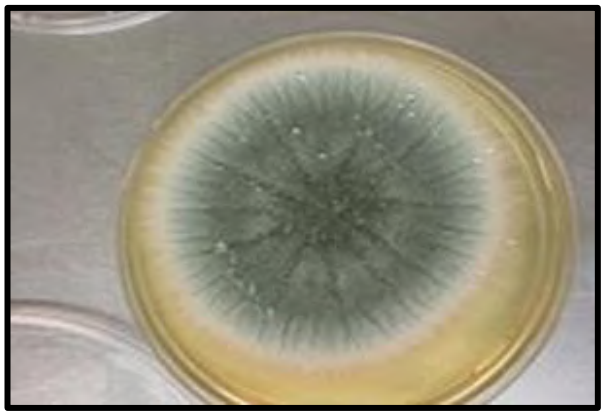
Culture: On Subouraud's dextrose agar with chloramphenicol after 25°C incubation for 1 to 4 days, there appear gray green colored colonies. Microscopic examination of these colonies shows septate hyphae bearing conidia in chain like fashion.

Other laboratory tests*:* Histological examination of Hematoxlin and Eosin stained and methenamine silver stain section shows septate hyphae branching dichotomously.

Treatment: Amphotericin B may be used. Fungus ball may be removed surgically.



Aspergillus fumigatus



Colony on SDA

Penicillium

Penicillium are of major importance in the natural environment as well as food and drug production. Some members of the genus produce penicillin, a molecule that is used as an antibiotic, which kills or stops the growth of certain kinds of bacteria. Other species are used in cheesemaking.

Penicilliosis:

is an infection caused by *Penicillium marneffei*. It is a dimorphic fungus.

Penicillium maneffei **(generalfeatures)**

1.It is the only dimorphic fungus of genus penicillium predominantly found in Southeast Asia spreading continuously in the surrounding areas like Southeastern China, Hong Kong, India, etc.

2. It is a dimorphic facultative intracellular fungus. It exists as mycelial form at 25°C and yeast like form at 37°C.

3.Unlike other yeasts, it divides by fission with formation of transverse septum.

Pathogenesis:

The yeast form can multiply in macrophages of host. The primary site of infection is reticuloendothelial system. Ultimately infection may result into granulomatous suppurative قيحية reaction to immunity. In immunocompromising patients necrotizing reaction may occur.This infection is chronic entity with incubation period of 4 weeks. Probably infection occurs by inhalation of airborne conidia of this fungus. It presents with low grade fever, chills, malaise, weight loss, cough, generalized popular skin rash with central umbilication, lymphadenopathy and hepatosplenomegaly.

laboratory diagnosis :

A. Indirect diagnosis: Microscopic examination of Wright's stained impression smear of skin, lymph node, bone marrow aspirate may be done. This fungus can be stained with Hematoxillin and Eosin, Calcoflur white staining, etc, is useful for the demonstration of yeast.

B. Culture: They can be cultured from blood, bone marrow, sputum, lymph nodes, pleural fluid, urine, etc. On Sabouraud's dextrose agar at 25°C grayish white colonies appear within 2 days and slowly become wooly growing to granular in texture and yellowish or gray in the center. The periphery of colony is white and has radical folds. The reverse is bright rose color. The hyaline short hyphae are septate and branched. The conidiophores are arranged laterally and terminally.

C. Immunological methods*:* They are include: immunofluorescence test , latex agglutination, immunodiffusion, PCR, etc.

Effective drugs are amphotericin B.

