

L 11:- Fungi (mycosis)

Fungi= Fungous

by Professor Dr. Nada Khazal

Basis for Comparison	Bacteria	Fungi
Definition	Bacteria are prokaryotes, can be grow at 37C. It is requiring several hour to days	fungi are eukaryotes. Most fungi grow best at room temperature 25C. It grow at slow rates, are requiring several days to weeks
pH	Bacteria grow best in the neutral environment of pH range 6.5-7.	Fungi mostly prefer a slightly acidic environment with pH value 4-6.
No. of cells	Bacteria are unicellular organisms with simpler cellular structure.	Most fungi are multicellular cellular. Some fungi like yeast might be unicellular.
Size	The size of bacteria ranges from 0.5 to 5 μm .	The size of the fungi ranges from 2 to 10 μm .
Cell wall	is made up of peptidoglycan	is made up of chitin. fungal membrane contains ergosterol,
Morphology	Bacteria are found to have three distinct shapes, round (cocci), spiral (Spirilla), and rod-shaped (bacillus).	Fungi are found to have varying shapes, but most of them are spotted in the form of a thread-like structure called hyphae.
Ribosomes	contain 70S ribosomes.	contain 80S ribosomes.
Reproduction	Bacteria reproduce by an asexual method like binary fission.	Fungi reproduce through both asexual and sexual methods. Sexual reproduction takes place through fungal spores.
Nutrition	Bacteria can be autotrophs or heterotrophs.	Fungi are mostly heterotrophs that feed on dead and decaying matter.

- **Modes of fungal growth:** Most fungi exist in one of two basic morphologic forms
 1. **filamentous mold** or **thallus**
 2. **unicellular (yeast)**. Single cell. Yeast-like fungi generally **reproduce by budding**.
 3. some fungi are **dimorphic** (that is, they switch between these two forms in response to environmental conditions).

In human (at 37 C)= yeast

In lab (at 25 C)= molds

The macroscopic aggregation (colony) of mold cells is called **thallus**, a thallus is composed of mass of strands called a **mycelium**, each strand is a **hyphae** .

vegetative hyphae grow on the surface of culture media, they form aerial hyphae , called **reproductive hyphae** , that bear asexual reproductive spores or conidia .

The hyphae that grow below the surface of culture media are called **rhizoidal hyphae**.

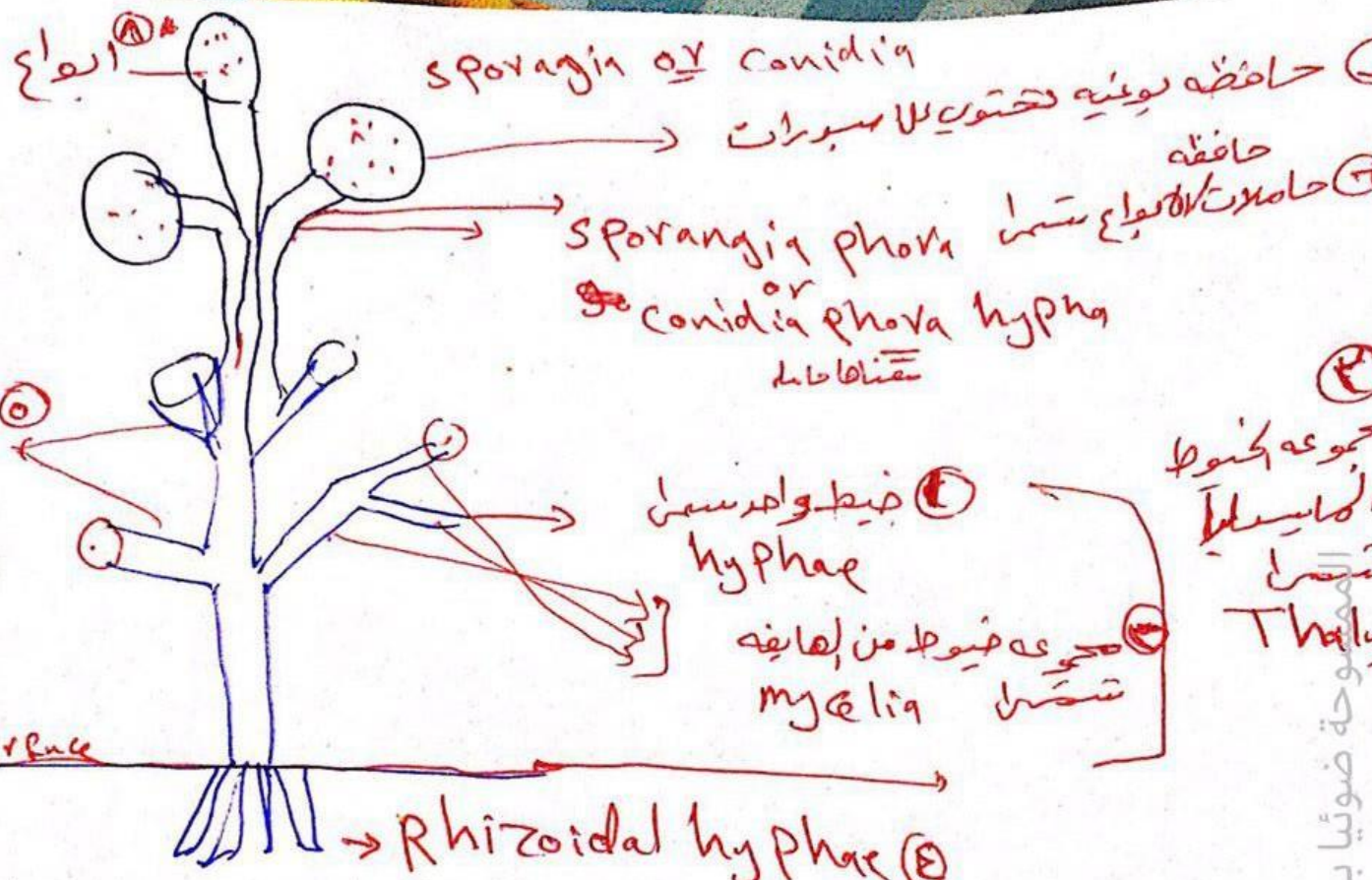
The hyphal strand of some molds may be separated by across wall called a septum. hyphae that contain septa are called **septate hyphae**.