Zygomycosis

Mucormycosis (zygomycosis) is an opportunistic mycosis caused by a number of molds classified in the order Mucorales of the Phylum Glomerulomycota and Subphylum Mucoromycotina. These fungi are ubiquitous thermotolerant saprobes. The leading pathogens among this group are species of the genera :

1. Mucor 2. Rhizopus. ….. et al.

Laboratory diagnosis:

1.Specimen:

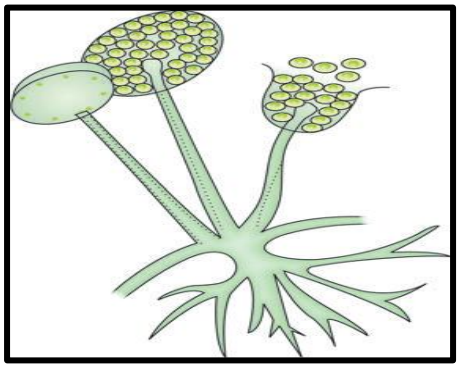
a)Skin lesion scraping b) Tissue biopsy

2.Direct microscopic examination: KOH preparation may show mycelial fragments and spores. For identification whether mucor or rhizopus, microscopic examination of this growth is helpful. Mucor colonies, microscopically are seen as non-septate hyphae having branched sporangiophores with sporangium at terminal end whereas in case of rhizopus there are non- septate hyphae and sporangiophores arise in groups exactly above rhizoids .

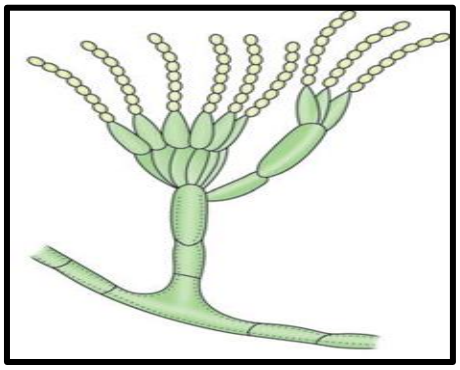
3. Culture: On Sabouraud's dextrose agar after 25°C incubation for 1 to 4 days there may be the growth of cottony colonies.

4.Histological sections: Microscopic examination shows broad, non-septate, irregular hyphae in thrombosed vessels or sinuses surrounded with leukocytes and giant cells.

Treatment: In some cases amphotericin B may be useful



Rhizopus



Penicillium

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Dermatophytes

Dermatophytoses are superficial infections of the skin and its appendages, commonly known as ringworm, Are slowly progressive eruptions of the skin and its appendages that may be nasty, but are not painful or life threatening. (Figure 45–1), athlete's foot. They are caused by species of three genera collectively known as dermatophytes.

What Is Ringworm?

Ringworm is a common fungal skin disorder otherwise known as "tinea" or dermatophytosis. It is caused by a fungus that can live on skin, surfaces like gym floors, and household items like towels, bedding, and clothes.

General characteristics of Dermatophytes

1.These fungi are highly adapted to the nonliving, keratinized tissues of nails, hair, and the stratum corneum of the skin.

2.The source of infection may be humans, animals, or the soil.

3.The three genera of medically important dermatophytes are *Epidermophyton, Microsporum,* and *Trichophyton*.

4.They are separated primarily by the morphology of their macroconidia and the presence of microconidia.

5.Most grow best at 25°C on Sabouraud's agar, which is usually used for culture.

6.Although teleomorphic (sexual) forms have been discovered, the medically important dermatophytes continue to be identified in their more familiar anamorphic (asexual) state.

7.The hyphae are septate, and their conidia may be borne directly on the hyphae or on conidiophores. Small microconidia may or may not be formed; however,the larger and more distinctive macroconidia are usually the basis for identification.

FIGURE 45–1. Ringworm. The ring-like lesions on this fore arm are due to advancing growth of *Trichophyton mentagrophytes*

TABLE 45–1 Agents of Superficial and Subcutaneous Mycoses

Fungus	In lesion	Fungal growth culture 25_c	Infection site	DISEASE
Dermatophytes				
Microsporum canis	**Septate hyphae**	**mold**	**Hair, skin**	**Ringwarm**
Trichophyton rubrum	**Septate hyphae**	**mold**	**Hair, skin. nails**	**Ringwarm**
Epidermophyton floccosum	**Septate hyphae**	**mold**	**skin**	**ringwarm**
Other superficial fungi				
Hortaea werneckiie	**Septate hyphae, ellipsoidal cells**	**Yeast(mold)**	**Skin(brown-black)**	**Tinea nigra**
Trichosporon cutaneum	**Septate hyphae**	**Mold**	**Hair (white)**	**White piedra**
Piedraia hortae	**Septate hyphae**	**Mold, ascospores**	**Hair (black)**	**Black piedra**
Subcutaneous fungi				
Sporothrix schenckii	**Cigar-shaped yeast**	**mold**	**Subcutaneous, lymphatic spread**	**Sporotrichosis**