Molds with hyphae that lack septa are called **coenocytic hyphae or aseptate hyphae**.

Fungi are **identified** primarily by examining their reproductive structures, morphological characteristics , and colony growth .

molds are **classified** primarily by their sexual stages of reproduction , they are also characterized and classified according to the appearance of the colony (ex. color ,size) organization of the hyphae (ex. septate or coenocytic) and the structure & organization of the spores (ex . sporangiospores ,conidispores).

S pores



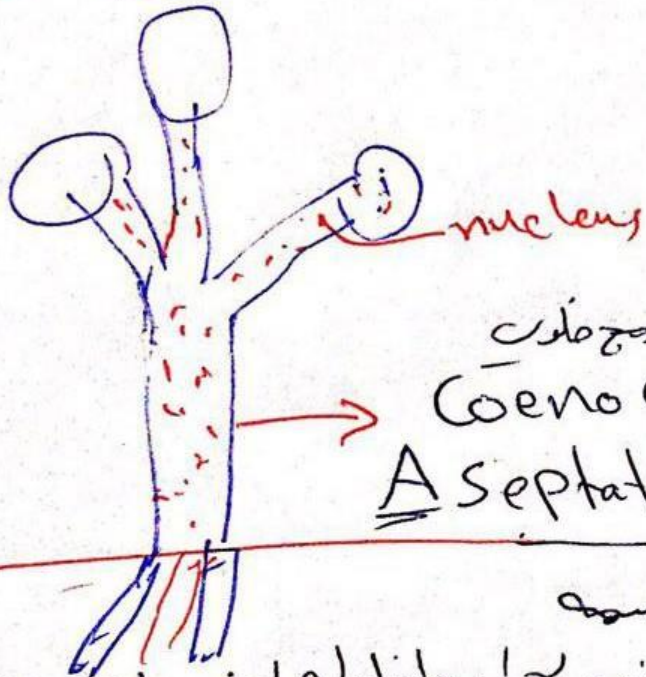
الخيوط فوق السطح
 خيوط هوائيه
 Aerial hyphae

خيوط ودرست
 hyphae
 مجموعه خيوط من الجانف
 mycelia

جموعه خيوط الهائيه
 Thalium

السطح الفائق
 Rhizoidal hyphae
 هافه الهياه الجذور
 السطح الفائق

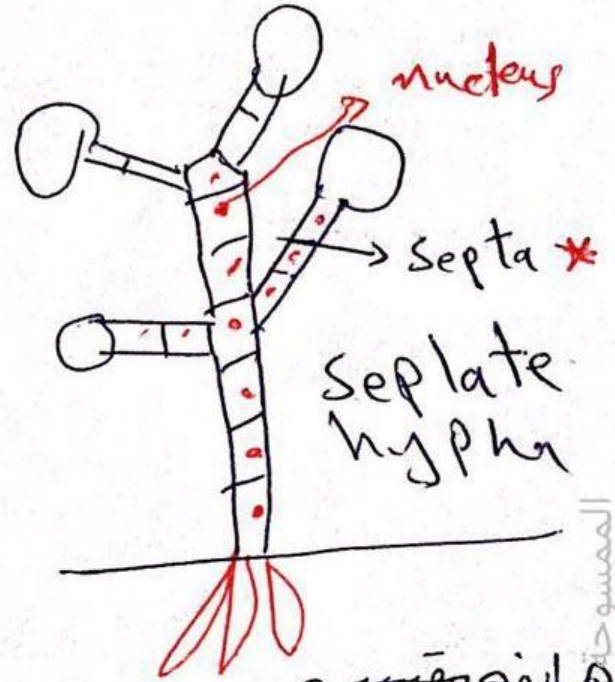
عند نضج الابواغ تنتفتح الجانفة ابوغيه وتنشر الابواغ بالهوار
 تتحلل لفرود ليه لغيره لانه وعندها تغير بيئه ملائمه تنبت وتكون فطر هيره



Coenocytic hypha
Aseptate hypha

هائفة غير مقسمة

تنتشر الأنوية اجزاء داخلها هائفة الغير مقسمة



هائفة مقسمة

تحتوي على اجزاء septa

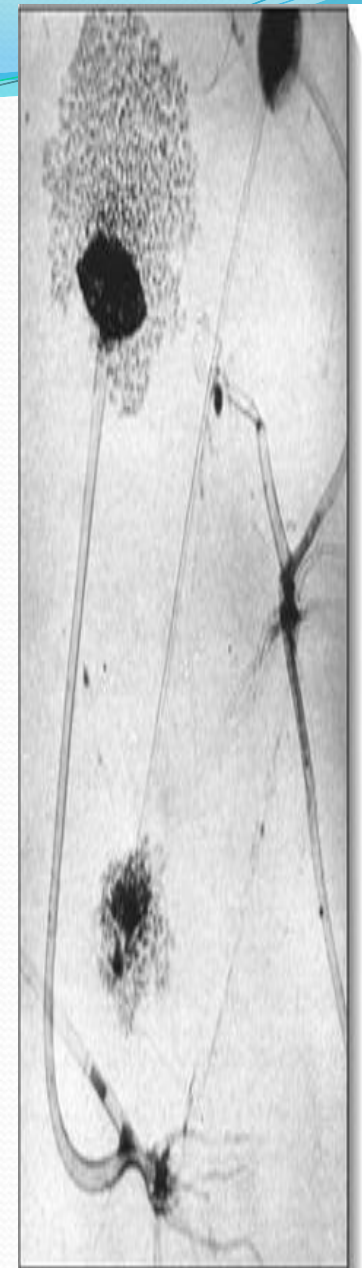
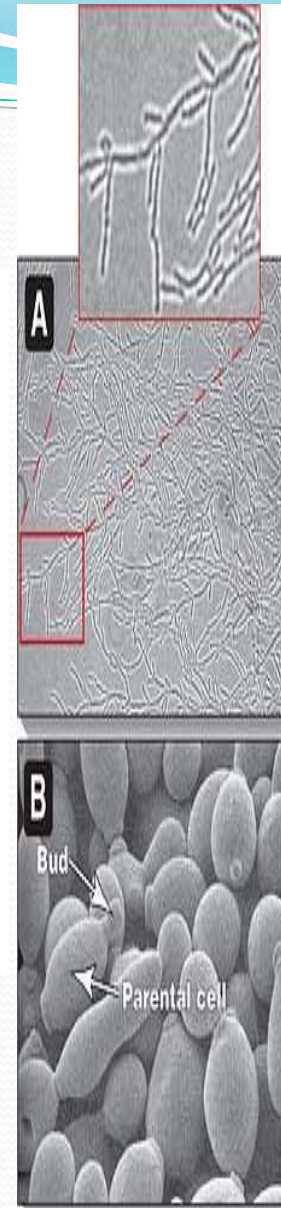
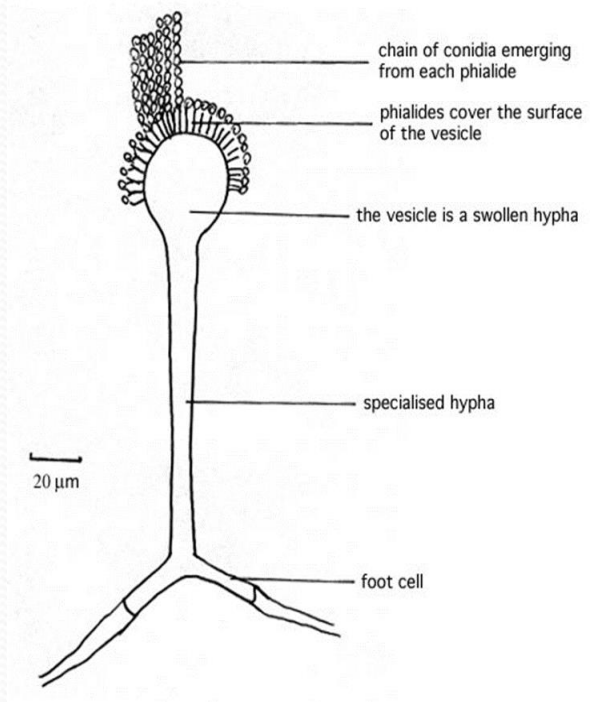
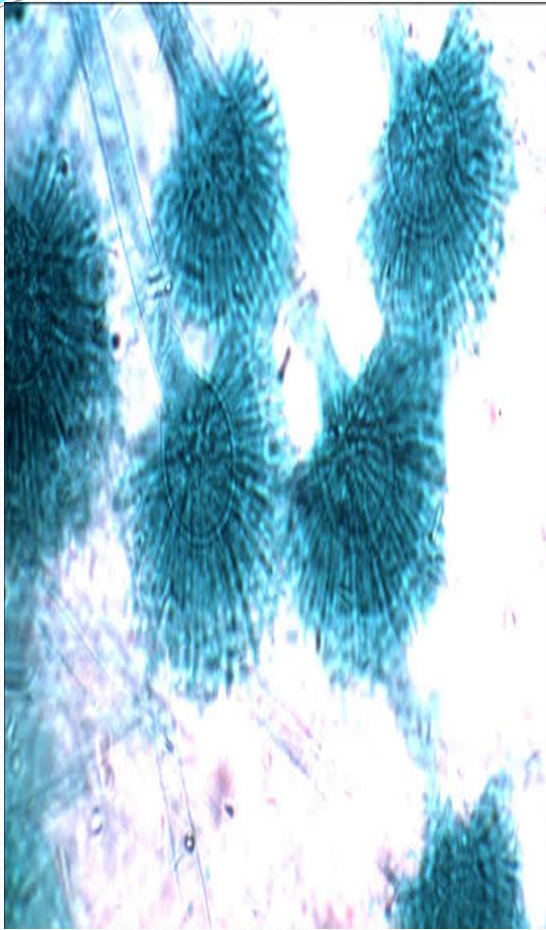
تضم كثيرا من غرف مرتبة