PATHOGENESIS of Dermatophytes

Dermatophytoses begin when minor traumatic skin lesions come in contact with dermatophyte hyphae or conidia shed from another infection. These forms may remain infectious for months in the environment.

The course of the infection depends on the : 1)anatomic location , 2)moisture, 3)the dynamics of skin growth and desquamation, 4)the speed and extent of the inflammatory response, and the infecting species.

Infection may spread from skin to other keratinized structures, such as hair and nails, or may invade them primarily. The hair shaft is penetrated by hyphae (**Figure 45–2**), which extend as arthroconidia either exclusively within the shaft (endothrix) or both within and outside the shaft (extothrix). The end result is damage to the hair shaft structure, which often breaks off. Loss of hair at the root and plugging of the hair follicle with fungal elements may result.

Invasion of the nail bed causes a hyperkeratotic reaction, which removes or distorts the nail.

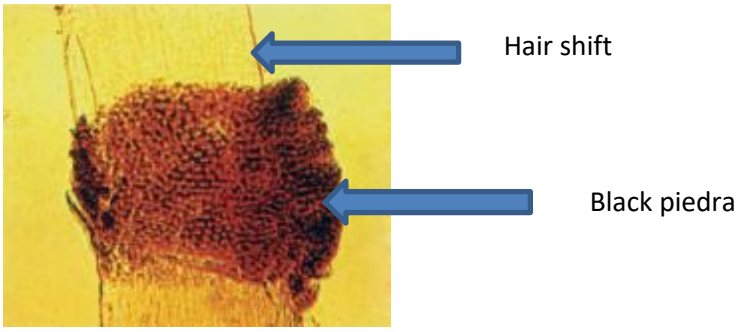


FIGURE 45–2. Black piedra.

Immunity

1.Most dermatophyte infections pass through an inflammatory stage to spontaneous healing.

2.Phagocytes are able to use oxidative pathways to kill the fungi .

3.Antibodies may be formed during infection but play no known role in immunity.

4.Most clinical and experimental evidence points to the importance of T-cell–mediated TH1 responses.

Laboratory diagnoses of Dermatophytes:

1. The most important step is microscopic examination of material taken from lesions to detect the fungus.
2. Potassium hydroxide (KOH) or calcifluor white preparations of scales scraped from the advancing edge of a dermatophyte lesion demonstrate septate hyphae. Examination of infected hairs demonstrate hyphae and arthroconidia penetrating the hair shaft.
3. Some species of dermatophyte fluoresce, and selection of hairs for examination can be aided by the use of an ultraviolet lamp
4. When KOH preparation is negative, The same material used for direct examination can be cultured for isolation and demonstration of typical conidia
5. Nucleic acid amplification procedures have been successfully applied to skin and nail scrapings, but their use is limited.

Reference

***SHERRIS MEDICAL MICROBIOLOGY,6th ed.2014**

Sporotrichosis

Sporotrichosis is a fungal infection of the skin caused by the fungus *Sporothrix schenckii*, which is found on decaying vegetation, rosebushes, twigs, hay, and mulch-rich soil. Because of its tendency to present after a thorn injury, it is also called rose gardener disease.

General characteristics of sporotrichosis

1. *Sporothrix schenckii* is naturally found in soil, hay, sphagnum moss, and plants.
2. It usually affects farmers, gardeners, and agricultural workers.
3. It enters through small cuts and abrasions in the skin to cause the infection.
4. In case of sporotrichosis affecting the lungs, the fungal spores enter through the respiratory pathways.
5. Sporotrichosis can also be acquired from handling cats with the disease; it is an occupational hazard for veterinarians.