تحتوي

كل غرفة لغاها واحدة

دكتور محمد

للاطلاع فقط



aspergillus

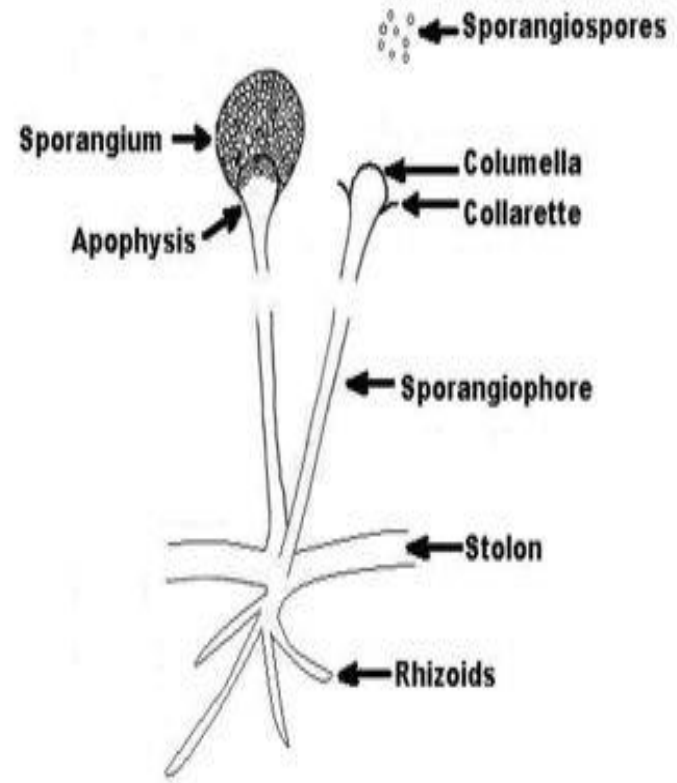
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Cladosporium

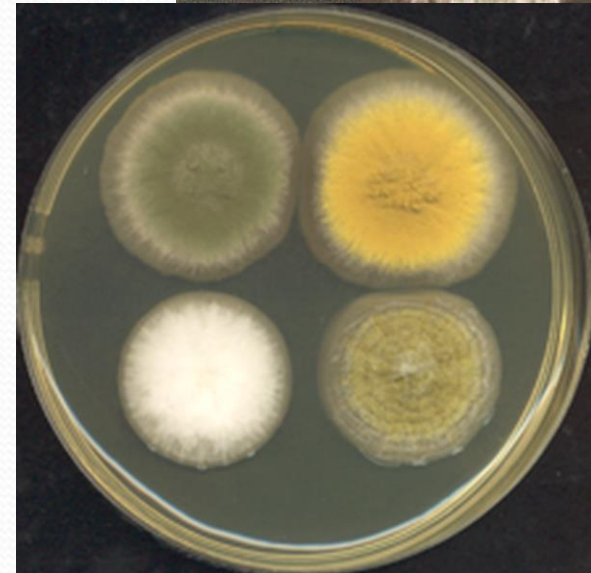
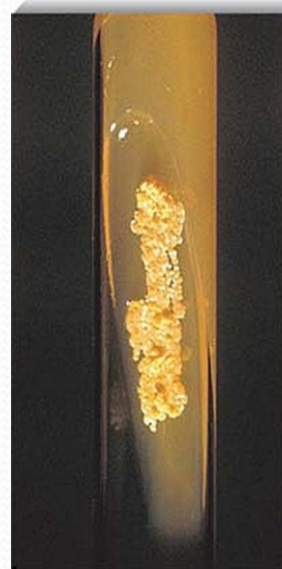


Rhizopus_oryzae_sporangia





-Penicillium-spp



Aspergillus_colonies_on_a_Petri_dish

• الفهم فقط

Habitat and nutrition

All fungi are heterotrophs; that is, they require some preformed organic carbon source for growth. Fungi do not ingest food particles as do organisms such as protozoa, but depend upon transport of soluble nutrients across their cell membranes. To obtain these soluble nutrients, **fungi secrete degradative enzymes (for example, cellulases, proteases, nucleases) into their immediate environment. It is this ability that enables fungi to live saprophytically on organic waste.** Therefore, the natural habitat of almost all fungi is soil or water containing decaying organic matter. [Note: Some fungi can be parasitic on living organisms. However, these parasitic infections usually originate from the individual's contact with fungus-infested soil, an exception being **Candida, which is part of the normal human mucosal flora**

Characteristics of Major Fungal Groups

Fungi can be distinguished from other infectious organisms such as bacteria or viruses because they are **eukaryotes**. Their characteristic **structures, habitats, and modes of growth and reproduction** are used to distinguish between different groups of fungi.

• **Cell wall and membrane components**

The fungal cell wall and cell membrane are fundamentally different from those of bacteria and other eukaryotes. **Fungal cell walls are composed largely of chitin, the fungal membrane contains ergosterol,** rather than the cholesterol found in mammalian membranes.

Types mycosis

1. **Cutaneous mycosis** : when limited to the epidermis
2. **Subcutaneous mycosis**: when the infection penetrates significantly beneath the skin
3. **Systemic mycosis**: when the infection is deep within the body or disseminated to internal organs.
4. **Opportunistic mycosis**: infecting in individuals who have predisposing conditions such as immunodeficiency, debilitating diseases.

- **Cutaneous Mycoses**

Also called **dermatophytoses**, these common diseases are caused by a group of related fungi, Dermatophytes fall into three genera, each with many sp: *Trichophyton*, *Epidermophyton*, & *Microsporum*.

- **Epidemiology**

The causative organisms of the dermatophytoses are often distinguished according to their natural habitats: **anthropophilic** (residing on human skin), **zoophilic** (residing on the skin of domestic and farm animals), or **geophilic** (residing in the soil). Most human infections are by anthropophilic and zoophilic organisms. Transmission from human to human or animal to human is by infected skin scales.

● Pathology

- A defining characteristic of the dermatophytes is the ability to use keratin as a source of nutrition. This ability allows them to **infect keratinized tissues** and structures, None invade underlying, nonkeratinized tissue.
- ***Trichophyton: attack the skin, hair, and nails***
- ***Epidermophyton: attack the skin, and nails***
- ***Microsporum: attack the skin, and hair***

Clinical significance

- Dermatophytoses are characterized by **itching, scaling skin patches that can become inflamed and weeping**. Specific diseases are usually identified according to affected tissue (for example, scalp, pubic area, or feet), but a given disease can be caused by any one of several organisms, and some organisms can cause more than one disease depending, for example, on the site of infection or condition of the skin. The following are the most commonly encountered dermatophytoses.

A. Tinea pedis (athlete's foot): Organisms most often isolated from infected tissue are *Trichophyton rubrum*, *Trichophyton mentagrophytes*, and *Epidermophyton floccosum*. The infected tissue is initially between the toes, but can spread to the nails, which become yellow and brittle. Skin fissures can lead to secondary bacterial infections, with consequent lymph node inflammation.



B. Tinea corporis (ringworm): Organisms most often isolated are *E. floccosum* and several species of *Trichophyton* and *Microsporum*. Lesions appear as advancing annular rings with scaly centers. The periphery of the ring, which is the site of active fungal growth, is usually inflamed and vesiculated. Although any site on the body can be affected, lesions most often occur on nonhairy areas of the trunk.



C.Tinea capitis (scalp ringworm): Several species of Trichophyton & Microsporum have been isolated from **scalp ringworm lesions**, the predominant infecting species depending on the geographic location of the patient. **Disease manifestations range from small, scaling patches, to involvement of the entire scalp with extensive hair loss.** The hair shafts can become invaded by Microsporum hyphae



D. Tinea cruris (jock itch): Causative organisms are *E. floccosum* and *T. rubrum*. Disease manifestations are similar to ringworm, except that lesions occur in the moist **groin area**, where they can spread from the upper thighs to the genitals.



E. Tinea unguium (onychomycosis): The causative organism is most often *T. rubrum*. **The nails are thickened, discolored, and brittle.** Treatment must be continued for three to four months until all infected portions of the nail grow out and are trimmed off.