Signs and symptoms

1.***Cutaneous or skin sporotrichosis***

This is the most common form of this disease. Symptoms of this form include nodular lesions or bumps in the skin, at the point of entry and also along lymph nodes and vessels. The lesion starts off small and painless, and ranges in color from pink to purple. Left untreated, the lesion becomes larger and look similar to a boil and more lesions will appear, until a chronic ulcer develops.

Usually, cutaneous sporotrichosis lesions occur in the finger, hand, and arm.

2. Pulmonary sporotrichosis

This rare form of the disease occur when *S. schenckii* spores are inhaled. Symptoms of pulmonary sporotrichosis include productive coughing, nodules and cavitations of the lungs, fibrosis, and swollen hilar lymph nodes. Patients with this form of sporotrichosis are susceptible to developing tuberculosis and pneumonia.

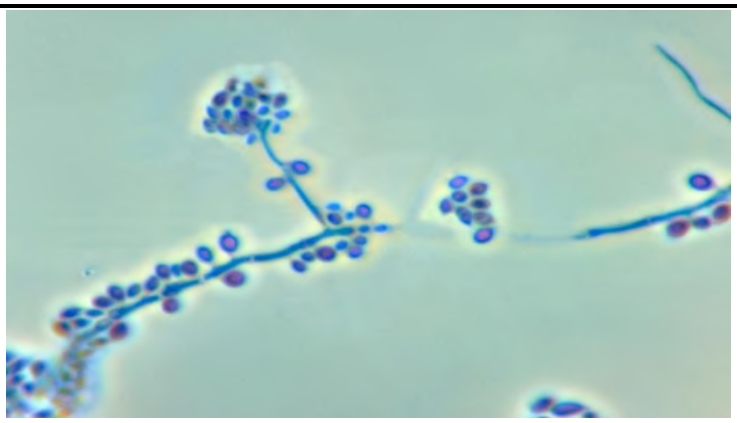
3. Disseminated sporotrichosis

When the infection spreads from the primary site to secondary sites in the body, the disease develops into a rare and critical form called disseminated sporotrichosis. The infection can spread to **joints and bones (called *osteoarticular sporotrichosis*)** as well as the **central nervous system and the brain (called *sporotrichosis meningitis*).**

The symptoms of disseminated sporotrichosis include weight loss, anorexia فقدان الشهية, and appearance of bony lesions نحول.

Laboratory Diagnosis:

1. Sporotrichosis is a chronic disease with slow progression and often subtle symptoms.
2. It is difficult to diagnose, as many other diseases share similar symptoms and therefore must be ruled out.
3. Patients with sporotrichosis will have antibody against the fungus *S. schenckii*, however, due to variability in sensitivity and specificity, it may not be a reliable diagnosis for this disease.
4. The confirming diagnosis remains culturing the fungus from the skin, sputum, synovial fluid, and cerebrospinal fluid. Smears should be taken from the draining tracts and ulcers.



Conidiophores and conidia of the
fungus *Sporothrix schenckii*

Prevention

The majority of sporotrichosis cases occur when the fungus is introduced through a cut or puncture in the skin while handling vegetation containing the fungal spores. Prevention of this disease includes **wearing long sleeves** and **gloves** while working with soil, hay bales بالات القش, rose bushesشجيرات الورد , pine seedlings, and sphagnum moss. Also, keeping cats indoors is a preventative measure.

Treatment

1. Oral potassium iodide
2. Itraconazole (Sporanox)
3. Fluconazole
4. Amphotericin B

Other animals infect with sporotrichosis

Sporotrichosis can be diagnosed in domestic and wild mammals. In veterinary medicine it is most frequently seen in cats and horses. Cats have a particularly severe form of cutaneous sporotrichosis and also can serve as a source of zoonotic infection to persons who handle them and are exposed to exudate from skin lesions.

References: https://en.wikipedia.org/wiki/Sporotrichosis