F. Tinea Barbae: The causative organism is most often *Trichophyton*.

Edematous erythematous lesion in beard hair



Category	Mycosis	Causative Fungal Agents
Superficial	Pityriasis versicolor Tinea nigra White piedra Black piedra	<i>Malassezia</i> species <i>Hortaea werneckii</i> <i>Trichosporon</i> species <i>Piedraia hortae</i>
Cutaneous	Dermatophytosis Candidiasis of skin, mucosa, or nails	<i>Microsporum</i> species, <i>Trichophyton</i> species, and <i>Epidermophyton floccosum</i> <i>Candida albicans</i> and other <i>Candida</i> species
Subcutaneous	Sporotrichosis Chromoblastomycosis Mycetoma Phaeohyphomycosis	<i>Sporothrix schenckii</i> <i>Phialophora verrucosa</i> , <i>Fonsecaea pedrosoi</i> , and others <i>Pseudallescheria boydii</i> , <i>Madurella mycetomatis</i> , and others <i>Exophiala</i> , <i>Bipolaris</i> , <i>Exserohilum</i> , and other dematiaceous molds
Endemic (primary, systemic)	Coccidioidomycosis Histoplasmosis Blastomycosis Paracoccidioidomycosis	<i>Coccidioides posadasii</i> and <i>Coccidioides immitis</i> <i>Histoplasma capsulatum</i> <i>Blastomyces dermatitidis</i> <i>Paracoccidioides brasiliensis</i>
Opportunistic	Systemic candidiasis Cryptococcosis Aspergillosis Hyalohyphomycosis Phaeohyphomycosis Mucormycosis (zygomycosis) <i>Pneumocystis pneumonia</i> Penicilliosis	<i>Candida albicans</i> and many other <i>Candida</i> species <i>Cryptococcus neoformans</i> and <i>Cryptococcus gattii</i> <i>Aspergillus fumigatus</i> and other <i>Aspergillus</i> species Species of <i>Fusarium</i> , <i>Paecilomyces</i> , <i>Trichosporon</i> , and other hyaline molds <i>Cladophialophora bantiana</i> ; species of <i>Alternaria</i> , <i>Cladosporium</i> , <i>Bipolaris</i> , <i>Exserohilum</i> and numerous other dematiaceous molds Species of <i>Rhizopus</i> , <i>Lichtheimia</i> , <i>Cunninghamella</i> , and other zygomycetes <i>Pneumocystis jiroveci</i> <i>Penicillium marneffeii</i>

Skin Disease	Location of Lesions	Clinical Features	Fungi Most Frequently Responsible
Tinea corporis (ringworm)	Nonhairy, smooth skin	Circular patches with advancing red, vesiculated border and central scaling. Pruritic	<i>Trichophyton rubrum</i> , <i>Epidermophyton floccosum</i>
Tinea pedis (athlete's foot)	Interdigital spaces on feet of persons wearing shoes	Acute: itching, red vesicular. Chronic: itching, scaling, fissures	<i>Trichophyton rubrum</i> , <i>Trichophyton mentagrophytes</i> , <i>Epidermophyton floccosum</i>
Tinea cruris (jock itch)	Groin	Erythematous scaling lesion in intertriginous area. Pruritic	<i>Trichophyton rubrum</i> , <i>Trichophyton mentagrophytes</i> , <i>Epidermophyton floccosum</i>
Tinea capitis	Scalp hair. Endothrix: fungus inside hair shaft. Ectothrix: fungus on surface of hair	Circular bald patches with short hair stubs or broken hair within hair follicles. Kerion rare. <i>Microsporum</i> -infected hairs fluoresce	<i>Trichophyton mentagrophytes</i> , <i>Microsporum canis</i> , <i>Trichophyton tonsurans</i>
Tinea barbae	Beard hair	Edematous, erythematous lesion	<i>Trichophyton mentagrophytes</i> , <i>Trichophyton rubrum</i> , <i>Trichophyton verrucosum</i>
Tinea unguium (onychomycosis)	Nail	Nails thickened or crumbling distally; discolored; lusterless. Usually associated with tinea pedis	<i>Trichophyton rubrum</i> , <i>Trichophyton mentagrophytes</i> , <i>Epidermophyton floccosum</i>
Dermatophytid (id reaction)	Usually sides and flexor aspects of fingers. Palm. Any site on body	Pruritic vesicular to bullous lesions. Most commonly associated with tinea pedis	No fungi present in lesion. May become secondarily infected with bacteria

Treatment

Removal of infected skin, followed by topical application of antifungal antibiotics such as miconazole or clotrimazole, is the first course of treatment. Refractory infections usually respond well to oral griseofulvin and itraconazole. Infections of the hair and nails usually require systemic (oral) therapy. Terbinafine is the drug of choice for onychomycosis.

Subcutaneous Mycoses

Subcutaneous mycoses are fungal infections of the dermis, subcutaneous tissue, and bone. Causative organisms reside in the soil and decaying or live vegetation. Subcutaneous fungal infections are almost always acquired through traumatic lacerations or wounds, often acquired from the prick of a thorn. As expected, these infections are more common in individuals who have frequent contact with soil and vegetation and wear little protective clothing. The subcutaneous mycoses are not transmissible from human to human under ordinary conditions.

Clinical Significance

A. Mycetoma (Madura foot): Mycetoma appears as a localized abscess on the feet, & Sinusitis (discharges pus, serum, and blood through sinuses channel). The infection can spread to the underlying bone. The color of the grains (black, white, red, or yellow). There is no effective chemotherapy for fungal mycetoma; the treatment is usually surgical excision.

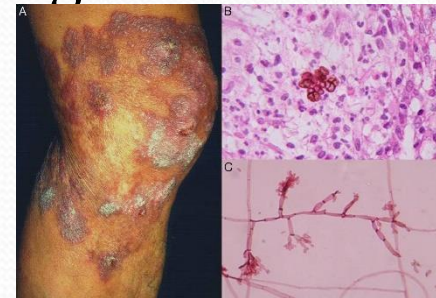


Clinical Significance

B. Sporotrichosis: The causative organism, *Sporothrix schenckii*, is a dimorphic fungus. This infection, characterized by a granulomatous ulcer at the puncture site, may produce secondary lesions along the draining lymphatics.



C. Chromo mycosis (also called chromoblastomycosis): This infection is characterized by warty nodules that spread slowly along the lymphatics and develop crusty abscesses. Pathogens causing this mycosis include several species of pigmented soil fungi



Systemic Mycoses

The organisms are dimorphic, responsible for systemic mycoses fall into two general categories:

1. those that infect normal healthy individuals (**immunocompetent**), and
2. those that primarily infect **immunocompromised individuals**.

Coccidioidomycosis, histoplasmosis, and blastomycosis are the most common systemic mycotic infections in the **immunocompetent host**,

while **Paracoccidioidomycosis** causes **immunocompromised host**.

Epidemiology and pathology

The fungal pathogens are found in the soil and can be aerosolized. Entry into the host is by inhalation of airborne spores, which germinate in the lungs. From the lungs, dissemination can occur to any organ of the body where the fungi can invade and destroy tissue.

Clinical manifestations of Histoplasmosis, Paracoccidioidomycosis, and Blastomycosis resemble those seen in tuberculosis (primary pulmonary infection)

while **Coccidioidomycosis** is disseminated disease, lesions occur in the bones, central nervous system (CNS) & meningitis

A. Coccidioidomycosis is caused by **Coccidioides immitis**, in cases of disseminated disease, lesions occur most often in the **bones and the central nervous system (CNS) & causes meningitis**. In the soil, the fungus generates spores by septation of hyphal filaments (arthrospores). These spores become readily airborne and enter the lungs, where they germinate and develop into large (twenty to forty μm) spherules filled with many endospores. Rupture of the spherule releases the endospores, each of which can form a new spherule.

B. Histoplasmosis: Pulmonary infections is caused by Histoplasma capsulatum. The wide range of clinical manifestations of histoplasmosis makes it a particularly complex disease. In the soil, the fungus generates conidia, which, when airborne, enter the lungs and germinate into yeast-like cells. These yeast cells become engulfed by macrophages in which they multiply. Pulmonary infections may be acute but relatively benign and self-limiting, or chronic, progressive, and fatal. **Dissemination is rare. Disseminated disease results in invasion of cells of the reticuloendothelial system**, which distinguishes this organism as the only fungus to exhibit intracellular parasitism. Definitive diagnosis is by isolation and culture of the organism, which is a slow process taking four to six weeks, or by detection of exoantigen, which can be completed in several days. The disease occurs worldwide, but is most prevalent in central North America. Soils that are laden with bird, chicken, or bat droppings are a rich source of *H. capsulatum* spores.

الفهم فقط C. Paracoccidioidomycosis

also called South American blastomycosis, is caused by *Paracoccidioides brasiliensis*. The clinical presentation is much like that of histoplasmosis and blastomycosis except that the most **common secondary site of infection is the mucosa of the mouth and nose, where painful, destructive lesions may develop**. Like other dimorphic pathogens, morphologic identification via conidia is slow, but the yeast form observed in infected tissue or exudates has a characteristic ship's steering wheel appearance caused by the presence of multiple buds. The disease is restricted to Central and South America, and over ninety percent of patients with symptomatic disease are mature males. It is speculated that female sex hormones may inhibit formation of the yeast form.

D. Blastomycosis

Blastomycosis is caused by *Blastomyces dermatitidis*. Like *Histoplasma*, the fungus produces microconidia, most often in the soil, which become airborne and enter the lungs. There they germinate into thick-walled yeast cells that often appear with buds. Initial pulmonary infections, rarely disseminate to other sites; however, when dissemination occurs, secondary sites include skin (seventy percent), bone (thirty percent), and genitourinary tract (twenty percent), where they manifest as ulcerated granulomas. Definitive diagnosis is accomplished by isolation and culture of the organism. Identifiable colonies can be obtained in one to three weeks, but identity can be established more rapidly by subjecting the young mycelial colonies to an exoantigen test

● Opportunistic Mycoses

● Opportunistic mycoses afflict debilitated or immunocompromised individuals, and are rare in healthy individuals. The use of immunosuppressive drugs for organ transplantation, widespread use of chemotherapy in cancer treatment, and the high frequency of immunodeficient individuals caused by the AIDS epidemic have resulted in significant expansion of the immunocompromised population, as well as increasing the spectrum of opportunistic fungal pathogens.

- **A. Candidiasis**
- **B. Cryptococcosis**
- **C. Aspergillosis**
- **D. Mucormycosis**
- **E. Pneumocystis**

A. Candidiasis (candidosis) is caused by the yeast *Candida albicans*, which are normal body flora found in the skin, mouth, vagina, and intestines. Although considered a yeast, *C. albicans* is dimorphic, and can form a true mycelium. Infections occur when competing bacterial flora are eliminated, for example, by antibacterial antibiotics, allowing the yeast to overgrow. *Candida* infections have various manifestations depending on the site.

Oral candidiasis (thrush) presents as raised, white plaques on the oral mucosa, tongue, or gums.

Systemic candidiasis is a potentially life-threatening infection that occurs in debilitated individuals, cancer patients (with neutropenia), individuals on systemic corticosteroids, and patients treated with antibiotics. Systemic candidiasis may involve the gastrointestinal tract, kidneys, liver, and spleen.

Vaginal candidiasis ; presents as itching and burning pain of the vulva and vagina, accompanied by a thick or thin white discharge.



B. Aspergillosis is caused by several species of the genus *Aspergillus*, *Aspergillus* is rarely pathogenic in the normal host, but can produce disease in immunosuppressed individuals. The disease has a worldwide distribution. They reside in dust and the soil, decomposing organic matter. In fact, hospital outbreaks affecting neutropenic patients (that is, those with decreased neutrophils in their blood)

Acute aspergillus infections: The most severe, and often fatal, form of aspergillosis is acute **invasive infection of the lung**, from which the infection can be **disseminated to the brain, gastrointestinal tract, and other organs**. A less severe, noninvasive lung infection gives rise to a **fungus ball (aspergilloma)**, a mass of hyphal tissue that can form in lung cavities derived from prior diseases, such as tuberculosis. **Although the lung is the most common primary site of infection, the eye, ear, nasal sinuses, and skin can also be primary sites.**

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C. Cryptococcosis is caused by the yeast *Cryptococcus neoformans* which is found worldwide. The organism is especially abundant in soil containing bird (especially pigeon) droppings, although the birds are not infected. The most common form of cryptococcosis is a **mild, subclinical lung infection. In immunocompromised patients, the infection often disseminates to the brain and meninges**, with fatal consequences. However, about half of patients with cryptococcal meningitis have no obvious immunologic defect. The organism has a characteristic thick capsule that surrounds the budding yeast cell.

D. Mucormycosis is caused most often by *Rhizopus oryzae*, like the aspergilli. Mucor infections occur worldwide, but are almost entirely restricted to individuals with some underlying predisposing condition, such as burns, leukemias, or acidotic states such as diabetes mellitus.

E. Pneumocystis jiroveci pneumonia is caused by the unicellular eukaryote, *P. jiroveci* (formerly, *P. carinii*). Before the use of immunosuppressive drugs and the onset of the AIDS epidemic, infection with this organism was a rare occurrence. It is one of the most common opportunistic diseases of individuals infected with HIV.

- **الفهم فقط**

- **Diagnosis and treatment**

Most fungi can be propagated on any nutrient agar surface. The standard medium is Sabouraud dextrose agar, which, because of its low pH (5.0), inhibits bacterial growth while allowing fungal colonies to form. Various antibacterial antibiotics can also be added to the medium to further inhibit bacterial colony formation. Cultures can be started from spores or hyphal fragments. Clinical samples may be pus, blood, spinal fluid, sputum, tissue biopsies, or skin scrapings. Identification is usually based on the microscopic morphology of conidial structures. Serologic tests and immunofluorescent techniques are also useful in identification of fungi from clinical isolates.

Definitive diagnosis of an aspergillus infection is afforded by detection of hyphal masses, and isolation of the organism from clinical samples. Aspergillus hyphae characteristically form V-shaped branches (septate hyphae) that are distinguished from Mucor species. Also, septae are present in aspergillus hyphae but absent from mucor hyphae. In culture, the spore-bearing structures of the aspergilli are unmistakable. Treatment of aspergillus infections is typically by amphotericin B and surgical removal of fungal masses or infected tissue. The antifungal drugs miconazole, ketoconazole, &itraconazole.